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Out-of-Hospital Deliveries in Finland

A Nationwide register study

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ACADEMIC DISSERTATION
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It always seems impossible until it's done.

Nelson Mandela

ABSTRACT

Background: Most infants are born in hospitals, but the rate of out-of-hospital deliveries has increased. Out-of-hospital deliveries are considered either unplanned or planned. Unplanned out-of-hospital deliveries have been associated with increased perinatal mortality and morbidity, while the outcome among planned out-of-hospital deliveries has been more favorable, especially if national guidelines and recommendations are followed.

Objectives: The aim was to establish perinatal and maternal mortality and morbidity data, incidence, incidence trends, and risk factors related to out-of-hospital deliveries. The further aim was to compare the incidence of long-term morbidity and mortality of children by school age.

Methods: The study cohort was derived from the Medical Birth Register. This national register study included all children born in Finland between 1996 and 2013 (n = 1 053 802). Infants with no information on site of birth were excluded (n = 1046). The remaining infants were analyzed in three groups by site of birth: unplanned out-of-hospital (n = 1420), planned out-of-hospital (n = 197) and in-hospital (n = 1 051 139). Mortality and morbidity of infants were established by linking data from different health registers. For one study, the data was collected from the medical files at Tampere University Hospital between years 1996 and 2011 including all out-of-hospital deliveries (n = 67) in the catchment area and the reference group (n = 134).

Results: The annual rate of unplanned out-of-hospital deliveries increased almost six-fold, from 46 to 260 per 100 000 births, during the study period, and the trend has continued to rise since. At the same time the number of delivery units decreased from 44 to 29. The rate of planned out-of-hospital deliveries increased almost five-fold, from 8.3 to 39.4 per 100 000 births. Perinatal mortality was five times higher in unplanned out-of-hospital deliveries than in in-hospital deliveries and did not change during the study period. Perinatal mortality was rare in planned out-of-hospital deliveries, but adverse perinatal outcomes were overrepresented even in the group of low risk parturients. Independent risk factors for unplanned out-of-hospital deliveries were smoking during the pregnancy, alcohol and or/drug

abuse, non-cohabitation, a small number of prenatal visits, previous deliveries, low birth weight, long distance to the delivery unit, short labor duration and giving birth outside the southern or southwestern area of Finland.

Risk factors for perinatal mortality among infants born in unplanned out-of-hospital deliveries were the out-of-hospital delivery itself, low birth weight, very preterm birth and being born in the eastern region of Finland. Risk factors for perinatal mortality or morbidity were low birth weight and preterm birth. Long-term mortality did not differ from those who were born in hospitals.

The hazard ratios of asthma or allergic diseases and infections were decreased by 7 years of age in children born out-of-hospital. The risk of neurological or mental disorders by seven years of age in the groups born out-of-hospital seemed to be similar to that of children born in-hospital.

Conclusion: In conclusion the rate of out-of-hospital deliveries increased significantly during the study period. At the same time the number of delivery units decreased. Unplanned out-of-hospital deliveries had significantly higher perinatal mortality rates, especially among preterm and small infants. Among the planned out-of-hospital deliveries mortality was rare. More than half of the planned out-of-hospital deliveries did not fulfill the current criteria for low-risk home delivery. Mortality by seven years of age did not differ between children born in-hospital and out-of-hospital. Children born outside a hospital were associated with a lower risk of asthma or allergies and infections than children born in-hospital. The risk of neurological or mental disorders seemed to be similar.

TIIVISTELMÄ

Taustaa: Sairaalan ulkopuolisten synnytysten määrä on lisääntynyt, vaikka suurin osa vauvoista syntyy edelleen sairaalassa. Sairaalan ulkopuoliset synnytykset voidaan jakaa suunnittelemattomiin ja suunniteltuihin synnytyksiin. Suunnittelemattomiin sairaalan ulkopuolisiin synnytyksiin on todettu liittyvän lisääntynyt varhainen seitsemän vuorokauden ikään mennessä tapahtuva kuolleisuus ja sairastavuus. Tutkimustulokset suunniteltuihin sairaalan ulkopuolisiin synnytyksiin liittyvän vastasyntyneiden kuolleisuuden ja sairastavuuden osalta ovat vaihtelevia, mutta useimmiten suotuisampia, jos kansallisia ohjeistuksia ja suosituksia on noudatettu.

Tutkimuksen tarkoitus: Tarkoituksena oli selvittää vastasyntyneiden varhaista, seitsemän vuorokauden ikään mennessä ilmaantuvaa kuolleisuutta ja sairastavuutta, äitien sairastavuutta ja kuolleisuutta, sairaalan ulkopuolisten synnytysten esiintyvyyttä sekä riskitekijöitä sairaalan ulkopuolisiin synnytyksiin liittyen. Lisätavoitteena oli verrata sairaalan ulkopuolella syntyneiden ja sairaalassa syntyneiden lasten seitsemän vuorokauden iän jälkeisen pitkäaikaissairastavuuden ja pitkäaikaiskuolleisuuden esiintyvyyttä kouluikään mennessä.

Menetelmät: Tutkimusjoukko muodostettiin syntymärekisteristä ja tähän kansalliseen rekisteritutkimukseen otettiin mukaan kaikki Suomessa vuosina 1996–2013 syntyneet lapset (n = 1 053 802). Lapset, joiden syntymäpaikka ei ollut tiedossa, suljettiin pois tutkimuksesta (n = 1046). Lopullisiin analyyseihin mukaan otetut lapset jaettiin kolmeen ryhmään syntymäpaikan mukaan; suunnittelematon sairaalan ulkopuolinen (n = 1420), suunniteltu sairaalan ulkopuolinen (n = 197) ja sairaala (n = 1 051 139). Kuolleisuutta ja sairastavuutta arvioitiin yhdistämällä eri rekistereiden tietoja toisiinsa. Yhteen osatyöhön tiedot kerättiin Tampereen yliopistollisen sairaalan potilasasiakirjoista vuosilta 1996–2011.

Tulokset: Vuosittainen suunnittelemattomien sairaalan ulkopuolisten synnytysten määrä lähes kuusinkertaistui tutkimusjakson aikana (46 per 100 000 syntynyttä - 260 per 100 000 syntynyttä) ja tämä trendi on jatkunut myös tutkimusjakson jälkeen. Synnytyssairaaloiden lukumäärä sen sijaan on vähentynyt, tutkimusjakson aikana suljettiin 15 synnytyssairaalaa. Suunniteltujen sairaalan ulkopuolisten synnytysten määrä lähes viisinkertaistui tutkimusjakson aikana (8.3

per 100 000 syntynyttä - 39.4 per 100 000 syntynyttä). Suunnittelemattomasti sairaalan ulkopuolella syntyneiden lasten varhainen kuolleisuus oli viisinkertainen sairaalassa syntyneisiin lapsiin verrattuna ja pysyi samanlaisena koko tutkimusjakson ajan. Suunnitellusti kotona syntyneiden joukossa oli vain kaksi alle seitsemän vuorokauden iässä kuollutta lasta, mutta huomattavaa oli, että myös matalan riskin synnyttäjien vastasyntyneillä esiintyi hoitoa tai huomioita vaatineita terveydellisiä ongelmia.

Itsenäisiä riskitekijöitä sairaalan ulkopuoliselle suunnittelemattomalle synnytykselle olivat raskaudenaikainen tupakointi, alkoholin tai päihteiden väärinkäyttö, eläminen ilman parisuhdetta, vähäisemmät raskaudenaikaiset tarkastuskäynnit, uudelleensynnyttäneisyys, pieni syntymäpaino, pidempi matka synnytyssairaalaan, synnytyksen lyhyt kesto ja syntyminen muualla kuin HUSin tai TYKSin erityisvastuualueilla. Riskitekijöitä suunnittelemattomasti sairaalan ulkopuolella syntyneiden lasten varhaiselle kuolleisuudelle olivat sairaalan ulkopuolella syntyminen itsessään, pieni syntymäpaino, hyvin ennenaikainen synnytys ja syntymä KYSin erityisvastuualueella. Riskitekijöitä puolestaan joko kuolemalle tai sairastavuudelle alle seitsemän vuorokauden iässä olivat pieni syntymäpaino ja ennenaikainen synnytys. Kuolleisuudessa viikon iästä kouluikään asti ei ollut eroa eri ryhmien välillä.

Kouluikään mennessä sairaalan ulkopuolella syntyminen joko suunnitellusti tai suunnittelemattomasti näytti olevan yhteydessä pienempään riskiin sairastua astmaan tai allergisiin sairauksiin sairaalassa syntyneisiin verrattuna. Suunnittelemattomasti tai suunnitellusti sairaalan ulkopuolella syntyneillä lapsilla esiintyi myös vähemmän sairaalahoitoa tai sairaalakäyntejä vaatineita infektioita. Neurologisten sairauksien riski ei näyttänyt olevan suurentunut sairaalan ulkopuolella syntyneillä sairaalassa syntyneisiin verrattuna.

Johtopäätökset: Johtopäätöksenä voidaan todeta, että sairaalan ulkopuolisten synnytysten määrä kasvoi merkittävästi tutkimusjakson aikana. Suunnittelemattomasti sairaalan ulkopuolella syntyneiden lasten varhainen kuolleisuus oli merkittävästi suurempaa sairaalassa syntyneisiin lapsiin verrattuna. Suunnitellusti kotona syntyneiden lasten varhainen kuolleisuus oli harvinaista. Sairaalan ulkopuolella syntyneiden lasten kuolleisuus viikon iästä kouluikään mennessä ei eronnut ryhmien välillä. Sairaalan ulkopuolella syntyneillä näytti olevan pienempi riski sairastua astmaan tai allergisiin sairauksiin sairaalan syntyneisiin lapsiin verrattuna ja myös sairaalahoitoa vaatineita infektioita esiintyi vähemmän. Neurologisten sairauksien riski ei ollut suurentunut sairaalan ulkopuolella syntyneillä lapsilla kouluikään mennessä.

CONTENTS

ABBREVIATIONS

AGA	appropriate for gestational age
ATC	Anatomical Therapeutic Chemical
CI	confidence interval
GA	gestational age
CRHC	Care Register for Health Care
EUROCAT	European Surveillance of Congenital Anomalies
HR	hazard ratio
ICD	International Classification of Diseases
IQR	interquartile range
SII	Social Insurance Institution of Finland
LGA	large for gestational age
MBR	Medical Birth Register
OHD	out-of-hospital delivery
OR	odds ratio
POHD	planned out-of-hospital delivery
SD	standard deviation
SGA	small for gestational age
THL	Finnish Institute for Health and Welfare
UOHD	unplanned out-of-hospital delivery

ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals I–IV.

I Ovaskainen K, Ojala R, Gissler M, Luukkaala T, Tammela O. Out-of-hospital deliveries have risen involving greater neonatal morbidity: Risk factors in out-of-hospital deliveries in one University Hospital region in Finland. Acta Paediatr. 2015;104(12):1248-1252.

II Ovaskainen K, Ojala R, Tihtonen K, Gissler M, Luukkaala T, Tammela O. Planned home deliveries in Finland, 1996-2013. J Perinatol. 2019;39(2):220-228.

III Ovaskainen K, Ojala R, Tihtonen K, Gissler M, Luukkaala T, Tammela O. Unplanned out-of-hospital deliveries in Finland: A national register study on incidence, characteristics and maternal and infant outcomes. Acta Obstet Gynecol Scand. 2020;99(12):1691- 1699.

IV Ovaskainen K, Ojala R, Gissler M, Luukkaala T, Tammela O. Is birth out-of-hospital associated with mortality or morbidity by seven years of age? PLoS ONE. 2021;16(4):e0250163.

1 INTRODUCTION

Deliveries that occur anywhere outside of hospital are called out-of-hospital deliveries. They can be divided into two completely different groups based on the intended place of delivery. Unplanned out-of-hospital deliveries (UOHDs) can occur in places like the car on the way to the hospital, in an ambulance, or in a bathroom, with or without the help of paramedics. Mortality and morbidity related to UOHDs during the perinatal period are well recognized and described in the literature (Combier et al., 2020; Lima et al., 2018; Engjom et al., 2017; Grzybowski et al., 2011; Gunnarsson et al., 2014; Gutvirtz et al., 2020; Hemminki et al., 2011; Lazić et al., 2011). Planned out-of-hospital deliveries (POHDs) differ from unplanned ones in many ways. The chosen place of delivery is usually the mother's home, and in high-income countries, home deliveries are a deliberate choice. Danger to mother and child can be minimized when only women at low risk attended by professionally educated, experienced midwives, deliver at home, but have access to a hospital setting (Hutton et al., 2019). However, even in optimal situations, the safety of planned out-of-hospital deliveries remains controversial (Grünebaum et al., 2020).

The proportion of POHDs remains small in high-income countries, especially if they are not well integrated into a health care system. The highest percentage is in the Netherlands, with almost 20% of all deliveries being planned out-of-hospital deliveries. However, in many high-income countries, this percentage is slowly rising (Grünebaum et al., 2020; Davies-Tuck et al., 2018). The trend in the percentage of UOHDs is more diverse, increasing in some countries while remaining stable in others (Combier et al., 2020; Gunnarsson et al., 2014; Viisainen et al., 1999).

The outcomes and incidences of both unplanned and planned out-of-hospital deliveries (OHDs) have been studied widely, but the risk factors for UOHDs and for poor outcomes related to OHDs, especially long-term morbidity and mortality of infants born out-of-hospital, have been studied less.

This study established perinatal and maternal mortality and morbidity data, incidence and incidence trends, and risk factors of OHDs. In addition, we established the long-term mortality and morbidity of infants born out-of-hospital.

2 REVIEW OF THE LITERATURE

2.1 Definitions

2.1.1 Gestational age

Term pregnancy is defined as delivery between 37^{+0} weeks and 41^{+6} weeks (World Health Organization, 2004). Births that occur between 37^{+0} weeks and 38^{+6} weeks are defined as early-term and those at 39^{+0} through 40^{+6} weeks as full-term (the American College of Obstetricians and Gynecologists, 2014; Spong, 2013). Births at 41^{+0} weeks through 41^{+6} weeks are late-term. Birth is post-term when gestational age (GA) is 42^{+0} weeks and beyond.

The World Health Organization defines preterm birth as a birth before 37 completed weeks of gestation (World Health Organization, 1977). Based on GA, preterm births can be categorized as extremely preterm (GA less than 28^{+0} weeks), very preterm (GA 28^{+0} to 31^{+6} weeks), moderately preterm (GA 32^{+0} to 33^{+6} weeks) and late preterm (GA 34^{+0} to 36^{+6} weeks).

2.1.2 Birth weight

Low birth weight is defined as birth weight less than 2500 grams. Very low birth weight is birth weight less than 1500 grams and extremely low birth weight less than 1000 grams (World Health Organization, 2004). Also, GA is taken into consideration when referring to small gestational age (SGA), appropriate for gestational age (AGA), and large for gestational age (LGA). SGA means that the birth weight is more than two standard deviations (SDs) below the mean weight for gestational age, and LGA means that the birth weight is more than two SDs over the mean weight for gestational age. AGA means that the birth weight is between -2 SD to +2 SD from the mean weight for gestational age (Pihkala et al.,

1989). New population-based references for birth weight were published after the end of our study period (Sankilampi et al., 2013).

2.1.3 Descriptives of mortality

The perinatal period commences at 22 completed weeks of gestation and ends seven completed days after birth. Perinatal mortality refers to the number of stillbirths and deaths in the first week of life. A stillborn infant is one who is born dead with a birth weight of at least 500 grams or after a pregnancy lasting 22 weeks or more (Tavares et al., 2016). The neonatal period refers to the period from birth to 28 days of age, and neonatal mortality refers to the number of deaths during that time.

2.2 Healthcare in Finland

In Finland, the right to social welfare and health care services is universal. According to Finland's constitution (Finnish legislation), adequate social, medical, and health services must be guaranteed for everyone. Free prenatal health care visits are offered at the maternity clinics during pregnancy. The amount of visits has decreased during the time being currently for at least nine times for primiparas and at least eight times for others (Finnish Institute for Health and Welfare, 2020). One of Finnish society's goals has also been to prevent social- and health-related problems. However, inequalities in health and welfare between socioeconomic groups still exist (Ministry of Social Affairs and Health, 2013).

2.2.1 Changes in delivery practices through the decades

Until the Second World War, women usually gave birth at home. In Finland, delivery generally occurred in a sauna or some other outbuilding. In 1945, 50% of all infants in Finland were born outside of hospital (Viisainen et al., 1999). Thereafter, the rate of OHDs declined up to 1973, when 0.01% of all deliveries in Finland, whether planned or unplanned, took place outside the hospital. Since the 1970s the rate of OHDs has increased (Hemminki et al., 2011). The trends have been quite similar in other high-income countries. For example, in the United Kingdom in 1959, the official view was that 70% of women should give birth in

the hospital, and British policy in 1970 stated that there should be enough resources for all women to have a hospital delivery. In 1900 in the United States, almost all deliveries occurred out-of-hospital. The proportion of OHDs had fallen to 44% by 1940 and to 1% by 1969, where it remained through the 1980s (MacDorman et al., 2019). There has been a recent increase in OHDs in United States, from 0.87% in 2004 to 1.36% in 2012 (Amorim et al., 2018). The situation is vastly different in low-income countries, where most deliveries are OHDs and the option to deliver in hospital does not even exist (Montagu et al., 2011).

2.2.1.1 Delivery units in Finland

More than half of Finland's delivery units have been closed since 1975, and because of this, travel times from home to the nearest delivery unit have grown longer in many parts of Finland (Viisainen et al., 1999). However, in most of Finland, delivery units are less than two hours away. The accessibility of delivery units in Finland as a function of their number and the yearly birthrate is illustrated in Table 1. The latest reform regarding delivery units was published by the Ministry of Social Affairs and Health in 2014. Childbirth requirements were tightened by law to ensure patient safety. Hospitals with at least 1000 deliveries per year are required to maintain sufficient emergency preparedness at all times. Hospitals with fewer than 1000 annual deliveries can still operate if required due to the availability of services or patient safety. Medical staff at smaller delivery units must meet minimum competency and adequacy thresholds, including immediate readiness for emergency caesarean sections. Delivery units must have on-call obstetricians and pediatricians present all the times. From 1996 to 2013, a total of 15 delivery units closed, reducing the number of delivery units from 44 to 29. These closed units are listed in Table 2. Small delivery units continued to close after 2013, and currently there are 23 delivery units in Finland. Current delivery units, coded by number of deliveries, are shown in Figure 1.

Table 1. Accessibility of delivery units as a function of average yearly births, expressed as a percentage (modified from Ministry of Social Affairs and Health 2012).

	Number of delivery units			
	30	25	20	15
Accessibility (hours)	%			
< 0.5	78.6	76.1	71.5	62.8
0,5–1	17.4	19.7	22.1	26.5
< 1	95.9	95.8	93.6	89.3
1–2	3.5	3.6	5.9	10.1
> 2	0.6	0.6	0.6	0.6
Median	13 min 42 sec	14 min 12 sec	16 min 17 sec	19 min 4 sec

Table 2. Delivery units in Finland that closed during the study period (1996–2013).

Year	Delivery unit
1998	Mänttä regional hospital
1999	Selkämeri regional hospital, Inari health center
2000	Jämsä health center
2001	Rauma regional hospital, Varkaus regional hospital
2002	Kuusankoski regional hospital, Lounais-Häme regional hospital (Forssa)
2003	Vakka-Suomi regional hospital (Uusikaupunki), Iisalmi regional hospital
2008	Kuusamo health center
2009	Loimaa regional hospital
2010	Länsi-Uusimaa regional hospital (Tammisaari)
2011	Raahe health center
2013	Vammala regional hospital

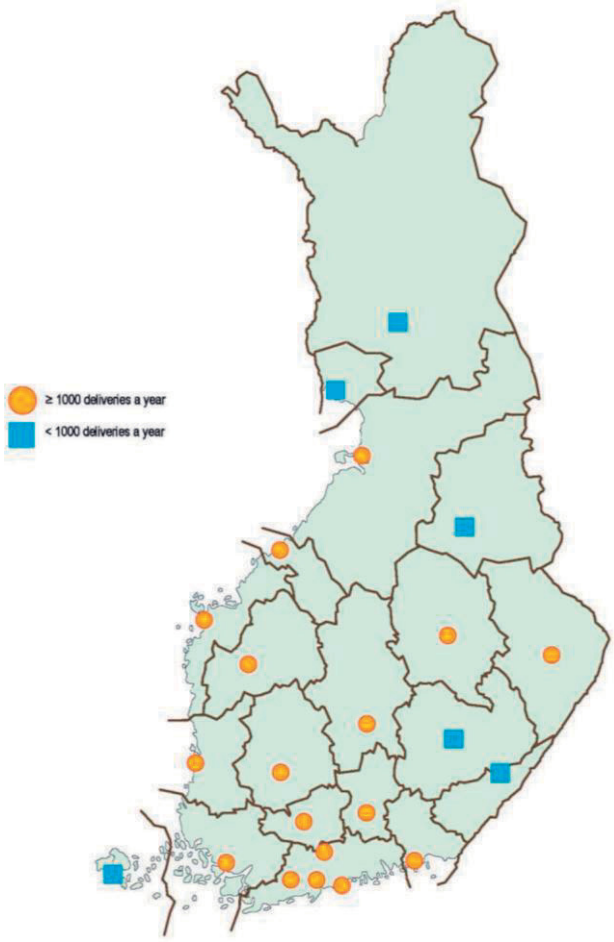

Figure 1. Delivery units in Finland (modified from THL 2021).

2.3 Current hospital network in Finland

There are 21 hospital districts in Finland, including Åland. Formed by municipalities, hospital districts are responsible for specialized medical care in their area. All children's hospitals and delivery hospitals in Finland are public, and almost all other hospitals are public as well. Private hospitals supplement public hospitals, for example, by providing outpatient surgeries. Each hospital district in a certain area belongs to one of the five university hospital catchment areas (southern, eastern, northern, western, and southwestern). University hospitals and

central hospitals in the hospital districts are responsible for the most demanding medical operations and for medical care. Hospitals can also be divided into three levels. Level three hospitals are considered tertiary hospitals providing all services. In Finland, deliveries of high-risk pregnancies, including imminent preterm birth before 32 gestational weeks and/or estimated fetal weight of less than 1500 grams are centralized in tertiary hospitals. These tertiary hospitals are university hospitals located in Helsinki, Kuopio, Oulu, Tampere and Turku. The centralization of very preterm deliveries has succeeded remarkably well in Finland compared to many other European countries. In 2017 the proportion of live-born very preterm infants delivered in tertiary hospitals was 95%, while in many other high-income countries this percentage is less than 50% (Helenius et al., 2019).

There are a total of 18 level two maternity hospitals capable of handling moderately and late preterm deliveries and infants. In addition, there are level one regional hospitals and local hospitals, such as city hospitals, but all delivery units belong to either level three or level two hospitals. POHDs are not recommended by health care professionals, and there are no free-standing birth centers in Finland. Specific catchment areas, hospital districts, university hospitals and central hospitals are shown in Figure 2.

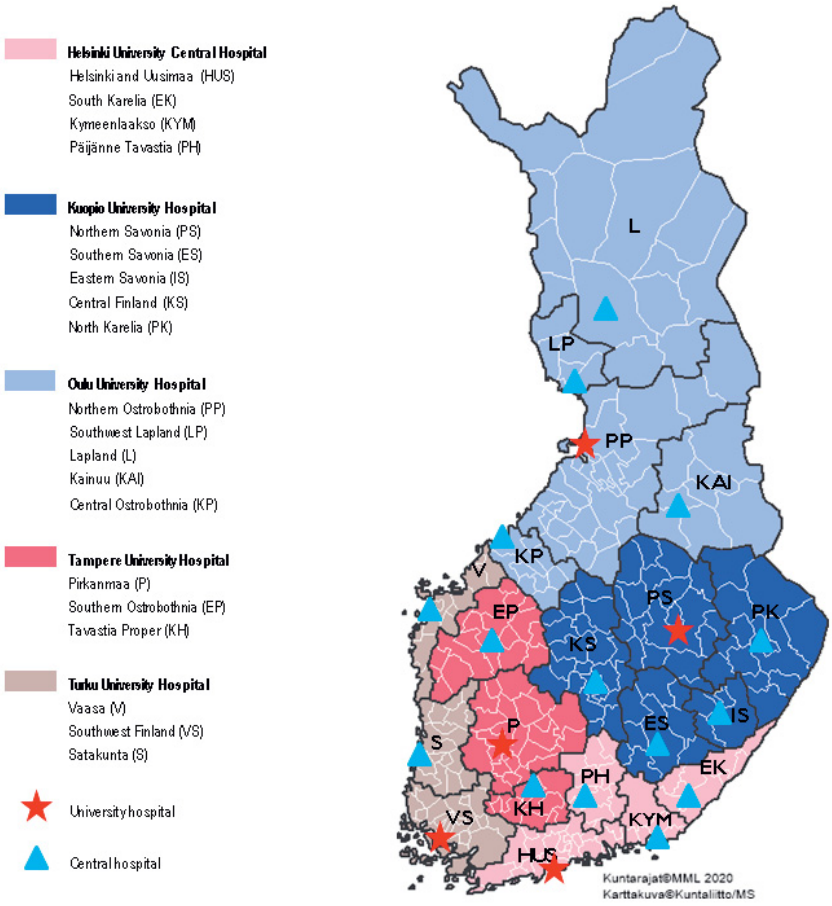

Figure 2. Specific catchment areas, hospital districts, university hospitals and central hospitals in Finland(modified from Kuntaliitto 2020).

2.4 Practices in sparsely populated areas in Finland

Although no official guidelines are available, women who live in sparsely populated areas far from their delivery unit may temporarily move closer to the unit as their due date approaches. For example, in Northern Finland, Ivalo, maternity clinic nurses advice women to contact the nurse on call immediately if the amniotic fluid or blood leaks. Instructions are similar when the due date approaches and contractions are regular for two hours. These women are advised to come to the health care center. If a woman lives more than 60 kilometers from the Ivalo health

care center, or there is a threat of preterm birth, she is advised to call an ambulance, which will bring a midwife to the patient, if possible. If the distances are far, women are advised to meet the arriving ambulance in their own car. If the labor is advancing quickly, the midwife may accompany the parturient all the way to the nearest delivery unit in Rovaniemi (300 kilometers from Ivalo). If the distance is even farther, as it is from Utsjoki to Rovaniemi (up to 500 kilometers), the midwife may come along in Ivalo. There are two midwives working at the Ivalo health care center now, since the Ivalo delivery unit closed in 1999 (O. Nykänen, public health nurse Ivalo health care center, personal communication, October 15, 2020). Midwives are not always on official duty, but the health care center nurse can call them at home if needed. Sometimes, if the travel distance is long, labor is initiated with less medical indications. These parturients create an individual plan with the maternity clinic (K. Hämeenoja, Head of Ob Gyn, Central Hospital of Lapland, personal communication, August 10, 2020).

2.5 Out-of-hospital deliveries

Out-of-hospital deliveries can be divided into planned and unplanned. The former are intended to take place out-of-hospital and the latter usually occur accidentally, when the labor is rapid, and may take place at home or on the way to the hospital, usually in the car or in an ambulance, with or without paramedic assistance. Deliveries that occur in the hospital by women who had originally planned to give birth at home are registered as in-hospital deliveries in the Finnish national birth register. Such births could be called as unplanned in-hospital deliveries. The categories of sites of birth are illustrated in Figure 3.

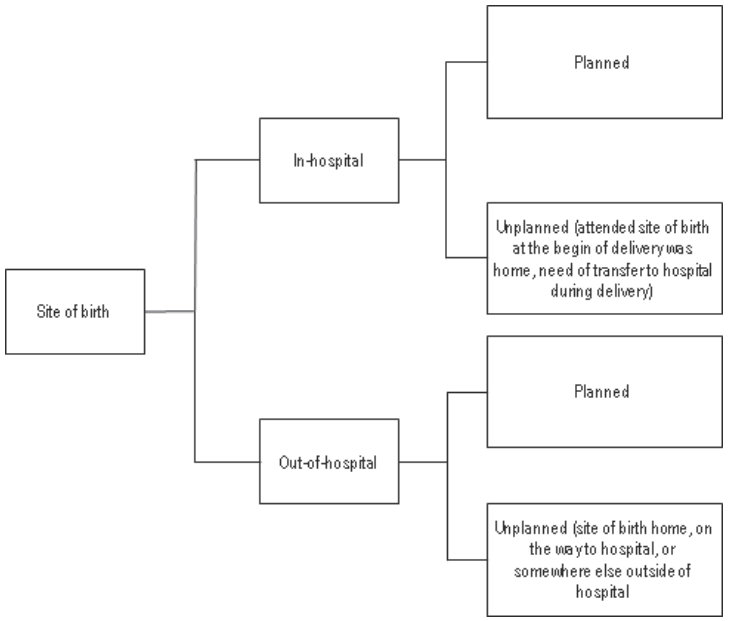

Figure 3. Categories of sites of birth.

2.6 Planned out-of-hospital deliveries

There are a variety of reasons why women want to consider POHD. In high-income countries, POHD is more a matter of choice than a lack of resources. The advantages of POHD are usually argued from the mother's, and not the infant's, point of view. Women may be dissatisfied with a previous hospital delivery, or they may wish to avoid delivery interventions and feel that home is the safest option (Bernhard et al., 2014; Boucher et al., 2010). Women may also feel that, at home, they have the freedom to make their own choices when it comes to delivery and have more continuity of care with a familiar midwife (Hauck et al., 2020). Different weightings of risks and benefits may affect the decision where to give birth. Comparing the results of previous studies is complex and difficult because the study designs, including the methods and the risk profiles of women and pregnancies, are diverse. First, most studies do not include women and/or infants transferred to the hospital during or after labor. Secondly, there is variation in how POHDs are integrated into the health care system. For example, in the Netherlands, the United Kingdom, Iceland, British Columbia (Canada), Ontario (Canada), and Washington State (USA), POHDs are well-integrated (Comeau et al.,

2018; Davies-Tuck et al., 2018). In comparison, POHDs are less well integrated into health care systems in Norway, Sweden, and Australia (Comeau et al., 2018). For example, national guidelines for POHD, qualifications for birth assistant(s), and availability of emergency care are well established if POHDs are firmly integrated into the health care system (National Institute for Health and Care Excellence, 2014).

2.6.1 Risks and advantages of planned out-of-hospital deliveries

The hospital is the safest option when it comes to perinatal and maternal mortality and sudden, unexpected complications during delivery (Danilack et al., 2015). Fetal monitoring began in the 1820s, when the ear was placed on the mother's abdomen to listen to the infant's heart beat in the womb. By the 1960s, a specialized monitor made it possible to monitor an infant's heart beat continuously. Midwives may use fetal Doppler intermittently during POHDs, but internal fetal monitoring is not possible at home, nor can fetal scalp sampling be performed for blood gas analysis during labor. Hospital, on the other hand, offers a variety of methods to augment labor and relieve pain. At home, there are only non-medical ways to treat labor and pain. Hospitals offer immediate access to emergency procedures for mother and child, for example, cesarean sections and immediate resuscitation of life-threatening postnatal conditions in newborns.

At home, women can avoid undesired interventions during delivery and give birth in a familiar environment (Zielinski et al., 2015; Bernhard et al., 2014; Cheng et al., 2013). One Canadian study also found that infants are more often exclusively breastfed if the mother has a POHD (91.5%) compared to in-hospital deliveries (84.2%) (Hutton et al., 2009). At-home deliveries might also prevent exposure to pathogenic microbes found in hospitals, thus decreasing the risk of puerperal and neonatal infections. It has been shown also, that infants born at home have more diverse bacteria in their gut (Combellick et al., 2018).

2.6.2 Differences in incidence in planned out-of-hospital deliveries in high-income countries

Home delivery rates have been rising recently in many high-income countries, but they still only make up approximately 1% of infants born in POHDs each year. The percentage of POHDs varies by country depending on, for example, whether

POHDs are integrated into the health care system, whether mothers are encouraged or discouraged in home deliveries by health care workers, and how POHDs are supported financially. POHDs are most common in the Netherlands, where 20% of women choose to deliver at home. However, the percentage has decreased recently in the Netherlands, while it has increased in most other high-income countries (Grünebaum et al., 2020; Davies-Tuck et al., 2018). The percentage of POHDs is 0.99% in the USA (MacDorman et al., 2019), 2% in Canada and the United Kingdom, 0.3% in Australia, and 3.4% in New Zealand (Davies-Tuck et al., 2018). In Nordic countries, the percentage is somewhere 1% and 2% in Denmark, 2.2% in Iceland, 0.07% in Sweden, and 0.2% in Norway (Blix et al., 2016). In the United States, a trend that has been rising since the mid-2000s has leveled off in the past few years (Grünebaum et al., 2020). In many low-income countries, the situation is completely different. For example, in Bangladesh, the home delivery rate is 95%, and in Mozambique, it is 41% (Amorim et al., 2018). These women don't have the choice of giving birth in the hospital.

2.6.3 Characteristics of parturients and deliveries

Mothers who deliver at home as planned are more often older (Cheng et al., 2013; Davis et al., 2011; Declercq et al., 2010; Grünebaum et al., 2013; Grünebaum et al., 2014; Grünebaum et al., 2017; Kennare et al., 2010; Li et al., 2015; Lindgren et al., 2008; MacDorman et al., 2019; Malloy et al., 2010), non-smokers (Danilack et al., 2015; Hutton et al., 2016; Lingren et al., 2008; MacDorman et al., 2019), married (Cheng et al., 2013; Declercq et al., 2010; Halfdansdottir et al., 2015), and have had more prior pregnancies (Davis et al., 2011; Li et al., 2015) and deliveries (Cheng et al., 2013; Davis et al., 2011; Grünebaum et al., 2013; Grünebaum et al., 2017; Halfdansdottir et al., 2015; Hutton et al., 2016; Kennare et al., 2010; Malloy et al., 2010), and the length of pregnancy is more often almost or more than 42 weeks (Cheng et al., 2013; de Jonge et al., 2009; Grünebaum et al., 2013; Grünebaum et al., 2014; Grünebaum et al., 2017; Hutton et al., 2016; Kennare et al., 2010; Li et al., 2015; Lindgren et al., 2008; van der Kooy et al., 2011) compared to women who deliver in-hospital. Socioeconomic status and/or education are usually higher among these women (Cheng et al., 2013; de Jonge et al., 2009; Declercq et al., 2010; Lindgren et al., 2008; Malloy et al., 2010).

2.6.4 Finnish national guidelines for planned out-of-hospital deliveries

Some countries have published national guidelines for POHDs, for example, the Netherlands, the United Kingdom, Canada, and Australia (Cheng et al., 2013). Current Finnish national guidelines for POHDs were published in 2013 (Klemetti et al., 2013). Finnish guidelines include the absence of any maternal pre-existing disease, uncomplicated singleton pregnancy, at least one previous delivery, vertex presentation, no previous cesarean section or operative vaginal delivery, absence of group B streptococcus colonization, gestational weeks between 38^{+0} and 41^{+6}, and two registered, certified midwives, or a midwife and a physician capable to manage the delivery including possible emergency situations. Transfer time from home to the delivery hospital should be less than 20 minutes. In Finland, home delivery preparations are the responsibility of the parturient, her family, and a midwife who handles home deliveries. All costs are paid for by the family, with no financial assistance from society. The family and/or midwife takes care of the supplies for the home delivery, including medication and first aid equipment. Equipment and medication are not provided by hospitals for POHDs. Health care professionals should inform families planning the home delivery about the risks and necessary arrangements. The delivery hospital should be informed about the intention to have a POHD.

Finnish guidelines also include follow-up instructions for newborn infants. At the age of two hours, an oxygen saturation screening test should be performed and if oxygen saturation is abnormal, the delivery hospital should be contacted immediately. The newborn's health should be checked at least once a day by a health care professional until the pediatric check-up at the delivery hospital. All newborn screening tests should be done appropriately, and vitamin K prophylaxis should be administered after birth. The birth data must be reported directly to the population register centre no later than the next business day following the birth. Health care professionals, who assist in a POHD, are also responsible for registering the birth with the Finnish Institute for Health and Welfare (THL). Nevertheless, Finnish guidelines recommend that everyone give birth in a hospital (Klemetti et al., 2013). For the families who meet the criteria established by pediatricians and obstetricians, it is also possible to check out the delivery hospital within 6-24 hours after the delivery.

2.6.5 Maternal outcomes

Study designs of POHDs differ widely and this makes comparing the results difficult. POHDs are associated with lower rates of obstetric interventions, severe perineal tears, and hemorrhages compared to deliveries in the hospital (Blix et al., 2012; Cheng et al., 2013; Homer et al., 2019; Hutton et al., 2016; Miller et al., 2012; Davies-Tuck et al., 2018; Nove et al., 2012; van der Kooy et al., 2011). In general, maternal morbidity is lower in POHDs, and maternal mortality is rare. De Jonge et al. found in their nationwide cohort study that the rate of severe acute maternal morbidity [admission to intensive care, uterine rupture, eclampsia or HELLP (hemolysis, elevated liver enzymes, and low platelet count) with liver hematoma, major obstetric hemorrhage (blood transfusion of four or more packed cells), and other severe acute maternal morbidity as diagnosed by the attending clinician] among planned primary care births for low-risk women is 2.0 per 1000 births. Among parous women, but not among nulliparous women, the difference in morbidity between POHDs versus planned hospital deliveries was statistically significant, showing a lower risk of severe maternal morbidity among low-risk women with POHDs compared to planned hospital deliveries (de Jonge et al., 2013). Reports from the United States are worrisome because the number of POHDs, regardless of contraindications, has increased since the 1990's (Zafman et al., 2018). The most common contraindications among mothers with POHDs are a body mass index greater than 35, post-term delivery, high blood pressure, a history of cesarean delivery, and breech position of the fetus (Grünebaum et al., 2015; Halfdansdottir et al., 2018; Davies-Tuck et al., 2018; Zafman et al., 2018). In one study, 19% of mothers having a POHD had at least one contraindication (Davies-Tuck et al., 2018). The risk of transfer from home to hospital and of postpartum hemorrhage increases if a mother with contraindications decides to give birth at home (Halfdansdottir et al., 2018; Davies-Tuck et al., 2018).

Also, so-called low-risk pregnancies run the risk of unexpected complications (Danilack et al., 2015). Transfer to the hospital during or after labor is needed in 8% to 45% of POHDs, usually before birth takes place (Blix et al., 2014; Blix et al., 2016; Grünebaum et al., 2020; Grünebaum et al., 2017). In a Dutch study by Amelink-Verburg et al., it was found that in 0.4% of all low-risk pregnancies, an emergency transfer was needed (Amelink-Verburg et al., 2010). A Japanese study established that transfers were made mostly due to the failure of labor to progress, postpartum hemorrhage, or non-reassuring fetal status (Hiraizumi et al., 2013). Blix et al. stated that the most common reasons for transfer were abnormal labor

progress, fetal distress, hemorrhage, fetal malpresentation, the need for pain relief and hypertension (Blix et al., 2016).

2.6.6 Infant morbidity and mortality

Study results related to infant morbidity and mortality are also varied and difficult to compare. Studies are conducted in different countries with different practices and a variety of home delivery providers. Study designs differ, and some studies include, for example, only low-risk mothers, while others do not even distinguish POHDs from unplanned ones. Also, there are variations in reports of outcomes like Apgar scores. Randomized, controlled comparisons of outcomes of POHDs and hospital deliveries are lacking. However, in many population-based studies, perinatal and neonatal mortality rates are higher among POHDs than among hospital deliveries (Bastian et al., 1998; Grünebaum et al., 2014; Grünebaum et al., 2017; Grünebaum et al., 2020; Malloy et al., 2010; Snowden et al., 2015). In contrast, there are also reports showing no difference in neonatal outcome parameters between planned out-of-hospital and in-hospital deliveries (de Jonge et al., 2009; Gaudineau et al., 2013; Homer et al., 2019; Hutton et al., 2016; Kennare et al., 2010; Li et al., 2015; Lindgren et al., 2008; van der Kooy et al., 2011). Some reports have shown, that infants born at home are admitted to neonatal intensive care units less often than those born in the hospital (Cheng et al., 2013; Snowden et al., 2015; Wax et al., 2010), but there are two studies showing more admissions (Halfdansdottir et al., 2015; Janssen et al., 2009). Perinatal and neonatal mortality is higher if the mother has contraindications for POHD (nulliparity, previous cesarean section, presentation other than vertex, multiple pregnancy, preterm birth, GA more than 41 weeks) (Bachilova et al., 2018; Grünebaum et al., 2020). Also, neonatal mortality rates in POHDs have been shown to be more than four times higher than hospital deliveries in the United States, even among low-risk parturients (Grünebaum et al., 2020). One study revealed that the most common risk factors for perinatal mortality in the high-risk group were various maternal medical complications (35% of perinatal mortality cases) (Davies-Tuck et al., 2018). On the other hand, in the latest published review and meta-analysis, there was no significant difference in perinatal and neonatal mortality or morbidity (admission to a neonatal intensive care unit, Apgar scores, need for resuscitation) between infants who were born in the hospital and those with POHD (Hutton et al., 2019). In an American study by Malloy et al., it was stated that the most common cause of

neonatal death among POHDs was congenital anomalies. In that study, infants born at home as planned needed mechanical ventilation more often, had more seizures, and their five-minute Apgar scores were four of lower more often (Malloy et al., 2010). In a recently published study, the authors stated that the cause of increased neonatal mortality rates in POHDs in the United States is the location, i.e., the home setting itself, and the failure to select only low-risk parturients (Grünebaum et al., 2020).

2.7 Unplanned out-of-hospital deliveries

Unplanned out-of-hospital deliveries occur either unexpectedly or due to irresponsible behavior by the mother, for instance, due to social or mental health problems.

2.7.1 Geographical differences in incidence

Rates of UOHDs are not always clearly documented, even in high-income countries. Sometimes, these rates may include POHDs. Clearly documented rates of UOHDs vary from 0.1% in Finland to 3.2% in Slovenia (Gunnarsson et al., 2014; Rodie et al., 2002; Sheiner et al., 2002; Viisainen et al., 1999). In addition, trends in the rates differ. For example in Finland and in France, the rate of UOHDs has increased in recent years and decades, while in Norway, the number of UOHDs has remained stable during the last few years (Combier et al., 2020; Gunnarsson et al., 2014). Geographical differences in Finland were examined in a study published in 2011, which showed that in the 1990s, UOHDs were more common in the northern parts of Finland, but thereafter, rates of UOHDs also increased in more densely populated areas. From 2006 to 2009, the differences between the areas largely disappeared (Hemminki et al., 2011).

2.7.2 Characteristics of parturients and deliveries

Previous studies have shown that mothers who give birth unplanned out-of-hospital tend to be particularly young (Boland et al., 2018; Declercq et al., 2010; Viisainen et al., 1999) or old (Blondel et al., 2011; Gunnarsson et al., 2014; Hadar et al., 2005; Viisainen et al., 1999), unmarried/not cohabiting (Declercq et al.,

2010; Gunnarsson et al., 2014; Viisainen et al., 1999), tend to smoke during the pregnancy (Declercq et al., 2010; Gunnarsson et al., 2014; Viisainen et al., 1999) and have less education or a lower socioeconomic status (Declercq et al., 2010; Hadar et al., 2005; Lazić et al., 2011), are more likely to abuse substances (Unterscheider et al., 2011), make no or fewer prenatal visits (Declercq et al., 2010; Lima et al., 2018; Gutvirtz et al., 2020; Pasternak et al., 2018; Renesme et al., 2013; Rodie et al., 2002; Sheiner et al., 2002), have more previous deliveries (Blondel et al., 2011; Declercq et al., 2010; Lima et al., 2018; Gunnarsson et al., 2014; Hadar et al., 2005; Lazić et al., 2011; Pasternak et al., 2018; Renesme et al., 2013; Rodie et al., 2002; Sheiner et al., 2002; Viisainen et al., 1999), have fewer previous cesarean deliveries (Pasternak et al., 2018), have shorter gestation times at delivery (Boland et al., 2018; Gunnarsson et al., 2014; Jones et al., 2011; Lazić et al., 2011; Rodie et al., 2002; Viisainen et al., 1999), and experience shorter labor durations (Rodie et al., 2002) compared to women who deliver in-hospital.

2.7.3 Characteristics of infants

Infants who are born out-of-hospital unplanned are more often preterm (Boland et al., 2018 ; Declercq et al., 2010; Gutvirtz et al., 2020) and have lower mean birth weight than those born in the hospital (Boland et al., 2018 ; Lima et al., 2018; Gutvirtz et al., 2020; Hadar et al., 2005; Lazić et al., 2011; Rodie et al., 2002; Sheiner et al., 2002; Viisainen et al., 1999).

2.7.4 Maternal outcomes

As far as we know, there are only a few studies showing serious adverse outcomes for mothers who deliver unplanned outside of a hospital. However, there is one report showing an association with maternal death (Combier et al., 2020) and another study showing a greater risk for postpartum hemorrhage compared to in-hospital deliveries (Hadar et al., 2005). More perineal injuries and puerperal infections compared to in-hospital deliveries have also been reported (Lima et al., 2018).

2.7.5 Infant morbidity and mortality

Compared to infants born in-hospital, infants born out-of-hospital require admissions to a neonatal care unit more often (Combier et al., 2020; Lima et al., 2018; Pasternak et al., 2018; Renesme et al., 2013; Lazić et al., 2011; Hadar et al., 2005; Rodie et al., 2002) have hypothermia more often (Pasternak et al., 2018; Renesme et al., 2013; Jones et al., 2011; Rodie et al., 2002; Moscovitz et al., 2000; Viisainen et al., 1999) and have prolonged hospital stays (Lima et al., 2018). Admitted infants have been reported to have infections, respiratory problems, prematurity, hypoglycemia, hypothermia and feeding difficulties (Combier et al., 2020; Lima et al., 2018; Rodie et al., 2002). Perinatal and neonatal mortality rates are significantly higher among UOHDs (Combier et al., 2020; Gutvirtz et al., 2020; Lima et al., 2018; Engjom et al., 2017; Gunnarsson et al., 2014; Grzybowski et al., 2011; Hemminki et al., 2011; Lazić et al., 2011; Rodie et al., 2002; Sheiner et al., 2002; Viisainen et al., 1999) and higher still among preterm infants (Boland et al., 2018; Engjom et al., 2017; Gunnarsson et al., 2014) compared to infants born in-hospital. Perinatal or neonatal mortality has been shown to be three to seven times higher compared to infants born in-hospital (Grünebaum et al., 2020; Lima et al., 2018; Hemminki et al., 2011). The perinatal mortality rate among UOHDs in the Norwegian study, for example, was 8.4 per 1000 births and 2.4 per 1000 births among midwife-led institutions (Engjom et al., 2017) and 51.7 per 1000 births in a British study and in the control group 8.6 per 1000 births (Rodie et al., 2002). According to one Australian population-based cohort study, most of deceased, very preterm infants died at the age of a few hours, and most deaths occurred before they arrived at an intensive care unit. In this study, all very preterm infant deaths occurred within three days of age (Boland et al., 2018).

2.7.6 Risk factors of unplanned out-of-hospital deliveries

There is limited current data about the risk factors related to UOHDs and adverse outcomes related to them. Mothers who have unplanned out-of-hospital deliveries more often have longer distance to travel to a hospital (Lima et al., 2018; Renesme et al., 2013). Longer travel time has been shown to increase the risk for UOHD (Combier et al., 2020; Engjom et al., 2017; Renesme et al., 2013), and it is also associated with neonatal mortality (Paranjothy et al., 2014; Pilkington et al., 2014; Grzybowski et al., 2011; Ravelli et al., 2011). On the other hand, in a French study, only neonatal hospitalization was associated with distance to hospital, but for other

adverse outcomes, distance had no association (Combier et al., 2020). Travel time and travel distance analyses are often estimations, because the exact location at the beginning of the active phase of delivery is difficult to pinpoint afterwards, at least in retrospective studies. In addition to long travel distance or travel times, low education and unemployment, high maternal age, high parity and lack of or poor prenatal care have been found to be independent risk factors for UOHD (Gunnarsson et al., 2014; Renesme et al., 2013; Hadar et al., 2005; Sheiner et al., 2002).

2.7.7 Risk factors of mortality in unplanned out-of-hospital deliveries

UOHDs themselves have been reported to be an independent risk factor for adverse neonatal outcomes. Maternal pathology, multiparity, lack of or poor prenatal care, prematurity, and neonatal hypothermia have been predictors of adverse outcome among infants born unplanned out-of-hospital (Javaudin et al., 2019; Sheiner et al., 2002; Moscovitz et al., 2000). The risk of stillbirth is increased in very preterm deliveries, when the birth occurs unplanned in out-of-hospital environment (Boland et al., 2018). These very preterm infants are also more likely to die within 28 days or within one year after birth (Boland et al., 2018). Preterm UOHD births have been associated with low maternal age, HIV-infection, lack of prenatal care, low temperature, low birth weight and need for endotracheal intubation (Jones et al., 2011).

Causes of infant deaths have been reported in only a few studies. Stillbirths account for a large proportion of deaths among very preterm infants (Boland et al., 2018), and a longer travel time increases the risk for stillbirth, infections and various conditions resulting from preterm birth (Paranjothy et al., 2014). Gunnarson et al. showed that the majority of perinatal mortality is caused by infections, placental- related causes (i.e. placental abruption or retroplacental hematoma) and neonatal causes, such as extreme prematurity, trauma, and suffocation (Gunnarsson et al., 2017).

2.8 Long-term outcomes of out-of-hospital born children

Child deaths in the general population are increasingly rare in high-income countries, and the majority of them occur during the neonatal period (Remes et al.,

2012; Public Health Agency of Canada, 2006). In the post-neonatal period, mortalities are often associated with congenital anomalies, sudden infant death syndrome, infections, and morbidity related to preterm birth (Official Statistics Finland 2016, Public Health Agency of Canada, 2008). Mortality during the post neonatal period (28 to 365 days of age) has also been attributed to social and environmental factors, for example low maternal education level (Chen et. al, 1998). From the age of one to 14 years, the most common causes of death are malignancies, congenital malformations, and chromosomal anomalies (Official Statistics of Finland 2016). Accidental deaths, drownings, and violence cause about one-third of deaths among children aged one to four years. Better parental education and higher income protect children from mortality, while single parenthood increases the risk (Remes, 2014; Arntzen et al., 2008). Low maternal education, multiple birth, and being male increase the odds of hospital readmission (Chen et al., 1998; Kosowan et al., 2019). Smoking during pregnancy increases risk of respiratory infections, asthma, atopy, otitis media and sudden infant death syndrome (Shea et al., 2008; Silvestri et al., 2015; Richardson et al., 2009). An Australian study found that UOHD-infants who were very preterm had higher neonatal and infant mortality, and only 41% of them were alive by the age of one year (Boland et al., 2018).

Data on the association between the birth setting and long-term childhood morbidity and mortality is lacking. In Australia, no differences in hospital readmissions were found within 28 days of age between infants who were born in hospital and infants who were born either at home or in birth centers (Homer et al., 2019).

To the best of our knowledge, there is only one recently published study about long-term outcomes related to UOHDs and no studies of childhood morbidity in children born at home as planned. In the previously mentioned Israeli study, researchers followed up with subjects until the age of 18 and found that hospitalization rates were lower among children who were born unplanned out-of-hospital. However, the study group stated that this result might be due to under-utilization of healthcare services among population who gave birth unplanned out-of-hospital rather than the UOHD itself (Gutvirtz et al., 2020).

3 AIMS OF THE STUDY

The aims of the study were to define the incidence, incidence trends, risk factors, morbidity, and mortality related to OHDs. The aim was also to establish possible regional differences in Finland.

The specific aims were to:

1. Evaluate incidence, incidence trends, perinatal mortality and morbidity and risk factors in detail for OHDs in the area of Tampere University Hospital between 1996 and 2011 (I).

2. Establish incidence and incidence trends of POHDs, and to compare perinatal and maternal mortality and morbidity in POHDs and in-hospital deliveries (II).

3. Evaluate incidence, incidence trends of UOHDs, to compare perinatal and maternal mortality and morbidity in UOHDs and assess the risk factors for UOHDs, perinatal mortality and morbidity related to UOHDs (III).

4. Evaluate the association of birth out-of-hospital with long-term childhood mortality and morbidity by analyzing the incidence of hospital visits, reimbursements for medical expenses, and disability allowances in various morbidities up to seven years of age (IV).

4 MATERIALS AND METHODS

4.1 Study design

This is a retrospective register study based on two cohorts of populations derived from medical records of births in the area of Tampere University Hospital between 1996 and 2011 (I) and from national health registers (II). The data from the national registers were linked by the register keepers. The primary cohort comprised all births in Finland between 1996 and 2013 according to the Medical Birth Register (MBR). Study materials, data sources, follow-up periods and study parameters are illustrated in Table 3.

Table 3. Study materials, data sources, follow-up periods and study parameters.

	Study I	Study II	Study III	Study IV
Included subjects	Infants delivered out-of-hospital (*n* = 67), infants delivered in-hospital (*n* = 134) 1996-2011 and their mothers	Infants delivered out-of-hospital as planned (POHD) (*n* = 197), (study group *n* = 170), infants delivered in- hospital (*n* = 1 051 139), (study group *n* = 720 047) 1996-2013 and their mothers	Infants delivered unplanned out-of-hospital (UOHD) (*n* = 1420), infants delivered in-hospital (*n* = 1 051 139) 1996-2013 and their mothers	Children who were delivered 1996-2013 out-of-hospital as planned (*n* = 176), unplanned out-of-hospital (*n* = 1338), in-hospital (*n* = 788 622) and were alive at age of seven days
Data sources	Tampere University Hospital database	the Medical Birth Register, the Register of Congenital Malformations, the Cause of Death Register	the Medical Birth Register, the Register of Congenital Malformations, the Cause of Death Register	the Medical Birth Register, the Care Register for Health Care, the Register of Congenital Malformations, the Social Insurance Institution, the Cause of Death Register
Follow-up period	Perinatal period	Perinatal period	Perinatal period	From the age of one week to seven years of age or by the year-end of 2018
Study parameters	Trends in incidence, risk factors for out-of-hospital delivery, perinatal morbidity	Perinatal and maternal mortality and morbidity in POHDs, incidence rates and incidence trends of POHDs	Perinatal and maternal mortality and morbidity in UOHDs, incidence rates and incidence trends of UOHDS. Risk factors for UOHDs, perinatal mortality and morbidity	Deaths, hospital visits, reimbursements for medical expenses, disability allowances. The association between site of birth and childhood morbidity and mortality

4.1.1 National health registers (II-IV)

4.1.1.1 Medical Birth Register

The Medical Birth Register (MBR) includes extensive data on all live births and stillbirths of fetuses with a birth weight of at least 500 grams or with a GA of at least 22 weeks, as well as data on the mothers. Data on mothers includes information on personal data, previous pregnancies and deliveries, the present pregnancy, and its follow-up and delivery. Infant data is taken up to the age of seven days or at discharge, and it includes detailed information about the infant and possible morbidities.

The socioeconomic classification used in the birth register is based on classifications by Statistics Finland and on the occupation reported by the mother. The information is supplemented by the mother's education if it is reported instead of occupation. The MBR is maintained by THL. Data sources for the register include maternity hospitals, the Population Information System of the Population Register Centre, and Statistics Finland. The MBR is well-established, providing comprehensive, reliable data (Gissler et al., 2002).

4.1.1.2 Care Register for Health Care

The Hospital Discharge Register was replaced by the Care Register for Health Care (CRHC) in 1994. The CRHC is maintained by THL. It includes data on patients discharged from inpatient care, the number of patients in inpatient care, and specialized outpatient health care at all public hospitals (the last entry was in 1998). Data on treatment received includes diagnoses coded according to the International Classification of Diseases, 10th Revision (ICD-10, used beginning in 1996). Data in this register are considered reliable (Sund, 2012).

4.1.1.3 National Register of Congenital Malformations

The Register of Congenital Malformations at THL was established in 1963. It monitors the prevalence and types of congenital anomalies and includes numbers and prevalence rates for congenital structural anomalies and chromosomal abnormalities for both live births and stillbirths. The data is received from hospitals, health care professionals, genetic laboratories, and other registers maintained by THL. Diagnoses are coded according to ICD codes. Although the Register of Congenital Malformations mainly collects data from an infant's first year, it also collects data on children's congenital anomalies detected later for statistics and research. The register's Statistical Report only provides information on major congenital anomalies. The exclusion of minor abnormalities is largely in keeping with the European Surveillance of Congenital Anomalies (EUROCAT). Our data included both minor and major congenital anomalies, and when needed, we excluded major anomalies using EUROCAT criteria (EUROCAT Guide 1.4 and reference documents, 2014).

4.1.1.4 Causes of Death Register, Statistics Finland

Statistics Finland produces statistics on causes of death and mortality trends. It also maintains death certificate archives, from which death certificate data are released for legal purposes. Data are supplemented by and verified against data from the Population Information System of the Population Register Center. Since 1987, causes of death have been defined as underlying causes of death, direct causes, intervening causes and contributing causes. For example, an underlying cause of death might be a disease that has triggered a series of illnesses leading directly to death, or it might be the circumstances surrounding an accident or act of violence that caused an injury or poisoning, leading to death. Causes of death are currently coded according to the ICD-10. Stillbirths include a fetus or newborn who shows no signs of life at the time of birth after a pregnancy lasting at least 22 weeks, or if the newborn weighs at least 500 grams. Perinatal mortality refers to the number of stillbirths and deaths during the first week of life (0–6 days after birth or children < 7 days old).

4.1.1.5 Social Insurance Institution (SII) register

The Social Insurance Institution of Finland (SII) provides social security coverage for Finnish residents, as well as benefits and services also for certain illnesses. SII provides disabled and chronically ill persons with a disability allowance for daily living. The amount of the allowance depends on the nature of the illness or disability and the restrictions the illness or disability causes. Children under 16 who have a disability or illness are eligible for the disability allowance. To be eligible, the child must have an illness, injury, or impairment that requires treatment, care, and rehabilitation lasting at least six months and requiring a level of effort, commitment to care, and additional expenditure greater than for a healthy child. There are three allowance levels (basic, middle, and highest). SII also reimburses patients for certain medication expenses for chronic diseases if they meet criteria set by SII. SII keeps a register of reimbursements for medical expenses and disease allowances.

4.2 Study population

4.2.1 Cohorts (I, II–IV)

The study populations were derived from births in the area of Tampere University Hospital (I) and from the cohort of MBR (II–IV). In the Tampere study, the study population (n = 201) and data were collected from medical files at Tampere University Hospital between 1996 and 2011 with certain ICD-10 codes indicating out-of-hospital births. The MBR study included all live births and stillbirths (n = 1 053 802) in Finland between 1996 and 2013. Infants with no information on site of birth (n = 1046) were excluded from studies II–IV. Other exclusion criteria varied depending on the study set and study question. In the national register on POHDs (II), we excluded UOHDs (n = 1420), all preterm infants, infants with no information on pregnancy duration or delivery method, and all operative deliveries (n = 331 119). In the study on UOHDs (III), we excluded POHDs (n = 197), and in the study on long-term outcomes (IV), perinatal deaths (n = 5322), major anomalies, operative deliveries, and infants with no information on delivery method (n = 257 296) were excluded. A flow chart of the study populations (II–IV) is presented in Figure 4.

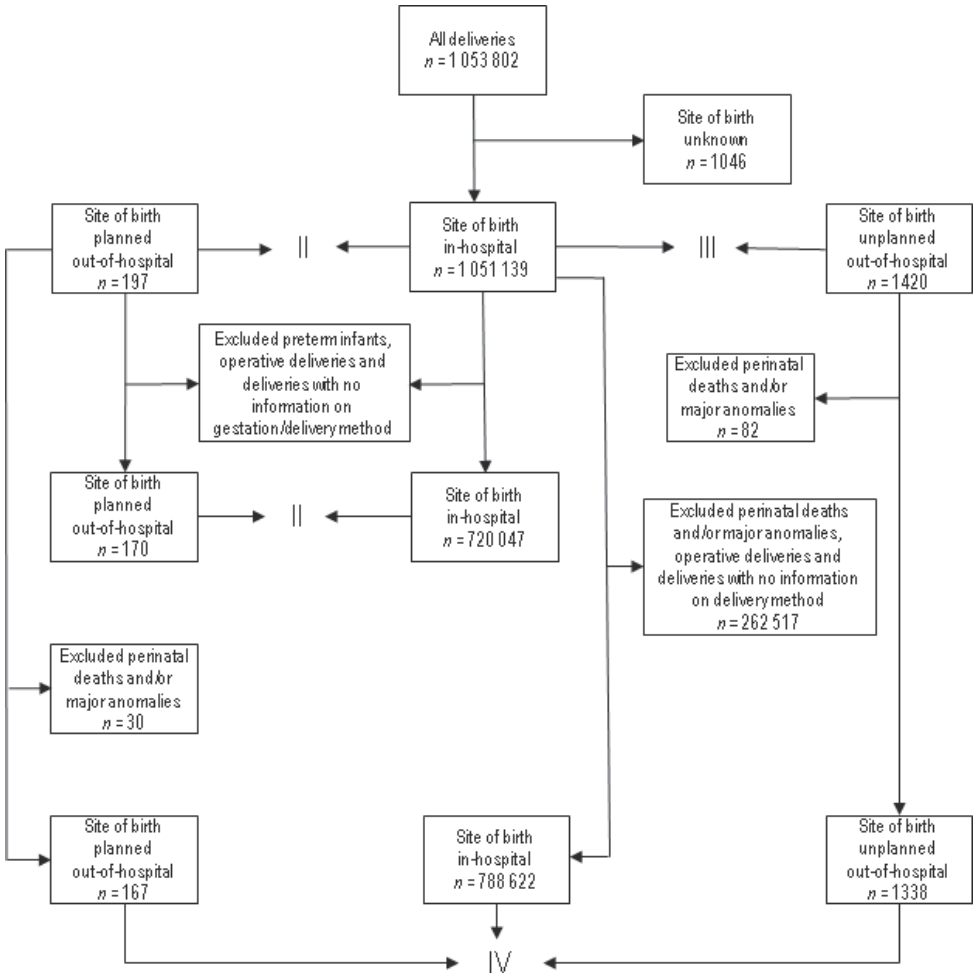

Figure 4. Flow chart of the study population, inclusions and exclusions in each study II–IV.

4.2.2 Groups based on site of birth (II-IV)

The remaining cohort of 1 052 756 infants and their mothers was divided into three subgroups according to site of birth: infants born in-hospital (n = 1 051 139), planned out-of-hospital (n = 197), and unplanned out-of-hospital (n = 1420) (II–IV).

4.3 Main outcomes

Main outcomes were perinatal mortality and morbidity (I, II, III). Diagnoses constituting the main end points in study IV were retrieved from the MBR, CRHC, and SII using ICD-10 codes. For the SII registers, we also used certain reimbursement codes and Anatomical Therapeutic Chemical (ATC) codes. ATC codes divide certain drugs into groups according to their therapeutic properties. Because the number of separate diagnoses was small, we combined certain diagnoses into larger groups (IV).

4.4 Variables (I, II–IV)

In study I, the site of birth was categorized as follows: in-hospital, on the way to the hospital, POHD, UOHD, and OHD with no information on whether the birth was planned or unplanned. Travel distances and travel times were divided into four categories: less than 5 km, 5–19.9 km, 20–34.9 km, and 35 km or more. Travel distances between the delivery unit and home municipality were calculated using a web-based route planner.

Variables on mothers included in the analysis were smoking during pregnancy, cohabitation, nationality, age, number of previous pregnancies and deliveries, number of prenatal visits, and duration of labor (I–III). In studies II and III, variables included for maternal morbidities were chorioamnionitis, genital tract trauma (including uterus rupture), bleeding during delivery or prenatally (including placental abruption and placenta previa), postpartum hemorrhage, and puerperal infection.

Variables on infants included length of gestation at delivery, birth weight, birth length (only in study I), Apgar scores, and admission to neonatal unit, and size for

GA (AGA/SGA/LGA). Diagnoses during hospital stays after the birth were collected (I-III).

One-minute and five-minute Apgar scores were divided into two categories: 0–6 and 7–10. Length of gestation in weeks and days was categorized as follows: < 32^{+0}, 32^{+0} to 36^{+6}, 37^{+0} to 42^{+0}, and more than 42^{+0}, and birth weight as 1500–2499 grams, 2500–4499 grams and 4500–5500 grams.

The following variables were tested for association with OHD in study I: smoking, cohabitation, mother's nationality, maternal age, parity, number of previous pregnancies, number of all prenatal visits to maternity clinics in health care centers or hospitals, home-to-hospital distance and travel time, length of gestation at delivery, duration of labor, duration of infant's hospital care, one- and five-minute Apgar scores, congenital anomaly, birth weight and birth length, SGA and LGA, admission to a neonatal unit, and diagnoses received. Variables included in the analyses in study III were the study period, the area of Finland, alcohol and/or drug abuse, cohabitation, smoking during pregnancy, primiparity, number of prenatal visits, length of gestation at birth, and birth weight. The results were reported as odds ratios (OR) with 95% confidence intervals (CI). Only variables with fewer than 10% of values missing were included in the logistic regression analyses. Infants and mothers with missing information were included in the analysis.

Defined diagnoses, coded according to the ICD-10, related to infant and mother morbidity were used. Asphyxia was registered in our study if there was diagnose P21* for birth asphyxia. Working from the birth register, we listed prenatal morbidity variables separately: resuscitation at birth (intubation and/or chest compression in the delivery unit), invasive ventilation (all endotracheal mechanically assisted ventilation), congenital malformation, and antibiotic therapy received during the first weeks of life. Results were also analyzed by specific catchment area (southern, eastern, northern, western, and southwestern).

In analyzing morbidity beyond the perinatal period (IV), three main groups of certain ICD-10 codes, ATC classification codes and reimbursement codes were created.

4.5 Data linkages (II–IV)

The study population was formed by THL. The personal identifiers of the study population were sent to other register controllers (such as Statistics Finland and

SII), who sent their own data to the researcher. The data from different registers were combined using the pseudonymised data with personal identity codes.

4.6 Statistical methods (I, II–IV)

Normally distributed continuous variables (maternal age and birth weight) were described by means and standard deviations (SD), and skew distributed variables were described by medians and interquartile ranges (IQR). The characteristics of infants and their mothers were expressed as numbers and percentages if the variables were categorical. Categorical variables were analyzed using Pearson's chi-squared test and Fisher's exact test. The Mann–Whitney U test and independent samples *t* test were used for continuous variables. P-values less than 0.05 were considered statistically significant.

Logistic (I–IV) and multinominal logistic (IV) regression analyses were performed to investigate the risk factors for UOHD, POHD, and OHD. Results were shown by ORs with 95% confidence intervals (CIs). All variables were entered simultaneously into the multivariable-adjusted models. The association between different sites of birth and childhood morbidity was sought using multivariable-adjusted Cox proportional-hazards regression analysis (IV). Statistically significant interactions with site of birth (UOHD, POHD and OHD, with in-hospital as the reference group) were included into the final models. Results were expressed as hazard ratios (HR) with 95% confidence intervals (95% CI). Statistical analyses were run with the statistical software package IBM SPSS Statistics for Windows, Version 22.0-26.0 (IBM Corp., Armonk, NY). The Cochran–Armitage trend test (StatXact version 4.0.1) was used to determine the statistical significance of the changes in the UOHD rates during the study period (II, III). R version 3.6.1 prop. trend.test was used to determine trends in mortality rates (III).

4.7 Ethics

This study was based on register data obtained from national registers (II–IV) and medical files (I). There was no patient or public involvement in defining the research question, designing the study, or interpreting the study results. Patients were not contacted, and study subjects were pseudonymised by codes in the

register-holding institutions. Permissions to use registries were obtained from THL (Dnro THL/535/5.05.00/2013, Dnro THL 1798/5.05.00/2019, Dnro THL/4101/14.02.00/2020), SII (Kela 36/522/2013, Kela 132/522/2019), and Statistics Finland (TK-53-556-13, TK-53-1863-18). The research project was approved by the Tampere Region Ethics Committee (ETL R12268).

5 RESULTS

5.1 Characteristics of parturients, deliveries, and infants (I, II–IV)

5.1.1 Mothers

Mothers who delivered out-of-hospital (I) smoked during pregnancy more often, cohabitated more often, and had more previous pregnancies and deliveries, fewer prenatal visits, longer distances to travel from home to a delivery unit and shorter labor durations (first and second phase) compared to mothers who delivered in the hospital.

Mothers, who delivered at home as planned (II) were older, had higher socioeconomic status, and smoked during pregnancy less often compared to those mothers who gave birth in the hospital. They also had more previous deliveries, fewer prenatal care visits, and shorter labor durations (first and second phase). Premature deliveries were less common compared to in-hospital deliveries. There were no differences in cohabitation, nationality, or distance from home to hospital between these groups.

Mothers who delivered unplanned out-of-hospital (III) were a heterogeneous group. However, as a whole group, compared to women who delivered in-hospital they had significantly more previous pregnancies and deliveries, and they were younger than 20 years or older than 34 years more often. They tended to have lower socioeconomic status, and they smoked during pregnancy and were of a nationality other than Finnish more frequently compared to in-hospital group. Substance abuse was also more common. They had fewer prenatal visits, fewer previous cesarean sections, and more multiple births. Their labor durations (first and second phase) were significantly shorter. Travel distances from their home municipality to the nearest delivery unit were significantly longer than for the in-hospital group. The mothers' characteristics are illustrated in Table 4.

5.1.2 Infants

In the study of Tampere University Hospital (I), characteristics such as length of gestation at delivery, birth weight, percentages of SGA or large birth weight (≥ 4500 grams and/or LGA), and length of hospital stay did not differ significantly between OHDs and hospital deliveries.

There were fewer preterm and post-term births among POHDs. Mean birth weight was higher among infants born at home, but 83% of the infants were appropriate for gestational age (II).

Infants born unplanned out-of-hospital were preterm and had low birth weight more often than infants born in-hospital (III). There were significantly fewer infants who were LGA compared to infants born in-hospital (III). The infants' characteristics are listed in Table 4.

Table 4. Characteristics of infants and their mothers.

Site of birth	Out-of-hospital I (n = 67)	Hospital I (n = 134)	Planned out-of-hospital II (n = 197)	Unplanned out-of-hospital III (n = 1420)	Hospital II, III (n = 1 051 139)
Mother					
Age in years, mean (SD)	29.0 (5.9)	29.1 (5.2)	31.8 (5.3)	30.3 (5.6)	30.0 (5.4)
Smoking, n (%)	10 (14.9)	8 (6.0)	11 (5.6)	223 (15.7)	157 009 (14.9)
Alcohol and/or drug abuse, n (%)	n/a	n/a	n/a	14 (1.0)	3044 (0.3)
Cohabitation, n (%)	46 (69.0)	119 (89.0)	172 (87.3)	1230 (86.6)	930 693 (88.5)
Socioeconomic status, n (%)					
Upper-level employee	n/a	n/a	43 (21.8)	154 (10.8)	168 579 (16.0)
Lower-level employee	n/a	n/a	52 (26.3)	423 (29.8)	375 728 (35.7)
Manual worker	n/a	n/a	7 (3.6)	225 (15.8)	152 846 (14.5)
Other	n/a	n/a	60 (30.5)	290 (20.4)	175 223 (16.7)
Finnish nationality, n (%)	63 (94.0)	128 (95.5)	160 (81.2)	1105 (77.8)	892 516 (84.9)
Area of Finland, n (%)					
Southern	n/a	n/a	n/a	424 (29.9)	367 335 (34.9)
Eastern	n/a	n/a	n/a	235 (16.5)	148 367 (14.1)
Northern	n/a	n/a	n/a	310 (21.8)	161 944 (15.4)
Western	67 (100)	134 (100)	n/a	274 (19.3)	205 920 (19.6)
Southwestern	n/a	n/a	n/a	167 (11.8)	160 356 (15.3)
Number of prenatal visits, MD (IQR)	13 (0-30)	16 (0-35)	12 (11-16)	14 (11-16)	16 (13-19)
First delivery, n (%)	9 (13.4)	55 (41.0)	25 (12.7)	139 (9.8)	334 393 (31.8)
Duration of labor, first phase, MD (IQR)	2:14* (0.25-17:47)	7:3* (1:23-23:28)	7:35 (5:18-11:40)	3:23 (1:50-3:22)	10:30 (6:40-16:40)
Length of gestation at birth, n (%)					
22+0–31+6	< 5 (1.5)	0 (< 0.1)	0 (< 0.1)	40 (2.8)	9986 (1.0)
32+0–36+6	< 5 (3.0)	<5 (1.5)	< 5 (0.5)	77 (5.4)	51 463 (4.9)
37+0–42+0	60 (89.6)	128 (95.5)	165 (83.8)	1250 (88.0)	938 498 (89.3)
> 42+0	0 (< 0.1)	<5 (3.0)	< 5 (1.5)	7 (0.5)	48 187 (4.6)
Infant					
Birth weight					
< 2500g, n (%)	6 (9.0)	< 5 (1.5)	< 5 (1.5)	107 (7.5)	46 180 (4.4)
Apgar 1 min 0–6, n (%)	< 5 (4.5)	5 (3.7)	8** (4.7)	116 (8.2)	56 231 (5.3)
Resuscitation at birth, n (%)	0 (< 0.1)	n/a	0** (<0.1)	11 (0.8)	9028 (0.9)
Asphyxia at birth, n (%)	0 (< 0.1)	<5 (1.5)	< 5** (1.2)	12 (0.8)	14 689 (1.4)
Invasive ventilation, n (%)	0 (< 0.1)	n/a	< 5** (1.2)	21 (1.5)	12 576 (1.2)
Antibiotic treatment, n (%)	5 (7.5)	0 (<0.1)	< 5** (2.4)	99 (7.0)	52 332 (5.0)
Congenital malformation, n (%)	7 (10.4)	6 (4.5)	7** (4.1)	117(8.2)	87 489 (8.3)

* Includes second phase of labor. **Morbidity was analyzed using a smaller group (n = 170) due to exclusion criteria.

5.2 Perinatal mortality of infants (I–III)

5.2.1 Out-of-hospital deliveries in the area of Tampere University Hospital

No perinatal deaths were registered in this study.

5.2.2 Planned out-of-hospital deliveries (II)

Two perinatal deaths occurred in the POHD group. The distance from home to the delivery unit in these cases was short. In these cases, multiple pregnancy and nulliparity were the known contraindications for the POHD, according to current Finnish national guidelines.

5.2.3 Unplanned out-of-hospital deliveries (III)

Perinatal mortality rate was 35 per 1000 births, five times higher than in-hospital births after adjusting for GA and birth weight. In total, 49 infants died, with 25 of them stillborn. Most deceased infants were preterm, 17 of stillborn infants and 13 of those who died before the age of one week. Intrauterine hypoxia, prematurity, chorioamnionitis, and umbilical cord complications were the main causes of death in stillborn infants. Chorioamnionitis and placenta-related causes, like ablation, were contributory causes of death in nine cases. The underlying cause of death was unknown in 12 of these cases.

Eighteen (75%) of the 24 infants who were born alive but died before the age of one week died on the day of birth, and the remaining six died during the first three days of life. Ten of these deceased infants were very preterm, and 13 of the infants had a birth weight less than 2500 grams. This group also included one set of twins. The cause of death was related to physical abuse of infant in almost half of the cases. Maternal and fetal infections and prematurity accounted for six deaths. Other underlying causes of death included nontraumatic intracranial hemorrhages, congenital urinary tract and cardiac anomalies and two unspecified causes. The underlying cause of death was unknown in one case. The specific numbers and percentages of causes of death are listed in Table 5.

Travel distance from home municipality to the nearest delivery unit (using 2015 locations) was ≥ 35 kilometers in 19 (39%) cases of death. Median travel distance

was 19.4 kilometers in this subgroup (IQR 60.9 km). The subjects were of Finnish nationality in most cases (n = 34, 69%), and 25 (51%) were cohabitating. The mothers' ages ranged from 20 to 34 years in 30 (61%) cases. Information about size for gestational age was missing in 19 cases, but seven (14%) were SGA.

Table 5. Underlying causes of death among infants born unplanned out-of-hospital.

Underlying cause of death	Number of stillborn infants	(%)	Number of live born infants	(%)
Physical abuse (proven or suspected)	0	< 0.1	10	42
Chorioamnionitis, perinatal infections	< 5	8.3	< 5	12.5
Asphyxia, umbilical cord complications	6	24	< 5	4.2
Causes of death related to prematurity or low birth weight	< 5	12.5	< 5	12.5
Unknown	12	48	< 5	4.2
Other	< 5	8.0	6	25
Total	25	100	24	100

5.3 Perinatal infant morbidity (I–III)

5.3.1 Planned out-of-hospital deliveries (I, II)

There were < 5 POHDs in the study population of Tampere University Hospital (I). In the national register study (II), the POHD group had lower one-minute Apgar scores, but only a few infants in this group were admitted to the neonatal unit (n = 7, 4.1%). Birth traumas were rare. Among those admitted infants there were infants with birth weight less than 2500 grams, infants who were treated with antibiotics, infants who needed invasive ventilation and/or had diagnoses of birth asphyxia or hypothermia. Other diagnoses for those admitted ones were pneumonia, a family history of substance abuse, and hypoglycemia. Fewer than five infants were registered with major congenital anomalies including cardiac and chromosomal anomalies. Perinatal morbidity in POHDs is listed in Table 4.

5.3.2 Unplanned out-of-hospital deliveries (I, III)

In the study population of the area of Tampere University Hospital (I), infants in OHD group had more often diagnosis for hypothermia and infections compared to in-hospital group. Infants who were born in the hospital had more often one- and five minute Apgar scores 7-10 compared to OHD-infants (I). In the national register study (III) in the UOHD group the one-minute Apgar scores were more often lower and hypothermia was more common, but the infants had less birth traumas compared to infants who were born in-hospital. The UOHD group infants received more often antibiotic treatment than those born in the hospital. Perinatal morbidity in UOHDs is illustrated also in Table 4. Infants in the OHD group were admitted more often to neonatal unit than infants born in-hospital in the study I, but the percentages of infants admitted to neonatal unit did not differ significantly between the groups in the national register study (III). In the national register study (III) in total 169 (11.9%) of the UOHD infants were admitted to neonatal care unit. The most common diagnoses among these infants were disorders related to prematurity and poor fetal growth (n = 54, 32.0%), respiratory disorders (n = 46, 27.2%), neonatal jaundice (n = 35, 20.7%), infections (n = 26, 15.4%), hypoglycemia (n = 23, 13.6%), congenital malformation (n = 15, 8.9%), hypothermia (n = 12, 7.1%), maternal substance abuse (n = 12, 7.1%) and birth asphyxia (n = 11, 6.5%).

5.4 Maternal Outcomes (II, III)

5.4.1 Planned out-of-hospital deliveries (II)

No maternal deaths or severe adverse maternal outcomes were registered in the national register. Significant adverse maternal and delivery outcomes included third- and fourth-degree perineal tears, the need for blood transfusions, prolapsed cord or other compressions of the cord, placental abruption, and labor dystocia. Interventions, including episiotomy (< 5 cases) were rare, while in the hospital, this rate was significantly higher (1.2% in the POHD group vs. 27.3% in the in-hospital-group, $p < 0.001$).

5.4.2 Unplanned out-of-hospital deliveries (III)

No maternal deaths or severe adverse outcomes were registered. Mothers in this group had fewer genital tract traumas (25 [2.2%] vs. 21 733 [3.7%], OR = 0.59, CI = 0.40-0.88), puerperal infections (< 5 [0.1%] vs. 2077 [0.4%], OR = 0.25, CI = 0.03-1.78), and hypertensive pregnancies (20 [1.4%] vs. 33 063 [3.1%], OR = 0.44, CI = 0.28-0.68) compared to those who delivered in the hospital.

5.5 Geographical differences in incidences of out-of-hospital deliveries in Finland (II–IV)

5.5.1 Planned out-of-hospital deliveries

Of the total number of births, POHDs occurred most often in Western Finland (Tampere University Hospital catchment area). In absolute numbers, POHDs were most common in Southern Finland (Helsinki University Hospital catchment area). Differences in geographical incidences are shown in Table 6.

Table 6. Occurrence of planned out-of-hospital deliveries in five university hospital catchment areas in 1996-2013 in Finland.

University hospital catchment area	Number of planned out-of-hospital deliveries	Percentage of all deliveries in the specific catchment area	Absolute percentage of all planned out-of-hospital deliveries in Finland
Southern (Helsinki)	75	0.02%	38%
Eastern (Kuopio)	13	0.01%	6.6%
Northern (Oulu)	18	0.01%	9.1%
Western (Tampere)	63	0.03%	32%
Southwestern (Turku)	28	0.02%	14%

5.5.2 Unplanned out-of-hospital deliveries (III)

In proportion to all deliveries in specific catchment area, UOHDs occurred most often in Northern Finland (Oulu University Hospital catchment area). However, the absolute number of UOHDs was highest in Southern Finland. Differences in geographical incidences are listed in Table 7. In addition, one infant was born unplanned out-of-hospital in the archipelago area, and nine infants born unplanned

out-of-hospital had no home municipality in Finland. Although the incidence of UOHDs was highest in the north, percentage of perinatal deaths in UOHD infants was lowest in Northern Finland (0.6%) and highest in Southwestern Finland (7.8%).

Table 7. Occurrence of unplanned out-of-hospital deliveries in different specific catchment areas from 1996 to 2013.

University hospital catchment area	Number of unplanned out-of-hospital deliveries	Percentage of all deliveries in specific catchment area	Absolute percentage of all unplanned out-of-hospital deliveries in Finland
Southern (Helsinki)	424	0.12%	30%
Eastern (Kuopio)	235	0.16%	17%
Northern (Oulu)	310	0.19%	22%
Western (Tampere)	274	0.13%	19%
Southwestern (Turku)	167	0.10%	12%

5.6 Incidence trends in Finland (I–III)

5.6.1 Out-of-hospital deliveries in the area of Tampere University Hospital

The relative number of OHDs increased from 0.09% in 1996 to 0.13% in 2011 ($p < 0.001$). The relative number was virtually unchanged between 1996 and 2005, but increased after this 2006-2011 (I).

5.6.2 Planned out-of-hospital deliveries (II)

The rate of POHDs per 100 000 births increased almost five-fold during the study period, from 8.3 in 1996 to 39.4 in 2013 ($p < 0.001$), growing toward the end of our study period and rising remarkably quickly afterward. Trends in POHDs are illustrated in Figure 5.

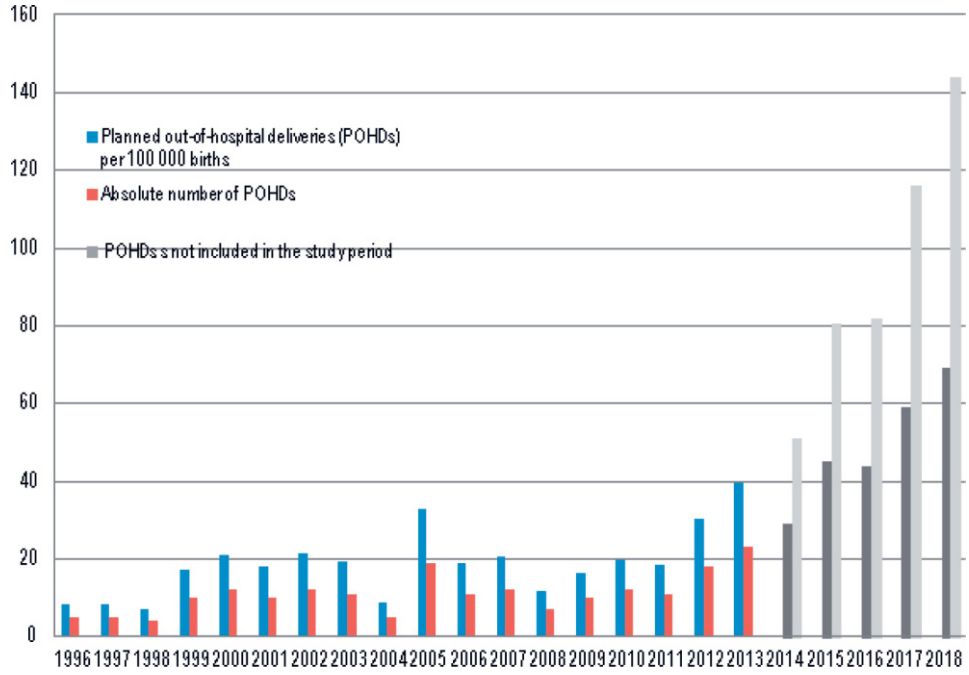

Figure 5. Rates of planned out-of-hospital deliveries across Finland from 1996 to 2018 (THL Medical Birth Register).

5.6.3 Unplanned out-of-hospital deliveries

The total rate of UOHDs remained virtually unchanged between 1996 and 2003 but increased through 2006 and then again in 2013. The rate rose significantly during the whole study period from 46 to 260 per 100 000 births ($p < 0.001$). The rate continued to rise after the end of our study period, as illustrated in Figure 6, where the UOHDs are separated into those that occurred on the way to hospital and those that occurred somewhere else out-of-hospital. Deliveries during transport and elsewhere out-of-hospital were not recorded separately until 2004. The numbers of UOHDs, delivery units, and perinatal deaths are illustrated together in Figure 7.

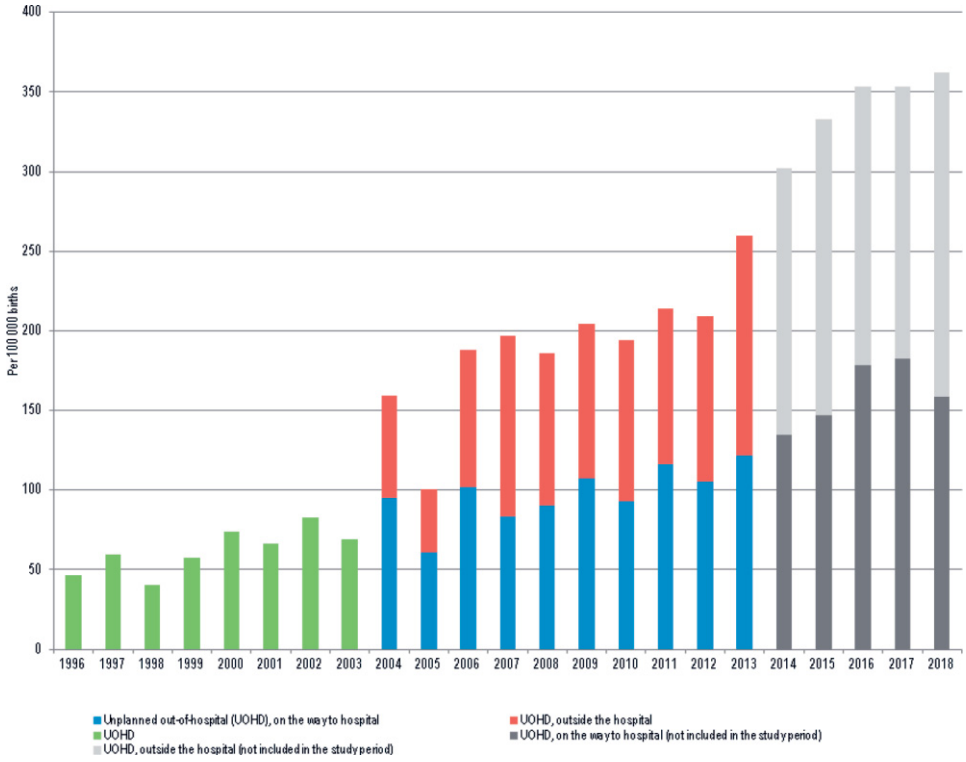

Figure 6. Rates of unplanned out-of-hospital deliveries across Finland from 1996 to 2018 (THL Medical Birth Register).

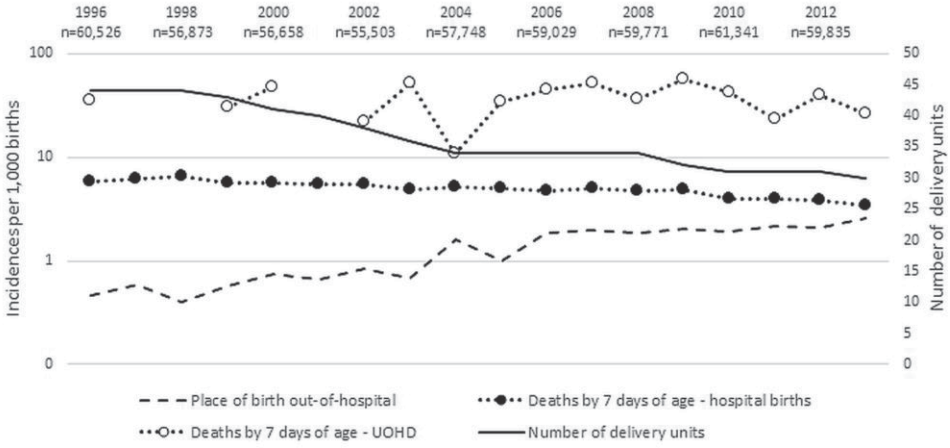

Figure 7. Rates in numbers of unplanned out-of-hospital deliveries, perinatal deaths, and delivery units from 1996 to 2013.

5.7 Predictors for planned out-of-hospital deliveries (II)

More than half (n = 125, 63%) of the 196 women who gave birth at home as planned had at least one risk factor for pregnancy and/or delivery or did not fulfill the criteria of current national recommendations for POHDs. There were 25 women who had no prior deliveries, and 14 mothers or deliveries with problems that included gestational diabetes, a history of stillbirth, a previous cesarean delivery, breech position of the fetus, and multiple pregnancy.

Five of the seven mothers whose children were admitted to the neonatal care unit lived in the same municipality as the delivery unit, though one mother lived more than 50 kilometers away. Among these seven mothers, fewer than five had no or only one prenatal visit, were nulliparous, or had a prior cesarean section. The length of gestation was 36 weeks in <5 cases and 42 weeks in <5 cases.

5.8 Predictors for unplanned out-of-hospital deliveries, perinatal mortality, and perinatal morbidity (I, III)

In the area of Tampere University Hospital (I), the independent risk factors associated with OHDs included non-cohabitation, smoking during pregnancy,

previous deliveries, < 13 prenatal visits, short labor duration, and a distance of ≥ 35 kilometers from home to the delivery unit. In the national register study (III), the independent risk factors of UOHDs were giving birth after the year 2001, giving birth outside Southern or Southwestern Finland, alcohol and/or drug abuse, non-cohabitation, having fewer than 13 prenatal visits, prior delivery/deliveries, and low birth weight.

Across the entire population, UOHD was one of the independent risk factors of mortality or morbidity and of mortality alone. Among the UOHD cases, the significant independent risk factors associated with perinatal mortality or morbidity included birth weight < 2500 grams and preterm delivery. Birth in the northern region seemed to be associated with a decreased risk of perinatal mortality or morbidity [OR 0.45 (CI 0.29-0.70)]. Independent risk factors of perinatal mortality were birth weight < 2500 grams, very preterm delivery, and birth in the eastern region of Finland. Among UOHDs, morbidity and mortality were not significantly associated with time period. Odd ratios and 95% confidence intervals for UOHD, perinatal mortality and mortality/morbidity are listed in Tables 8 and 9.

Table 8. Risk factor analyses for unplanned out-of-hospital deliveries.

		Unplanned out-of-hospital deliveries (*n* = 1420; 0.13%)		
Risk factors	N	n	Multivariable OR	95% CI
Study period				
1996–2001	346 574	198	1.00	
2002–2007	345 545	462	**2.45**	**[2.07-2.90]**
2008–2013	360 440	760	**3.76**	**[3.21-4.40]**
Area of Finland				
Southern	367 759	424	1.00	
Eastern	148 602	235	**1.39**	**[1.19-1.64]**
Northern	16 254	310	**1.48**	**[1.27-1.72]**
Western	206 194	274	**1.27**	**[1.09-1.49]**
Southwestern	160 523	167	0.99	[0.82-1.18]
Alcohol and/or drug abuse				
No	1 049 144	1407	1.00	
Yes	3415	13	**2.14**	**[1.22-3.74]**
Cohabitation				
Yes	931 923	1230	1.00	
No	59 049	94	**1.30**	**[1.05-1.61]**
Smoking during pregnancy				
No	868 686	1074	1.00	
Yes	157 232	223	**1.19**	**[1.03-1.38]**
Primipara				
No	616 285	1234	**4.76**	**[4.17-5-56]**
Yes	435 460	173	1.00	
Number of prenatal visits				
< 13	182 310	527	**2.01**	**[1.78-2.26]**
13–17	496 935	608	1.00	
> 17	355 897	212	**0.55**	**[0.47-0.64]**
Length of gestation at birth				
37+0–42+0	959 282	1250	1.00	
22+0–31+6	10 026	40	1.29	[0.84-1.99]
32+0–36+6	51 540	77	0.83	[0.63-1.10]
> 42+0	28 660	7	**0.32**	**[0.15-0.68]**
Birth weight				
< 2500g	46 287	107	**1.57**	**[1.16-2.12]**
≥ 2500g	1 005 551	1305	1.00	

Table 9. Risk factor analyses for perinatal mortality/morbidity and for perinatal mortality alone in unplanned out-of-hospital deliveries.

Multivariable risk factors of		Mortality or morbidity (*n* = 337, 23.7%)			Mortality (*n* = 49, 3.5%)		
	N	n	OR	95% CI	n	OR	95% CI
Study period							
1996–2001	198	41	1.00		<	1.00	
2002–2007	462	132	1.40	[0.89-2.20]	17	1.51	[0.28-8.14]
2008–2013	760	164	0.88	[0.57-1.37]	28	2.38	[0.51-11.2]
Area of Finland							
Southern	424	102	1.00		12	1.00	
Eastern	235	71	1.25	[0.84-1.87]	13	**5.32**	**[1.38-20.5]**
Northern	310	39	**0.45**	**[0.29-0.70]**	2	0.64	[0.09-4.77]
Western	274	72	0.92	[0.62-1.38]	9	1.34	[0.34-5.28]
Southwest	167	51	1.03	[0.65-1.63]	13	3.22	[0.84-12.4]
Alcohol and/or drug abus e							
No	1407	333	1.00		48	1.00	
Yes	13	< 5	0.51	[0.12-2.21]	<	0.32	[0.02-4.99]
Cohabitation							
Yes	1230	269	1.00		25	1.00	
No	94	30	1.17	[0.69-1.98]	<	1.01	[0.21-4.78]
Smoking during pregnancy							
No	1074	216	1.00		19	1.00	
Yes	223	60	1.19	[0.82-1.74]	<	0.20	[0.03-1.17]
Primipara							
No	1243	256	0.77	[0.50-1.19]	17	0.38	[0.14-1.05]
Yes	173	77	1.00		28	1.00	
Number of prenatal visits							
< 13	527	144	1.04	[0.75-1.44]	33	2.30	[0.61-8.68]
13–17	608	118	1.00		<	1.00	
> 17	212	46	1.23	[0.82-1.83]	<	0.93	[0.10-9.16]
Length of gestation at birth							
37+0–42+0	1250	229	1.00		7	1.00	
22+0–31+6	40	40	-	-	24	**15.4**	**[2.64-90.2]**
32+0–36+6	77	40	**2.83**	**[1.60-4.98]**	6	2.12	[0.37-12.0]
> 42+0	7	< 5	0.71	[0.08-6.02]	0	-	-
Birth weight							
< 2500g	107	79	**3.06**	**[1.67-5.60]**	33	**9.41**	**[2.21-40.1]**
≥ 2500g	1305	252	1.00		11	1.00	

5.9 Child mortality and morbidity up to seven years of age (IV)

5.9.1 Mortality

No deaths were detected in OHD group after the perinatal period up to the age of seven years or the end of year 2018.

5.9.2 Morbidity

Numbers and percentages of children who had hospital visits, medication reimbursements and disability allowances are illustrated in Tables 10-12. The percentage of children, who visited hospital due to infections, was significantly lower in the children born planned out-of-hospital, and in the group of children born out-of-hospital in total in comparison with children born in-hospital (Table 11). The percentage of children who needed hospital visits and received disability allowances due to neurological or mental health disorders was higher in the UOHD group and in the children born out-of-hospital in total, compared to children born in- hospital (Table 12).

5.9.2.1 Asthma and allergies

The risk of hospital admissions and outpatient visits for asthma or allergies in children born either planned or unplanned out-of-hospital did not differ significantly from those born in-hospital. However, when these groups were combined, the children born out-of-hospital had a significantly lower risk of asthma or allergies than the children born in-hospital. The result remained significant in the analysis with interactions (Table 13).

5.9.2.2 Infections

The risk of hospital admissions and outpatient visits for infections by age seven was significantly lower in the POHD and UOHD groups and in children born out-of-hospital as a whole compared to those born in-hospital. The analysis with interactions showed that low one-minute Apgar scores seemed to be associated

with an increased risk of infections in the children born out-of-hospital. However, the decreased risk of infections in children born out-of-hospital remained significant in this analysis (Table 13).

5.9.2.3 Neurological and mental disorders

The risk of hospital admissions and outpatient visits for neurological or mental disorders by age seven in the POHD group was similar to the risk for children born in-hospital. On the other hand, the risk seemed to be higher in the UOHD group and in the combined group of children born out-of-hospital. However, the statistical significance disappeared in the analysis with interactions (Table 13).

Table 14 summarizes our main results.

Table 10. Morbidity of asthma and allergies.

	Planned out-of-hospital delivery (*n* = 176)		Unplanned out-of-hospital delivery (*n* = 1338)		In-hospital delivery (*n* = 788 622)		Out-of-hospital delivery, planned or unplanned (*n* = 1514)	
Asthma or allergies								
Hospital visits, *n* (%)	16	(9.1)	156	(11.7)	98 817	(12.5)	172	(11.4)
Number of hospital visits, MD (IQR)	4.5	(2.25–17.25)	3	(1-7.75)	3	(2–8)	3	(1–8)
Age at first hospital visit, in years, MD (IQR)	1.1	(0.6–2.0)	1.3	(0.7-3.1)	1.5	(0.7-3.2)	1.3	(0.7–3.0)
Reimbursement for medical expenses, *n* (%)	< 5	(2.3)	52	(3.9)	28 681	(3.6)	56	(3.7)
Age at first reimbursement, in years, MD (IQR)	2.75	(0.36–5.13)	1.72	(0.74-3.39)	2.02	(0.67–4.15)	1.7	(0.7–3.4)
Disability allowance, *n* (%)	< 5	(1.1)	22	(1.6)	14 690	(1.9)	24	(1.6)

Table 11. Morbidity of infections.

Infections	Planned out-of-hospital delivery (*n* = 176)		Unplanned out-of-hospital delivery (*n* = 1338)		In-hospital delivery (*n* = 788 622)		Out-of-hospital delivery, planned or unplanned (*n* = 1514)	
Hospital visits, *n* (%)	38	(21.6)	439	(32.8)	273 958	(34.7)	477	(31.5)
Number of the hospital visits, MD (IQR)	2	(1–3.25)	2	(1–3)	2	(2–8)	2	(1–3)
Age at first hospital visit, in years, MD (IQR)	1.1	(0.5-2.1)	1.5	(0.6-2.6)	1.4	(0.7-3.2)	1.4	(0.6-2.5)
Pneumonia								
Hospital visits, *n* (%)	8	(4.5)	57	(4.3)	30 530	(3.9)	65	(4.3)
Number of the hospital visits, MD (IQR)	1	(1–1.75)	2	(1–2)	1	(1–2)	n/a	n/a
Age at first hospital visit, in years, MD (IQR)	1.2	(0.6-2.6)	1.9	(1.1-3.9)	2.2	(1.3–3.7)	1.9	(1.1–3.7)
Bronchitis or bronchiolitis								
Hospital visits, *n* (%)	9	(5.1)	123	(9.2)	67 840	(8.6)	132	(8.7)
Number of the hospital visits, MD (IQR)	2	(1.5–3.5)	2	(1–3)	2	(1–3)	n/a	n/a
Age at first reimbursement in years, MD (IQR)	0.3	(0.1–0.6)	0.9	(0.3–1.8)	1.0	(0.4–1.9)	0.7	(0.3–1.6)

Table 12. Morbidity of neurological and mental disorders.

Neurological or mental disorders	Planned out-of-hospital delivery (*n* = 176)		Unplanned out-of-hospital delivery (*n* = 1338)		In-hospital delivery (*n* = 788 622)		Out-of-hospital delivery, planned or unplanned (*n* = 1514)	
Hospital visits, *n* (%)	10	(5.7)	100	(7.5)	42 653	(5.4)	110	(7.3)
Number of the hospital visits, MD (IQR)	2	(1–22)	4	(1–10)	3	(1–10)	4	(1–10.5)
Age at first hospital visit, in years, MD (IQR)	5.8	(1.0–6.6)	4.9	(3.3–6.0)	5.0	(3.0–6.0)	4.9	(3.3–6.0)
Reimbursement for medical expenses, *n* (%)	< 5	(0.6)	< 5	(0.3)	3044	(0.4)	5	(0.3)
Age at first reimbursement, in years, MD (IQR)	0.10	-	3.70	(0.84–5.87)	3.42	(1.41–5.29)	1.6	(0.4–5.9)
Disability allowance, *n* (%)	< 5	(1.1)	60	(4.5)	17 952	(2.3)	62	(4.1)

Table 13. Cox hazard regression models regarding hospital visits for asthma or allergies, infections and neurological or mental disorders.

							Planned and / or unplanned out-of-hospital deliveries vs. deliveries in-hospital					
							Univariable		Multivariable without interactions		Multivariable with interactions	
	N	n	(%)	Pyrs	Risk	(95% CI)	HR (95% CI)		HR (95% CI)		HR (95% CI)	
Ashtma or allergy	**790 136**	**98 989**	**(12.5)**	**5 048 310**	**196**	**(195-197)**						
In-hospital	788 622	98 817	(12)	5 038 578	196	(195-197)	1.00		1.00		1.00	
Planned out-of-hospital	176	16	(9)	1141	140	(72-208)	0.72	(0.44-1.17)	0.71	(0.44-1.17)	0.63	(0.35-1.10)
Unplanned out-of hospital	1338	156	(12)	8592	182	(153-210)	0.93	(0.79-1.09)	0.86	(0.73-1.004)	0.83	**(0.69-0.996)**
In-hospital	788 622	98 817	(12.5)	5 038 578	196	(195-197)	1.00		1.00		1.00	
Out-of-hospital	1514	172	(11.4)	9733	177	(151-203)	0.90	(0.78-1.05)	0.84	(0.72-0.98)	0.80	**(0.67-0.96)**
Infections	**790 136**	**274 435**	**(34.7)**	**5 414 948**	**507**	**(505-509)**						
In-hospital	788 622	273 958	(34.7)	5 404 641	507	(505-509)	1.00		1.00		1.00	
Planned out-of-hospital	176	38	(21.6)	1207	315	(216-413)	0.59	(0.43-0.80)	0.59	(0.43-0.81)	0.49	**(0.34-0.72)**
Unplanned out-of-hospital	1338	439	(32.8)	9101	482	(438-526)	0.94	(0.85-1.03)	0.87	(0.79-0.96)	0.80	**(0.71-0.89)**
In-hospital	788 622	273 958	(34.7)	5 404 641	507	(505-509)	1.00		1.00		1.00	
Out-of-hospital	1,514	477	(31.5)	10 307	463	(422-503)	0.89	(0.81-0.98)	0.84	(0.76-0.92)	0.76	**(0.68-0.84)**
Neurological or mental disorder	**790 136**	**42 763**	**(5.4)**	**4 134 687**	**103**	**(102-104)**						
In-hospital	788 622	42 653	(5.4)	4 126 554	103	(102-104)	1.00		1.00		1.00	
Planned out-of-hospital	176	10	(5.7)	1028	97	(37-157)	1.05	(0.56-1.95)	1.11	(0.60-2.07)	1.19	(0.62-2.29)
Unplanned out-of-hospital	1338	100	(7.5)	7106	141	(112-168)	1.40	(1.15-1.70)	1.24	(1.01-1.51)	1.04	(0.83-1.31)
In-hospital	722 622	42 653	(5.4)	4 126 554	103	(102-104)	1.00		1.00		1.00	
Out-of-hospital	1514	110	(7.3)	8134	135	(110-160)	1.36	(1.12-1.64)	1.22	(1.01-1.48)	1.06	(0.85-1.31)

Table 14. Summary of the main results in studies I-IV.

Study	Study groups	Main results
Study I	OHD (out-of-hospital delivery) group (*n* = 67), in-hospital group (*n* = 134)	Smoking, short duration of labor, a higher number of previous deliveries, single status and longer distance from home to delivery unit were associated with OHDs.
Study II	POHD (planned out-of-hospital delivery) group (study group *n* = 170), in-hospitalgroup (study group *n* = 720 047)	More than half of the women had at least one risk factor for pregnancy and/or delivery or did not fulfill the criteria of current national recommendations for POHDs. The annual rate of POHDs increased during the study period.
Study III	UOHD (unplanned out-of-hospital delivery) group (*n* = 1420), in-hospital group (*n* = 1 051 139)	Cause of perinatal death was related to physical abuse in 42% of all dead infants. Predictors of perinatal morbidity and mortality included preterm delivery and low birth weight. The annual rate of UOHDs increased during the study period.
Study IV	UOHD group (*n* = 1338), POHD group (*n* = 176), OHD group (*n* = 1540), in-hospital group (*n* = 788 622)	Morbidity related to asthma or allergic diseases and infections by seven years of age appeared to be lower in children born out-of-hospital. Birth out-of-hospital seemed to not be associated with increased risk for neurological morbidity nor early childhood mortality.

6 DISCUSSION

6.1 Planned out-of-hospital deliveries (II)

The outcomes of POHDs might be affected by several factors, including who is assisting the delivery, whether these persons are properly trained and experienced, what the maternal risk profile is, how the POHDs are generally integrated to the health care system, how, by who and when the decision of transfer the mother to the delivery hospital is made, how the transfer is organized, and how long is the delay in the case of emergency transfer.

POHDs were rare, but the rate increased during the study period. The findings in our study showed that also women with current contraindications, as defined by the national guidelines, planned at-home deliveries. However, these guidelines were not published until at the end of the study period in 2013. Perinatal deaths occurred when the current national guidelines were not followed. This is consistent with an Australian study in which nearly 60% of women with POHDs had at least one risk factor according to the criteria of publicly funded homebirth program (Sassine et al., 2020). In addition, even in the subgroup of women who met the criteria of a low-risk pregnancy and delivery, there were adverse infant outcomes.

It has been claimed that when national guidelines and systems for transfer to a hospital are available, there is either minimal or no increased risk associated with POHD for low-risk women (de Jonge et al., 2013). Previous studies have reported conflicting results of perinatal mortality and morbidity across various countries and populations of women, and it is difficult to draw any conclusions from these results because of the different study settings. In our study, number of deceased infants was low—only two infants—so it is difficult to establish whether POHDs are associated with higher perinatal mortality in Finland.

Benefits of POHD include lower rates of maternal morbidity, such as postpartum hemorrhage and perineal lacerations, and lower rates of interventions. Our findings are in line with those of many previously published studies (MacDorman et al., 2019; Li, 2015; Grünebaum et al., 2017; Homer et al., 2019, Davies-Tuck et al., 2018; Snowden et al., 2015). However, while interventions should clearly be considered negative outcomes, they may in fact have been

necessary and potentially prevented other adverse outcomes such as perinatal mortality or morbidity. The differences in intervention rates might actually be a case of over- or undertreatment. Furthermore, the opportunity for interventions is limited during POHDs.

Maternal outcomes in our study were favorable. They have consistently been in favor of POHDs also in previously published studies (Cheng et al., 2013; Homer et al., 2019). The ideal statistical method would be to conduct a randomized, controlled trial, but it is neither feasible nor ethical to conduct a study of perinatal and maternal outcomes of POHDs compared to hospital deliveries.

The mother's right to choose a POHD does not preclude additional risks for the infant. It is still widely accepted that a hospital delivery, with ready access to and use of technology, is optimal for safe childbirth. The challenge is to optimize maternal and infant health outcomes, as well as the mother's experience of childbirth, with the least possible interventions. Many delivery units are trending toward more family-centered policies, and new hospital delivery units offer a more homelike environment, with accommodations for the whole family and the option of even a water birth. There is also the possibility of early discharge at many hospitals, as soon as six hours after birth, if mother and newborn meet the criteria. POHDs should be made safer by following national guidelines, including, at the very least, ruling out pregnancies and deliveries with contraindications. Despite this measure, the safety of POHDs remains unproven.

6.2 Unplanned out-of-hospital deliveries (I, III)

6.2.1 Trends in unplanned out-of-deliveries

In both the Tampere University Hospital area and in Finland as a whole, the rate of UOHDs has increased by time. After 2004, the number of deliveries during transport increased less than the number of UOHDs elsewhere.

The annual UOHD rate in our study population was virtually the same as in the latest studies published in Finland (1.0 to 2.5 per 1000 births, Viisainen et al., 1999; Hemminki et al., 2011) but lower than in the study from Norway (6.8 per 1000 births, Gunnarsson et al., 2014). The annual rate of UOHDs has increased significantly over time, throughout the country. This is in contrast to a Norwegian

study (Gunnarsson et al., 2014) reporting that the UOHD rate remained stable over 15 years despite a declining number of delivery units.

6.2.2 Deliveries during transport

Half of UOHDs occurred during transport to hospitals. As the number of delivery units has decreased, the distances from home to delivery hospital has increased. Deliveries during transport in the study population did not, however, explain most of the increase in UOHDs in the past 10 years. Indeed, a previous study in Finland suggested that the rise in UOHDs might not be explained entirely by the increasing distance between homes and delivery units (Pirneskoski et al., 2016). Other reasons, such as short labor durations and maternal mental and social issues, might explain a remarkable proportion of UOHDs. UOHDs during transport can be prevented by developing more effective emergency response centers, ambulances and helicopter services.

6.2.3 Predictors and maternal outcomes in unplanned out-of-hospital deliveries

UOHDs are more likely to involve mothers who are particularly young (Viisainen et al., 1999; Boland et al., 2018; Declerq et al., 2010) or old (Gunnarsson et al., 2014; Viisainen et al., 1999; Blondel et al., 2011), are unmarried and not cohabiting (Gunnarsson et al. 2014; Viisainen et al. 1999; Declerq et al. 2010), are smokers (Gunnarsson et al., 2014; Viisainen et al., 1999; Declerq et al., 2010), have less education or lower socioeconomic status (Lazić et al., 2011; Declerq et al., 2010; Renesme et al., 2013; Hadar et al., 2005), have less or no access to prenatal care, (Rodie et al., 2002, Sheiner et al., 2002, Lima et al., 2018; Declerq et al., 2010; Renesme et al., 2013; Pasternak et al., 2018), have had more previous deliveries (Gunnarsson et al., 2014; Rodie et al., 2002; Sheiner et al., 2002; Viisainen et al., 1999; Lazić et al., 2011; Lima et al., 2018; Declerq et al., 2010; Blondel et al., 2011, Renesme et al., 2013, Hadar et al., 2005; Pasternak et al., 2018), have fewer previous cesarean deliveries (Pasternak et al., 2018), have lower GA at delivery (Gunnarsson et al., 2014; Rodie et al., 2002; Viisainen et al., 1999; Lazić et al., 2011; Boland et al., 2018; Declercq et al., 2010), and experience shorter labor durations (Rodie et al., 2002). Thus, our data did not contradict previous studies. In our material, the study group had significantly shorter labor durations, but maternal

complications in the groups were comparable, including postpartum hemorrhage, which contradicts earlier report (Hadar et al., 2005).

Maternal outcome was favorable in most UOHDs. Mothers with UOHDs had less genital tract traumas, uterine ruptures, puerperal infections, and hypertensive pregnancies. Rates of diabetic and hemorrhagic complications did not differ between UOHDs and in-hospital deliveries.

6.2.4 Infant outcomes in unplanned ouf-of-hospital deliveries

In line with previous knowledge, infants delivered by mothers with UOHDs are more likely to be preterm (Lazić et al., 2011; Boland et al., 2018; Declercq et al., 2010), have lower mean birth weight (Rodie et al., 2002; Sheiner et al., 2002; Viisainen et al., 1999; Lazić et al., 2011; Boland et al., 2018; Hadar et al., 2005; Pasternak et al., 2018), are more likely to be admitted to neonatal care units (Rodie et al., 2002; Lazić et al., 2011; Lima et al., 2018; Renesme et al., 2013; Pasternak et al., 2018), and have more often hypothermia (Renesme et al., 2013; Moscovitz et al., 2000; Pasternak et al., 2018) than those born in-hospital. Prematurity was most strongly associated with adverse infant outcomes in UOHDs, as found in earlier studies (Gunnarsson et al., 2014; Engjom et al., 2017; Boland et al., 2018; Jones et al., 2011; Javaudin et al., 2019). To improve their skills, paramedics need to be adequately educated, and equipment suitable for managing preterm infants should be made available to emergency services. Special attention should be paid to monitoring and recording the body temperatures of infants to prevent hypothermia.

Higher perinatal and neonatal mortality rates in UOHDs are well established in certain populations and countries (Gunnarsson et al., 2014; Rodie et al., 2002; Sheiner et al., 2002; Viisainen et al., 1999; Engjom et al., 2017; Lazić et al., 2011; Hemminki et al., 2011; Grzybowski et al., 2011; Lima et al., 2018). No change in the perinatal mortality rate was seen over the study period for UOHD cases. In contrast, the perinatal mortality rate decreased in infants delivered in hospitals. As supposed earlier (Gunnarsson et al., 2014), infants born in hospitals might benefit from access to bigger hospitals capable of performing emergency cesarean sections and effective neonatal resuscitation at any time.

The causes of death we detected were partly in line with a previously published Norwegian study (Gunnarsson et al., 2017). A significant percentage of live births

in our material died as a consequence of abuse, i.e., under vague circumstances. Such cases seem unpreventable and are unlikely to be associated with distance to the nearest delivery unit. Mental health and/or social issues, as well as drug and alcohol abuse, may underlie some of these cases. Multidisciplinary interventions for the mother and her family, including substance abuse treatment, psychiatric therapy, and focused social work support, are needed to improve pregnancy outcomes in such circumstances.

Birth between 2008 and 2013 and birth in areas with low population density were associated with an increased risk of UOHDs, but not with perinatal morbidity or mortality associated with UOHDs. Thus, this does not support the hypothesis that such adverse events in UOHDs are associated with increasing distances due to the declining number of delivery hospitals. The association of delivery in the eastern region with an increased risk of perinatal mortality might be explained by chance because of the small number of cases.

6.3 Long-term outcomes in out-of-hospital deliveries (IV)

POHD group had the lowest percentage of children, who needed hospital admissions or outpatient visits due to infections by seven years of age. Mothers who deliver at home as planned are more often older (Cheng et al., 2013; Grünebaum et al., 2017; Li et al., 2015; Lindgren et al., 2008; MacDorman et al., 2019), non-smokers (Danilack et al., 2015; MacDorman et al., 2019), and married (Cheng et al., 2013; Halfdansdottir et al., 2015). Socioeconomic status and/or education are also usually higher among these women (Cheng et al., 2013; Declercq et al., 2010; Malloy et al., 2010). Thus, both the perinatal, demographic and socioeconomic factors in combination might provide conditions, which make these children less prone to infections causing need of hospital care.

Previous studies have showed that mothers who give birth unplanned out-of-hospital are younger (Boland et al., 2018; Declercq et al., 2010) or older (Blondel et al., 2011; Gunnarsson et al., 2014), more often unmarried/not cohabiting (Declercq et al., 2010; Gunnarsson et al., 2014), smoke more often during the pregnancy (Declercq et al., 2010; Gunnarsson et al., 2014), have less education or a lower socioeconomic status (Declercq et al., 2010, Lazić et al., 2011), are more likely substance abusers (Unterscheider et al., 2011), have lack of or less visits to prenatal care (Lima et al., 2018; Gutvirtz et al., 2020; Pasternak et al., 2018; Renesme et al., 2013), and have lower length of gestation at delivery (Boland et al.,

2018; Gunnarsson et al., 2014; Jones et al., 2011; Lazić et al., 2011; Rodie et al., 2002) compared to mothers with in-hospital deliveries. In our population, the children born unplanned out-of-hospital were also more often preterm, SGA and needed more often assisted ventilation and admissions to neonatal unit. These are obvious risk factors for future need of hospital care and disability allowances due to neurodevelopmental problems.

The earlier study reported long term morbidity of 3580 children born unplanned out-of-hospital in a single tertiary hospital area in Israel (Gutvirtz et al., 2020). The study population included altogether 243 682 singleton deliveries. The hospitalization rates by 18 years of age of the children born unplanned out-of- hospital due to respiratory, infectious and neurological causes were lower than in children born in-hospital. The author suggested that factors related to UOHDs might also be related to under-utilization of health care services. Under-utilization seems to be an unlikely phenomenon and avoiding/reluctance to visit health care is probably rare in a Finnish public health insurance and social security system. This improves reliability for our results.

The children born out-of-hospital in total is a very heterogeneous group in terms of perinatal, demographic and socioeconomic factors. In most cases the children born planned out-of-hospital remained at home environment during their perinatal period and only five (2.9%) infants in the study group were admitted to a neonatal care unit after birth. Instead, the children born unplanned out-of-hospital, were mostly transported after birth to hospital with their mothers and 169 (11.9%) of them were even admitted to the neonatal unit. The only factors in common in this population were that these children were not born in the delivery room environment. A quite significant percentage of mothers delivering in-hospital received intrapartum antibiotics. An American study reports that 38.3% of mothers received antibiotics for reasons such as GBS-positivity, suspected maternal infection, cesarean section, preterm labor or prolonged membrane rupture (Lin et al., 2011). According to unpublished data from the Finnish Medical Birth Register, 5.1% of women received intrapartum antibiotic prophylaxis during vaginal delivery to prevent GBS disease in their infants (years 2017–2019), excluding Southern Finland with no statistics available before 2020. Instead, intrapartum exposure to antibiotics is lacking in all OHDs. Both the association of the environment at birth and possible intrapartum exposure to antibiotics at birth might have impact on children's skin and gut microbiome (Tapiainen et al., 2019). These above-mentioned factors could have had protective or harmful effects on the prevalence of allergic and infectious diseases during childhood.

6.4 Strengths and limitations (I–IV)

As far as we are aware, this is the largest study conducted on OHDs in Finland and the only study in Finland of long-term outcomes up to seven years of age. We studied a long period of time, and the data was population-based and included all registered OHDs and deliveries in hospitals. Finnish national health registers are dependable, and their data have been shown to be reliable (Sund et al., 2012; Gissler et al., 2002).

The results of our study cannot be generalized to all high-income countries. However, in Nordic countries, health care systems are organized in similar ways, and paramedics and other medical staff are similarly educated. Our study groups, especially in the study on POHDs, were constrained by low numbers. This may have caused us to miss some small but potentially important differences in rare outcomes.

The POHD and UOHD groups differed significantly in terms of maternal, pregnancy and infant characteristics, which inevitably led to difficulties in comparing these groups to in-hospital deliveries. We tried to adjust the reference group for variables like length of gestation at delivery, infant gender, birth method and number of fetuses, but this model was not applicable in statistical way. Our study groups were small because of low out-of-hospital delivery rates in Finland, indicating that statistical significance in results may be difficult to show. Thus, we realize that our results need to be interpreted with caution.

In a retrospective register study some information may be missing, misclassified or inaccurately registered but, in general, register data is reliable and accurate (Gissler et al., 2002; Sund et al., 2012). In the study on the area of Tampere University Hospital (I), it was possible to obtain more detailed information by reading through the medical files, but it was not feasible with the larger cohort (II–IV). Some variables had several missing values, partly due to circumstances, such as Apgar scores given outside hospitals. Retrospective register studies run the risk of inappropriately assigning some diagnostic codes. For example, hypothermia was most likely underdiagnosed or unrecorded. In addition, the register data did not include admission temperatures or information about delivery attendants. Also, data on parental asthma, possible postnatal smoke exposure, and duration of breastfeeding were lacking in the national registers.

One great limitation is that we could not detect those women who were planning to give birth at home but who were transferred during labor from home to hospital. Currently, these cases are registered as in-hospital deliveries and in-

hospital births. We also could not find out who assisted with the POHDs and UOHDs, and whether they had any medical education or experience. This missing information is crucial in analyzing the risks of POHDs. The registers need to be refined so that these data can be collected in the future.

Accurate travel distances among UOHDs are difficult to determine. We analyzed travel distances from the home address (I) or the home municipality (III) to the nearest delivery unit based on delivery units in operation in 2015. Our method was not able to detect those women whose planned delivery unit was other than the nearest one, for example, due to traveling. In Finland, high-risk pregnancies and deliveries are centralized in tertiary units, and some women choose a smaller delivery unit instead of the nearest one. Paranjothy et al., showed that 15.6% of women travel to hospitals that are further away, possibly due to management of maternal, fetal, or pregnancy-related conditions (Paranjothy et al., 2014). Especially when it comes to sudden preterm birth, the location of a specific delivery unit can vary widely.

6.5 Future considerations and clinical implications

Sites of birth should be categorized according to both the planned and actual place of delivery. POHDs in Finnish registers should include deliveries that ended at a hospital after being transferred. That way, it would be possible to analyze the outcomes of POHDs more thoroughly. Accurate categorization is also essential when analyzing the possible long-term neurological morbidity of POHDs. It has been shown that infants born in the hospital after transfer from an ongoing POHD are at the highest risk (Blix et al., 2016). We have no information on whether the decision to transfer is made by the midwife, the mother, or someone else and what the actual time delay is in emergency transfers.

Equipment and medications are not provided by hospitals for POHDs in Finland. Physician has responsibility of the usage of prescribed medicine and this is why the physician has also right to refuse prescribing medicines needed in POHD. On the other hand this may lead to higher risks in POHDs if for example oxytocin or vitamin K is not available because of lacking prescriptions. We did not study patient injuries in our study, but the risk of patient injuries related to OHDs and the question of who has the responsibility of them has also being under debate.

Midwives attending POHDs and health care professionals should inform families properly and honestly about the risks of POHDs. It is also important to

find ways to influence public opinion and attitudes by providing positive information on modern family-friendly delivery units and in-hospital deliveries via the media. It would be interesting to know, why some women choose to endure the risk of POHD against the current national guidelines. Detailed information on the association of contraindications with morbidity, mortality, and transfers to the hospital is also needed in Finland.

Future studies should focus especially on UOHDs that occur on the way to the hospital and determine how to reduce their morbidity and mortality. OHD is rare event for paramedics, especially what it comes to preterm delivery. Paramedics should be better educated about the issue, and we need to offer more theoretical and practical education on this subject and especially simulations involving newborns. Paramedics should have the skills to deliver and resuscitate newborns without help from midwives or physicians. Proper resuscitation and care immediately after birth is crucial, especially for preterm infants. On the other hand, hospital guidelines and protocols for preterm births are not all feasible when the birth occurs in out-of-hospital setting. Preventing hypothermia is crucial, since excessive heat loss can predispose infants to other morbidities, such as apneas and pulmonary hypertension.

Cooperation and communication between paramedics, home birth attendants and delivery unit personnel could be improved and enhanced to ensure patient safety. Home birth attendants should inform the delivery unit when the labor has initiated. It is also important to find ways to identify at-risk populations with no prenatal care and with social and mental health issues, who might benefit from multidisciplinary support.

Mothers who deliver unplanned out-of-hospital are heterogeneous, and not all UOHDs can be prevented, but we need to be better at identifying high-risk groups for UOHDs. Finally, the goal is to minimize and stop the rising trend of UOHDs and make POHDs a less attractive option for families by counseling and listening better their hopes what it comes to delivery. We should provide a homey yet safe birth environment in the hospital where all the facilities are available in unexpected emergency situations. Every single injury, lifetime disability or death of mother and infant should be prevented whenever it is possible.

7 CONCLUSIONS

The following conclusions can be drawn:

1. The number of OHDs was small in the area of Tampere University Hospital, but the rate increased up to 0.13% of all births by 2011. No perinatal deaths were detected. Infants in OHD group needed more often admission to neonatal care unit compared to in-hospital group. Independent risk factors for OHD were smoking during pregnancy, short duration of labor, previous deliveries, no cohabitation, residence ≥ 35 kilometers from the delivery unit and < 13 prenatal visits.

2. The number of POHDs in Finland were small, but the rate increased up to 39.4 per 100 000 births by 2013. More than half of the POHDs did not fulfill the criteria of current national guidelines for POHD and low-risk delivery. Severe perinatal morbidity appeared to exist even among low-risk POHDs. Maternal morbidity was rare.

3. The rate of UOHDs increased significantly during the study period reaching 260 per 100 000 births. The proportion of deliveries during transport to the delivery unit remained stable during the study period and did not explain the increase in UOHDs. Living in an area with low population density and short labor duration seemed to be factors explaining the increased incidence of UOHDs. UOHDs had significantly higher perinatal mortality rates, especially among preterm and small infants, but the number of deaths was very small. The perinatal mortality rate was high but stabile in UOHDs, but it decreased among hospital births. Perinatal morbidity and mortality in UOHDs did not seem to be related to the area or time period of birth. The decreasing number of delivery units seems unlikely to be associated with increased perinatal morbidity and mortality associated with UOHDs.

4. Mortality by seven years of age did not differ between children born in-hospital and out-of-hospital. Children born outside a hospital were associated with a lower risk of asthma or allergies and infections than children born in-hospital. The risk of neurological or mental disorders seemed to be similar.

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ORIGINAL PUBLICATIONS

PUBLICATION I

Out of hospital deliveries have risen involving greater neonatal morbidity: Risk factors in out-of-hospital deliveries in one University Hospital region in Finland

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REGULAR ARTICLE

Out-of-hospital deliveries have risen involving greater neonatal morbidity

Risk factors in out-of-hospital deliveries in one University Hospital region in Finland

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ABSTRACT

Aim: Most Finnish births take place in hospital, but out-of-hospital deliveries (OHDs) have increased. This study evaluated trends and reasons for OHDs in the Tampere University Hospital catchment area.

Methods: The study cohort included all planned and unplanned OHDs in the Hospital area from 1996 to 2011; the control group comprised two hospital births for each OHD. Trends in incidence and risk factors for OHDs, including neonatal morbidities, were established and compared to the controls.

Results: OHDs accounted for 67 (0.10%) of the 76 773 births in the area, the proportion remaining unchanged between 1996 and 2005, but then increasing. Risk factors associated with OHDs were smoking during pregnancy, short labour, higher number of previous births, single status, residence more than 35 kilometres from the delivery unit and fewer prenatal visits. OHD cases were more likely to be admitted to the neonatal care unit than controls and to be treated for suspected infections and hypothermia.

Conclusion: Smoking, short duration of labour, a higher number of previous births, single status and longer distances from the delivery unit were associated with OHDs. Eight (12%) mothers had OHDs without antenatal care, and their infants had more neonatal morbidities.

INTRODUCTION

Increased neonatal morbidity and mortality rates have been shown among unplanned OHDs (1–7). Infants born accidentally out-of-hospital have more often been of low birthweight (1,3,4,6), preterm (1,3,5,8) and small for gestational age (SGA) (2). Hypothermia has been the most common morbidity (1,5,7,9–11). The mean admission body temperature of preterm infants surviving an OHD has been significantly higher compared with those who did not survive (12).

OHDs have been associated with multiparity (1–5,10,11), smoking (3,8), single-mother status (3,5,13), unemployment (10), deficient or lacking antenatal care (2,4,5,8,10), shorter education (4,5,8), higher (4) and younger maternal age (8,13), nonwhite race (8), shorter duration of labour (1), postpartum haemorrhage (4) and delayed hospital discharge (4,8). The risk of an unplanned OHD seems to increase if the travel time to the nearest delivery unit is longer than 45 minutes (10), or the distance to the nearest delivery unit is 30 km or more (14). Results of studies related to the safety of planned homebirths diverge widely (15–17).

In Finland, up to the Second World War deliveries took place at home. In 1945, 50% of all babies in Finland were born outside hospital (18). Thereafter, the rate of OHDs

Abbreviations
LGA, Large for gestational age; OHD, Out-of-hospital delivery; SGA, Small for gestational age.

Key Notes

- Most Finnish babies are born in hospital, but out-of-hospital deliveries (OHDs) have increased.
- We evaluated OHDs in one hospital catchment area from 1996 to 2011, comparing cases with hospital-born controls.
- OHDs were associated with smoking, short duration of labour, a higher number of previous births, single status and longer distances from the delivery unit, together with greater numbers of NICU admissions and neonatal morbidities.

declined up to 1973, when 0.01% of all births in Finland took place outside hospital (18). The percentage has since increased (19). In 2012, 0.2% of approximately 60 000 births in Finland occurred outside hospital, either planned or unplanned (20). Since 1975, more than half of Finland's delivery units, mainly smaller ones, have been closed (3) and travelling times from home to the nearest delivery unit have become longer, thus increasing the number of OHDs (3). The aim of this study was to establish whether the number of OHDs has increased over time in the region of Tampere University Hospital, to identify risk factors associated with OHDs and to establish whether infants born out-of-hospital were more prone to neonatal morbidities compared to infants delivered in hospital.

PATIENTS AND METHODS

Data were collected retrospectively from the medical files of Tampere University Hospital. During the years 1996–2011, there were 76 773 births in the catchment area, 67 of them occurring out-of-hospital. The hospital district is a joint municipal authority of 23 municipalities having (in 2013) 521 700 residents and comprising in addition to Tampere ten smaller cities. The catchment area has been the same during the study period, and until 2013, there was also another delivery unit in the area with 481 deliveries per year. The control group consisted of 134 infants and their mothers, chosen for each OHD case by selecting the births immediately preceding and following. Home addresses at the time of birth were gathered from the Central Population Register, and the distance between home and the delivery unit was calculated using the web-based route planner Fonecta (www.fonecta.fi). We selected the fastest route option from the planner.

Place of birth was categorised as follows: in hospital, on the way to hospital, planned OHD, unplanned OHD, and OHD with no information of whether the birth was planned or unplanned.

Travel distance and travel time were divided into four categories: <5 km, 5–19.9 km, 20–34.9 km and 35 km or more. One-minute and five-minute Apgar scores were divided into two categories: 0–6 and 7–10. Length of gestation in weeks and days was categorised as follows: <32 + 0, 32 + 0 to 36 + 6, 37 + 0 to 42 + 0 and more than 42 + 0, and birthweight into the following: 1500–2499 g, 2500–4499 g and 4500–5500 g. There were no infants of birthweight below or above these ranges.

Hypothermia was defined as a temperature ≤36.5°C and severe hypothermia as <36.1°C. An infection was recorded if the infant evinced symptoms and at least one of the following: white cell count $<5 \cdot 10^9$/L or more than $30 \cdot 10^9$/L, neutrophil count $<1 \cdot 10^9$/L, immature to total neutrophil ratio more than 0.2, platelet count $<150 \cdot 10^9$/L and C-reactive protein more than 10 mg/L (21). Intravenous antibiotics were used in these cases. SGA was either birthweight or both birthweight and birth length <2 standard deviations (SDs) below the mean according to the Finnish sex-specific growth curves (21). A large newborn was of birthweight more than 2 SDs above the mean (22) or birthweight 4500 g or more. A premature infant was defined as born at a gestational age <37 + 0 weeks and post-term at a gestational age more than 42 + 0 weeks. Hyperbilirubinaemia was defined as a need for phototherapy based on plasma bilirubin threshold levels (23). Hypoglycaemia was defined as treatment for the condition in the neonatal care unit at the discretion of the attending physician (intravenous glucose infusion and/or gavage feedings). Plasma glucose <2.6 mmol/L was used as threshold in the unit.

Statistical analyses

The following preselected variables were tested for association with OHD: smoking (yes/no), living in partnership (yes/no), mother's nationality (Finnish/other), maternal age (years), parity, number of previous pregnancies, number of all prenatal visits to maternity clinics in health centres or hospital, home-to-hospital distance (kilometres) and travel time (minutes), length of gestation (weeks), duration of labour (minutes), duration of hospital care (days), one- and five-minute Apgar scores, congenital anomaly (yes/no), birthweight (grams) and birth length (centimetres), SGA and LGA (yes/no), admission to neonatal unit and diagnoses received. Infants and mothers with missing information were included in analyses.

To describe the data, medians and ranges were given for skew-distributed continuous variables and means and standard deviations for normally distributed variables. For categorical variables, frequencies and percentages were used. Groups were compared using Mann–Whitney *U*-tests for skew-distributed continuous variables, independent sample *t*-test for normally distributed continuous variables and chi-square test or Fisher's exact test for categorical variables, as appropriate. Statistical significance was defined as $p < 0.05$. Logistic regression was used to identify variables independently associated with OHD using the control group as reference. The following variables were included in the final model: smoking during pregnancy, duration of labour, living in partnership, previous pregnancies, maternal age, distance to the delivery unit, prenatal visits, gestational age at birth, SGA and LGA. For logistic regression, the continuous variables home-to-hospital distance and travel time were recategorised based on the uppermost quartile (35 km or more and 30 minutes and more), and duration of labour was recategorised based on the lowest quartile (2 hours and 46 minutes). All univariate significant variables were entered simultaneously into the final multivariate model. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). The analyses were carried out on IBM SPSS Statistics for Windows (version 22.0, released 2013; IBM Corp., Armonk, NY, USA). Trends for number of OHDs related to hospital births were analysed by Cochran–Armitage trend test to measure direction in binomial proportions across the levels of a single variable. The two-level variable represents the response, and the other represents an

explanatory variable with ordered levels. The null hypothesis is that of no trend; that is, the binomial proportion is the same for all levels of the explanatory variable. The trend test was carried out on StatXact-4 version 4.0.1 (Cytel Software Corporation, Cambridge, MA, USA).

RESULTS

During the study period, a total of 67 OHDs were recorded, accounting for 0.10% of all births in the hospital area. The relative number increased from 0.09% in 1996 to 0.13% in 2011 ($p < 0.001$, Figure S1). The proportion of OHDs remained virtually unchanged between 1996 and 2005, but increased thereafter. Thirty-one (46%) OHDs occurred on the way to the delivery unit and 22 (33%) unplanned outside the hospital, while one (1.5%) was a planned home delivery.

A total of 20 (30%) infants were born in an ambulance, 9 (13%) in a health centre, 4 (6%) on the way to the hospital, 8 (12%) at home with the help of medical staff, and 11 (16%) at home before the ambulance had arrived.

Data on the parturient, pregnancy and delivery are presented in Table S1.

We excluded from the OHD group 13 (19%) cases with no possibility to establish whether the OHD was planned or unplanned, one with missing home address and the one planned OHD when we analysed the distance to the hospital. This OHD subgroup comprised 52 mothers, 25 (47%) living at a distance of at least 35 km fromthe hospital compared to 17 (13%) in the control group. One (2.0%) mother in the OHD subgroup and 8 (6.0%) in the control group lived <5 km from the hospital. The significance remained the same ($p < 0.001$) when we analysed all OHDs without the above-mentioned exclusions.

Eight (12%) OHD mothers and one mother (0.7%) in the control group had made no visits to prenatal care. The reason for this was in most cases impossible to ascertain. The distance to the delivery unit was 6.9–208.8 km. Three of the mothers in question claimed that they were not aware of their pregnancies. Three smoked during pregnancy and five lived in partnership. Two mothers, one with a substance and the other with an alcohol abuse problem, gave birth in a toilet, and one infant was born on the way to hospital. Three of these mothers were living at a distance of at least 35 km from the delivery unit. Two of eight infants were treated at the neonatal care unit.

Data on the infants

Only one full-term OHD infant needed stimulation and oxygen from ambulance staff. This was a planned home-birth, and the medical staff arrived after the birth. The infant' s body temperature was 34.7°C upon arrival at hospital, and the infant was kept in the neonatal unit for one day due to hypoglycaemia.

Characteristics of infants at birth are presented in Table S2.

No neonatal or maternal deaths were recorded. The data on neonatal morbidity, including all congenital anomalies among the infants, are presented in Table S3. There were no culture-proven infections.

Risk factors for out-of-hospital births

According to the logistic regression analysis, six independent risk factors were associated with OHDs: smoking during pregnancy (OR 6.54, CI 1.33–32.22), short duration of labour (less than lowest quartile; 2 hours and 46 minutes) (OR 18.79, CI 5.96–59.29), single-mother status (OR 13.01, CI 3.37–50.23), number of previous births (OR: 7.02, CI 1.83–26.95), distance to the delivery unit at least 35 km (OR: 5.02, CI 1.80–14.04) and <13 prenatal visits (OR 2.73, CI 0.95–7.84) when all independently significant variables were entered simultaneously into the multivariate model.

DISCUSSION

The numbers of OHDs and their proportion increased after the year 2006, although the catchment area and the number of delivery units in the region remained the same. Women giving birth out-of-hospital were more often smokers, single, had shorter duration of labour and fewer prenatal care visits. Distance to the delivery unit was longer. Almost one-third of the OHD infants had hypothermia, and about one-fifth of them were admitted to the neonatal unit.

The long study period can be regarded as a strength in our study. Our data were population-based and covered all OHD infants born in the hospital region. Multiple data sources were used to improve data quality, as a large body of information was missing from the hospital birth registers. Only few studies have reported as many variables in OHDs, especially Apgar scores, diagnoses of infants and travel distance to the delivery unit.

A limitation to the study was the rather small number of OHDs. Other limitations were missing values for maternal education or socioeconomic status or the use of alcohol or drugs. Data were based on self-reporting and found in only a small number of cases.

According to the findings here, it remains difficult to recognise the risk of an OHD unless the mother has had a short labour in her earlier pregnancies. The higher proportion of smokers and mothers without antenatal care among the OHD group suggests that these parturients have shorter education and/or lower socioeconomic status than parturients in general (24). The percentage of mothers not attending antenatal care is substantially lower than in the Finnish population in general (0.3%, unpublished data from the Medical Birth Register). It seems that mothers with indicators of lower socioeconomic status, and on the other hand those living at a long distance from the delivery hospital, form two partly independent groups.

In contrast to previous OHD studies, there were no maternal or neonatal deaths there and OHD infants showed no significant risk of being SGA or premature.

This is probably due to the small number of cases. Apgar scores given by the mother or laypersons might differ from scores given by paediatricians or midwives. Apgar scores were for obvious reasons often mistimed or not given at all, which resulted in a substantial amount of missing data.

Plasma glucose was probably measured more often if the infant was born out-of-hospital and in the case of control infants only due to symptoms or a risk of hypoglycaemia. This may have caused a systematic error in the difference in numbers of hypoglycaemia diagnoses between OHDs and controls. Also the OHD infants might have received antibiotics more often due to much closer observation compared to controls and a lower threshold for treatment with antibiotics.

Hypothermia could be better preventable by means of education of pregnant women and paramedics. Excessive heat loss increases oxygen consumption and leads to hypoglycaemia, metabolic acidosis, apnoea and pulmonary hypertension (25). In our infants, severe hypothermia was seen only in the OHD group. The condition was not, however, significantly associated with the outcome of the infant and did not lead automatically to the infant's admission to the neonatal unit.

In conclusion, OHDs were associated with poorer attendance at antenatal care, number of previous births, distance to the delivery unit, maternal smoking, single status and higher infant morbidity. OHDs would thus seem to be poorly preventable. Hypothermia, need for hospitalisation, administration of antibiotics for infections and jaundice were common problems. OHDs are still rare in the catchment area of Tampere University Hospital, but their incidence is increasing. We should therefore concentrate on the training of ambulance staff and develop and implement a protocol to educate attendants working in the alarm units.

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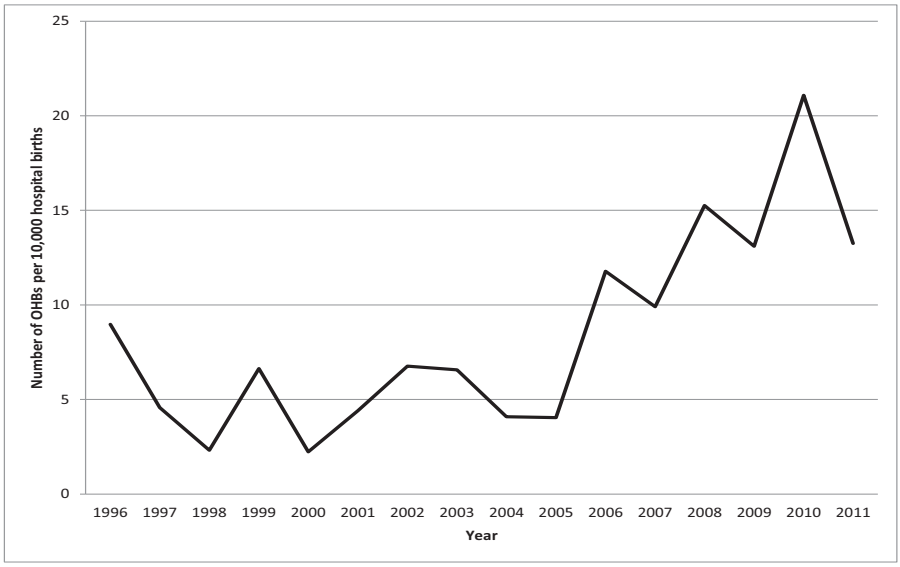
SUPPORTING INFORMATION

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

Figure S1 Number of out of hospital deliveries (OHDs) related to hospital births.

Table S1 Data on the parturient, pregnancy and delivery.
Table S2 Data on the infants delivered out of hospital (OHDs) and control infants.
Table S3 Diagnoses during hospital stay in infants born out of hospital (OHDs) and control infants.

Figure S1 Number of out of hospital deliveries (OHDs) related to hospital births



The proportion of OHDs remained virtually unchanged between 1996-2005, but increased thereafter.

Table S1 Data on the parturient, pregnancy and delivery

Variable	OHDs (n = 67)	Controls (n = 134)	p*
Smoking during pregnancy, N (%)	10 (15%)	8 (6.0%)	<0.001
Living in partnership and/or married, N (%)	46 (69%)	119 (89%)	<0.001
Finnish nationality, N (%)	63 (94%)	128 (96%)	0.467
Age in years, mean, SD, (range)	29.0, 5.9 (15-47)	29.1, 5.2 (18-41)	0.906
Number of previous pregnancies, median (range)	1 (0-18)	1 (0-11)	0.001
Parity, median (range)	1 (0-16)	1 (0-9)	<0.001
Number of prenatal visits, median (range)	13 (0-30)	16 (0-35)	<0.001
Distance from home to delivery unit (shortest route, kilometers), median (range)	23.0 (2.8-208.8)	13.3 (1.5-125.4)	<0.001
Distance to delivery unit (fastest route, minutes), median (range)	23.5 (4-171)	15.0 (2-107)	<0.001
Duration of labor (1. and 2. phase), median (range)	2 h 14 min (15 min-17 h 28 min)	7 h 3 min (1h 14 min-23 h 17 min)	<0.001

*Differences between OHDs (out of hospital deliveries) and controls were tested by Pearson's Chi-Square / Fisher's exact test/ Mann-Whitney U-test / Independent sample t-test

Tables

Table S2 Data on the infants delivered out of hospital (OHDs) and control infants

Variable	OHDs (n= 67)	Controls (n=134)	p*
Length of gestation at birth (weeks + days), median (range)	39+5 (31+642+0)	40+0 (34+3-42+3)	0.077
Birth weight (g), mean and SD, (range)	3460 573 (1835-4570)	3575 516 (1680–4630)	0.105
Birth length (centimeters), median (range)	50.0 (41.0-54.0)	51.0 (42.0-56.1)	0.005
One-minute Apgar scores 7-10, N (%)	45 (67%)	129 (96%)	<0.001
Five-minute Apgar scores 7-10, N (%)	45 (67%)	133 (99%)	<0.001
Infant treated in the neonatal unit, N (%)	13 (19%)	4 (3.0%)	<0.001
Small for gestational age, N (%)	4 (6.0%)	4 (3.0%)	0.445
Large newborn, N (%)	2 (3.0%)	8 (6.0%)	0.501
Length of hospital stay (days counted from the date of the infant's birth), median (range)	3 (0-29)	3 (0-75)	0.833

*Differences between OHDs and controls were tested by Pearson's Chi-Square / Fisher's exact test/ Mann-Whitney U-test / Independent sample t-test

Table S3 Diagnoses during hospital stay in infants born out of hospital (OHDs) and control infants

Diagnosis	**OHDs (n = 67)**	**Controls (n=134)**	***p**
Hypothermia, N (%) Severe hypothermia **, N (%)	21 (31%) 15 (22%)	1 (0.7%) (0.0%)	<0.001
Unspecified infection, N (%) Culture proven infection	5 (7.5%) (0.0%)	(0.0%) (0.0%)	0.004
Congenital anomaly (ICD-10 Q00-Q99), N (%)	7 (10%)	6 (4.5%)	0.130
Transient tachypnea, N (%)	3 (4.5%)	1 (0.7%)	0.109
Neonatal jaundice, N (%)	9 (13%)	7 (5.2%)	0.054
Neonatal hypoglycemia, N (%)	5 (7.5%)	4 (3.0%)	0.163

*Differences between OHDs and controls were tested by Pearson's Chi-Square / Fisher's exact test

**Temperature < 36.1 °C

PUBLICATION
II

Planned home deliveries in Finland, 1996-2013

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Planned home deliveries in Finland, 1996- 2013

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ABSTRACT

Objective: To evaluate trends and perinatal outcomes of planned home deliveries in Finland.

Study Design: All infants born in 1996 -2013, excluding those born preterm, by operative delivery, and without information on birth mode or gestational age, were studied. The study group included 170 infants born at home as planned, 720 047 infants born at hospital were controls.

Result: The rate of planned home deliveries increased from 8.3 to 39.4 per 100 000. In the study group 63%, containing two perinatal deaths, were not low-risk pregnancies according to national guidelines. The rate of hypothermia, asphyxia and need of invasive ventilation was increased in low-risk home deliveries. One infant had a major congenital malformation. Maternal outcomes were favorable.

Conclusion: The rate of planned home deliveries increased. Guidelines for low-risk deliveries were not followed in a majority of cases, including two perinatal deaths. Even in low-risk home deliveries, the neonatal morbidity appeared to be increased.

INTRODUCTION

In many studies perinatal and neonatal mortality rates are higher among planned home deliveries than among hospital deliveries(1-5), although there are also reports showing no difference between them(6-14). Data on neonatal outcome and morbidity are also controversial. Infants born at home are admitted less often to neonatal intensive care units than those born in the hospital(1,15,16), but there are two studies showing more admissions(17,18).

Mothers who deliver at home as planned are more often older(2-4,9,12,14,15,19-21), non-smokers(6,12,21), married(15,17,21), and have had more earlier pregnancies(14,19)and deliveries(3,4,9,10,15,17,19,20), and the length of pregnancy is more often almost or more than 42 weeks(2,3,7,9-12,14,15,20). Socioeconomic status and/or education are usually better among these women(4,7,12,15,21). Intrapartum interventions and adverse maternal outcomes occur less often in planned home deliveries(6,15).

Comparison of the mortality and morbidity results between different countries on different regions is difficult, but could be improved by taking account the variation in governmental support and regional integration of planned home births to the health care system. The settings of the previous studies as also patient selection and health care facilities(3) of the studies have been variable. In some studies strict selection criteria have been used for women planning home delivery with trained certified midwives highly integrated to the public health care system(7,10).

Unexpected complications cannot be ruled out even in so-called low-risk pregnancies(22). In spite of this, even some mothers with risky pregnancies have had planned home deliveries(23). Transfer to hospital during or after labor is needed in 8- 32% of home deliveries, usually before the birth(24,25).

The primary purpose of this study was to establish perinatal and maternal mortality and morbidity data in planned home deliveries compared with in-hospital deliveries. We also wanted to establish prevalence rates and trends in connection with planned home deliveries in Finland.

METHODS

The data were collected from the Medical Birth Register and the Register of Congenital Malformations maintained by the National Institute for Health and Welfare. The Medical Birth Register contains data related to all live births and stillbirths from the gestational age of 22+0 weeks onward and/or birth weight of at least 500 g. The register collects data on planned and unplanned home deliveries separately. This information is collected not until the infant is born. It includes diagnoses and treatments of infants by the age of seven days or at discharge. Information concerning Apgar scores at five minutes of age is not available for the period between October 1990 and December 2003. This partly explains why 66% of these scores were missing and because of that we analyzed only 1-minute Apgar scores. The data in the Medical Birth Register also include maternal and delivery characteristics and obstetric procedures. Causes of death were collected from the Cause of Death Register maintained by Statistics Finland. Travel distances between delivery unit and home municipality were calculated by using a web-based route planner. We used the shortest distance between the home municipality and the nearest delivery unit according to the location of these units in 2015. Rural and urban municipalities were categorized according to Statistics Finland(26).

This national retrospective study included all planned home deliveries in Finland from 1996 to 2013. During these years 1 053 802 infants were born in Finland. Of these infants, 197 were born at home as planned and a total of 1 051 139 infants were born at hospital. We excluded unplanned out-of-hospital deliveries (n=1420) and newborns with no information on the place of birth (n=1046). We also reclassified seven cases which were clearly misclassified as planned home deliveries, having, for example, indications for elective cesarean section.

To compare perinatal and maternal mortality and morbidity reliably we excluded preterm births (length of gestation at birth less than 37+0 weeks), deliveries with no information on

gestational age, cesarean sections, vacuum extractions, forceps deliveries and deliveries without information about the mode of childbirth. After exclusions, there were 170 infants in the study group and 720 047 infants in the control group. In total, seven infants in the planned home delivery group were admitted to a neonatal care unit but only five of them were included in the study group and analysis, on the basis of the exclusion criteria mentioned above. One of the excluded infants was preterm and the other's gestational age at birth was not mentioned in the birth register.

Birth weight related to gestational age at birth was analyzed using Finnish growth curves(27). Small for gestational age (SGA) means that weight at birth is two or more standard deviations (SD) below the population average. Large for gestational age (LGA) is a weight two or more SDs greater than the average. Socioeconomic status was defined by using the mother's occupation and was divided into four groups: upper-level and lower-level employees, manual workers and others. The group of "other" included students, housewives and unclassifiable cases. Maternal age, parity, gestational age, birth weight and Apgar scores were also divided into categories and analyzed both as dichotomous and categorized variables. Post-term pregnancy was defined as at length of gestation at birth of 42+0 weeks or more. Congenital anomalies were divided into major and minor anomalies according to classification of European surveillance of congenital anomalies(28). We report only major congenital anomalies, since the reporting of minor anomalies varies by time and place.

For analysis of maternal morbidity we included diagnoses of chorioamnionitis, retained placenta, placenta accreta, placenta previa, placental abruption, antepartum hemorrhage, hemorrhage during delivery, postpartum hemorrhage, perineal tears, uterine rupture,

thromboembolism and maternal sepsis or other puerperal infections. Maternal deaths were reported separately.

Current Finnish national guidelines for planned home delivery include the following: absence of any maternal preexisting disease, uncomplicated singleton pregnancy, at least one previous delivery, vertex presentation, no previous cesarean section or operative vaginal delivery, absence of group B streptococcus colonization, gestational weeks between 38+0 and 41+6 and two registered and certified midwives, or a midwife and a physician managing the labor(29). Transfer time to hospital should not be more than twenty minutes. We analyzed a subgroup of women who fulfilled the above-mentioned criteria that we could detect in the registers used.

Statistical analyses

To describe the data, medians, ranges and interquartile ranges were calculated for skew-distributed continuous variables and means and standard deviations for normally distributed variables. Frequencies and percentages were used for categorical variables. The infants born at home as planned and a control group were compared by using Mann Whitney *U* tests for skew-distributed continuous variables, independent sample *t*-tests for normally distributed continuous variables, and chi-square tests or Fisher's exact tests for categorical variables, as appropriate. Logistic regression analyses were also performed, with results shown as odds ratios (ORs) with 95 % confidence intervals (CIs). Values of $p < 0.05$ were considered statistically significant. The analyses were carried out by using IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp., Armonk, NY). The Cochran Armitage trend test (StatXact version 4.0.1) was used in order to determine statistical significance of change of the planned home delivery rates during the study period.

RESULTS

Trends in rates of planned home deliveries

During the study period, a total of 197 infants, on average 23.6 infants per 100 000 births were born at home as planned. Finland is divided into five specific catchment areas. Related to the number of deliveries, planned home births occurred most often in the western Finland area (37.6 per 100 000 births). According to the statistical grouping of municipalities the home municipality was defined as rural in 124 (63%) cases(26). The rate of planned home deliveries rose almost fivefold from 8.3 (in 1996) to 39.4 (in 2013) per 100,000 ($p<0.001$) but they are still very rare (Figure 1).

Maternal characteristics and outcomes

Mothers who delivered at home as planned were older (mean 31.8 vs. 30.0 years, $p<0.001$), had better socioeconomic positions, smoked less often, had more previous deliveries, had fewer prenatal visits and shorter durations of labor (first and second phase). There were no differences in the rate of living in a partnership, in nationality or in distance from home to the delivery unit (Table 1). In 125 (63%) cases pregnancies prior to planned home deliveries deviated from national recommendations, i.e. they were not low-risk pregnancies. A total of 25 (12.7%) of the mothers were nulliparous. Four (2.0%) mothers had gestational diabetes without need of insulin treatment. One mother (0.5%) had had a previous cesarean section and seven mothers (3.6%) had a history of stillbirth. In the planned home delivery group there was one (0.5%) twin delivery and one (0.5%) fetus in breech position at the time of birth. The median length of gestation was longer and premature deliveries were statistically significantly less common in the planned home delivery group. Lengths of gestation at birth are given in Table 2.

No maternal deaths or adverse maternal outcomes were registered during the study period in the study group. Episiotomy was performed significantly less often in cases of planned home births; (**2** (1.2%) vs. **196 744** (27.3%), p<0.001). No third- or fourth-degree perineal tears, need for blood transfusion postpartum, chorioamnionitis (infections of the amniotic sac and membranes), umbilical cord complications (prolapsed cord or other forms of compressions of the cord), or cases of placental abruption or labor dystocia were recorded in the study group. Unfortunately we could not identify the number or characteristics of those mothers who were transferred from home to hospital during labor, since registration is based on the actual place, not the intendent place of birth.

Infant characteristics and outcomes

Infant outcomes and characteristics are listed in Tables 2, 3, 4 and 5. Most of the infants in the planned home delivery group were of a size appropriate for gestational age. Infants in the home delivery group were heavier (mean birth weight 3592 g vs. 3505 g, p=0.01) and more frequently had one-minute Apgar scores less than 7. Congenital anomalies were rare within the study group. However, there were four infants with major congenital anomalies including diagnoses of patent ductus arteriosus (GA more than 37 weeks), a non-specified syndrome, trisomy 18 (Edwards syndrome), Klinefelter's syndrome and left heart hypoplasia syndrome. Infants in the study group suffered significantly fewer birth traumas.

Five infants (2.9%) in the study group and **41 905** (5.8%) infants born at hospital were admitted to a neonatal care unit after birth (p=0.11).

In the study group there were two deaths, a couple of twins born at 37+4 week's gestation. Twin A had a birth weight of 2390 g. He did not need resuscitation, but he needed invasive ventilator therapy. He had a diagnosis of severe birth asphyxia and the official cause of death

was hypoxic-ischemic encephalopathy. Twin B was stillborn and his cause of death remains unknown. No Apgar scores were mentioned in either case. Their mother was a 28-year-old healthy woman living in the same city where the delivery unit was located. The known risk factors associated with the delivery were having a multiple pregnancy, and nulliparity. Overall, deaths were rare in both the study and control groups.

After the exclusion of mothers who did not meet the above-mentioned current national guideline criteria there were 72 mothers who delivered at home as planned, and 219 062 controls. None of their infants died during the perinatal period. As regards other perinatal outcomes, infants who were born at home had higher risks of invasive ventilation and hypothermia (Table 4). However, a lower percentage of these infants had at least one of the adverse outcomes listed in Tables 3 and 4 compared with infants who were born at the hospital; 5 (6.9%) vs. 30 297 (13.8%), although the difference was not statistically significant (p=0.09). There were no significant differences in mortality or morbidity between those infants whose mothers met the criteria for planned home deliveries and those whose mothers did not (Table 5).

DISCUSSION

Each country has a maternity care system of its own and home deliveries are integrated into them in different ways. In Finland, we have a low perinatal mortality rate, approximately 0.4%, which reflects a high-quality maternal health care system, and delivery and neonatal units. We have national guidelines for planned home deliveries, but hospital deliveries are nevertheless recommended in every case.

The American Academy of Pediatrics (AAP) (30)and the American College of Obstetricians and Gynecologists (ACOG) (31) have published criteria for planned home births and even stricter guidelines have been published in Finland(29). The purpose of the recommendations is to prevent planned home deliveries in high-risk pregnancies.

Our first finding was, that planned home deliveries are relatively rare in Finland (0.02%) compared, for example, with the Netherlands (20%), where planned home deliveries have traditionally been common(7). This reflects the common attitude in favor of hospital deliveries in our country. Our results show, however, a rising trend in the occurrence of planned home deliveries. Some regional differences were also found.

Planned home delivery rates are also increasing in other developed countries, especially in the United States(32,33). On the other hand, the home-birth rate has decreased in the Netherlands during the last two to three decades(32,33). Women choosing a planned home delivery may feel dissatisfaction with a previous hospital delivery. They may wish to avoid delivery interventions and feel that home is the safest option, with a peaceful environment(34,35). Regional differences in the planned OHD rates exist in spite of the fact that the guidelines for planned home deliveries are the same in whole Finland.

Our second finding was that the majority of women who plan to deliver at home do so regardless of the national recommendations. In our population this was associated to two perinatal deaths. This highlights the importance of the safety recommendations and calls for the responsibility of the health care professionals, who assist planned deliveries at home.

Out third finding in was that even in those home deliveries that fulfilled the criteria of low-risk pregnancy and delivery, untoward neonatal outcomes, including hypothermia, asphyxia and need of invasive ventilation, were overrepresented. In addition, although by a chance, our study group included infants with major congenital malformations. Thus, it is impossible to

predict the course of delivery even in cases of low-risk labor. Rare but serious complications are not totally avoidable. The central issue of planned home delivery is the limited possibility to intervene when necessary. Continuous monitoring of fetal heart rate and contractions is unlikely to be available at home. Neonatal and also maternal complications can occur unexpectedly and may require immediate emergency cesarean section or other forms of intervention, and/or effective resuscitation of the infant. In these cases delay because of home delivery is always too long. These facts should be included in the counseling of pregnant women.

From the maternal point of view planned home deliveries may appear to be relatively safe, with some benefits compared with hospital deliveries. The lower rate of episiotomies can be partly explained by maternal characteristics such as the fact that most women were multiparous, the duration of labor was shorter, and there were no LGA infants in the group of planned home deliveries. However, it is also possible that episiotomy may be favored in a hospital setting, since the episiotomy rate among multiparas varied from 15% to 5% during the study period in Finland(36), while in the study group it was only 1.2%. Our findings of fewer episiotomies and no increase in maternal morbidity are consistent with the results of other studies(37).

Furthermore, no emergency obstetric complications such as placental abruption, uterine rupture or retained placenta were registered in the study group, even though multiparity is a risk factor of these conditions. Likewise, the need for blood transfusion was not increased in the study group, reflecting no severe postpartum hemorrhage complications. However, these severe complications are rare – for example the incidence of placental abruption has been reported to be 0.4 /1 000 deliveries in Finland(38) and our limited amount of material does not allow us to estimate the risks of these rare but life-threatening complications in a home-

delivery setting. Furthermore, there were no serious maternal infections in the planned home-delivery group. This could be a result of the shorter duration of labor and fewer invasive procedures such as episiotomies. A home setting does also not particularly expose a woman to infections.

It is, however, very likely that all the above-mentioned complications are underreported in planned home delivery cases, because complicated cases require a transfer and treatment in hospital.

Although Finnish pediatricians and obstetricians do not support home birth, it is important to find out how to promote physiological birth where appropriate. Interventions during labor should be driven by clinical need. Increasing popularity of planned home deliveries challenges the staff working in delivery units to re-evaluate which routine procedures are necessary for safety in labor.

The greatest limitation of our study is that we had no data on the intended place of birth before the delivery. This may lead to underestimation of perinatal mortality and morbidity, because transfers to hospital during delivery are classified in Finland as hospital births or as transfer births. Previous studies have shown that neonatal mortality and morbidity are increased if there has been a transfer to hospital during labor(9). The Medical Birth Register would be improved by collecting information on the intended place of birth at the onset of labor. In addition, the professions of health care workers attending home deliveries should be registered.

Another limitation is the substantial proportion of missing data concerning home deliveries. Midwives taking care of home deliveries should send the data to the Medical Birth Registry, but these data are often less complete than for hospital births. Additionally, our planned home delivery group was limited by a small sample size and absolute figures in some outcomes

remained small, but on the other hand we had a long study period covering all births and stillbirths in Finland in an 18-year study period.

CONCLUSIONS

Planned home deliveries are relatively rare in Finland but their number increased during the study period.

Planned home deliveries seemed to have some advantages to the mother compared with hospital deliveries, such as fewer episiotomies and shorter duration of labor. As regards the infants, planned home deliveries were associated with lower Apgar scores but fewer cases of birth trauma. It is notable that infant deaths in the planned home delivery group occurred to the ones whose mother didn't fulfill the national criteria for planned home deliveries. Even in low risk home deliveries, the occurrence of asphyxia, hypothermia and need of assisted ventilation appeared to be increased, although the absolute number of them was low. Such facts should be included in the counseling of pregnant women, who are aiming to deliver at home. It is also important to develop the hospital environment and seek ways to promote physiological birth where appropriate in delivery units.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Figure 1.Regional differences in trends of planned home deliveries in Finland (southern, eastern, northern, western, southwest, and the whole country)

PUBLICATION III

Unplanned out-of-hospital deliveries in Finland: A national register study on incidence, characteristics and maternal and infant outcomes

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Unplanned out-of-hospital deliveries in Finland: A national register study on incidence, characteristics and maternal and infant outcomes

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Abstract

Introduction: Unplanned out-of-hospital deliveries (UOHDs) have earlier been related to higher perinatal mortality and morbidity, but recent research has not paid much attention to them. Our aim was to evaluate the incidence, characteristics, risk factors, and maternal and perinatal mortality and morbidity in UOHDs in Finland.

Material and methods: We conducted a national register study on births, causes of death and congenital anomalies for all live and stillbirths during 1996-2013. The study group included 1420 infants delivered by mothers with UOHDs. The 1 051 139 infants born in hospitals during the study period were the reference group. Data on maternal and delivery characteristics, obstetric procedures, infants' characteristics, neonatal care unit admissions, diagnoses, congenital anomalies and causes of death were collected.

Results: The annual rate of UOHDs increased in 1996-2013 from 46 to 260 per 100 000 deliveries, whereas the number of delivery units decreased from 44 to 29. UOHD infants had five times higher perinatal mortality rates than those delivered in hospitals. The perinatal mortality rate did not change by time in the UOHDs, whereas it diminished among in-hospital deliveries. Maternal morbidity in UOHDs was low. The predictors for UOHDs were delivery after the year 2001, delivery in sparsely populated areas, alcohol, drug abuse and/or smoking during pregnancy, being single, fewer prenatal visits, having delivered earlier and birthweight <2500 g. UOHD was one of the predictors of perinatal morbidity and mortality. Among the UOHD cases, the predictors of perinatal morbidity or mortality included low birthweight and preterm delivery. Time period seemed not to predict morbidity or mortality.

Conclusions: The UOHD rate increased, probably due to multifactorial causes, including living in area with low population density and short duration of labor. UOHD was a significant predictor of perinatal morbidity or mortality, but the numbers were very small. Neonatal morbidity and mortality in UOHDs did not seem to be related to the area or time period of birth.

Abbreviations: CI, confidence interval; GA, gestational age; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision; OR, odds ratio; SD, standard deviation.

KEYWORDS
infant, out-of-hospital birth, perinatal morbidity, perinatal mortality, risk factor, unplanned

1 | INTRODUCTION

The annual birth rate in Finland has decreased to less than 50 000 in recent years. In recent decades, smaller delivery units with fewer than 1000 births annually were closed, and deliveries have been centralized in fewer and larger units to maintain resources for emergency cesarean sections and newborn resuscitation at any time, any day. There has been concern about whether these closures might increase the rates of unplanned out-of-hospital deliveries (UOHD), especially in areas with low population density. UOHDs carry an increased risk of perinatal and neonatal mortality,[1-9] including infants born preterm and low birthweight.[1,5,9-11] We assessed risk factors associated with UOHDs in our earlier work and showed that risk factors associated with UOHDs were smoking during pregnancy, short labor, higher number of previous deliveries, single status, a distance from home to the delivery unit of more than 35 km and fewer prenatal visits.[12] One previous study, revealing risk factors for adverse neonatal outcome,[13] found that multiparity, prematurity, maternal pathology and neonatal hypothermia were independent risk factors of neonatal mortality and morbidity.

The aim of this study was to examine whether the number of UOHDs has risen over time and to establish risk factors of UOHDs as well as perinatal morbidity and mortality in UOHDs. We also aimed to determine whether the risk of mortality and morbidity in UOHDs might increase over time with the decreasing number of delivery units.

Key message

The rate of unplanned out-of-hospital deliveries increased during the study period, 1996-2013, in Finland. Perinatal mortality was high but stable among unplanned out-of-hospital deliveries but decreased among in-hospital births.

2 | MATERIAL AND METHODS

This national register study included all deliveries in Finland from 1996 to 2013 for a total of 1 053 802 infants. The study population consisted of 1420 UOHD infants and 1 051 139 infants born in hospitals. We also used these data in our previous work.[14] Infants for whom there was no information on place of birth (n = 1046, 0.10%) or planned home deliveries (n = 197, 0.02%) were excluded.

The study drew on data from the Medical Birth Register and the Register of Congenital Malformations maintained by the Finnish Institute for Health and Welfare. The Medical Birth Register included data on maternal and delivery characteristics and obstetric procedures as well as data on all live births and stillbirths from a gestational age (GA) of 22^{+0} weeks onward and/or with birthweight of at least 500 g. The register included diagnoses and treatments of infants up to 7 days old (or discharge if earlier). The Medical Birth Register includes data of Apgar scores at 5 minutes of age since 2004. These scores were not analyzed in our study due to missing data including all information from the first 8 years. Three time periods (birth years 1996-2001, 2002-2007, and 2008-2013) were compared. After our study period, the most recently published register data is available for years 2014-2018 (the Finnish Institute for Health and Welfare, 2018). Diagnoses related to pregnancy and duration of labor were available from 2004. The register form was changed in 2004 to record separately the UOHDs during transport to hospital, UOHDs elsewhere outside hospitals, and births with no information whether the delivery was unplanned or planned outside hospital. Births with no information on whether the delivery was unplanned or planned outside hospital were excluded from the study.

Subgroups of preterm birth by GA were moderately and late preterm (32^{+0}-36^{+6} weeks), very preterm (28^{+0}-31^{+6} weeks) and extremely preterm (<28^{+0} weeks). Post-term birth was defined as a gestation of more than 42^{+0} weeks. Birthweight related to GA was analyzed using Finnish growth curves.[15] Small-for-gestational-age infants were defined as those with a birthweight more than two standard deviations (SD) less than the mean weight for GA. Large-for-gestational-age infants were those with birthweight more than two SDs greater than the mean weight for GA. Socioeconomic status was defined by maternal occupation, divided into four groups: upper-level employees, lower-level employees, manual workers and others, including students, housewives and other unclassifiable cases. Maternal age, parity, GA, birthweight and 1-minute Apgar scores were also divided into categories and analyzed as both dichotomous and categorized variables. Hypothermia was detected using the ICD-10 code P80*.

Congenital anomalies were categorized as major and minor anomalies according to the European Surveillance of Congenital Anomalies classification.[16] We reported only major congenital anomalies because reporting of minor anomalies varies by time, region and hospital.

Causes of death were collected from the Cause of Death Register maintained by Statistics Finland. To analyze causes of death, we categorized them into seven groups: physical abuse or drowning, chorioamnionitis and other infections, placenta-related causes, asphyxia or/and umbilical cord complications, preterm birth and/or small birthweight, unknown causes and other causes.

For maternal morbidities, we included chorioamnionitis, genital tract trauma (including uterus rupture), bleeding during delivery or antenatally (including placental abruption and placenta previa),

postpartum hemorrhage and puerperal infections. Maternal deaths were reported separately.

2.1 | Statistical analyses

Medians with interquartile ranges were calculated for the skew-distributed continuous variables and means with SDs were computed for the normally distributed variables. Frequencies and percentages were used for the categorical variables. The reference population and infants delivered by mothers with UOHDs were compared with the Mann-Whitney *U* test for the skew-distributed continuous variables and Chi-square test or Fisher's exact test for the categorical variables, as appropriate.

Logistic regression analyses were performed to investigate the multivariable-adjusted risk factors for UOHDs and perinatal mortality and morbidity in the whole population and separately among UOHD cases and among infants born in hospital. Variables included in the analyses were study period, area of Finland, alcohol and/or drug abuse, living in a partnership, smoking during pregnancy, primiparity, number of prenatal visits, length of gestation at birth and birthweight. The results were reported as odds ratios (OR) with 95% confidence intervals (CI). Only variables with less than 10% missing valuables were included in logistic regression analyses. Values of $P < .05$ were considered to be statistically significant. The analyses were carried out with IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). The Cochran-Armitage trend test (StatXact version 4.0.1) was used to determine the statistical significance of the changes in the UOHD rates during the study period. R statistical software package (R Core Team 2018: R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/) version 3.6.1 was used to determine trends in mortality rates.

3 | RESULTS

During the study period 1996-2013, 1420 of 1 052 559 infants had UOHDs, for an average of 135 infants per 100 000 births. The proportion of UOHDs remained unchanged between 1996 and 2003 but increased through 2006 and then again in 2013. The UOHD rate rose from 46 to 260 per 100 000 deliveries, a nearly sixfold increase, during the study period ($P < .001$) (Table 1, Figure S1). Since 2004, 579 (51%) of the UOHDs were registered as births during transport to hospitals and 557 (49%) as births elsewhere outside hospitals. Birth rates during transport increased much less than UOHDs elsewhere ($P < .001$) (Figure 1). The UOHD rate was highest in northern Finland and lowest in southwestern Finland. The numbers of delivery units decreased from 44 to 29 during the study period (Figure 2). The increase of the proportion of UOHDs continued after the end of our study period, although the absolute number of UOHDs has decreased along with the declining birth rates since 2016. In the year 2018, the rate was 382 per 100 000 deliveries, representing eightfold rise since the beginning of our study period (the Finnish Institute for Health and Welfare, 2018).

3.1 | Maternal and infant characteristics and outcomes

Compared with women who delivered in hospitals, women with UOHDs had more previous deliveries and pregnancies. Significantly more of these mothers were either younger than 20 years or older than 34 years of age (Table 1). Mothers with UOHDs more often had disadvantaged socioeconomic positions, had higher smoking rates and were of nationalities other than Finnish (Table 1). They also more often had a history of earlier and current drug and alcohol abuse (n = 14 [1.0%] vs. n = 3044 [0.3%]) (Table S1) and had fewer prenatal visits (Table 1), previous cesarean section deliveries (n = 68 [4.8%] vs. n = 111 857 [10.6%]), Table S2) and multiple births (n = 14 [1.0%] vs. 31 873 [3.0%]; $P < .001$).

In the UOHD group, the median length of gestation and duration of labor (first and second phases) were shorter than in the reference population, with first phase duration of less than 3 hours in 258 (18.2%) cases in the UOHD group and 22 589 (2.1%) cases in the reference group ($P < .001$). Extremely and very preterm deliveries were more common, post-term deliveries were less common, and travel distances from home to hospitals were significantly longer than in in-hospital deliveries. The UOHD mothers had less genital tract trauma and fewer puerperal infections and hypertensive pregnancies (Tables 1, S1 and S2). No maternal deaths occurred among UOHDs.

Tables S2 and S3 present the infant characteristics and outcomes. The study group infants had lower mean birthweight (3346 g [SD 672 g] vs. 3505 g [SD 582 g]; $P < .001$) and a greater proportion of them weighed <2500 g compared with those born in hospitals. The UOHD group had a higher percentage of premature infants (n = 117, 8.2%) than the reference population (n = 61 449, 5.8%; $P < .001$)

Compared with the reference population, infants in the UOHD group significantly more often had low 1-minute Apgar scores (n = 116 [8.2%] vs. n = 56 231 [5.3%]) but significantly fewer birth traumas (n = 12 [0.8%], vs. n = 24 115 [2.3%]). They more frequently had antibiotic treatment (n = 99 [7.0%] vs. n = 52 332 [5.0%]) and hypothermia (n = 16 [1.1%] vs. n = 418 [<0.1%]) (Table S3). The percentages of infants admitted to neonatal care units after birth did not differ significantly (169 [11.9%] infants in the UOHD group vs. 109 551 [10.4%] infants in the reference population; $P = .06$).

In the UOHD group, 49 infants were stillborn or died before the age of 7 days. Of these, 32 (65%) were born elsewhere than during transportation to the hospital and 30 (61%) were preterm. The perinatal mortality rate was 35 per 1000 births in the UOHD group and 5 per 1000 births in the reference population ($P < .001$). During the study period, the trend of average perinatal mortality rate did not change in the study group ($P < .001$), whereas it diminished among hospital births (Figure 2, $P < .001$). After adjusting for GA and

TABLE 1 Characteristics of the Patients, Pregnancies, and Deliveries

	Place of birth			
	Out-of-hospital (n = 1420)	Hospital (n = 1 051 139)	P^*	Univariable: birth out-of-hospital vs. in hospital OR (95% CI)
Study period, y, n (%)				
1996-2001	198 (13.9) 57[b]	346 376 (33.0)	<.001	1.00
2002-2007	462 (32.5) 122[b]	345 083 (32.8)		2.34 (1.98-2.77)
2008-2013	760 (53.5) 211[b]	359 680 (34.2)		3.70 (3.16-4.32)
Area of Finland, n (%)				
Southern	424 (29.9)	367 335 (34.9)	<.001	1.00
Eastern	235 (16.5)	148 367 (14.1)		1.37 (1.17-1.61)
Northern	310 (21.8)	161 944 (15.4)		1.66 (1.43-1.92)
Western	274 (19.3)	205 920 (19.6)		1.15 (0.99-1.34)
Southwest	167 (11.8)	160 356 (15.3)		0.90 (0.75-1.08)
Age in years, n (%)				
20-34	1058 (74.5)	812 745 (77.3)	.02	1.00
≤19	34 (2.4)	18 729 (1.8)		1.40 (0.99-1.96)
≥35	328 (23.1)	219 665 (20.9)		1.15 (1.01-1.30)
Living in partnership, n (%)				
Yes	1230 (86.6)	930 693 (88.5)	.08	1.00
No	94 (6.6)	58 955 (5.6)		1.21 (0.98-1.49)
Unknown	96 (6.8)	61 491 (5.8)		1.18 (0.96-1.45)
Socioeconomic status, n (%)				
Upper-level employee	154 (10.8)	168 579 (16.0)	<.001	1.00
Lower-level employee	423 (29.8)	375 728 (35.7)		1.23 (1.02-1.48)
Manual worker	225 (15.8)	152 846 (14.5)		1.61 (1.31-1.98)
Other	290 (20.4)	175 223 (16.7)		1.81 (1.49-2.20)
Unknown	328 (23.1)	178 763 (17.0)		2.01 (1.66-2.43)
Nationality, n (%)				
Finnish	1105 (77.8)	892,516 (84.9)	<.001	1.00
Other	122 (8.6)	50,413 (4.8)		1.96 (1.62-2.36)
Unknown	193 (13.6)	108 210 (10.3)		1.44 (1.24-1–68)
Parity, n (%)				
0	139 (9.8)	334 393 (31.8)	<.001	1.00
1-2	792 (55.8)	507 423 (48.3)		3.76 (3.13-4.50)
3-4	318 (22.4)	148 507 (14.1)		5.15 (4.22-6.29)
5 or more	167 (11.8)	600 896 (5.7)		6.69 (5.34-8.38)
Unknown	4 (0.3)	727 (0.1)		13.2 (4.89-35.9)
Distance from home to delivery unit (shortest route, kilometers), Md (IQR)	32 (0-76)	8.3 (0-35)	<.001	
<5.0	422 (29.7)	506 794 (48.2)		1.00
5.0-19.9	70 (4.9)	91 718 (8.7)		0.92 (0.71-1.18)
20.0-34.9	236 (16.6)	184 918 (17.6)		1.53 (1.31-1.80)
≥35.0	683 (48.1)	265 397 (25.2)		3.09 (2.74-3.49)
Not known	9 (0.6)	2312 (0.2)		4.68 (2.41-9.09)

(Continues)

TABLE 1 (Continued)

	Place of birth			
	Out-of-hospital (n = 1420)	Hospital (n = 1 051 139)	P*	Univariable: birth out-of-hospital vs. in hospital OR (95% CI)
Number of previous pregnancies, Md (Range)	2 (0-18)	1 (0-24)	<.001	
Smoking during pregnancy, n (%)			<.001	
No	1,074 (75.6)	867 612 (82.5)		1.00
Yes	223 (15.7)	157 009 (14.9)		1.15 (0.99-1.33)
Unknown	123 (8.7)	26 518 (2.5)		3.75 (3.11-4.52)
Number of prenatal visits, Md (IQR)	14 (11-16)	16 (13-19)	<.001	
Time period, 2004-2013[a]	Out–of–hospital (n = 1137)	Hospital (n = 592 768)		
Duration of labor, first phase, Md (IQR) hours: minutes	3:23 (1:50-3:22)	10:30 (6:40-16:40)	<.001	
Duration of labor, second phase, minutes, Md (IQR)	3 (1-9)	15 (7-33)	<.001	

Note: OR = odds ratio; CI = 95% confidence interval; Md = median; IQR = interquartile range.

[a]Diagnoses are available from the Medical Birth Register from 2004 to the present.

[b]Number of UOHDs per 100,000 deliveries.

*Differences between unplanned out-of-hospital deliveries and controls were assessed using Pearson's Chi-Square, Fisher's exact, Mann-Whitney *U*, and independent samples t-tests, as appropriate.

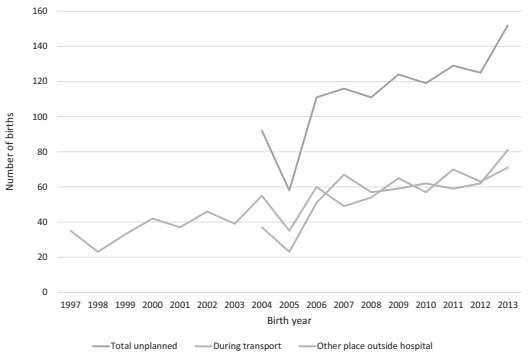

FIGURE 1 Trends in rates of unplanned deliveries out-of-hospital. Deliveries during transport and elsewhere out-of-hospital were recorded separately from year 2004 onwards

birthweight, the UOHD group had a fivefold higher perinatal mortality rate (OR 5.34, 95% CI 3.73-7.63) than the reference population.

Stillbirths accounted for 25 (51%) cases of perinatal mortality in the study group. Fourteen (56%) of the stillborn infants were very preterm. The main causes of death related to stillbirths were intrauterine hypoxia, prematurity, chorioamnionitis and complications related to the umbilical cord. The underlying cause of death was unknown in 12 (48%) cases.

Twenty-four (49%) liveborn infants in the UOHD group died before age of 7 days. Eighteen of them (75%) died on the day of birth and the remaining six during the first 3 days of life. Ten (42%) of these deceased infants were very preterm and 13 (54%) had a birthweight <2500 g. This group also included one set of twins. The causes of death were diverse and 10 (42%) cases were related to physical abuse. Maternal and fetal infections and prematurity accounted for six (25%) deaths. In one (4.2%) case, the underlying cause of death was unknown.

The perinatal death rate in UHOD infants was lowest in the northern Finland (n = 2, 0.6%) and highest in southwestern Finland (n = 13, 7.8%) (Table S5).

3.2 | Risk factors for out-of-hospital births and perinatal morbidity and mortality

In the logistic regression analysis, the independent risk factors of UOHDs were birth after the year 2001, birth outside southern or southwestern Finland, alcohol and/or drug abuse, living without a partner, fewer than 13 prenatal visits, earlier delivery/deliveries and small birthweight (Table 2). In the whole population, UOHD was one of the independent risk factors of mortality or morbidity and mortality (OR 1.32, 95% CI 1.17-1.49) and mortality (OR 7.09, 95% CI 5.33-9.44). Among the UOHD cases, the significant independent risk factors associated with perinatal mortality or morbidity included birthweight <2500 g (OR 3.06, 95% CI 1.67-5.60) and preterm delivery (OR 2.83, 95% CI 1.60-4.98). Birth in the northern region seemed to be associated with a decreased risk for perinatal mortality or morbidity (OR 0.45, 95% CI 0.29-0.70). The

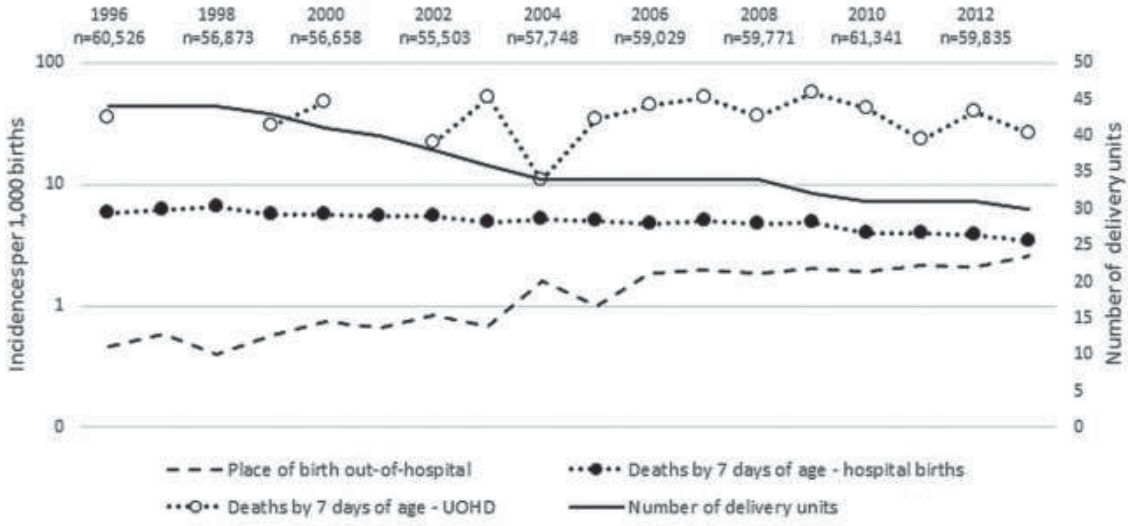

FIGURE 2 Rates of unplanned out-of-hospital births, perinatal deaths, and numbers of delivery units in Finland, 1996-2013

independent predictors for perinatal mortality were birthweight <2500 g (OR 9.41, 95% CI 2.21-40.1), very preterm delivery (OR 15.4, 95% CI 2.64-90.2) and birth in the eastern region of Finland (OR 5.32, 95% CI 1.38-20.5) (Table S4). Among the UOHDs, the morbidity and mortality were not significantly associated with time period (Table S4).

4 | DISCUSSION

In this large national register study, we found that in recent years the rate of UOHDs in Finland has increased. During the past 10 years, the number of deliveries during transport has increased less than the number of UOHDs elsewhere. Risk factors for UOHDs included later study periods, birth outside southern or southwestern Finland, ie in areas with a lower population density, alcohol and/or drug abuse during pregnancy, living without a partner, fewer prenatal visits, mother having delivered earlier and small birthweight. Adverse maternal outcomes related to UOHDs were rare. Infants delivered by mothers with UOHDs had a five-fold higher perinatal mortality rate than the reference population, with the highest ratio concerning premature infants. The majority of the UOHD deaths were stillbirths and a significant percentage of the causes of early neonatal deaths were related to abuse. In the whole population, UOHD was one of the independent risk factors of morbidity or mortality and mortality. Among the UOHDs, prematurity and low birthweight were the most important predictors of the infant's adverse outcome. The infants' adverse outcomes did not seem to be associated with time period of birth.

The main strength of our study was the long study period covering all deliveries and stillbirths in Finland over 18 years. We were also able to obtain detailed data on diagnoses, complications and causes of death from Finnish national health registers providing comprehensive, reliable data. The main limitation of the study was that some variables had several missing values, partly due to circumstances such as Apgar scores given outside hospitals. Retrospective register studies run the risk of not inappropriately assigning some diagnostic codes. For example, hypothermia was most likely underdiagnosed or unrecorded. In addition, the register data did not include admission temperatures or information about delivery attendants. In future studies it is important to register the attendance of medical personnel (paramedics, midwifes, physicians) and analyze their role in minimizing the perinatal morbidity and mortality.

The reasons for delivery during transportation or somewhere else out-of-hospital could not be detected from the retrospective register data. Data on home address at time of delivery is available, but the mother's accommodation or location at the onset of labor might be somewhere else, for example due to vacation, Thus the mother's actual traveling distance to the delivery unit during labor cannot be documented reliably from the register data.

The annual UOHD rate in our study population was higher than in earlier studies in Finland (1.0-2.5 per 1000 births[4]) and Norway (6.8 per 1000 births[1]). In Finland, the annual rate of UOHDs increased significantly over the study period, with a similar trend throughout the country. Our results differ from those in a Norwegian study[1] finding that the UOHD rate remained stable over 15 years despite a decreasing number of delivery units.

Half of the UOHDs occurred during transport to hospitals. As the number of delivery units has decreased, the distances from home to delivery hospitals have increased. One would expect the risk of delivery during transport to increase respectively. However, deliveries during transport in the study population did not explain most of the increase in UOHDs in the past 10 years.

TABLE 2 Risk factor analysis for unplanned out-of-hospital deliveries

		Unplanned out-of-hospital birth (n = 1420; 0.13%)		
Risk factors	**N**	**n**	**Multivariable OR**	**(95% CI)**
Study period				
1996-2001	346 574	198	1.00	
2002-2007	345 545	462	2.45	(2.07-2.90)
2008-2013	360 440	760	3.76	(3.21-4.40)
Area of Finland				
Southern	367 759	424	1.00	
Eastern	148 602	235	1.39	(1.19-1.64)
Northern	162 254	310	1.48	(1.27-1.72)
Western	206 194	274	1.27	(1.09-1.49)
Southwest	160 523	167	0.99	(0.82-1.18)
Alcohol and/or drug abuse				
No	1 049 144	1407	1.00	
@@Yes	3415	13	2.14	(1.22-3.74)
Living in partnership				
Yes	931 923	1230	1.00	
No	59 049	94	1.30	(1.05-1.61)
Smoking during pregnancy				
No	868 686	1074	1.00	
Yes	157 232	223	1.19	(1.03-1.38)
Primipara				
No	616 285	1234	1.00	
Yes	435 460	173	0.21	(0.18-0.24)
Number of prenatal visits				
<13	182 310	527	2.01	(1.78-2.26)
13-17	496 935	608	1.00	
>17	355 897	212	0.55	(0.47-0.64)
Length of gestation at birth				
37 + 0-42 + 0	959 282	1250	1.00	
22 + 0-31 + 6	10 026	40	1.29	(0.84-1.99)
32 + 0-36 + 6	51 540	77	0.83	(0.63-1.10)
>42 + 0	28 660	7	0.32	(0.15-0.68)
Birthweight				
<2500 g	46 287	107	1.57	(1.16-2.12)
≥2500 g	1 005 551	1305	1.00	

Likewise, a previous study in Finland stated that rise in UOHDs could not be explained entirely by the increasing distance between homes and delivery units.[17] Our results also support the conclusion that other reasons, such as short duration of labor or maternal mental and social problems, might explain a remarkable proportion of UOHDs. Whether the women's knowledge and attitudes to leaving home before start of labor have changed during the study period, needs to be studied further. Prevention of UOHDs during transport can be promoted by developing more effective emergency response center, ambulance and helicopter services.

UOHDs are more likely to involve mothers who are younger[4,10,18] or older,[1,4,19] are unmarried,[1,4,18] smokers,[1,4,12,18] have less education or a lower socioeconomic status,[6,18,20,21] have a lack of or less access to prenatal care,[2,3,9,18,20,22] have more previous deliveries,[1-4,6,9,18-22] have fewer previous cesarean deliveries,[22] have lower GA at delivery,[1,2,4,6,10,18] and experience shorter duration of labor.[2,12] Our findings are in line with previous studies. In our material, the study group had a significantly shorter labor, but the maternal complications in the groups were comparable, including postpartum hemorrhages, which is in contrast to earlier reports.[21] The UOHD group had a significantly lower incidence of chorioamnionitis,[12] which has

been associated with prolonged labor, primiparity and multiple vaginal examinations,[23] to which the study group were obviously less exposed.

Compared with in-hospital births, infants delivered by mothers with UOHDs are more likely to be preterm,[6,10,18] have lower mean birthweight,[2-4,6,10,21,22] be admitted to neonatal care units[2,6,9,12,20,22] and have hypothermia.[2,4,11,12,20,22,24] Our results confirm these previous findings. To improve preparedness, paramedics need to be adequately educated and have equipment suitable for the management of preterm infants. Emergency teams should be prepared to monitor and record the body temperatures of the infants to prevent hypothermia.

Higher perinatal or neonatal mortality rates in UOHDs are well established in different populations and countries.[1-9] In the present study, the perinatal mortality rate did not change over the study period for UOHD cases, but did decrease for infants delivered in hospitals. As supposed in an earlier study,[1] infants born in hospitals seem to reap the benefit of the centralization of deliveries into bigger hospitals with emergency cesarean sections and effective neonatal resuscitation available at any time, any day.

The causes of death we detected were partly in line with a previously published Norwegian study.[25] We also detected that a significant percentage of the liveborn cases in our material died as consequence of abuse, ie in indistinct circumstances. Such cases seem to be hardly preventable and are unlikely to be associated with distance to the nearest delivery unit. Mental health problems, drug and alcohol abuse, and social exclusion may lay behind some of these cases. Multidisciplinary interventions for the mother and her family, including substance abuse treatment, psychiatric therapy and focused social work support, are needed to improve the pregnancy outcome in such complicated situations.

Our data indicate an increased risk of preterm delivery outside hospitals. This risk was also obviously associated with fewer prenatal visits. Supporting previous findings, UOHD risk factors also included multiparity, living alone and smoking during pregnancy.[1,12,20,21] Prematurity was most strongly associated with adverse infant outcomes of UOHDs, as found in earlier studies.[1,5,10,11,13]

Birth during the most recent time period, 2008-2013, and delivery in areas with low population density were associated with an increased the risk of UOHDs but not with perinatal morbidity or mortality associated with UOHDs. Thus, this does not support the suspicion that such adverse events in UOHDs might be associated with increasing distances due to decreased numbers of delivery hospitals. The association of delivery in the eastern region with an increased risk of perinatal mortality might be explained by a chance, because of the small numbers of the cases.

5 | CONCLUSION

The increased incidence of UOHDs may be due to various factors such as living in area with low population density and short duration of labor. UOHDs had significantly higher perinatal mortality rates, especially among preterm and small infants, but the numbers of deaths were very small, and mostly hardly preventable. Neonatal morbidity and mortality in UOHDs did not seem to be related to the area or time period of birth. The decreasing number of delivery hospitals seems unlikely to be associated with increases in perinatal morbidity and mortality associated with UOHDs.

CONFLICT OF INTEREST

None.

ETHICAL APPROVAL

There was no patient or public involvement in setting the research question, designing the study or interpreting the study results. The research project has been approved by the Ethics Committee of the Tampere region 8.1.2013 (R12268).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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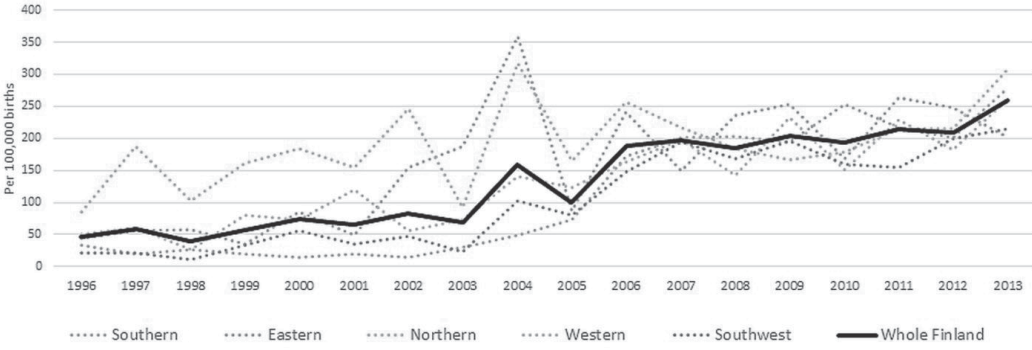
400
350
300
250
200
150
100
50
0
Per 100,000 births
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Southern
Eastern
Northern
Western
Southwest
Whole Finland

Figure S1

Table S1 Maternal Morbidity

	Place of birth						
Time period 1996–2013	Out-of-hospital (n=1420)		Hospital (n=1 051 139)		p*	Univariable: birth out-of-hospital vs. in hospital	
	n	(%)	n	(%)		OR	(95% CI)
Previous cesarean delivery	68	(4.8)	111 857	(10.6)	<0.001	0.42	(0.33–0.54)
Previous miscarriage	327	(23.0)	218 172	(20.8)	0.002	1.15	(1.01–1.30)
Previous intrauterine death	19	(1.3)	7402	(0.7)	<0.001	1.92	(1.22–3.02)
Artificial pregnancy	6	(0.4)	13 655	(1.3)	0.004	0.32	(0.14–0.72)
Alcohol and/or drug abuse	14	(1.0)	3044	(0.3)	<0.001	3.43	(2.02–5.81)
Diabetic complications	116	(3.3)	83 823	(8.0)	0.79	1.03	(0.85–1.24)
Postpartum hemorrhage, blood transfusion	47	(4.9)	33 244	(3.2)	0.75	1.05	(0.78–1.40)
Complications related to hypertension	20	(1.4)	33 063	(3.1)	<0.001	0.44	(0.28–0.68)
Breech delivery	16	(1.1)	33 231	(3.2)	<0.001	0.35	(0.21–0.57)
Shoulder dystocia	0	(<0.1)	1468	(0.1)	0.28	-	(–)
Time period 2004–2013**	Out-of-hospital (n=1137)		Hospital (n=592 768)		p*	Out-of-hospital vs. in hospital	
	n	(%)	n	(%)		OR	(95% CI)
Uterine bleeding	14	(1.2)	8,281	(1.4)	0.634	0.88	(0.52–1.49)
Obstetric trauma in the genital area	25	(2.2)	21,733	(3.7)	0.008	0.59	(0.40–0.88)
Puerperal infections	1	(0.1)	2,077	(0.4)	0.200	0.25	(0.03–1.78)
Chorioamnionitis	2	(0.2)	4,113	(0.7)	0.035	0.25	(0.06–1.01)

* Differences between unplanned out-of-hospital deliveries and controls were tested with Pearson's Chi-Square and Fisher's exact tests, as appropriate. ** Diagnosis are available from the Medical Birth Register from 2004 onwards.

Table S2 Infants' Characteristics

	Place of birth							
	Out-of-hospital (n=1420)		Hospital (n=1 051 139)			Birth out-of-hospital vs. in hospital		
					p*	OR	(95 % CI)	
Length of gestation at birth (weeks + days), median (IQR)	39+4	(38+3–40+3)	39+6	(38+6–40+5)	<0.001			
Length of gestation at birth, n (%)					<0.001			
37+0–42+0	1250	(88.0)	938 498	(89.3)		1.00		
22+0–31+6	40	(2.8)	9986	(1.0)		3.07	(2.24–4.21)	
32+0–36+6	77	(5.4)	51 463	(4.9)		1.15	(0.91–1.44)	
>42+0	7	(0.5)	48 187	(4.6)		0.19	(0.09–0.39)	
Unknown	46	(3.2)	3005	(0.3)		11.7	(8.72–15.8)	
Birthweight (g), n (%)					<0.001			
2500–3999	1132	(79.7)	816 893	(77.7)		1.00		
4000–5500	173	(12.2)	187 353	(17.8)		0.67	(0.57–0.78)	
1500–2499	70	(4.9)	37 190	(3.5)		1.36	(1.07–1.73)	
500–1499	37	(2.6)	8990	(0.9)		2.97	(2.14–4.12)	
Unknown	8	(0.6)	713	(0.1)		8.10	(4.02–1.63)	

					<0.001	
Birthweight adjusted for gestational age, n (%)						
Appropriate for GA	1309	(92.2)	992 207	(94.4)	1.00	
Small for GA	37	(2.6)	25 246	(2.4)	1.11	(0.80–1.54)
Large for GA	20	(1.4)	29 392	(2.8)	0.52	(0.33–0.80)
Not known	54	(3.8)	4294	(0.4)	9.53	(7.25–12.5)

* Differences between unplanned out-of-hospital deliveries and controls were tested with Pearson's Chi-Square, Fisher's exact test, and Mann-Whitney *U*-test, as appropriate.

Table S3 Morbidity and Mortality among Study Case and Control Infants Excluding Those without Information on Mode/Place of Birth (n=1 052 559)

	Place of birth							
	Out-of-hospital (n=1420)		Hospital (n = 1 051 139)			Univariable: birth out-of-hospital vs. in hospital		
	n	(%)	n	(%)	p*	OR	(95% CI)	
One-minute Apgar scores					<0.001			
0–6	116	(8.2)	56 231	(5.3)		2.03	(1.68–2.47)	
Resuscitation**	11	(0.8)	9028	(0.9)	0.731	0.90	(0.50–1.63)	
Asphyxia at birth	12	(0.8)	14 689	(1.4)	0.076	0.60	(0.34–1.06)	
Birth trauma	12	(0.8)	24 115	(2.3)	<0.001	0.36	(0.21–0.64)	
Meconium aspiration	5	(0.4)	1979	(0.2)	0.202	1.87	(0.78–4.51)	
Respiratory distress**	43	(3.0)	26 801	(2.5)	0.253	1.19	(0.88–1.62)	
Pulmonary hypertension**	4	(0.3)	751	(0.1)	0.020	3.95	(1.48–10.6)	
Antibiotic treatment**	99	(7.0)	52 332	(5.0)	0.001	1.43	(1.17–1.76)	
Invasive ventilation**	21	(1.5)	12 576	(1.2)	0.328	1.24	(0.81–1.91)	
Hypothermia**	16	(1.1)	418	(<0.1)	<0.001	28	(17–47)	
Congenital malformation	117	(8.2)	87 489	(8.3)	0.909	0.99	(0.82–1.20)	
Perinatal mortality	49	(3.5)	5271	(0.5)	<0.001	7.09	(5.32–9.44)	
At least one of mentioned above	337	(23.7)	200 387	(19.1)	<0.001	1.32	(1.17–1.49)	

* Differences between unplanned out-of-hospital deliveries and controls were tested with Pearson's Chi-Square and Fisher's exact test.

** Before age 7 days

Odds ratios (OR) with 95% confidence intervals (CI)

Table S4 Multivariable risk factor analysis for mortality and mortality or morbidity

		Mortality or morbidity			Mortality		
		(n=337, 23.7%)			(n=49, 3.5%)		
Multivariable risk factors of UOHD	N=1,420	n	OR	(95% CI	n	OR	(95% CI)
Study period							
1996-2001	198	41	1.00		4	1.00	
2002-2007	462	132	1.40	(0.89-2.20)	17	1.51	(0.28-8.14)
2008-2013	760	164	0.88	(0.57-1.37)	28	2.38	(0.51-11.2)
Area of Finland							
Southern	424	102	1.00		12	1.00	
Eastern	235	71	1.25	(0.84-1.87)	13	5.32	(1.38-20.5)
Northern	310	39	0.45	(0.29-0.70)	2	0.64	(0.09-4.77)
Western	274	72	0.92	(0.62-1.38)	9	1.34	(0.34-5.28)
Southwest	167	51	1.03	(0.65-1.63)	13	3.22	(0.84-12.4)
Alcohol and/or drug abuse							
No	1407	333	1.00		48	1.00	
Yes	13	4	0.51	(0.12-2.21)	1	0.32	(0.02-4.99)
Living in partnership							
Yes	1230	269	1.00		25	1.00	
No	94	30	1.17	(0.69-1.98)	4	1.01	(0.21-4.78)
Smoking during pregnancy							
No	1074	216	1.00		19	1.00	
Yes	223	60	1.19	(0.82-1.74)	2	0.20	(0.03-1.17)
Primipara							
No	1243	256	0.77	(0.50-1.19)	17	0.38	(0.14-1.05)
Yes	173	77	1.00		28	1.00	
Number of prenatal visits							

< 13	527	144	1.04	(0.75-1.44)	33	2.30	(0.61-8.68)
13-17	608	118	1.00		4	1.00	
> 17	212	46	1.23	(0.82-1.83)	1	0.93	(0.10-9.16)
Length of gestation at birth							
37+0-42+0	1,250	229	1.00		7	1.00	
22+0-31+6	40	40	-	-	24	15.4	(2.64-90.2)
32+0-36+6	77	40	2.83	(1.60-4.98)	6	2.12	(0.37-12.0)
>42+0	7	1	0.71	(0.08-6.02)	0	-	-
Birthweight							
<2500g	107	79	3.06	(1.67-5.60)	33	9.41	(2.21-40.1)
≥2500g	1,305	252	1.00		11	1.00	

Categories of missing values are not shown.

Odds ratios (OR) with 95% confidence intervals (CI)

Table S5 Stillbirths and Deaths at Less than Seven Days Old

	Out-of-hospital births (n=1420)		Stillbirths (n=25)		Deaths 0-7 days (n=24)		All perinatal deaths (n=49)	
University hospital catchment area	n	(%)	n	(%)	n	(%)	n	(%)
Southern	424	(30.0)	5	(20.0)	7	(29.2)	12	24.5
Eastern	235	(16.5)	7	(28.0)	6	(25.0)	13	26.5
Northern	310	(21.8)	1	(4.0)	1	(4.2)	2	4.1
Western	274	(19.3)	5	(20.0)	4	(16.7)	9	18.4
Southwest	167	(11.8)	7	(28.0)	6	(25.0)	13	26.5
Time Period								
1996-2001	198	(13.9)	2	(8.0)	2	(8.3)	4	8.2
2002-2007	462	(32.5)	9	(36.0)	8	(33.3)	17	34.7
2008-2013	760	(53.5)	14	(56.0)	14	(58.3)	28	57.1

PUBLICATION IV

Is birth out-of-hospital associated with mortality or morbidity by seven years of age?

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RESEARCH ARTICLE

Is birth out-of-hospital associated with mortality and morbidity by seven years of age?

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Data Availability Statement: Relevant data are within the manuscript and its tables. The original register data with identification codes are confidential and available only for the study group and the holding register worker. The original data

Abstract

Background and aims

Compared to in-hospital births, the long-term outcome of children born out-of-hospital, planned or unplanned, is poorly studied. This study aimed to examine mortality and morbidity by seven years of age in children born out-of-hospital compared to those born in-hospital.

Methods

This study was registered retrospectively and included 790 136 children born in Finland between 1996 and 2013. The study population was divided into three groups according to birth site: in-hospital (n = 788 622), planned out-of-hospital (n = 176), and unplanned out-of-hospital (n = 1338). Data regarding deaths, hospital visits, reimbursement of medical expenses, and disability allowances was collected up to seven years of age or by the year-end of 2018. The association between birth site and childhood morbidity was determined using multivariable-adjusted Cox hazard regression analysis.

Results

No deaths were reported during the first seven years after birth in the children born out-of-hospital. The percentage of children with hospital visits due to infection by seven years of age was lower in those born planned out-of-hospital and in the combined planned out-of-hospital and unplanned out-of-hospital group compared to those born in-hospital. Furthermore, the percentage of children with hospital visits and who received disability allowances due to neurological or mental disorders was higher among those born unplanned out-of-hospital and out-of-hospital in total when compared to those born in-hospital. In the multivariable-adjusted Cox proportional hazard regression analysis, the hazard ratio for hospital visits due to asthma and/or allergic diseases (HR 0.84; 95% CI 0.72–0.98) was lower in

received from register holders cannot be shared publicly; however, researchers who meet the criteria for access to confidential data may apply for data access from Findata, the Health and Social Data Permit Authority (https://www.findata.fi/en/).

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Competing interests: The authors have declared that no competing interests exist.

children born out-of-hospital when compared to those born in-hospital. A similar decreased risk was found due to infections (HR 0.76; 95% CI 0.68–0.84). However, the risk for neurological or mental health disorders was similar between the children born in-hospital and out-of-hospital.

Conclusions

Morbidity related to asthma or allergic diseases and infections by seven years of age appeared to be lower in children born out-of-hospital. Birth out-of-hospital seemed to not be associated with increased risk for neurological morbidity nor early childhood mortality. Our study groups were small and heterogeneous and because of this the results need to be interpreted with caution.

Introduction

Compared to in-hospital births, the possible long-term risks and outcomes for children delivered planned out-of-hospital (POHD) and unplanned out-of-hospital (UOHD) are poorly known. Previous studies on the possible risks of out-of-hospital deliveries (OHDs) for mothers and offspring are limited almost completely to the perinatal or neonatal period. In our previous studies, we analyzed register-based data on POHDs and UOHDs during the perinatal period [1–3]. We found that perinatal mortality and morbidity rates were significantly higher among UOHD infants compared to children born in-hospital [3]. Such differences were less significant when we compared POHDs to in-hospital deliveries [1]. There are only a limited number of studies establishing the long-term outcomes of infants born out-of-hospital. A recently published study [4] showed that hospitalization rates were lower in UOHD children compared to those born in-hospital. Moreover, an Australian population-based cohort study showed that very preterm UOHD infants were significantly more likely to die within 28 days or one year of age compared to those born in-hospital. Furthermore, the study showed that only 41% of very preterm UOHD infants were alive at one year of age [5]. To our knowledge, these are the only studies related to this issue.

This study aimed to examine the association between neonatal, infant, and childhood mortality and morbidity between children delivered out-of-hospital and those delivered in-hospital.

Material and methods

This national retrospective register study included all births in Finland between 1996 and 2013 registered in the Medical Birth Register, which contains data related to all live births and stillbirths from the gestational age of 22+0 weeks onward or those with a birth weight of at least 500 g. In addition, data in the Medical Birth Register includes maternal and delivery characteristics and obstetric procedures. During the study years, 1 053 802 infants were born in Finland. Infants who were stillborn or died before the age of seven days (n = 5322) were excluded in order to avoid overlapping with our previous reports [1, 3]. Infants with missing data regarding birth site (n = 1046), and at least one major congenital anomaly as well as operative deliveries (n = 257 296) were also excluded. Operative deliveries were excluded as a potential confounder in the analysis due to lack of operative deliveries in the out-of-hospital birth group. Overall, 790 136 children born in Finland between 1996 and 2013 were assessed.

The data from the Medical Birth Register was linked to the Care Register for Health Care and the Register of Congenital Malformations maintained by the Finnish Institute for Health and Welfare; to health insurance data from the Social Insurance Institution; and to the Cause-of-Death Register, maintained by Statistics Finland.

Morbidity data was collected from the Care Register for Health Care, including data on inpatient visits, admissions to public hospitals, specialized health care outpatient visits (available since 1998), and admission and discharge dates. Primary health care visits were not included. Data regarding reimbursements of medicine expenses and disability allowances was obtained from the Social Insurance Institution. In Finland, reimbursements of medicine expenses and disability allowances can be granted for children if they require long-term therapy for a disease. The follow-up time was up to seven years of age or by the year-end of 2018.

Finnish growth curves were used to analyze birth weight in relation to gestational age [6]. Small for gestational age (SGA) was defined as a birth weight two or more standard deviations (SDs) below the population average. Large for gestational age (LGA) was defined as a birth weight two or more SDs above the average. Socioeconomic status was defined by using the mother's occupation and divided into four groups: upper-level employees, lower-level employees, manual workers, and others. "Others" included students, housewives, and unclassifiable cases. Congenital anomalies were divided into major and minor anomalies according to the classification of the European surveillance of congenital anomalies [7]. Only major congenital anomalies were reported because the reporting of minor anomalies varies depending on time period and the reporting unit. The Medical Birth Register includes data regarding Apgar scores at one and five minutes, but data on five- minute Apgar scores has only been available since 2004. Five-minute Apgar scores were not analyzed in our study due to missing data including all information from the first eight years of our study period.

For the analysis of morbidity, three main groups based on certain ICD-10 codes, Anatomical Therapeutic Chemical (ATC) classification codes, and reimbursement codes were created: asthma and allergy (ICD-10 codes: J45‾ asthma, L20.0 atopic dermatitis, L27.2 dermatitis due to ingested food, K52.2 allergic and dietetic gastroenteritis and colitis, J30.10 allergic rhinitis due to pollen, and J30.3 other allergic rhinitis; ATC-codes: R03 drugs for obstructive airway diseases and V06DF milk substitutes; and reimbursement codes: 203 chronic asthma and 505 and 506 milk allergy), central nervous system-associated problems, including neurological and mental health diseases and sensory impairments (ICD-10 codes: G40‾ epilepsy, G41‾ status epilepticus, G80‾-G83‾ cerebral palsy and other paralytical syndromes, F90-98‾ behavioral and emotional disorders, F70-79‾ intellectual disabilities, F82, F83, F84‾ different developmen-tal disorders, H90‾ hearing loss, and H54‾ blindness; ATC-codes: N03‾ drugs for epilepsy, andN06‾ antidepressants, psycholeptics, etc.; and reimbursement codes 111, 181, 182, 183, 199 epilepsy, 112 severe psychosis and other severe mental disorders, and 113 behavioral disorders with intellectual disabilities) and infections (ICD-10 codes: H65‾-H66‾ otitis media, J06‾ upper respiratory infections, B34.9 unspecified viral infection, J12‾-J18‾ pneumonia, and J20‾-J21‾ acute bronchitis and bronchiolitis). Based on the data in the Care Register for Health Care and the Social Insurance Institution, we determined incidences for the previously men- tioned morbidity groups. The age at diagnosis for certain morbidity groups was defined according to the first detection in one of the aforementioned registers. Hospital visits included all hospitalizations: inpatient visits at all hospitals and specialized health care outpatient visits at public hospitals.

Based on the age at the time of death, mortality after the perinatal period was divided into three categories: seven to 27 days, 28 days to 11 months and one year or older.

There was no patient or public involvement in setting the research question, designing the study, or interpreting the study results. The research project was approved on behalf of the

whole country of Finland by the Ethics Committee of the Tampere Region (Date: 8.1.2013, No: R12268).

Statistical analyses

The characteristics of the infants in this study and reference groups and those of their mothers were described with medians with an interquartile range in skew distributions. Variables which were categorical were described with percentages. Logistic and multinomial logistic regression analyses were performed to investigate the factors of UOHDs, POHDs, and out-of-hospital deliveries (OHDs) in comparison to in-hospital deliveries. The results were shown via odds ratios with 95% confidence intervals (CIs). All variables were entered simultaneously into the multivariable-adjusted models. The associations between birth site and childhood morbidity were determined using Cox hazard regression models for hospital visits for asthma or allergy, infection and neurological or mental disorder by the age of seven years. Risk factors included in the multivariable-models were: maternal age, mother living in partnership, socioeconomic status, smoking during pregnancy, primipara, sex, length of gestation at birth less than 37^{+0} weeks (preterm) vs. 37^{+0} weeks or more (term), appropriate for gestational age (AGA)/SGA/LGA, one- minute Apgar score, treatment in a neonatal care unit and antibiotic treatment. Statistically significant ($p < 0.05$) interactions between birth site and other risk factors were included into the final multivariable-adjusted model. Cox proportional assumptions were tested and found valid according to the site of birth. The results were expressed as hazard ratios (HRs) with 95% CIs. The analyses were carried out using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY).

Results

The study population consisted of 176 POHD infants and 1338 UOHD infants. The reference group consisted of 788 622 infants born in-hospital. The characteristics of the mothers and infants are presented in Tables 1 and 2. Compared to the children born in-hospital, mothers' low socioeconomic status was less prevalent in the POHD group (4% vs. 14.6%), but the percentage of missing data was almost 20% for this variable. Nationality was more often other than Finnish in the POHD group (8.6% vs. 4.7%), and there were fewer primiparas among the POHD (11.4%) and UOHD mothers (9.6%) than among those who gave birth in-hospital (35.8%). Furthermore, mothers with POHDs smoked less often during pregnancy (6.3% vs. 14.9%). Post term ($> 42^{+0}$ weeks) births were more frequent in the POHD (1.7%) group, but less frequent in the UOHD group (0.5%) when compared to the in-hospital group (2.4%). The POHD infants had higher birth weights, while admissions to the neonatal unit (2.8% vs. 10.7%), need of ventilator treatment (0.6% vs. 1.2%), and treatment with antibiotics (1.1% vs. 6.1%) were less frequent when compared to infants born in-hospital.

Mortality

No childhood deaths were registered after the perinatal period among the POHD or UOHD children. The group born in-hospital had 1024 deaths (1.3 deaths per 1000 births) during the study period. Overall, 119 infants (11.6%) died at the age of seven to 27 days, 406 (39.7%) at the age of 28 days to 11 months, and 499 (48.8%) at the age of one to seven years.

Morbidity

Asthma and allergic diseases. The need for hospital visits, reimbursement of medications, and disability allowances appeared to be similar in all groups, regardless of birth site

Table 1. Characteristics of mothers (n = 790 136).

Site of birth	Planned home (n = 176)		Unplanned out-of-hospital (n = 1338)		In-hospital (n = 788 622)	
	n	(%)	n	(%)	n	(%)
Study period, years						
1996 – 2001	42	(23.9)	187	(14.0)	265 792	(33.7)
2002 – 2007	59	(33.5)	427	(31.9)	257 896	(32.7)
2008 – 2013	75	(42.6)	724	(54.1)	264 934	(33.6)
Area of Finland						
Southern	62	(35.2)	408	(30.5)	269 098	(34.1)
Eastern	11	(6.3)	213	(15.9)	111 408	(14.1)
Northern	17	(9.7)	302	(22.6)	124 570	(15.8)
Western	60	(34.1)	258	(19.3)	156 979	(19.9)
Southwestern	26	(14.8)	147	(11.0)	121 494	(15.4)
Mothers' age, years						
< 19	0	(< 0.1)	29	(2.2)	14 927	(1.9)
20 – 34	120	(68.2)	1002	(74.9)	619 992	(78.6)
> 35	56	(31.8)	307	(22.9)	153 773	(19.5)
Cohabitation						
Yes	159	(90.3)	1177	(88.0)	700 314	(88.8)
No	11	(6.3)	88	(6.6)	43 753	(5.5)
Unknown	6	(3.4)	73	(5.5)	44 555	(5.6)
Socioeconomic status						
Upper-level employee	36	(20.5)	147	(11.1)	123 098	(15.6)
Lower-level employee	50	(28.4)	406	(30.3)	280 383	(35.5)
Manual worker	7	(4.0)	207	(15.5)	115 417	(14.6)
Other	54	(30.7)	277	(20.7)	138 499	(17.5)
Unknown	29	(16.5)	301	(22.5)	131 733	(16.7)
Nationality						
Finnish	150	(85.2)	1047	(78.3)	673 340	(85.4)
Other	14	(8.0)	115	(8.6)	37 372	(4.7)
Unknown	12	(6.8)	176	(13.2)	77 910	(9.9)
Smoking						
No	153	(86.9)	1033	(77.2)	651 891	(82.7)
Yes	11	(6.3)	214	(16.0)	117 778	(14.9)
Unknown	12	(6.8)	91	(6.8)	18 953	(2.4)
Primipara						
No	155	(88.1)	1210	(90.4)	506 097	(64.2)
Yes	20	(11.4)	128	(9.6)	282 174	(35.8)
Unknown						
Length of gestation at birth, weeks+days						
22+0 – 31+6	0	(< 0.1)	15	(1.1)	2562	(0.3)
32+0 – 36+6	1	(0.6)	68	(5.1)	28 740	(3.6)
37+0 – 42+0	151	(85.8)	1205	(90.1)	737 361	(93.4)
> 42+0	10	(5.7)	18	(1.3)	18 613	(2.4)
Unknown	14	(8.0)	32	(2.4)	1894	(0.2)

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(Table 3). In the Cox regression analysis, the hazard ratios for admission and outpatient visits to a hospital related to asthma or allergy for either the POHD or UOHD group children did not significantly differ from those born in-hospital. However, when POHD and UOHD groups

Table 2. Characteristics of infants alive at age of seven days (n = 790 136).

Site of birth	Planned home (n = 176)		Unplanned out-of-hospital (n = 1338)		In-hospital (n = 788 622)	
	n	(%)	n	(%)	n	(%)
Infant						
Boys	82	(46.6)	664	(49.6)	395 586	(50.2)
Birth weight, grams						
2500 – 3999	130	(73.9)	1098	(82.1)	627 315	(79.5)
4000 – 5500	31	(17.6)	169	(12.6)	140 820	(17.9)
1500 – 2499	1	(0.6)	57	(4.3)	18 571	(2.4)
500 – 1499	0	(< 0.1)	12	(0.9)	1701	(0.2)
Unknown	14	(8.0)	2	(0.1)	215	(< 0.1)
Gestational weight						
SGA (small for gestational age)	0	(< 0.1)	27	(2.0)	12 442	(1.6)
AGA (appropriate)	159	(90.3)	1259	(94.1)	755 431	(95.8)
LGA (large)	0	(< 0.1)	19	(1.4)	18 603	(2.4)
Unknown	17	(9.7)	33	(2.5)	2146	(0.3)
Apgar score 1min 0 – 6	7	(4.0)	85	(6.4)	25 457	(3.2)
Admission to neonatal unit	5	(2.8)	157	(11.7)	57 246	(7.3)
Invasive ventilation	1	(0.6)	17	(1.3)	4193	(0.5)
Resuscitation at birth	0	(< 0.1)	5	(0.4)	2808	(0.4)
Antibiotic therapy in the first week of life	2	(1.1)	90	(6.7)	27 828	(3.5)

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were combined into one group (OHD group), the children born out-of-hospital appeared to exhibit significantly lower hazard ratios for asthma and allergy than the children born in-hospital. No significant interactions were found (Table 6).

Infections

The percentage of children with hospital visits due to infection was significantly lower in the POHD group and in the combined OHD group than in the born in-hospital group. Children in the POHD group had their first hospital visit due to pneumonia and bronchitis or bronchiolitis at a younger age compared to those born in-hospital (Table 4). In the Cox regression analysis, the risk of hospital visits due to infection by seven years of age was significantly lower among the children in the POHD group, in the UOHD group, and in the OHD group in total than among those born in-hospital. The decreased risk of infections in the children in the OHD group remained significant in the analysis with interactions (Table 6).

Table 3. Morbidity related to asthma or allergy (n = 790 316).

	Site of birth							
Asthma or allergy (J45[ʢ], L20.0, L27.2, J30.10, J30.3, K52.2)	**Planned home (n = 176)**		**Unplanned out-of-hospital (n = 1338)**		**In-hospital (n = 788 622)**		**Out-of-hospital (planned or unplanned) (n = 1514)**	
Hospital visits, n (%)	16	(9.1)	156	(11.7)	98 817	(12.5)	172	(11.4)
Number of hospital visits, median MD (InterQuartile Range IQR)	4.5	(2.25 – 17.25)	3	(1 – 7.75)	3	(2 – 8)	3	(1 – 8)
Age at 1st hospital visit in years, MD (IQR)	1.1	(0.6 – 2.0)	1.3	(0.7 – 3.1)	1.5	(0.7 – 3.2)	1.3	(0.7 – 3.0)
Reimbursement for medication, n (%)	4	(2.3)	52	(3.9)	28 681	(3.6)	56	(3.7)
Age at 1st reimbursement in years, MD (IQR)	2.75	(0.36 – 5.13)	1.72	(0.74 – 3.39)	2.02	(0.67 – 4.15)	1.7	(0.7 – 3.4)
Disability allowance due to, n (%)	2	(1.1)	22	(1.6)	14 690	(1.9)	24	(1.6)

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Table 4. Morbidity related to infections (n = 790 316).

Infections (H65[-]_H66[-], J06[-], B34.9, J12[-]-J18[-], J20[-]-J21[-])	Site of birth							
	Planned home (n = 176)		Unplanned out-of-hospital (n = 1338)		In-hospital (n = 788 622)		Out-of-hospital (planned or unplanned) (n = 1514)	
Hospital visits, n (%)	38	(21.6)	439	(32.8)	273 958	(34.7)	477	(31.5)
Number of hospital visits, median MD (Interquartile range IQR)	2	(1 – 3.25)	2	(1 – 3)	2	(1 – 3)	2	(1 – 3)
Age at 1st hospital visit in years, MD (IQR)	1.1	(0.5 – 2.1)	1.5	(0.6 – 2.6)	1.4	(0.7 – 2.7)	1.4	(0.6 – 2.5)
Pneumonia (J12[-]-J18[-])								
Hospital visits, n (%)	8	(4.5)	57	(4.3)	30 530	(3.9)	65	(4.3)
Number of hospital visits, MD (IQR)	1	(1 – 1.75)	2	(1 – 2)	1	(1 – 2)	n/a	n/a
Age at 1st hospital visit in years, MD (IQR)	1.2	(0.6 – 2.6)	1.9	(1.1 – 3.9)	2.2	(1.3 – 3.7)	1.9	(1.1 – 3.7)
Bronchitis or bronchiolitis (J20[-]-J21[-])								
Hospital visits, n (%)	9	(5.1)	123	(9.2)	67 840	(8.6)	132	(8.7)
Number of hospital visits, MD(IQR)	2	(1.5 – 3.5)	2	(1 – 3)	2	(1 – 3)	n/a	n/a
Age at 1st hospital visit in years, MD (IQR)	0.3	(0.1 – 0.6)	0.9	(0.3 – 1.8)	1.0	(0.4 – 1.9)	0.7	(0.3 – 1.6)

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Neurological or mental health disorders. The percentage of children with hospital visits and who received disability allowances due to neurological or mental health disorders was higher in the UOHD and OHD groups than in the in-hospital group (Table 5). In the Cox regression analysis, the HRs for admissions or outpatient visits to a hospital due to neurological or mental disorders by seven years of age increased in UOHD children and OHD children in total, compared to children born in-hospital. The statistical significance was, however, lost in the analysis with interactions (Table 6).

Discussion

The POHD and UOHD groups differed significantly in terms of maternal, pregnancy and infant characteristics, which inevitably led to difficulties in comparing these groups to in-hospital deliveries. There is also a risk of selection bias in the analyses. Differences between these groups, i.e. more preterm deliveries, lower socioeconomic position, and smoking among

Table 5. Morbidity related to neurological or mental health disorders (n = 790 316).

Neurological or mental health disorder (G40-G41, G80[-]-83[-], F90-98[-], F70-79[-], F82, F83, F84, H90[-], H54[-])	Site of birth							
	Planned home (n = 176)		Unplanned out-of-hospital (n = 1338)		In-hospital (n = 788 622)		Out-of-hospital (planned or unplanned) (n = 1514)	
Hospital visits, n (%)	10	(5.7)	100	(7.5)	42 653	(5.4)	110	(7.3)
Number of hospital visits, median MD (interquartile range IQR)	2	(1 – 22)	4	(1 – 10)	3	(1 – 10)	4	(1 – 10.5)
Age at 1st hospital visit in years, MD (IQR)	5.8	(1.0 – 6.6)	4.9	(3.3 – 6.0)	5.0	(3.0 – 6.0)	4.9	(3.3 – 6.0)
Reimbursement for medication n (%)	1	(0.6)	4	(0.3)	3044	(0.4)	5	(0.3)
Age at 1st reimbursement in years, MD (IQR)	0.10		3.70	(0.84 – 5.87)	3.42	(1.41 – 5.29)	1.6	(0.4 – 5.9)
Disability allowance due to, n (%)	2	(1.1)	60	(4.5)	17 952	(2.3)	62	(4.1)

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Table 6. Cox hazard regression models regarding hospital visits for asthma or allergy, infection, and neurological or mental disorder by the age of 7 years in the children born in-hospital, planned out-of-hospital, and unplanned out-of-hospital.

							Planned and/or unplanned out-of-hospital births vs. births in-hospital					
							Univariable		Multivariable without interactions		Multivariable with interactions	
	N	n	(%)	Pyrs	Risk	(95 % CI)	HR	(95 % CI)	HR	(95 % CI)	HR	(95 % CI)
Asthma or allergy	**790 136**	**98 989**	**(12.5)**	**5 048 310**	**196**	**(195–197)**						
In-hospital	788 622	98 817	(12)	5 038 578	196	(195 – 197)	1.00		1.00		1.00	
Planned out-of-hospital	176	16	(9)	1141	140	(72 – 208)	0.72	(0.44 – 1.17)	0.71	(0.44 – 1.17)	0.63	(0.35 – 1.10
Unplanned out-of-hospital	1338	156	(12)	8592	182	(153 – 210)	0.93	(0.79 – 1.09)	0.86	(0.73 – 1.004)	0.83	(0.69 – 0.996)
In-hospital	788 622	98 817	(12.5)	5 038 578	196	(195 – 197)	1.00		1.00		1.00	
Out-of-hospital	1514	172	(11.4)	9733	177	(151 – 203)	0.90	(0.78 – 1.05)	0.84	(0.72 – 0.98)	0.80	(0.67 – 0.96)
Infections	**790 136**	**274 435**	**(34.7)**	**5 414 948**	**507**	**(505–509)**						
In-hospital	788 622	273 958	(34.7)	5 404 641	507	(505 – 509)	1.00		1.00		1.00	
Planned out-of-hospital	176	38	(21.6)	1207	315	(216 – 413)	0.59	(0.43 – 0.80)	0.59	(0.43 – 0.81)	0.49	(0.34 – 0.72)
Unplanned out-of-hospital	1338	439	(32.8)	9101	482	(438 – 526)	0.94	(0.85 – 1.03)	0.87	(0.79 – 0.96)	0.80	(0.71 – 0.89)
In-hospital	788 622	273 958	(34.7)	5 404 641	507	(505 – 509)	1.00		1.00		1.00	
Out-of-hospital	1,514	477	(31.5)	10 307	463	(422 – 503)	0.89	(0.81 – 0.98)	0.84	(0.76 – 0.92)	0.76	(0.68 – 0.84)
Neurological or mental disorder	**790 136**	**42 763**	**(5.4)**	**4 134 687**	**103**	**(102–104)**						
In-hospital	788 622	42 653	(5.4)	4 126 554	103	(102 – 104)	1.00		1.00		1.00	
Planned out-of-hospital	176	10	(5.7)	1028	97	(37 – 157)	1.05	(0.56 – 1.95)	1.11	(0.60 – 2.07)	1.19	(0.62 – 2.29)
Unplanned out-of-hospital	1338	100	(7.5)	7106	141	(112 – 168)	1.40	(1.15 – 1.70)	1.24	(1.01 – 1.51)	1.04	(0.83 – 1.31)
In-hospital	722 622	42 653	(5.4)	4 126 554	103	(102 – 104)	1.00		1.00		1.00	
Out-of-hospital	1514	110	(7.3)	8134	135	(110 – 160)	1.36	(1.12 – 1.64)	1.22	(1.01 – 1.48)	1.06	(0.85 – 1.31)

Cox hazard regression models regarding hospital admissions for asthma or allergy, infection and neurological or mental disorder by the age of seven years were shown by person-years until seven age-years (Pyrs), risk per 10,000 person-years (Risk) and Cox proportional hazard regression estimates (HR) with 95% confidence intervals (CI). Statistically significant ($p<0.05$) interactions between the site of birth with other risk factors were included into the final multivariable-adjusted model.

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UOHDs may have had an association with the risk of morbidities we studied. Thus, we realize that our results need to be interpreted with caution. Our study groups were small due to low out-of-hospital delivery rates in Finland, indicating that statistical significance may be difficult to show.

The findings of our study showed that the percentage of children with hospital visits due to infection by seven years of age was lower in those born planned and out-of-hospital in total than those born in-hospital. The percentage of children who had hospital visits and received disability allowances due to neurological or mental disorders was higher in those born unplanned out-of-hospital and out-of-hospital in total than in those born in-hospital. In the Cox regression analysis corrected with interactions the hazard ratios for visits to a hospital due to asthma or allergic diseases or due to infection were lower among the children born out-of-hospital.

The POHD group had the lowest percentage of children who needed hospital visits due to infection by seven years of age. Mothers who deliver at home as planned are more often older [8‐18], non-smokers [12, 18‐20], and married [14, 17, 21]. In addition, socioeconomic status and/or education are usually higher among these women [10, 12, 14, 17, 22, 23]. In our population, the POHD group children were of higher birth weights, rarely needed assisted ventilation, and had fewer admissions to the neonatal unit. Thus, when perinatal, neonatal, demographic, and socioeconomic factors are combined, it might result in conditions that make these children in the POHD group less prone to infections requiring hospital care.

Previous studies have shown that mothers who give birth unplanned out-of-hospital tend to be younger [5, 17, 24] or older [24–27], unmarried/not cohabiting [17, 24, 25], smoke during pregnancy [17, 25], have less education or a lower socioeconomic status [17, 27, 28], more likely substance abusers [29], not visit or have fewer prenatal care visits [4, 17, 30–34], and exhibit a lower length of gestation at delivery [5, 24, 25, 28, 30, 35]. These are obviously risk factors for requiring future hospital care and disability allowances due to neurodevelopmental problems.

One study previously reported on the long-term morbidity of 3580 children born unplanned out-of-hospital in a single tertiary hospital area in Israel [4]. The study population included 243 682 singleton deliveries. The hospitalization rates of the UOHD children by 18 years of age due to respiratory, infectious, and neurological causes were lower when compared to children born in-hospital. The author suggested that socioeconomic and demographic factors related to UOHDs might also be related to the under-utilization of health care services. Such under-utilization may be an unlikely phenomenon, and avoiding/reluctance toward health care visits is probably rare in the Finnish free public health insurance and uniform social security system.

Children born out-of-hospital in total is a very heterogeneous group in terms of perinatal, demographic, and socioeconomic factors. In most cases, the POHD group children remained in a home environment during their perinatal period. In contrast, the UOHD group children were mostly transported after birth to the hospital with their mothers, and some were even admitted to the neonatal unit. The only factor in common among this population was that these children were not born in a delivery room environment. A quite significant percentage of mothers delivering in-hospital receive intrapartum antibiotics. An American study reported that 38.3% of mothers received antibiotics for reasons such as group B Streptococcal (GBS)-positivity, suspected maternal infection, cesarean section, preterm labor, or prolonged membrane rupture [36]. According to unpublished data from the Finnish Medical Birth Register, 5.1% of women received intrapartum antibiotic prophylaxis during vaginal delivery to prevent GBS disease in their infants (years 2017 – 2019, excluding Southern Finland). In addition, women receive intrapartum antibiotic treatment, but number of these women is not studied or published in Finland. Instead, intrapartum exposure to antibiotics is lacking in all out-of-hospital deliveries. The association between the environment and possible intrapartum exposure to antibiotics at birth might have an impact on the children' s skin and gut microbiome [37]. These above-mentioned factors may have protective or harmful effects on the prevalence of allergic and infectious diseases during the childhood.

The main strength of this study is the reliable data obtained from the Finnish national registers [38–41]. We included all OHD infants alive at the age of seven days—except those born after operative delivery or with major malformations.

One of the limitations of this retrospective register study is that we were only able to collect data for a limited range of variables available from the registers. This is why we were unable to analyze certain parameters, such as the prevalence of breastfeeding or smoking after pregnancy. We were also unable to gather information on whether the mother received antibiotic treatments during her pregnancy or delivery or whether inheritable risk factors, such as parental asthma, existed. Because of our study design, infants born at the end of the study period had shorter follow-up times than those born in earlier years. However, even the youngest children born toward the end of the study period were aged at least 5 years at the end of the period when the data was collected.

Future studies are indicated, in order to obtain more information on whether children born planned or unplanned out-of-hospital need additional follow-up during their childhood and whether there is increased risk for certain morbidities. This would be important in order

to set a proper follow-up for such children and share this information with families who are planning for a home birth.

Conclusions

The risk of childhood morbidity related to asthma and allergic diseases, and infections seemed to be smaller among children born out-of-hospital. A reason for this could not be detected in our study, but is presumably multifactorial, including a possible lack of intrapartum antibiotic prophylaxis or treatment for mothers. Furthermore, birth out-of-hospital seemed to not be associated with childhood mortality. Our study groups were small and heterogeneous and because of this the results need to be interpreted with caution.

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