Tampere University

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Major Traumas and Reproductive Health in Women

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ABSTRACT

To date, only a few studies have assessed the effects of previous major trauma (pelvic fractures, spine fractures, etc.) on the reproductive health of fertile-aged women, as most studies focus either on traumas of the reproductive system, traumas occurring during pregnancy, or on the delivery mode after traumas. Moreover, the studies assessing the effects of major orthopedic traumas, such as pelvic fractures and spine fractures, are limited to small or local studies. Pelvic fractures and spine fractures are known to increase the rate of cesarean section (CS), but there is scarcity of studies assessing the effect of these fractures on neonatal health or complications during pregnancy. In addition, although traumatic brain injuries (TBIs) are known to cause disorders in the menstrual cycle and increase the risk for amenorrhea, the long-term effects of TBIs on subsequent pregnancies, deliveries, and neonatal health have not been studied previously.

The overall aim of this nationwide retrospective cohort study was to calculate the incidences of skeletal or brain traumas in fertile-aged women, and to analyze reproductive health after these major traumas in a nationwide setting. In study I, we calculated the incidence of pelvic fractures and surgeries among fertile-aged women and analyzed the effects of these on later pregnancies and neonatal outcomes. In study II, we calculated the incidence of spine fractures, spine fracture surgeries, and fusion surgeries for other reasons in fertile-aged women and analyzed the effects of these on later pregnancy outcomes. In study III, we calculated the incidence of TBIs in fertile-aged women and analyzed the effects of these on subsequent pregnancies and neonatal outcomes. In study IV, we calculated incidence of major traumas (pelvic fractures, spine fractures, TBIs, and hip or thigh fractures) in fertile-aged women and calculated the subsequent birth rate after these traumas. In addition, the risk for a woman to have a pregnancy leading to birth after major traumas when compared to minor traumas was analyzed in study IV. The risk for fractures among

women who smoked when compared to no-smokers, using the smoking status found in the medical birth register (MBR), was analyzed in study V.

The participants in this study were gathered from two nationwide registries: the National Medical Birth Register (MBR) and the Care Register for Health Care. The registers were linked using the unique pseudonymized identification code of each person selected for the study. The study period was from 1998 to 2018. Information on trauma hospitalizations and surgeries was obtained from the Care Register for Health Care and the information on pregnancies was gathered from the MBR. A total of 628 908 women with 1 192 825 deliveries was found in the MBR. In studies I, II, and III, pregnancies occurring after specific traumas formed the patient group, which was then compared to pregnancies without preceding trauma. In study IV, patients with major trauma were compared to patients with palmar fracture and the hazard for the event of giving birth after trauma was analyzed. In study V, the risk for fractures after pregnancy were compared between smoking and non-smoking women. In statistical analyses, logistic regression models (studies I, II, and III) and Cox proportional hazard models (studies IV, and V) were used. The results were interpreted as adjusted odds ratios (aOR), hazard ratios (HRs), or adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs).

The probability for preterm deliveries (aOR 1.32, 95 % CI 1.01 – 1.69), CS (aOR 1.57, 95% CI 1.34 – 1.83), and weakened health of the neonate (aOR 1.31, 95% CI 1.07 – 1.58) was higher among women with previous pelvic fracture in study I. In study II, the probability for CS (aOR 1.30, 95% CI 1.17 – 1.45), and weakened health of the neonate (aOR 1.19, 95% CI 1.05 – 1.34) was higher after spine fracture. Further, after fusion surgery due to instability, the probability for CS (aOR 1.63, 95% CI 1.34 – 1.96) and weakened health of the neonate (aOR 1.35, 95% CI 1.07 – 1.68) was higher. Especially after fusion surgery in lumbar spine, the probability for CS was higher (aOR 1.80, CI 1.38 – 2.34). In addition, the incidence of spine fusion surgeries unrelated to fracture increased strongly during the study period (156%). In study III, the probability for preterm deliveries (aOR 1.19, 95% CI 1.11 – 1.28), CS (aOR 1.25, 95% CI 1.19 – 1.31), and weakened health of the neonate (aOR 1.26, CI 1.19 – 1.33) was higher among women with TBI before pregnancy. Furthermore, the incidence of TBIs increased during our study period from 103 per 100 000 person-years in 1998 to 257 per 100 000 person-years in 2018. In study IV, women with fractures of hip or thigh had the lowest birth rate during the 5-year follow-up period after the fracture (12.4%). Interestingly, women with TBI had the highest birth rate during the 5-year follow-up (19.0%), which was also higher than for women in the reference group with palmar fractures (18.7%). The risk for a pregnancy leading to birth during a 5-year follow-up for women with hip or thigh fracture was lower in the 15-24 years age group (HR 0.72, CI 0.58 – 0.88) and the 15-34 years group (HR 0.65, CI 0.52 – 0.82), when compared to palmar fractures. Women with pelvic fracture in the 25-34 years age group also had a lower risk for a pregnancy leading to birth during a 5-year follow-up (HR 0.79, CI 0.64 – 0.97), when compared to control group. In study V, the overall risk for fractures after pregnancy was higher at 1-year follow-up (aHR 1.73, CI 1.53 – 1.96) and 5-year follow-up (aHR 1.74, CI 1.64 – 1.84) for smoking women when compared to non-smoking women. The risk was also higher for all anatomic regions, polytraumas, severe (hospitalization period over one day), and non-severe fractures (hospitalization period less than a day).

Our result suggests that vaginal delivery is generally possible for the mother and safe for the neonate after pelvic fracture, spine fracture or surgery, and TBI. Preterm deliveries, the need for intensive care for the neonate, labor analgesia, and instrumental vaginal deliveries, were more prevalent in women with previous TBI, indicating that a history of TBI should be identified as a possible factor affecting the delivery and health of the neonate. Further, our results also suggest that women with pelvic, hip, or thigh fractures had a lower birth rate in 5-year follow-up after trauma. Our results also show that maternal smoking during pregnancy is associated with a higher risk for sustaining a fracture after giving birth.

TIIVISTELMÄ

Suurten traumojen (lantionmurtuma, selkärankamurtuma jne.) vaikutuksista naisten myöhempään lisääntymisterveyteen on tehty vain muutamia tutkimuksia, sillä suurin osa tutkimuksista on keskittynyt pääasiassa joko lisääntymiselimistön traumoihin, raskaudenaikaisiin vammoihin tai ainoastaan aikaisempien traumojen vaikutuksista synnytystapaan. Tutkimukset, jotka keskittyvät isojen ortopedisten vammojen, kuten lantio- ja selkärankamurtuminen vaikutuksiin rajoittuvat pääasiassa pieniin tutkimuksiin. Lantio- ja selkämurtumien tiedetään lisäävän riskiä keisarileikkauksille, mutta niistä on hyvin vähän tutkimuksia liittyen vastasyntyneen terveyteen tai raskaudenaikaisiin ongelmiin. Lisäksi aivovammojen tiedetään lisäävän riskiä amenorrealle ja aiheuttavan häiriöitä kuukautiskierrossa. Aivovammojen pitkäaikaisvaikutuksia tuleviin raskauksiin ja vastasyntyneiden terveyteen ei ole kunnolla tutkittu aikaisemmin. Suurin osa aihetta aikaisemmin tutkineista tutkimuksista on tapauskertomuksia tai pieniä paikallisia tutkimuksia.

Tämän retrospektiivisen tutkimuksen tavoitteena oli raportoida suurten traumojen ilmaantuvuudet lisääntymisikäisten naisten keskuudessa ja tutkia näiden traumojen vaikutuksia lisääntymisterveyteen käyttäen valtakunnallisia rekistereitä. Tutkimuksessa I laskimme lantiomurtumien ja leikkaushoitojen ilmaantuvuudet lisääntymisikäisille naisille ja analysoimme näiden vaikutuksia tuleviin raskauksiin ja vastasyntyneen terveyteen. Tutkimuksessa II laskimme selkärankamurtumien ja selkärankamurtumaoperaatioiden, sekä muiden selkärankaoperaatioiden ilmaantuvuudet lisääntymisikäisille naisille ja analysoimme näiden vaikutuksia tuleviin raskauksiin. Tutkimuksessa III laskimme aivovammojen ilmaantuvuudet lisääntymisikäisille naisille ja analysoimme näiden vaikutuksia myöhempiin raskauksiin ja vastasyntyneen terveyteen. Tutkimuksessa IV laskettiin suurten vammojen ilmaantuvuudet lisääntymisikäisillä naisilla ja analysoitiin riskiä

tapahtumalle, jossa nainen tulee raskaaksi suuren trauman jälkeen verrattuna pieniin vammoihin. Tupakoitsijoiden riskiä saada murtuma raskauden jälkeen verrattuna tupakoimattomiin naisiin perustuen synnytysrekisterin tupakointitunnukseen analysoitiin tutkimuksessa V.

Potilastiedot kerättiin kansallisesta synnytysrekisteristä ja hoitoilmoitusrekisteristä. Rekisterit yhdistettiin käyttäen pseudonymisoitua tunnistuskoodia jokaiselle henkilölle, jotka olivat mukana tutkimuksessa. Tutkimusjakso oli vuodesta 1998 vuoteen 2018. Tiedot traumoista saatiin hoitoilmoitusrekisteristä ja informaatio raskauksista kerättiin kansallisesta synnytysrekisteristä. Yhteensä 628 908 eri naisella oli 1 192 825 raskautta tutkimusjakson aikana. Tutkimuksissa I, II ja III, tutkimuksessa mukana olevien traumojen jälkeiset raskaudet muodostivat potilasryhmän, jota vertailtiin raskauksiin ilman aikaisempaa kyseistä traumaa. Tutkimuksessa IV, riskiä tapahtumalle, jossa nainen tulee raskaaksi trauman jälkeen, analysoitiin. Potilaita, jotka olivat saaneet suuren trauman, vertailtiin kämmenen murtuman saaneisiin potilaisiin. Tutkimuksessa V, riskiä murtumille raskauden jälkeen vertailtiin tupakoitsijoiden ja tupakoimattomien kesken. Tilastollisina analyyseina käytettiin tilastollisten testien lisäksi logistista regressiomallia ja Coxin regressiomallia.

Todennäköisyys ennenaikaisille synnytyksille (aOR 1.32, 95 % CI 1.01-1.69), keisarileikkauksille (aOR 1.57, 95% CI 1.34 – 1.83), ja vastasyntyneen heikentyneelle terveydelle (aOR 1.31, 95% CI 1.07 – 1.58) oli korkeampi naisten keskuudessa, jolla on ollut aikaisempi lantiomurtuma. Tutkimuksessa II, selkärankamurtuman jälkeen todennäköisyys keisarileikkaukselle (aOR 1.30, 95% CI 1.17 – 1.45) ja vastasyntyneen heikentyneelle terveydelle (aOR 1.18, 95% CI 1.08 – 1.29) oli korkeampi. Murtumaan liittymättömän selän luudutusleikkauksen jälkeen, todennäköisyys keisarileikkaukselle (aOR 1.63, 95% CI 1.34 – 1.96), ja vastasyntyneen heikentyneelle terveydelle (aOR 1.35, 95% CI 1.07 – 1.68) oli korkeampi. Erityisesti selän luudutusleikkaus lannerangassa lisäsi todennäköisyyttä keisarileikkaukselle (aOR 1.80, CI 1.38 – 2.34). Lisäksi murtumaan liittymättömien selän luudutusleikkausten ilmaantuvuus nousi viii voimakkaasti tutkimuksen aikana (156 %). Tutkimuksessa III, todennäköisyys ennenaikaisille synnytyksille (aOR 1.19, 95% CI 1.11 – 1.28), keisarileikkauksille (aOR 1.25, 95% CI 1.19 – 1.31), ja vastasyntyneen heikentyneelle terveydelle (aOR 1.26, CI 1.19 – 1.33) oli korkeampi naisten keskuudessa, joilla oli ollut aikaisempi aivovamma. Lisäksi aivovammojen ilmaantuvuus kasvoi reilusti tutkimusjakson aikana, kasvaen 103 per 100 000 henkilövuodesta (1998) 257 per 100 000 henkilövuoteen (2018). Tutkimuksessa IV havaittiin, että lisääntyvyys oli alhaisempi lonkka- tai reisimurtumaryhmässä ikäryhmissä 15–25 vuotta (HR 0.72, CI 0.58–0.88) ja 15–34 vuotta (HR 0.65, CI 0.52 – 0.82), kun verrattiin kämmenen murtuman saaneisiin. Lisäksi naisilla, joilla oli lantiomurtuma ikäryhmässä 25–34 vuotta oli alhaisempi lisääntyvyys (HR 0.79, CI 0.64 – 0.97) kämmenmurtuma ryhmään verrattuna. Tutkimuksessa V tupakoivien naisien riski murtumille oli korkeampi yhden vuoden seurantajaksolla (aHR 1.73, CI 1.53 – 1.96), sekä viiden vuoden seurantajaksolla (aHR 1.74, CI 1.64 – 1.84) kuin tupakoimattomilla naisilla. Riski oli korkeampi myös murtumille kaikilla anatomisilla alueilla, polytraumoille, vakaville murtumille (yli vuorokauden hoitojaksoa vaativille), sekä lieville murtumille (alle vuorokauden hoitojaksoa vaativille).

Tulostemme perusteella alatiesynnytys on yleisellä tasolla äidille mahdollinen ja yleisesti turvallinen lantiomurtumien, selkärankamurtumien tai -operaatioiden, sekä aivovammojen jälkeen. Ennenaikaiset synnytykset, toimenpiteelliset alatiesynnytykset, puudutukset synnytyksen yhteydessä, sekä vastasyntyneen tehohoidon tarve olivat kuitenkin yleisempiä aivovamman jälkeen. Aivovammojen historia tulisi tiedostaa mahdollisena tekijänä vaikuttamassa synnytykseen ja vastasyntyneen terveyteen. Lisäksi totesimme, että naisilla, joilla on lonkan, reiden, tai lantion murtuma on alhaisempi lisääntyvyys viiden vuoden ajan trauman jälkeen. Raskauden aikana tupakoivilla naisilla on suurempi riski saada murtuma synnytyksen jälkeen kuin tupakoimattomilla.

CONTENTS

ABBREVIATIONS

aHR	Adjusted hazard ratio
aOR	Adjusted odds ratio
CI	Confidence interval
CS	Cesarean section
DAG	Directed acyclic graph
HR	Hazard ratio
ICD-10	International Classification of Diseases version 10
LBW	Light birth weight
MBR	Medical Birth Register
OR	Odds ratio
SD	Standard deviation
SES	Socioeconomic status
TBI	Traumatic brain injury
THL	National institute of Health and Welfare
WHO	World Health Organization

ORIGINAL PUBLICATIONS

Publication I Vaajala M, Kuitunen I, Nyrhi L, Ponkilainen V, Kekki M, Mattila VM. Pregnancy and delivery after pelvic fracture in fertile-aged women: A nationwide population-based cohort study in Finland. Eur J Obstet Gynecol Reprod Biol. 2022 Mar;270:126-132.

Publication II Vaajala M, Kuitunen I, Nyrhi L, Ponkilainen V, Kekki M, Huttunen T, Mäntymäki H, Mattila V. Pregnancy and delivery after spine fracture or surgery: A nationwide population-based register study in Finland. PLoS One. 2022 Aug 5;17(8):e0272579.

Publication III Vaajala M, Kuitunen I, Nyrhi L, Ponkilainen V, Kekki M, Luoto T, Mattila VM. Pregnancy and delivery after traumatic brain injury: a nationwide population-based cohort study in Finland. J Matern Fetal Neonatal Med. 2022 Dec;35(25):9709-9716.

Publication IV Vaajala M, Kuitunen I, Nyrhi L, Ponkilainen V, Kekki M, Huttunen TT, Mattila VM. Birth rate after major trauma in fertile-aged women: a nationwide population-based cohort study in Finland. Reprod Health. 2022 Mar 24;19(1):73.

Publication V Vaajala M, Kuitunen I, Nyrhi L, Ponkilainen V, Huttunen TT, Mattila VM. Smoking is associated with an increased risk for fractures in women after childbirth: a nationwide population-based cohort study in Finland. Acta Orthop. 2022 Nov 25;93:859-865.

1 INTRODUCTION

Major trauma can negatively affect the quality of life for many years following the initial trauma. Indeed, common problems, such as pain and discomfort, changes in normal activities, reduced mobility, anxiety and depression, and limited autonomy, can persist long after sustaining the trauma (Ulvik et al., 2008). Women are at higher risk for developing these posttraumatic complications (Born et al., 2006; Ulvik et al., 2008). Major trauma is known to affect reproductive health in both psychologic and physiologic ways (Born et al., 2006). However, to date, most studies have focused mainly on trauma and abnormalities of the reproductive system, especially of the uterus and ovaries, and the literature on the effects of other major traumas (skeletal, neural) is quite scarce (Taylor & Gomel, 2008). Moreover, although there is a great deal of information about traumas that occur during pregnancy, there is little about those that occur before pregnancy.

There are, however, some studies on the effects of major trauma, such as pelvic fractures, spine fractures, or traumatic brain injuries (TBIs), on the reproductive health of women. According to a literature review conducted in 2002, fractures of the pelvis and acetabulum during pregnancy can result in increased maternal and fetal mortality rates (Leggon et al., 2002). In addition, it appears that even though pelvic fractures can have an effect on the delivery mode, delivery vaginally is still possible after pelvic fracture in most cases (Madsen et al., 1983; Vallier et al., 2012b). According to the findings of a previous systematic review, those women who sustain a pelvic fracture have a notably higher rate of cesarean sections (CS), although the reason for this is not completely understood (Riehl, 2014).

The association between spine fractures and reproductive health is quite poorly studied, as most studies focus solely on spinal cord injuries. However, multiple studies have reported that anterior spinal surgery or scoliosis surgery can affect the mode of delivery, increase the number of CS cases, and lead to a higher rate of preterm deliveries when compared to the population who have not been operated on (Lavelle et al., 2009; Orvomaa et al., 1997; Visscher et al., 1988). Furthermore, women who have had spine surgery are reported to sustain higher rates of pregnancy and delivery-related complications (Albright et al., 2015).

The effect of TBIs on reproductive health is poorly studied. Although women who have suffered from menstrual or sexual dysfunctions after a concussion may have a lower likelihood of becoming pregnant, there is currently a lack of research exploring the impact of TBIs on reproductive health and subsequent pregnancies (Anto-Ocrah et al., 2021). Indeed, studies assessing the effects of TBI on delivery are limited to a few case reports in acute cases, where TBI has led to acute CS after performing craniotomy to lower intracranial pressure (Neville et al., 2012; Tawfik et al., 2015). TBIs can lead to menstrual cycle disturbances in women of reproductive age, with nearly half of affected women experiencing amenorrhea following the injury (Colantonio et al., 2010; Ripley et al., 2008).

2 REVIEW OF THE LITERATURE

The topic of this dissertation is major traumas and reproductive health in women. The types of traumas considered to be major in this study include fractures of the pelvic circle, fractures of the spine, traumatic brain injuries (TBIs), and fractures of the hip or thigh. This study mainly focuses on the prior traumas before pregnancies, not the pregnancy, or delivery-related traumas that occur during pregnancy. The surgical operations included in this study are those operations related to these major traumas or these anatomic locations (e.g., spine fusion surgeries due to instability). However, surgeries on the hip or thigh are not included in this study.

2.1 Pelvic fractures and surgical treatment

2.1.1 Causes, types, and severity

Due to all the strong ligaments around the area of the pelvis, the pelvic ring is a highly stable structure, which makes high-energy collisions the most common reason behind pelvic fractures (Perry et al., 2021). In addition, the pelvic ring has to be disrupted in at least two sites for displacement to occur (Perry et al., 2021). In the younger population, high-energy collisions, such as falls from height or traffic collisions, are typical causes of fractures (Lundin, Huttunen, Berg, et al., 2021). In the older population, falls from standing height are a more common cause of fracture, as the bones of the pelvic ring deteriorate with age, making them more susceptible to fractures (Boskey & Coleman, 2010; Davis et al., 2021). The severity of pelvic fractures ranges from low-energy, generally lateral compression injuries, to life-threatening unstable fracture patterns (Langford et al., 2013).

The Orthopedic Trauma Association classifies pelvic fractures into three subgroups using Tile's classification (Tile A, Tile B, and Tile C) (Tile, 1996). The classification is based on the stability and integrity of the posterior sacroiliac complex. Tile A-type fractures are stable injuries usually treated non-operatively. Tile's B-Type fractures are rotationally unstable but vertically stable fractures. They present an incomplete disruption of the posterior arch, and they can be further divided into subgroups (B1, -B3). B1 means external rotation (open-book injury), B2 means internal rotation (lateral compression injury), and B3 is bilateral. Tile's C-Type fractures are identified by translational instability resulting from the complete disruption of the posterior arch (Meinberg et al., 2018). Fracture lines are used for evaluating the overlapping and complex configuration of pelvic anatomic structures (Yeap & Budak, 2021). The basic fracture lines are shown in figure 1.

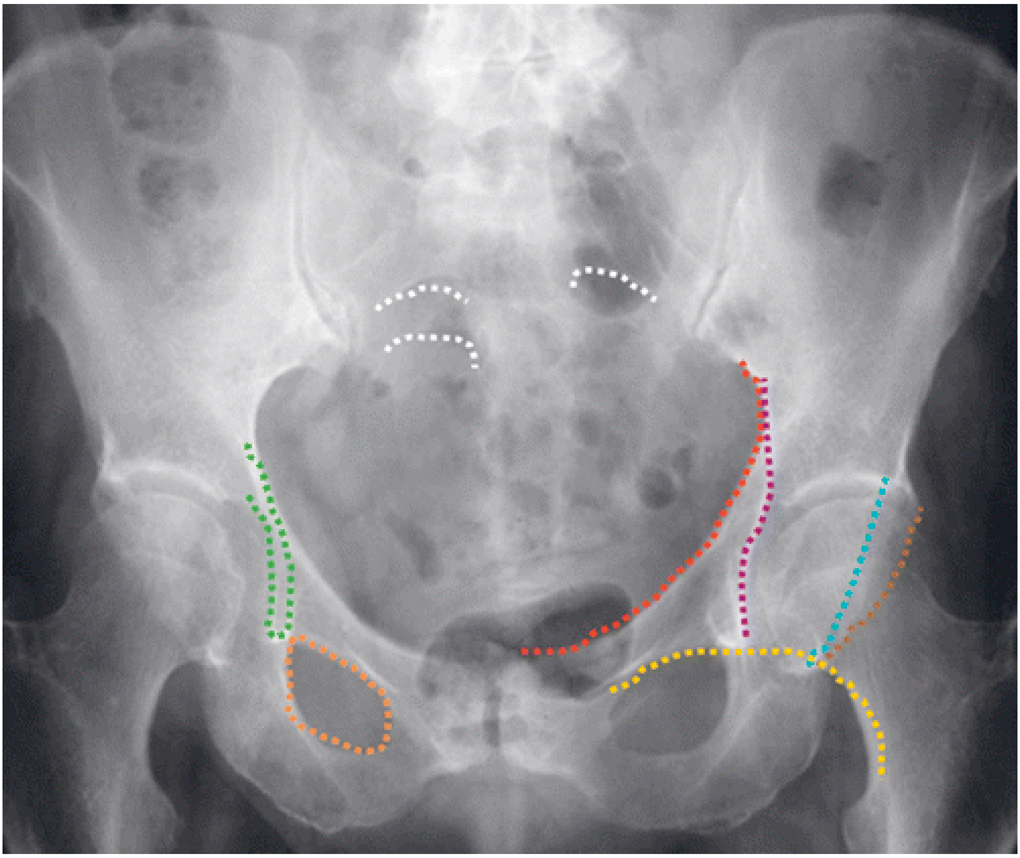

Figure 1. The key contour lines for evaluating the pelvis in an anterior-posterior radiograph: teardrop (green), obturator (orange), iliopectineal (red), ilioischial (purple), Shenton (yellow), anterior rim (blue), posterior rim (brown), and sacral arcs (white). Picture borrowed from the original source (Khurana et al., 2014).

The annual mortality rate after sustaining an unstable pelvic fracture during the last decade was estimated to be between 2.4% and 7.8%. Furthermore, the trend during this period was decreasing. (H.-T. Chen et al., 2019) A nationwide register study in Sweden, however, found that during the years 2001-2016, the 1-year mortality rate was more than 20% for patients aged 50 years and older, but less than 2% for the 18-49 years age group, meaning that pelvic fractures appear to be more often fatal in the older population (Lundin, Huttunen, Enocson, et al., 2021).

2.1.2 Epidemiology

Pelvic fractures make up around 1.5% to 3% of all skeletal injuries (Hodgson, 2009). In Sweden, the incidence of pelvic fractures among the whole female population ranged from 64 to 80 per 100 000 person-years, and the incidence of acetabular fractures from 58 to 73 per 100 000 person-years (Lundin, Huttunen, Berg, et al., 2021). According to the same study, the incidence of pelvic fractures in the younger population was approximately 20 per 100 000 person-years (Lundin, Huttunen, Berg, et al., 2021). In Finnish adults, the overall incidence of hospitalization for a pelvic fracture increased from 34 to 56 per 100 000 person-years between 1997 and 2014. The same study observed that the incidence of pelvic fracture surgery also increased between 1997 and 2014, increasing from 3.0 in 1997 to 4.3 per 100 000 person-years in 2014 (Rinne et al., 2020).

2.1.3 Surgical treatment of pelvic fractures

The choice of diagnostic and therapeutic approaches employed in treating pelvic ring fractures is contingent upon several factors, including the patient's attributes, the mechanism of injury, and their hemodynamic condition upon admission (McCormack et al., 2010). According to a study published in 2011, conservative treatment is the treatment of choice for Tile's type A fractures, and an external fixator can be used for treating Tile's type B fractures (including all 18 subtypes) (Grubor et al., 2011). An internal fixation as monotherapy or together with an external fixator can be used for treating Tile's type C fractures (Grubor et al., 2011).

Among the Finnish adult population between 1997 and 2014, approximately 8.2% of all pelvic fractures required surgical treatment (Rinne et al., 2020). The main aim of the surgical treatment of a pelvic fracture is to restore stability and allow mobilization and healing (Kleweno et al., 2020). In addition, surgical intervention for pelvic fractures can result in quicker patient mobilization and a shortened recovery period compared to conservative treatment, ultimately leading to decreased overall treatment expenses (Grubor et al., 2011). Plate fixation for anterior ring stabilization alone has conventionally been the recommended treatment for open-book injuries; however, some reports have shown treatment failures using this approach (Moed et al., 2019). As a result, this management strategy has been reconsidered. According to an international survey among experienced trauma surgeons, complications with anterior fixation alone have led many surgeons, especially those who entered clinical practice more recently, to add posterior fixation, even though the data determining its indications is currently limited (Moed et al., 2019). Moreover, according to the latest study on complications after the surgical treatment of pelvic fractures, the rate of urgent reoperation after pelvic fracture surgery was high, as well as the rate of other adverse events treated non-surgically (Lundin & Enocson, 2022).

2.1.4 Prior pelvic fracture and pregnancy

Pelvic fractures before, or during pregnancy are relatively rare and most of the studies that focus on these events are case reports (Lo et al., 2009). In a literature review conducted in 2002, fractures of the pelvic ring or acetabulum during pregnancy were associated with a high maternal and higher fetal mortality rate (Leggon et al., 2002). In the same study, when assessing the potential causes of fetal mortality, direct trauma to the fetus, placenta, or uterus was not associated with a higher fetal mortality rate when compared with maternal hemorrhage (Leggon et al., 2002).

The physiologic changes occurring during pregnancy and delivery, include an increase in anterior, and posterior width (Morino et al., 2019), small changes in the pubic area, and greater separation of anterior portions of sacroiliac joints (Sakamoto et al., 2021). It has been also reported, that anterior width changes of the pelvis are not recovered at one-month post-childbirth (Morino et al., 2019). The width of the pubic symphysis may reach 9 mm during pregnancy (Stolarczyk et al., 2021). Pregnant women who do not exhibit symptoms typically have a symphyseal width of 6.3 mm on average, whereas those with a width of 9.5 mm or greater are more likely to experience symphyseal pain (Schoellner et al., 2001). Plating of the injured pubic symphysis reduces the diastasis of the pubic symphysis regardless of the fixation method (Grimshaw et al., 2012).

To date, studies assessing deliveries and pregnancies after pelvic fractures are limited to a few studies. Even though pelvic fractures have affected the delivery mode, it seems that delivery vaginally is still possible after pelvic trauma in most cases (Madsen et al., 1983; Vallier et al., 2012b). Indeed, vaginal delivery was possible even after operatively treated pelvic fracture with associated damaged pubic symphysis (Cannada & Barr, 2010). However, pelvic ring fractures can impact the sexual wellbeing of women of childbearing age, leading to discomfort during sexual intercourse and sexual dysfunction (Cannada & Barr, 2010).

A previous systematic review reported that women who sustain a fracture of the pelvis have a notably higher proportion of CS, the proportion increasing up to 60% (Riehl, 2014). However, the reason for this is not fully understood (Riehl, 2014). Fracture patterns, retained hardware, and minor malalignment are not absolute indications of CS (Vallier et al., 2012b). In fact, a prior pelvic fracture did not have a demonstrable effect on pregnancy outcomes in the systematic review, and the higher rate seemed to be at least partly caused by patient and obstetrician bias (Riehl, 2014). According to Copeland et al., patients who experienced pelvic fractures with dislocations greater than 5 mm were at a higher risk for CS (Copeland et al., 1997). However, the same study also reported that previous pelvic fractures did not have an important effect on miscarriage or fertility (Copeland et al., 1997).

When the mode of delivery itself is not considered, there have been no published studies that have reported major challenges during pregnancy after pelvic fracture. However, chronic symphyseal instability, which can also be caused by the trauma of the pelvis, is known to be a challenging problem during pregnancy (Amorosa et al., 2013; Herren et al., 2016). The summary of the previous literature on pregnancies and deliveries with a history of pelvic fractures is shown in table 1.

Table 1. Summary of the previous literature on pregnancies and deliveries with a history of pelvic fractures.

Author and year	Study design	Patients	Aim	Conclusion
(Madsen et al., 1983)	Follow-up study	34 women with 34 pregnancies	Evaluate the pregnancy outcomes of obstetric patients with a history of pelvic fracture	When it comes to subsequent parturition, separation of the symphysis due to a pelvic fracture is a more severe complication than displacement of the bony birth canal
(Copeland et al., 1997)	Retrospective review	123 women	Evaluate the impact of a pelvic fracture on a woman's physical, sexual, and reproductive functioning	Female patients who experienced pelvic trauma had their reproductive function negatively impacted, leading to an increased rate of cesarean section
(Jeys et al., 2003)	Questionnaire of women from a prospectively kept database	8 women with 8 pregnancies	Investigate the fears of patients who required surgical stabilization for pelvic fractures, and assess the pregnancy outcomes	Numerous patients express concerns regarding future pregnancies and the potential for complications after experiencing a pelvic injury
(Cannada & Barr, 2010)	Retrospective review	26 women with 26 pregnancies	Questionnaire for women with a history of pelvic fractures about the subsequent pregnancies	Although a high rate of cesarean section was observed, vaginal delivery was still a viable option even for patients who underwent surgical fixation without affecting the pubic symphysis.
(Vallier et al., 2012b)	Retrospective review with prospective collection of obstetric information.	16 women with 25 pregnancies	Evaluate outcomes of pregnancy after pelvic ring injury	Despite pelvic fractures, pregnancies and deliveries without complications are still possible.
(Riehl, 2014)	Systematic review	148 women with 148 pregnancies	Examine the caesarean section rate in patients with prior pelvic fractures.	Patients with prior pelvic fractures have higher cesarean section rates, but the reason for this is not entirely understood

2.2 Spine fractures and surgical treatment

2.2.1 Causes and severity

Spinal fractures commonly result from high-impact injuries among young individuals and from low-impact incidents in older adults. Such fractures usually occur anatomically near the junction of the thoracic and lumbar spine (most commonly in thoracic vertebrae 10-12) (Wood et al., 2014). According to the published literature, in younger patients, the most common cause of spine fractures is falling from a height, followed by traffic collisions and collisions in sports (Leucht et al., 2009). In younger patients, the majority of spine fractures are caused by high-energy collisions and are located in the thoracic or lumbar vertebrae (Leucht et al., 2009). A large epidemiologic study in China reported that cervical spine fractures were significantly more common among patients injured in traffic collisions, and lumbar spine fractures were more common among patients with accidental falls (Wang et al., 2012). However, the most common area of fracture was still the thoracolumbar spine (Wang et al., 2012).

The current classification for thoracolumbar spine fractures is based on three major groups, in order of increasing severity: A meaning compression injuries, B meaning distraction injuries, and C meaning displacement/translational injuries (Aebi, 2010). Computer-generated 3D images of different types of fractures in the thoracolumbar spine are shown in Figure 2. According to a national follow-up study in Korea, mortality after vertebral fractures was higher in younger patients. The higher mortality was caused by multiple factors, such as neurologic, circulatory, respiratory, or digestive disorders, muscular diseases, or neoplasms (Choi et al., 2020).

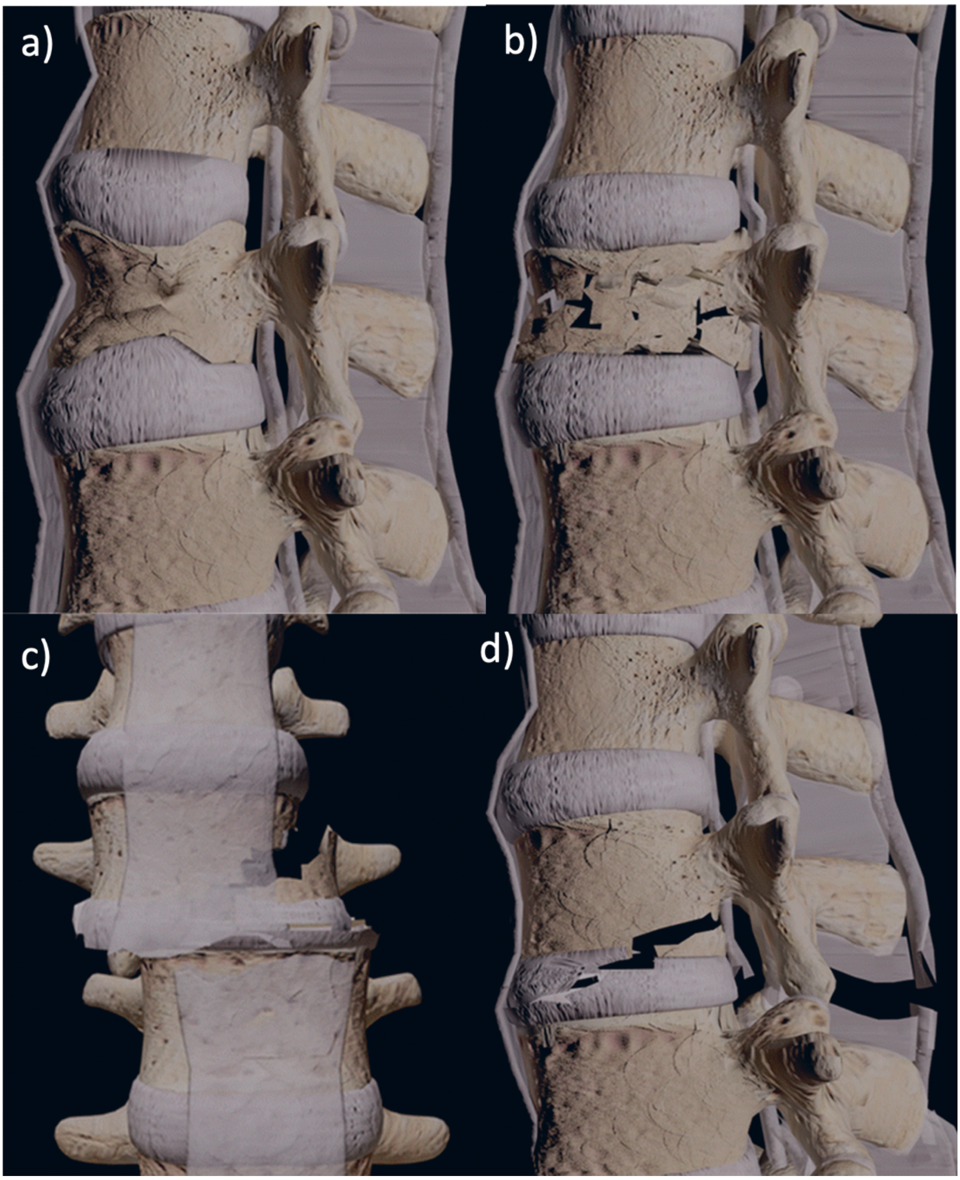

Figure 2. Computer-generated 3D images showing the different types of thoracolumbar spine fractures: compression fracture (a), compression with burst fracture (b), translation or rotation injury (c), and distraction injury (d). Images borrowed from the original source (Khurana et al., 2013).

2.2.2 Epidemiology

In Finland, the incidence of spine fracture hospitalizations increased from 57 per 100 000 person-years (1998) to 89 per 100 000 person-years (2017) among Finnish adults over 20 years of age (Ponkilainen et al., 2020). A corresponding increase was also observed in the incidence of spine fracture surgeries, which increased from 5.3 per 100 000 person-years (1998) to 8.8 per 100 000 person-years (2017) (Ponkilainen et al., 2020). Among women, a strongly increasing trend in the rate of spine fracture surgeries (147%) was observed (Ponkilainen et al., 2020). In Norway, the incidence of cervical spine fractures was estimated to be approximately 11.8 per 100 000 person-years (Fredø et al., 2012). Scoliosis surgery is also a common procedure in younger populations. Between 2000 and 2013, the estimated annual incidence of scoliosis surgery in Sweden was 12.5 per 100,000 person-years, with women showing a noticeable trend of increasing rates (Von Heideken et al.). Generally, the published literature about the epidemiology of spine fractures and major spine surgeries is quite limited.

2.2.3 Surgical treatment of the spine

Surgical treatment of the spine is known to be a clinically beneficial procedure in many situations, such as spinal stenosis decompression, symptomatic lumbar disc herniation, and decompression and fusion surgery for degenerative spondylolisthesis, providing an important clinical benefit in the face of serious back and radicular pain when compared with conservative treatment (Allen et al., 2009). In addition, the surgical treatment of lumbar and thoracic spine fractures is known to be a relatively safe and effective procedure and postoperative complications are rare events (Verlaan et al., 2004). Furthermore, the functional outcome after a surgically treated spine fracture seems to be better than can be believed (Verlaan et al., 2004). However, women are reported to have more complex lumbar spine surgeries than men (Grotle et al., 2019a).

Spine fusion surgery is a highly effective procedure for many conditions, including instability and deformity due to tuberculosis, scoliosis, and traumatic injury (Reisener et al., 2020). The indications for spine fusion surgery have broadened over time, with the procedure also being a solution for diseases, such as congenital or degenerative deformity, spinal tumors, spondylolisthesis, and pseudarthrosis, with degenerative disorders being the most common indication (Reisener et al., 2020) (Figure 3).

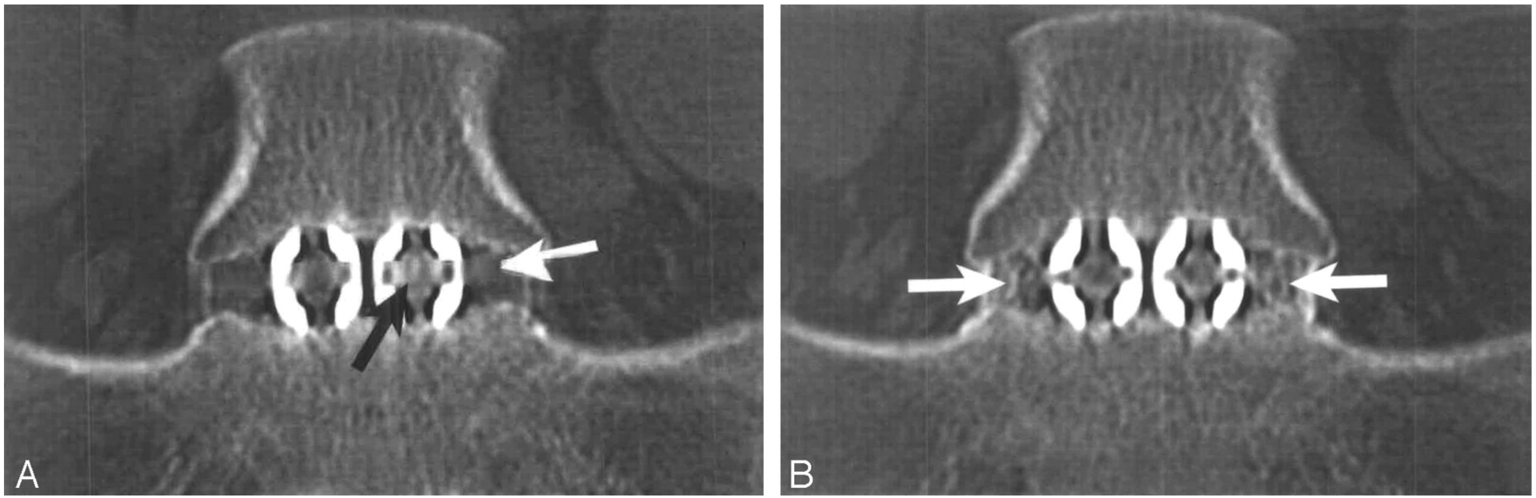

Figure 3. The normal progression of an interbody fusion in a coronal CT image at 6 months (A) and 10 months (B) in a 28-year-old woman. New bone formation is evident within (black arrow) and adjacent to (white arrow) (A). After 10 months, additional new bone formation, especially lateral to the fusion devices (white arrows) can be seen. Borrowed from the original source (Williams et al., 2005).

2.2.4 Prior spine fracture or surgery and pregnancy

Pregnancy-related osteoporosis increases the risk of multiple vertebral fractures, and it is often promoted as a risk factor before or during pregnancy (Laroche et al., 2017). According to the findings of a recent multicenter case series, spinal surgical procedures performed during pregnancy seem to be safe (Butenschoen et al., 2021). Nonetheless, strict criteria must be met for surgery to be recommended, and surgical interventions during pregnancy ought to be reserved exclusively for emergency situations (Butenschoen et al., 2021). Indeed, positioning issues with spine surgery during pregnancy have been reported and the operation should therefore be planned carefully (Bongetta et al., 2020).

The current literature on the effects of spine fractures and surgeries on subsequent pregnancies is truly limited. When compared to conservatively treated women, anterior spinal surgery or scoliosis surgery increased the number of CS cases and led to a higher rate of preterm deliveries (Lavelle et al., 2009). Furthermore, women undergoing spine surgery have been reported to have increased rates of pregnancy and delivery-related complications (Lavelle et al., 2009). However, a previous local study examining pregnancy outcomes after surgically treated scoliosis did not observe important differences in delivery rates or in neonatal health (Orvomaa et al., 1997). In addition, a small study in 2012 about pregnancies after microsurgery for lumbar disc herniation found high rates of low back and leg pain during pregnancy (Berkmann & Fandino, 2012). However, no delivery or fetal outcomes were reported in this study (Berkmann & Fandino, 2012). Also, women with scoliosis have been reported to have a higher rate of premature births, but the rates of other adverse reproductive events appear not to be increased (Visscher et al., 1988). A summary of the previous literature on pregnancies and deliveries with a history of spine fractures or spine surgeries is shown in table 2

Table 2. Summary of the previous literature on pregnancies and deliveries with a history of spine fractures or spine surgeries.

Author and year	Study design	Number of patients	Aim	Conclusion
(Visscher et al., 1988)	Retrospective cohort study	1409 women with 1733 pregnancies	Study reproductive outcomes in patients with scoliosis	When compared with the expected rates, scoliosis patients showed a higher incidence of premature births, but there was no important difference in their rates of other unfavorable reproductive events.
(Orvomaa et al., 1997)	Prospective follow-up study	142 women with 142 pregnancies	Study the pregnancy course and outcome in patients operated by the Harrington method for idiopathic scoliosis	The proportion of cesarean section deliveries among children was higher than that of the general population, but this finding should only be considered suggestive and requires further investigation.
(Lavelle et al., 2009)	Retrospective chart review combined with a telephone questionnaire	19 women with 19 pregnancies	Determine the fertility, cesarean section rate, and the use of neuraxial anesthesia in women with prior anterior spinal surgery.	Despite the seemingly high rate of cesarean sections, it aligns with current obstetrical trends.
(Berkmann & Fandino, 2012)	Retrospective study combined with a questionnaire	26 women with 39 pregnancies	Report the course of pregnancies after lumbar discectomy	The occurrence of radicular pain during pregnancy following microsurgical discectomy for lumbar disc herniation was found to be 18%. Additionally, the incidence and prevalence of low back pain were noted to be among the highest reported in the literature.

2.3 Traumatic brain injuries and surgical treatment

2.3.1 Causes and severity

Traumatic brain injury (TBI) may occur as a result of trauma, which can vary from a minor impact to the head to a penetrating injury that affects the brain (Georges & M Das, 2022). Traffic accidents, falls, and high-impact sports activities are the most frequent causes of TBIs (Ng & Lee, 2019).

Patients with TBIs are reported to have higher mortality rates when compared to the general population (Groswasser & Peled, 2018; Miller et al., 2021). However, the mortality rate depends a lot on the severity of the injury (Groswasser & Peled, 2018; Miller et al., 2021). The overall mortality rate, including all TBI severities, is approximately 3% (Georges & M Das, 2022). However, the morbidity of TBIs is more challenging to estimate (Georges & M Das, 2022). In a previous Finnish study assessing the mortality rate of TBIs, the mortality rate was estimated to be approximately 18 per 100 000 person-years. In addition, the mortality rate was reported to be higher among women (Koskinen & Alaranta, 2008).

2.3.2 Epidemiology

TBIs have been recently found to be an increasing global health problem (Johnson & Griswold, 2017). Indeed, it has been estimated that TBIs are annually affecting more than 10 million people worldwide (Hyder et al., 2007). According to a comprehensive investigation conducted in the United States, around 1.7 million individuals experience TBIs each year (Georges & M Das, 2022). In addition, the population most likely to sustain a TBI was found to be adolescents between the ages of 15 and 19, and adults aged 65 and older (Georges & M Das, 2022). An international study assessing the worldwide incidence of TBIs estimated the global incidence of TBIs is approximately 369 per 100 000 person-years (GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators). As per reports, the average rate of hospitalized TBI for women in Finland between 1991-2005 was around 80 per 100 000 person-years. (Koskinen & Alaranta, 2008).

2.3.3 Types of traumatic brain injuries

There are 5 commonly encountered types of TBI: concussions, extra-axial hematomas, contusions, traumatic subarachnoid hemorrhages, and diffuse axonal injuries (Georges & M Das, 2022).

Concussion, also known as mild TBI, is known to be a common public health concern affecting millions of people annually. A concussion is defined as a traumatically induced transient disturbance of brain function (Harmon et al., 2013). A concussion can occur as a result of either a direct or due to indirect hit to the head, such as movement of the brain within the skull (Ferry & DeCastro, 2022). A direct traumatic blow to the head is considered a significant cause of concussion by healthcare providers (Ferry & DeCastro, 2022). However, forces on the body can also indirectly cause a concussion (McCrory et al., 2017). Experimental evidence suggests that the brain is less responsive to usual neural activation after concussions (Harmon et al., 2013). In addition, premature cognitive or physical activity occurring before complete recovery of the brain may cause prolonged dysfunction (Harmon et al., 2013).

Extra-axial hematomas include both epidural and subdural hematomas. Both are common clinical entities after TBI, and they are often occurring in the same patient (Aromatario et al., 2021). Subdural hematomas are generally associated with high-energy collisions, especially traffic accidents (Karasu et al., 2010). Epidural hematomas are most commonly caused by motor vehicle accidents and fall from height (Basamh et al., 2016). According to an analysis of a Singapore neurotrauma database, subdural hematomas are much more frequently caused by severe TBIs than epidural hematomas (Han et al., 2017). In addition, subarachnoid hemorrhage is usually caused by high-energy injuries, and it is known to be severe trauma (Modi et al., 2016).

Cerebral contusion is caused by trauma to the head and can cause permanent damage to tissues of the cerebrum (Pellot & De Jesus, 2022). Contusions are known to progress and expand and in many patients, other hemorrhagic contusions are present (Pellot & De Jesus, 2022). Hemorrhagic contusions are found to overlie brain parenchyma and cause loss of function (Pellot & De Jesus, 2022). Diffuse axonal injuries can underlie mild to moderate TBI and potentially result from any twisting, shearing, or stretching injuries to the axons of the neurons (Georges & M Das, 2022).

2.3.4 Surgical treatment of head traumas

The current available surgical options to head traumas are cisternostomy, decompressive craniectomy, and other methods, mainly to divert cerebrospinal fluid (e.g., placement of an external ventricular drain) (Bullock et al., 2006). The main aim of these options is to control increased intracranial pressure and to prevent secondary brain damage in the setting of severe TBIs (Bullock et al., 2006). Cerebral hematomas, especially subdural and epidural hematomas, are the most common type of TBIs requiring surgical treatment (Bullock et al., 2006). During a craniotomy, a section of the skull is temporarily taken out to gain access to the brain and perform an intracranial procedure. Brain tumors, aneurysms, arterio-venous malformations, subdural empyema or hematomas, and intracerebral hematomas are the most common conditions treated with this procedure (Fernández-de Thomas & De Jesus, 2022). Craniectomy is a procedure, where the bone flap is not placed back into the skull during the same operation, which is usually a decompressive procedure for the treatment of malignant brain edema (Fernández-de Thomas & De Jesus, 2022). Cisternostomy seems to be a more physiological approach to brain swelling, but this topic has had some controversies (Giammattei et al., 2018).

2.3.5 Prior traumatic brain injury and pregnancy

The literature about the effects of TBI on the subsequent fertility, pregnancies, and deliveries of women is currently limited. TBIs are reported to cause disorders in the menstrual cycle, and nearly half of the women with TBIs report amenorrhea following the trauma (Colantonio et al., 2010; Ripley et al., 2008). Even though women who have experienced menstrual or sexual dysfunctions after a concussion are found to have a decreasing incidence of pregnancies, there are no previous studies assessing the effects of TBIs on subsequent reproductive health and pregnancies (Anto-Ocrah et al., 2021). Indeed, studies assessing the effects of TBI on delivery are limited to a few case reports in acute cases, where TBI has led to acute CS after performing craniotomy to lower intracranial pressure (Neville et al., 2012; Tawfik et al., 2015). However, the long-term effects of TBIs on subsequent fertility, deliveries, and neonatal health have not been studied previously. A summary of the previous literature on pregnancies and deliveries with a history of TBIs is shown in table 3.

Table 3: Summary of the previous literature on pregnancies and deliveries with a history of traumatic brain injuries (TBIs).

Author and year	**Study design**	**Number of patients**	**Aim**	**Conclusion**
(Ripley et al., 2008)	Telephone interview	30 women	To determine the impact of TBI on female menstrual and reproductive functioning	The seriousness of TBI was indicative of the length of amenorrhea, with more severe cases having longer periods of amenorrhea, and less severe cases having shorter periods.
(Colantonio et al., 2010)	Retrospective cohort study	104 women	To examine the health outcomes relevant to premenopausal women 5-12 years after injury	The aforementioned discoveries provide insights into the prognosis for women following a TBI and emphasize the importance of long-term monitoring of health outcomes and heightened support after childbirth.
(Anto-Ocrah et al., 2021)	Longitudinal cohort study	102 women	To evaluate pregnancy outcomes after concussion in a cohort of reproductive-aged women	Our study has the potential to raise awareness about the enduring reproductive impacts of concussions in females.

2.4 Hip or thigh fractures

2.4.1 Causes, classification, and severity

In the younger population, hip fractures, and thigh fractures are usually caused by high-energy trauma, such as motor-vehicle collisions or falls from height (Denisiuk & Afsari, 2022; Emmerson et al., 2022). Patients with hip fractures have most likely incurred multiple injuries (Denisiuk & Afsari, 2022; Emmerson et al., 2022). In the elderly population, however, falls have been estimated to cause over 95% of hip fractures (Parkkari et al., 1999). There are numerous risk factors for falls in the older population. However, the most common factors with a strong independent association are a previous history of falls, the use of walking aids, gait abnormalities, Parkinson's disease, vertigo, and antiepileptic medications (Parkkari et al., 1999). Another type of hip fracture is pathological hip fracture, which is caused by a disease process and is not related to trauma (Emmerson et al., 2022). Malignancy and bisphosphonate use are the most common types of pathological hip fractures (Emmerson et al., 2022). However, pathological hip fractures caused by osteoporosis might be much more common, but this group is rarely labeled in this way (Emmerson et al., 2022).

There are currently three different classifications for hip fractures: Garden's classification (Figure 4a), Pauwel's classification (Figure 4b), and AO/OTA (Figure 4c) (Lu & Uppal, 2019). The Garden classification relies on anteroposterior radiographs of the hip, which comprise four fracture types (Type I-IV). Type I includes incomplete and valgus impacted fractures, Type II complete and nondisplaced fractures, Type III complete and partially displaced fractures, and Type IV complete and fully displaced fractures (Kazley et al., 2018). Pauwel's classification determines the shearing stress and compressive force by calculating. The angle between the fracture line of the distal fragment and the horizontal line. There are three types of fractures in this classification: Type I fractures have an angle of less than 30°, type II fractures have an angle between 30° and 50°, and type III fractures have an angle greater than 50° (Shen et al., 2016). The AO/OTA classification system is used for the classification of all fractures but is mostly used for research purposes (Lu & Uppal, 2019).

Especially in the elderly, hip fractures are associated with high mortality rates (Cree et al., 2000; Guzon-Illescas et al., 2019). It is estimated that the mortality of elderly patients is over 20% during one-year follow-up after hip fracture (Schnell et al., 2010). According to a retrospective study in 2021, the leading causes of mortality were pneumonia (19.4%), diseases of the circulatory system (16%), and dementias (13.9%) (Barceló et al., 2021). A total of 3.2% of the patients died from causes directly related to hip fractures or surgery (Barceló et al., 2021). In the younger population, however, it appears that the survival rate is relatively high. A study in 2014 found that the 10-year survival rate for the population aged between 20 and 40 was over 90% (Lin et al., 2014). In addition, the 10-year complication-free rates were around 70% (Lin et al., 2014). A recently published study in Finland found that the mortality rate after hip fractures was 7% at 1 month, 22% at 12 months, and 87% at 14 years (Tiihonen et al., 2022). However, men have been found to have higher mortality after hip fractures than women (Kannegaard et al., 2010). According to a Finnish study, the lifetime risk for hip fractures was ranging between 6% and 18% in women and between 5% and 6% in men (Kannus et al., 1996).

The severity of thigh fractures depends a lot on the type of fracture, but these are known to cause increased mortality and mortality (Kobbe et al., 2013). A study investigating the incidence of different types of femoral fractures found that the incidence of stable fractures was 14.3 per 100,000 per year, the incidence of borderline fractures was 1.8 per 100 000 per year, the incidence of unstable fractures was 0.8 per 100 000 per year, and the incidence of extremis fractures was 0.5 per 100,000 per year (Enninghorst et al., 2013). Patients with bilateral femoral shaft fractures tend to experience more severe abdominal injuries and blood loss, leading to a higher mortality rate.

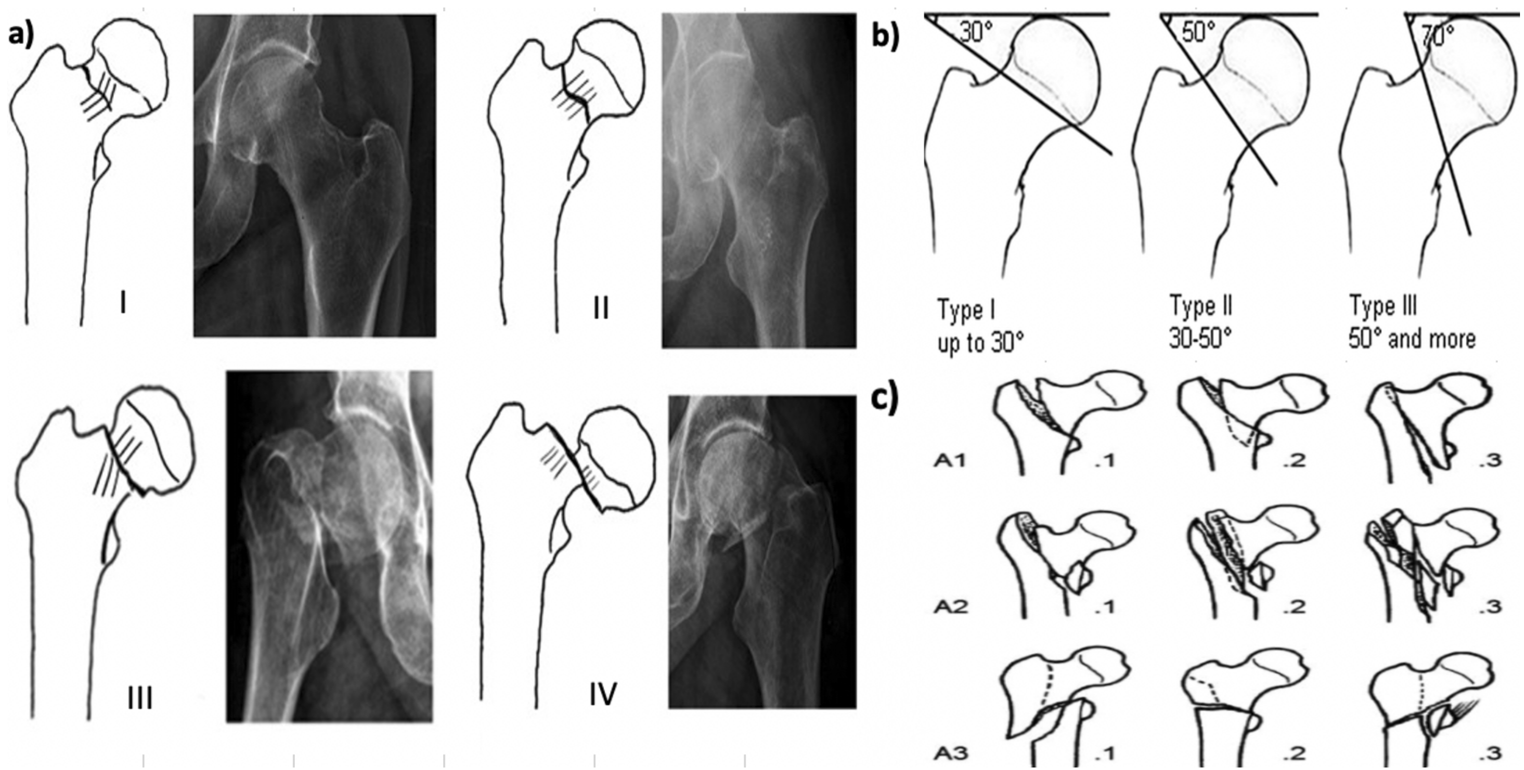

Figure 4. Three types of classifications for hip fractures: Garden's classification (a), Pauwel's classification (b), and AO/OTA (c). The pictures are borrowed from the original sources (Kazley et al., 2018; Lu & Uppal, 2019; Shen et al., 2016).

2.4.2 Epidemiology

The rates for hip fractures were highest in North Europe and the United States, and the lowest in Latin America and Africa (Dhanwal et al., 2011). Especially Norway and Sweden had a high incidence of hip fractures among women. The reported annual incidence rate of hip fracture is 920 per 100 000 persons in Norway, and the incidence has been found to be decreasing in Sweden. (Lofthus et al., 2001; Meyer et al., 2021) In addition, the incidence of hip fractures has had a decreasing trend during the last decades in Finland (Kannus et al., 2018). Especially among women, the age-adjusted incidence has decreased from 538 per 100 000 persons in 1997 to 344 per 100 000 persons 344 in 2016 (Kannus et al., 2018).

The global annual incidence of femoral shaft fractures ranges between 10 and 21 per 100,000 (Denisiuk & Afsari, 2022). However, according to a Finnish study, the incidence of femoral shaft fractures was 9.9 fractures per 100 000 person-years (Salminen et al., 2000). Injuries to the femoral shaft are frequently encountered and treated by orthopedic surgeons. (Denisiuk & Afsari, 2022).

2.4.3 Hip or thigh fracture and pregnancy

Femoral fractures during pregnancy are truly rare complications. The incidence of these was reported to be approximately 1% of all pregnancies (Harold et al., 2019). The main causes of hip fractures during pregnancy were reported to be transient osteoporosis of the hip and occult stress fractures of the femoral (Meyer & Modig, 2021).

There are few studies about the effects of hip fracture history on subsequent reproductive outcomes. According to a study in 2015, women who experience proximal thigh trauma are more likely to suffer from sexual dysfunction, especially those who are younger (Shulman et al., 2015). However, the same study found that after a one-year follow-up, the majority of women with proximal thigh traumas only reported mild or no sexual dysfunction, with few exceptions. (Shulman et al., 2015). Most studies on this topic have focused on the reproductive outcomes after total hip replacement. In 2001, a small study concluded that vaginal delivery is possible after a total hip replacement (McDowell & Lachiewicz, 2001). A study in 2005 found that childbirth was not affected among women with a total hip replacement, but in these patients, pain in the hip is common during pregnancy (Sierra et al., 2005). However, a Finnish study in 2019 found that women with previous total hip replacement had a higher risk for emergency CS, and neonates have an increased risk of low birth weight, preterm births, stillbirths, and small for gestational age (Kuitunen et al., 2019). The summary of the previous literature on pregnancies and deliveries with a history of hip fractures or operations is shown in table 4.

Table 4: Summary of the previous literature on pregnancies and deliveries with a history of hip or thigh fractures or operations.

Author and year	**Study design**	**Number of patients**	**Aim**	**Conclusion**
(McDowell & Lachiewicz, 2001)	Prospective cohort study	5 women with 5 pregnancies	To report on a series of women who had completed a pregnancy after a total hip arthroplasty	There is evidence to suggest that a successful pregnancy and uncomplicated vaginal delivery can take place without risk following total hip arthroplasty.
(Shulman et al., 2015)	Retrospective analysis of prospectively collected data.	70 women	To investigate the prevalence and longitudinal improvement of patient-reported sexual dysfunction after 5 common nonpelvic orthopedic traumatic conditions	Sexual dysfunction is a common issue experienced by a high number of patients following a hip fracture, with women reporting a higher incidence of dysfunction compared to men.
(Sierra et al., 2005)	Telephone questionnaire	108 patients with 108 pregnancies	To study pregnancy and childbirth in a large group of patients who had undergone a total hip replacement and to determine the effect of childbirth on the subsequent survival of the implant	Childbirth is not affected by the presence of a total hip replacement, but the pain in the hip is common during pregnancy in these patients
Kuitunen et al., 2019)	Retrospective cohort study	1190 women with 1190 pregnancies	To evaluate whether maternal total hip replacement affects pregnancy outcomes on a population-based level.	Neonates who are born to mothers who have undergone total hip replacement are at a heightened risk of stillbirth, being small for gestational age, having low birth weight, and being born prematurely. Additionally, there is a higher likelihood of a trial of labor resulting in an emergency cesarean section.

2.5 Pregnancy and delivery

2.5.1 Pregnancies and deliveries in Finland

According to Statistics Finland and the Finnish Institute for Health and Welfare (THL), the total number of deliveries in Finland has been decreasing since 2010, which is partly explained by the decreasing number of fertile-aged females living in Finland (Nordberg, 2020; THL, 2018b) (Figure 5).

Since 2007, the most common methods of pain relief during vaginal delivery were epidural anesthetics (40-48%), nitrous oxide (49-55%), and non-pharmaceutical pain relief. The use of non-pharmaceutical pain relief techniques, such as water birth, and transcutaneous electrical nerve stimulation, has increased from 23% in 2007 to 56% in 2020 (THL, 2018b).

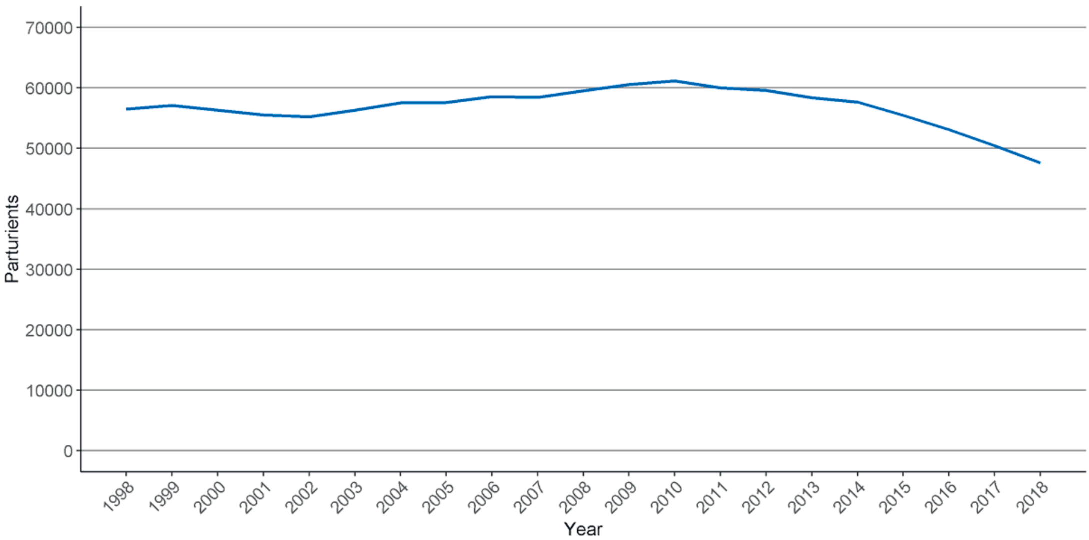

Figure 5. The annual number of parturients born in Finland during the study period (1998-2018). The data were obtained from Statistics Finland (stat.fi).

2.5.2 Delivery methods, briefly

In the Finnish national Medical Birth Register, the mode of delivery is categorized as spontaneous vaginal, vacuum or forceps delivery, breech delivery, or cesarean section (CS) (THL, 2018b). It has been reported, that of all full-term singleton vaginal deliveries, approximately 80% are spontaneous vaginal deliveries (Desai & Tsukerman, 2022). However, the number of women with spontaneous vaginal delivery has decreased over time, and the rate of labor induction has increased ("ACOG Practice Bulletin No. 107," 2009).

The utilization of forceps or a vacuum extractor to aid vaginal delivery is a crucial aspect of the obstetric practice (Keriakos et al., 2013). Indications for an operative vaginal delivery are non-reassuring fetal status, no progress from 30 minutes of adequate active pushing, maternal exhaustion, or medical indications to avoid Valsalva (Sentilhes et al., 2008). According to the findings of a large register-study in Ireland, the incidences of operative vaginal deliveries were 11.4 per 100 deliveries, when all deliveries were included, and 13.6 per 100 deliveries, when only vaginal deliveries were included (Hehir et al., 2013). In Finland, the rate for vacuum or forceps deliveries was 8% to 10% during the years 2007-2020. However, the proportion of forceps deliveries in Finland has decreased strongly, and today they are truly rare events (THL, 2018b).

A breech presentation occurs in 3-4% of all full-term pregnancies (Gray & Shanahan, 2022). However, in Finland, the rate for breech deliveries is approximately 2.2% (Macharey, 2018). Breech presentation is a term used to describe the position of a fetus in which the buttocks or lower extremities are positioned to enter the pelvis first, while in a longitudinal lie (Gray & Shanahan, 2022).

Breech presentation can be classified into three types: frank breech, complete breech, and incomplete breech. A fetus with a frank breech has both hips flexed, and its legs are straight with feet positioned near the fetal face in a pike position (Gray & Shanahan, 2022). Complete breech occurs when the fetus sits with both hips flexed and both legs in a tucked position, while incomplete breech can present in various ways, with the fetus having one or both hips extended (Gray & Shanahan, 2022).

The delivery itself is a rough event for the musculoskeletal system, as the pelvic floor and spine are exposed to high pressure and stretch during vaginal delivery. It has been reported that approximately half of all pregnant women are likely to experience lower back pain either during pregnancy or in the postpartum period (Katonis et al., 2011). Stretching of the pelvic floor is a normal phenomenon during labor, but only some women experience injury (Ashton-Miller & DeLancey, 2009). Vaginal delivery is, however, associated with prolapse of the pelvic floor (Ashton-Miller & DeLancey, 2009).

2.5.3 Cesarean section

Cesarean section (CS) involves delivering the fetus through a surgical incision in the abdomen (laparotomy) and uterus (hysterotomy) (Sung & Mahdy, 2022). Although it carries potential risks for both short-term and long-term complications, it may be the safest or only option for some women to give birth to a healthy neonate (Sung & Mahdy, 2022). In Finland, CS can be performed as an elective, urgent, or emergency procedure. The overall proportion of CS during the last decades in Finland was approximately 16%. Since 2007, however, the annual rate for emergency CS has only been approximately 1% (THL, 2018b).

There are numerous indications for elective CS, and the decision can be made either by maternal request or suggested by a physician. According to a systematic review conducted in 2020, mothers may request an elective CS for reasons such as concerns about fetal injury or death, fear of labor pain, anxiety related to childbirth, desire to avoid long labor, previous negative delivery experiences, abnormal prenatal examination results, pelvic floor or vaginal trauma, urinary incontinence, delivery time, past infertility issues, anxiety towards the gynecologic examination, insufficient medical staff support, emotional factors, and infant's weight at birth. (Jenabi et al., 2020).

While CS is generally considered a relatively safe and efficient operation, that has played a remarkable role in decreasing mortality in neonates, it has been reported to be associated with many disadvantages for the mother and neonate following the operation. Studies have shown that neonates delivered via CS have a higher likelihood of developing asthma, obesity, and poor cardiorespiratory health later in life (Ekstrom et al., 2020; Li et al., 2013; Mueller et al., 2019). Mothers who undergo CS have been found to experience shorter breastfeeding duration and may also be at risk of future subfertility and complications in subsequent pregnancies (Hobbs et al., 2016; Keag et al., 2018; S. Liu et al., 2007; M. Ometti Bettinelli, G. ,. Candiani, M. ,. &. Salini, V., 2020).

2.5.4 Neonate outcome

The global perinatal mortality rate is estimated to be approximately 53 per 1000 live births, and the neonatal mortality rate is estimated to be approximately 36 per 1000 live births. Therefore, 7.5 million perinatal deaths and 5.1 million neonatal deaths occur annually, with 90% of these deaths occurring in low-income countries (Yu, 2003). In Finland, the mortality rate is only 1.9 per 1000 live births (The World Bank, 2020). The main reasons for neonatal mortality globally are complications of preterm birth, intrapartum-related causes, and infections (Blencowe & Cousens, 2013). Preterm labor (34%) and intrapartum asphyxia (21%) were found to be the leading obstetric causes of neonatal mortality (Jehan et al., 2009). The final causes of neonatal death were categorized as immaturity-related birth, asphyxia or hypoxia, and infection (Jehan et al., 2009). Reducing neonatal mortality is possible and maternal health should be the main focus, with free antenatal care and centralized deliveries with healthcare personnel attending the birth (Saugstad, 2011).

Preterm birth is defined as the delivery of a live-born infant before the completion of 37 weeks of gestation. According to the classification by the World Health Organization (WHO) (WHO, 2018b), preterm deliveries are categorized into 3 classes: moderate to late preterm (32 to 37 weeks), very preterm (28 to 32 weeks), and extremely preterm (less than 28 weeks). The WHO estimates that 15 million babies are born preterm every year, in other words, more than 1 in 10 babies. The global rate of preterm births is estimated to be about 11% (Walani, 2020). The annual number of children dying due to complications caused by preterm birth was estimated to be approximately 1 million (L. Liu et al., 2016). In Finland, the rate of preterm deliveries increased from 5.1% in the late 1980s to 5.4% in the late 1990s but then decreased to 5.2% between 2001 and 2005 (Jakobsson et al., 2008). In 2018, the rate for preterm deliveries in Finland was 5.8% (THL, 2018b).

According to the WHO, low birthweight (LBW) is defined as a birthweight below 2500 g, regardless of gestational age, and is usually applied to live births only (WHO, 2018a). The estimated worldwide LBW prevalence in 2000 was 17.5% and 14.6% in 2015 (Blencowe et al., 2019). According to THL, the annual rate of neonates born LBW in Finland has remained stable. In 2020, the rate for LBW neonates was approximately 4%. In addition, the rate for very LBW (under 1500 g) was 0.8% in 2020 (THL, 2018b).

2.5.5 Diabetes mellitus and gestational diabetes mellitus

Diabetes is a clinically important chronic disease that affects maternal and neonatal health. Pregnancy-related complications in women with diabetes include pre-eclampsia, preterm labor, polyhydramnios, a greater likelihood of operative delivery, and an increased risk of infection (Kulshrestha & Agarwal, 2016). These complications can be minimized with optimal glycemic control (Kulshrestha & Agarwal, 2016). Furthermore, pregnancies in women with pregestational diabetes may have diabetes-related complications, such as hypoglycemia, worsening of nephropathy, diabetic ketoacidosis, and retinopathy (Kulshrestha & Agarwal, 2016). According to the Finnish Diabetes Association, there are about 50 000 people with type 1 diabetes and 400 000 people with type 2 diabetes in Finland (Finnish diabetes association, 2022). Thus, the prevalence of diabetes is almost 10% of the whole population of Finland (Finnish diabetes association, 2022).

Gestational diabetes mellitus (GDM) is the most common medical complication that occurs during pregnancy (Alfadhli, 2015). It is known to be associated with adverse outcomes for both the mother and neonate (Alfadhli, 2015). GDM is characterized by any level of glucose intolerance that develops or is identified for the first time during pregnancy (Quintanilla Rodriguez & Mahdy, 2022). The etiology of gestational diabetes is apparently associated with either dysfunction of the beta cells in the pancreas, resulting in a delayed response to glycemic levels, or significant insulin resistance due to hormonal release from the placenta (Quintanilla Rodriguez & Mahdy, 2022). It has been found that the rates of GDM have been increasing during the past decade (Shah et al., 2021).

2.6 Birth rate

2.6.1 Birth rate

In the 1950s, each woman had an average of five children, but the current global average has decreased to around 2.5 children per woman (Our World in Data, 2017). Falling fertility rates worldwide have been suggested to be the primary driver behind the rapid aging of populations, even overpowering the positive effects of reduced mortality (David E. Bloom, David Canning, Günther Fink, 2010). The birth rate in Finland has had a decreased trend since the beginning of the 20th century according to Statistics Finland's data on population changes (Nordberg, 2020) (Figure 6).

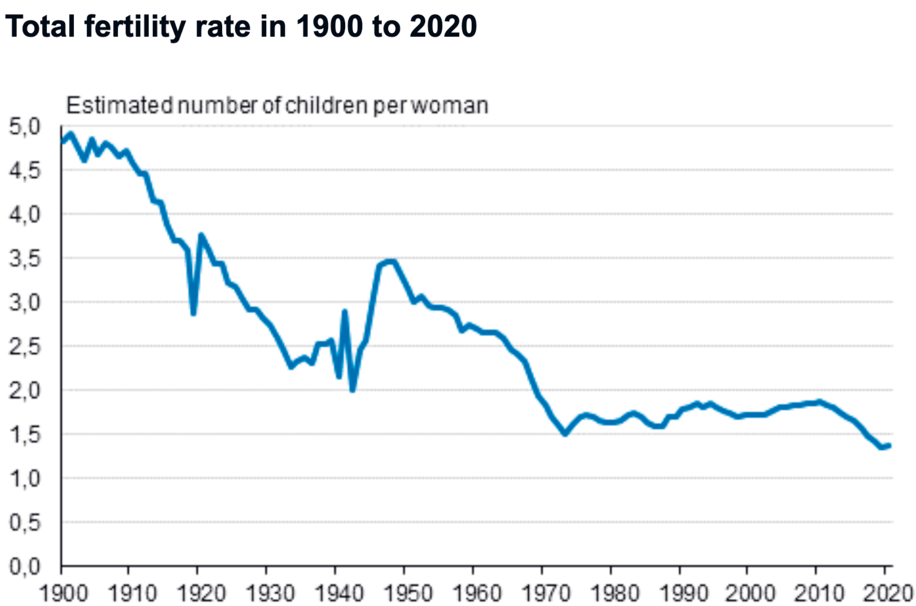

Figure 6. The total fertility rate (calculated average number of children per fertile-aged woman) from 1900 to 2020 in Finland, according to statistics Finland. Borrowed from the original source:(Nordberg, 2020) https://www.stat.fi/til/synt/2020/synt_2020_2021-04-23_tie_001_en.html

2.6.2 Trauma or orthopedic surgery and birth rate

Despite the widespread research on the incidence and impact of major trauma on health, there has been a lack of research on how it affects women's fertility. Previous studies have predominantly concentrated on trauma-related abnormalities of the reproductive system, particularly the uterus, and ovaries (Taylor & Gomel, 2008). Studies have indicated that musculoskeletal trauma involving the pelvic ring and femur can lead to sexual dysfunction and dyspareunia (Shulman et al., 2015; Walton et al., 2021). Furthermore, research conducted in Finland has shown that women who have undergone total hip replacement have a lower rate of childbirth than women in the general population (Artama et al., 2016).

2.7 Smoking

2.7.1 Prevalence and mortality

Smoking is a major worldwide health concern and is responsible for causing approximately 5 million fatalities annually (Jafari et al., 2021). A recent systematic review suggests that approximately 17% of women in the general population worldwide are estimated to be smokers (Jafari et al., 2021). The pooled prevalence of women who have never smoked was the highest in Europe (38%) (Jafari et al., 2021). In Finland, the proportion of smokers in the adult population has decreased during the last two decades from 19% in 2000 to 13% in 2018 (THL, 2018c). However, between 20% and 80% of the whole population is still exposed to the effects of passive smoking (Bartal, 2001). In Finland, less well-educated individuals tend to smoke more than those who attend higher education (THL, 2018c).

2.7.2 Smoking and pregnancy

The findings of a large systematic review conducted in 2018 reported that the estimated worldwide prevalence of smoking during pregnancy was 1.7%. The prevalence was highest in the European region (8.1%), followed by the Americas (5.9%), and Southeast Asia (1.2%). According to the same study, 72.5% of pregnant women who smoked were daily smokers and the rest were occasional smokers (Lange et al., 2018). A study in the Finnish population reported that the overall smoking rate during early pregnancy remained stable at around 15% between 1991 and 2015. The same study also found that the smoking rate was increasing among teenage girls and young women (Rumrich et al., 2019).

Maternal smoking during pregnancy is linked to various detrimental developmental consequences in the child, such as growth restriction, premature delivery, miscarriage, increased risk of sudden infant death syndrome, and persistent behavioral and psychiatric disorders in the long term (Shea & Steiner, 2008). In addition, smoking puts the fetus at higher risk for deformities, such as deformed extremities, polycystic kidneys, aortopulmonary septum defects, gastroschisis, and skull deformation (Haustein, 1999). In addition to the toxic chemicals found in tobacco, nicotine likely plays an important role in the adverse health effects on neonates. Nicotine use leads to a decrease in uteroplacental blood flow, resulting in reduced maternal weight gain and subsequently resulting in adverse fetal outcomes (Kataoka et al., 2018).

2.7.3 Smoking and bone metabolism

Smoking has been found to disrupt the balance of bone turnover, rendering smokers more susceptible to reduced bone density and osteoporosis (Al-Bashaireh et al., 2018). The impact of tobacco smoke on bone density occurs through a direct influence on osteogenesis and angiogenesis of bone (Al-Bashaireh et al., 2018). The indirect effects of smoking tobacco are caused by the alteration of body weight, parathyroid hormone-vitamin D axis, sex hormones, adrenal hormones, and increased oxidative stress on bony tissues (Al-Bashaireh et al., 2018). Smokers often experience complications with fractures, such as delayed bone healing, even when they have already stopped smoking, as some adverse effects can persist for a prolonged period (Hernigou & Schuind, 2019).

The mechanisms that cause osteoporosis in individuals who smoke cigarettes have not been fully investigated. However, there are some pathophysiologic ways found to likely affect bone metabolism. It has been reported that smoking may indirectly impact bone metabolism by changing the way calciotropic hormones are metabolized (Krall & Dawson-Hughes, 1999), causing derangements in the production, metabolism, and binding of estradiol (Cassidenti et al., 1990), causing alterations in adrenal cortical hormone metabolism (Baron et al., 1995), and have direct effects on osteogenesis including alteration in the RANK–RANKL–OPG system (Lappin et al., 2007; Tang et al., 2009), collagen metabolism (Sørensen et al., 2010), and bone angiogenesis (Ma et al., 2010).

The potential risk for fractures among smokers might be divisive, as it may be caused by the weakened health of bone (osteoporosis, weakened circulation, etc.) leading to a higher number of low-energy fractures (J. S. Chen et al., 2011), or by risky behavior, which has been found to be more common among people with a lower socioeconomic status (SES) (Geckova et al., 2002; Hiscock et al., 2012), leading to accident proneness.

3 AIMS OF THE STUDY

The overall aim of the present study was to provide important nationwide information on the reproductive health of fertile-aged women with prior skeletal or brain traumas. The specific aims of the studies were to investigate the following:

1. To assess the progress of the pregnancy, the success of the delivery, and neonatal outcomes in a patient group who had previously sustained a pelvic fracture or undergone pelvic fracture surgery.

2. To assess the progress of the pregnancy, the success of the delivery, and neonatal outcomes in a patient group who had previously sustained a spine fracture or undergone fusion surgery.

3. To assess the progress of the pregnancy, the success of the delivery, and neonatal outcomes in a patient group who had previously sustained a traumatic brain injury (TBI).

4. To calculate the incidence of major trauma hospitalizations (TBI, spine fracture, pelvic fracture, and hip or thigh fracture) in fertile-aged women, report the birth rates of these women, and analyze the risk for a pregnancy leading to birth after major trauma during a 5-year follow-up.

5. To evaluate the association between smoking and the risk for fracture hospitalizations (different anatomic regions, polytraumas, and severe and non-severe trauma) in women during a one-year and 5-year follow-up after childbirth.

4 PATIENTS AND MEDHODS

4.1 Study design

This nationwide cohort study was conducted by retrospectively analyzing data from two national registers in Finland: The Medical Birth Register (MBR) and the Care Register for Health Care. To combine information from these registers, we utilized the unique pseudonymized identification code assigned to each individual included in the study. The study period found in our data was from January 1, 1998, to December 31, 2018.

4.2 Registers

Finland has a long history of local population registers. The first population registers were established in the 16th century and the first population health registers during the 20th century. The purpose of population health registers is to enhance the quality of healthcare services and provide data for national statistics and research (Statistics Finland, 2018).

The Finnish data permit authority Findata grants access for the secondary use of the data contained in the registers (Findata, 2022). The pseudonymization was also made by Findata. The pseudonymization key, which is under the custody of Findata, was not accessible to the authors.

4.2.1 The Medical Birth Register (MBR)

The MBR is a nationwide mandatory register, which is maintained by THL. It was created in 1987 and has been updated in 1990, 1996, 2004, and 2017 with the aim of gathering information for research, statistics, and improving reproductive health in Finland. The current register coverage is almost 100%, and its quality is considered to be high (Gissler M., 1995; Vuori E, 2016.). The MBR comprehensively records data on all pregnancies, delivery statistics, and perinatal outcomes of births with a birthweight of ≥500 grams or a gestational age ≥22+0. In the present study, we collected all the live and stillbirths recorded in the MBR during the years 1998- 2018, but only singleton deliveries were included in studies I, II, and III.

The most important missing variables from the register data were the lack of delivery durations as well as the lack of 5-minute Apgar points and maternal pre-pregnancy BMI since they were not included in the register until 2004. Further, the coding for CS was two-parted (elective or urgent CS) instead of the current coding (elective, urgent, emergency CS). The MBR uses electronic reporting from the delivery hospitals, and midwives assisting the delivery in planned home deliveries report the births to the register. A current list of the information that is recorded in the MBR can be found on the MBR's homepage (THL, 2018b). The MBR comprises variables that are routinely collected either in maternity clinics, using a maternity counseling card that contains information related to the health and habits of the mother (such as smoking status), or in maternity hospitals, where information on the mode of delivery and the health of the neonate is recorded. This information is then sent to the register either at the time of discharge or when the neonate is 7 days old, if still in the hospital. During pregnancy, information about maternal smoking status is obtained from women and child welfare clinics, and it is recorded as a non-smoker, smoking during the 1st trimester, smoking after the 1st trimester, or unknown in the MBR. Maternal diabetes is classified as either pregestational or gestational, with gestational diabetes being diagnosed by a pathological glucose tolerance test. The diagnosis of gestational diabetes is made using the 75 g 2-hour oral glucose tolerance test.

4.2.2 The Care Register for Health Care

The Care Register for Health Care is the updated version of the Hospital Discharge Register, which collected data on patients discharged from hospitals between 1969 and 1993. The Hospital Discharge Register was replaced by the Care Register for Health Care in 1994, which provides more comprehensive data on the use of services and service users. The Care Register for Health Care includes information on patients discharged from inpatient care, the number of patients in inpatient care in health centers and hospitals as of December 31st, day surgeries, and specialized outpatient care. To identify specific trauma patients in each study, we used ICD-10 (International Classification of Diseases, 10th revision) codes that begin with S (for traumatic injuries) found in the Care Register for Health Care. The NOMESCO (Nordic Medico-Statistical Committee) operation codes, also found in the Care Register for Health Care, were used to identify patients who underwent surgery. Our data included NOMESCO operation codes starting with N (Musculoskeletal system) or A (Traumatic brain injury). An up-to-date list of the information recorded in the Care Register for Health Care can be found on the homepage of the register (THL, 2018a). The quality and coverage of the Care Register for Health Care are good (Sund, 2012).

4.3 Patients and outcomes

Information on a total of 628 908 women with 1 192 825 deliveries between 1998 and 2018 was found in the MBR. In studies I, II, and III, the patient group was formed of pregnancies occurring after the specific trauma hospitalization or operation included in that study. Pregnancies occurring without the preceding specific trauma hospitalization included in that study were placed in the control group. As the cohorts in studies I, II, and III are created only based on whether there is a prior trauma before each pregnancy, the same mother can have pregnancies in both study groups. The trauma hospitalizations and surgeries were found in the Care Register for Health Care based on specific ICD-10 codes. The identification of the fracture patients with subsequent deliveries was based on the date of the fracture recorded in the Care Register for Health Care and the date of the pregnancy recorded in the MBR. The start date of the pregnancy is calculated using the date of the delivery and the length of the pregnancy. In study IV, the risk of giving birth after different trauma hospitalizations was calculated using the date of the pregnancies found in the MBR. In study V, the risk for fractures after giving birth was calculated using the smoking status variable found in the MBR. In studies I, II, and III, pregnancies with multiple fetuses found in the MBR were excluded, but in study IV and study V, they were included. The pregnancies with multiple fetuses were excluded in study I, II, and III, as they are known to cause complications during pregnancy and delivery (Norwitz et al., 2005), and are therefore not comparable with singleton deliveries in terms of pregnancy outcomes. Due to missing data and different inclusion criteria, the number of participants differs between studies I and V. This is described in more detail in the following sections.

4.3.1 Study I

A total of 2878 women had pelvic fracture hospitalization during our study period. Of these, 126 fractures were treated surgically. The definition of pelvic fracture for this study was based on hospitalization records that had at least one of the ICD-10 codes listed in Table 5. A total of 596 women had 1024 singleton deliveries after pelvic fracture hospitalization. These women were divided into two groups based on the need for surgical treatment of the fracture. To enhance clarity, the fracture group was presented as a single entity in the tables, with notable findings being presented separately. In total, 2282 women had no pregnancies after pelvic fracture during our study period. The NOMESCO operation codes for the surgical procedures included in this study are presented in Table 5. In total, 26 women had 49 singleton deliveries after surgically treated pelvic fractures. The no-fracture group comprised 621 141 women with 1 156 378 singleton deliveries. Women with missing information on the mode of delivery were excluded. The forming of the study groups is shown as a flowchart in Figure 7.

The primary outcomes analysed in study I was a risk for preterm deliveries, the risk for CS, and the risk for neonatal intensive care unit. The secondary outcomes for the health of neonates collected in the study I was neonatal sex, birth length, and birthweight, perinatal and neonatal mortality, 1-minute Apgar score, delivery-related asphyxia, phototherapy, neonatal status after one week. The secondary maternal outcomes were labor analgesia, amniotomy, use of oxytocin, episiotomy, manual placenta removal, and uterine curettage. Maternal age, maternal smoking during pregnancy, maternal diabetes during pregnancy, and previous CS, were used as adjusting variables. The selection of adjustment variables is explained in the statistics section (4.4.3 and 4.5). All the variables are routinely collected in the MBR.

Table 5. Definitions of ICD-10 codes (International Classification of Diseases 10th revision) and NOMESCO (Nordic Medico-Statistical Committee) classification codes for the operations included in study I.

ICD-10-code	
Diagnosis code	Definition
S32.1	Fracture of sacrum
S32.3	Fracture of ilium
S32.4	Fracture of acetabulum
S32.5	Fracture of pubis
S32.7	Multiple fractures of lumbar spine and pelvis
S32.8	Fracture of other parts of pelvis
S32.9	Fracture of unspecified parts of lumbosacral spine and pelvis
Nomesco classification of surgical procedure	
Operation code	Definition
NEA 20	Exploration of soft tissue of pelvis
NEG 30	Excision, reconstruction, and fusion of joint of pelvis
NEH 99	Miscellaneous operations on joint of pelvis
NEJ 40	Closed reduction of fracture of pelvis
NEJ 50	Operation of fracture of pelvic ring
NEJ 70	External fixation of fracture of pelvis
NEJ 86	Reoperation or late fracture surgery of pelvis
NEK 10	Excision of fragment of bone of pelvis
NEK 20	Fenestration or forage of bone of pelvis
NEK 99	Other operation on bone of pelvis
NEL 10	Freeing of muscle of pelvis
NEQ 10	Hemipelvectomy
NEQ 48	Revision of amputation or exarticulation stump of pelvis
NER 20	Incomplete excision of soft tissue tumor of pelvis
NER 30	Extended excision of soft tissue tumor of pelvis
NER 50	Other operation for tumor of pelvis
NES 10	Incision and debridement of infection of joint of pelvis
NES 20	Incision and debridement of infection of bone of pelvis
NET 50	Removal of foreign body from tissue of pelvis
NET 99	Other operation on pelvis
NEU 10	Removal of external fixation device from pelvis
NEU 20	Removal of internal fixation device from pelvis
NEU 99	Removal of other implant from pelvis
NEW 00	Repair of wound dehiscence in surgery of pelvis
NEW 10	Reoperation for deep infection in surgery of pelvis

NEW 99 Other reoperation in surgery of pelvis

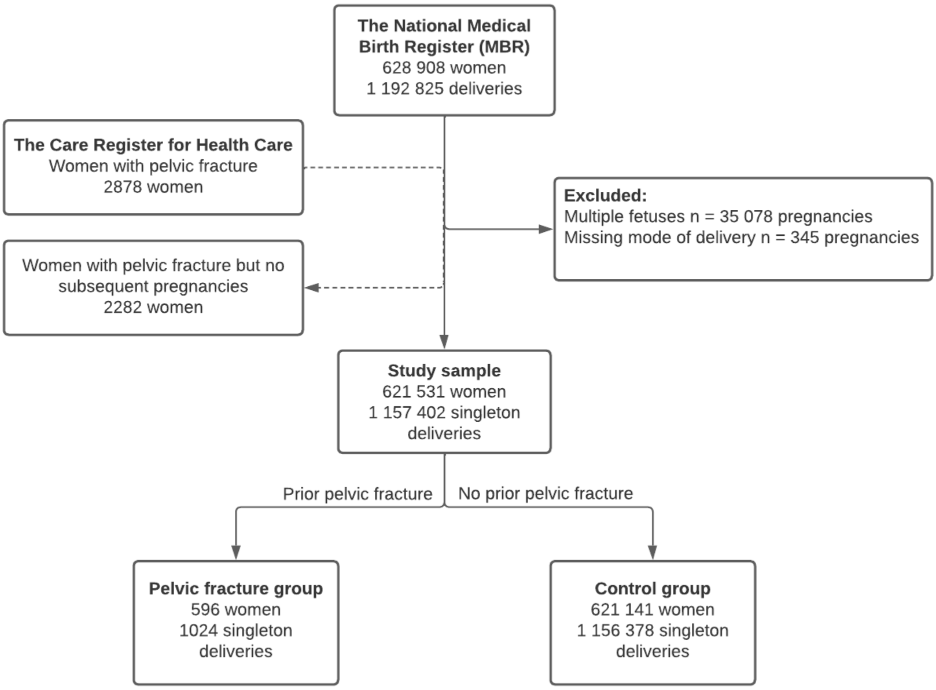

Figure 7. Flowchart of the study population in study I. Data from the MBR were combined with data on the diagnosed pelvic fractures in the Care Register for Health Care. In the pelvic fracture group, a total of 26 women had 49 singleton pregnancies after surgically treated pelvic fracture.

4.3.2 Study II

In this study, the deliveries of the women in the MBR were divided into 4 study groups based on whether the women had had preceding spine fracture hospitalizations, surgically treated spine fractures, fusion surgery for other reasons, or no previous spine fracture or surgery. During our study period, a total of 14 006 women had spine fracture hospitalizations or surgery. Spine fracture was defined as a hospitalization period with one of the ICD-10 codes shown in Table 6. In total, 1371 women had 2301 singleton deliveries after spine fractures. Of these, 734 women with 1234 deliveries sustained a fracture in the lumbar spine. Patients with conservatively treated fractures (1329 women with 2224 singleton deliveries) and those with surgically treated fractures (42 women with 77 singleton deliveries) were analyzed separately. However, for presentation purposes, these patients are combined as the fracture group in tables, and only important findings have been presented separately. In addition, 416 women had 632 singleton deliveries after fusion surgery unrelated to fracture. Of these, 206 women with 309 deliveries underwent fusion surgery for other reasons in the lumbar spine. The NOMESCO operation codes for fracture-related surgeries and fusion surgery for other reasons are shown in Table 6. A control group was formed of 620 093 women who had 1 154 469 singleton deliveries and had not undergone spine fracture hospitalization or fusion surgery before pregnancy, in order to compare with the study group. Forming of the study groups is shown as a flowchart in Figure 8.

The primary outcomes analysed in study II were a risk for CS and a risk for neonatal intensive care unit. The secondary outcomes for the health of neonates collected in study I were birthweight, preterm pregnancy, perinatal mortality, 1-minute Apgar score, and neonatal status after one week. The secondary maternal outcomes were labor analgesia. Maternal age, maternal smoking during pregnancy, maternal diabetes during pregnancy, and previous CS, were used as adjusting variables. The selection of adjustment variables is explained in the statistics section (4.4.3 and 4.5). All the variables are routinely collected in the MBR.

Table 6. Definitions for spine fracture ICD-10-codes (International Classification of Diseases 10th revision) and NOMESCO (Nordic Medico-Statistical Committee) classification codes for fracture-related and other major spine operations included in this study II.

ICD-10 Code	Definition
S12.0	Fracture of first cervical vertebra
S12.1	Fracture of second cervical vertebra
S12.2	Fracture of third cervical vertebra
S12.7	Multiple fractures of cervical vertebra
S12.8	Fracture of other parts of neck
S12.9	Fracture of neck, unspecified
S22.0	Fracture of thoracic vertebra
S22.1	Multiple fractures of thoracic vertebra
S32.0	Fracture of lumbar vertebra
Procedure code	**Definition**
NAJ 10	Anterior reduction of fracture of cervical spine
NAJ 12	Posterior reduction of fracture of cervical spine
NAJ 20	Anterior reduction of fracture of thoracic spine
NAJ 22	Posterior reduction of fracture of thoracic spine
NAJ 30	Anterior reduction of fracture of lumbar spine
NAJ 32	Posterior reduction of fracture of lumbar spine

Procedure code	Definition
NAG 40	Anterior fusion of cervical spine without fixation
NAG 41	Anterior fusion of cervical spine with fixation
NAG 42	Posterior fusion of cervical spine with or without fixation
NAG 50	Anterior fusion of thoracic spine without fixation
NAG 51	Anterior fusion of thoracic spine with fixation
NAG 52	Posterior or lateral fusion of thoracic spine with fixation, 2-3 vertebrae
NAG 53	Posterior or lateral fusion of thoracic spine with fixation, more than 3 vertebrae
NAG 57	Anterior and posterior fusion of thoracic spine

NAG 60	Anterior fusion of lumbar spine with fixation
NAG 61	Posterior fusion of lumbar spine without fixation
NAG 62	Posterior fusion of lumbar spine with fixation, 2-3 vertebrae
NAG 63	Posterior fusion of lumbar spine with fixation, more than 3 vertebrae
NAG 65	Anterior and posterior fusion of lumbar spine
NAG 66	Posterior interbody fusion of lumbar spine, 2 vertebrae
NAG 67	Posterior interbody fusion of lumbar spine, more than 2 vertebrae

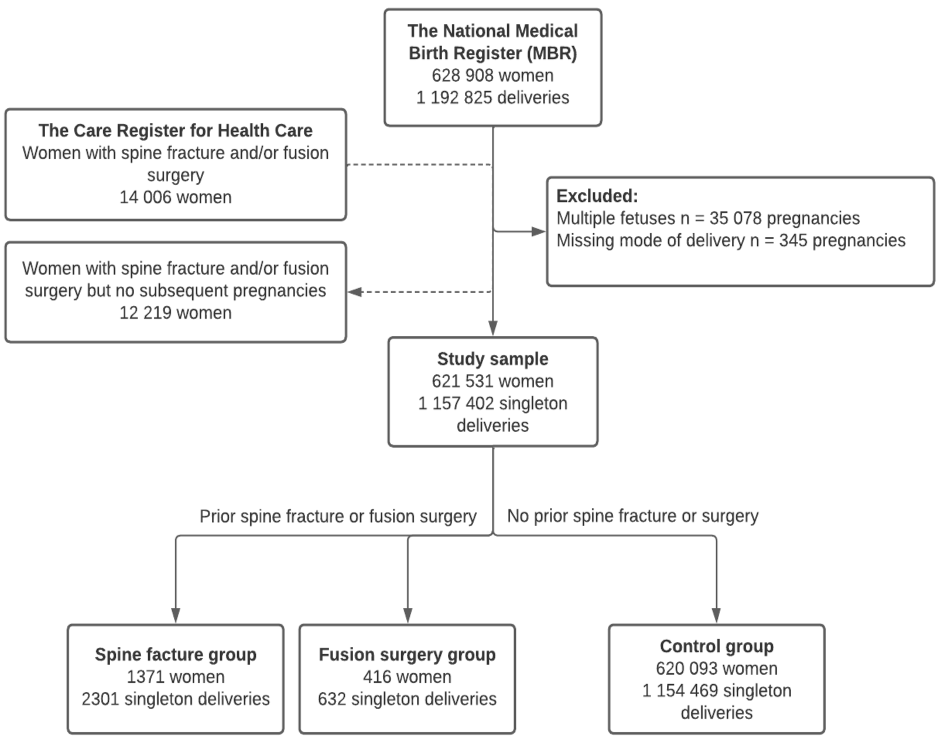

Figure 8. Flowchart of the study population in study II. Data from the MBR were combined with data on the diagnosed spine fractures and spine operations recorded in the Care Register for Health Care. In the spine fracture group, a total of 42 women had 77 singleton pregnancies after surgically treated spine fracture.

4.3.3 Study III

In this study, the deliveries of the women were divided into two groups based on whether the women had had a TBI before the pregnancy or not. A total of 40 028 women sustained a TBI during our study period. TBI was defined as a hospitalization period with one of the ICD-10 codes shown in Table 7. Of these, 8048 women had 13 448 singleton deliveries after TBI. These women were further divided into three subgroups (non-admitted, admitted, and operated) based on the length of the hospitalization period and the need for surgical treatment. TBIs with a hospitalization period lasting more than one day were considered admitted TBIs, and TBIs with a hospitalization period lasting less than one day were considered non-admitted TBIs. In total, 41 women had 64 deliveries after surgically treated TBI. Only procedure codes performed during the same hospitalization period and associated with TBI diagnosis codes were included, as these operations may also be performed for reasons other than TBI. The NOMESCO operation codes for surgical procedures included in this study are shown in Table 7. The control group was composed of 615 144 women who had 1 143 954 singleton deliveries. Forming of the study groups is shown as a flowchart in Figure 9.

The primary outcomes analysed in study I was a risk for preterm deliveries, the risk for CS, and the risk for neonatal intensive care unit. The secondary outcomes for the health of neonates collected in the study I were birthweight, induction of labor, perinatal mortality, 1-minute Apgar score, and neonatal status after one week. The secondary maternal outcomes were labor analgesia. Maternal age, maternal smoking during pregnancy, maternal diabetes during pregnancy, and previous CS, were used as adjusting variables. The selection of adjustment variables is explained in the statistics section (4.4.3 and 4.5) All the variables are routinely collected in the MBR.

Table 7. Definitions of ICD-10 codes (International Classification of Diseases 10th revision) and NOMESCO (Nordic Medico-Statistical Committee) classification codes for the operations included in study III.

ICD-10-code	Definition
S06.0	Concussion
S06.1	Traumatic cerebral edema
S06.2	Diffuse traumatic brain injury
S06.3	Focal traumatic brain injury
S06.4	Epidural hemorrhage
S06.5	Traumatic subdural hemorrhage
S06.6	Traumatic subarachnoid hemorrhage
S06.8	Other specified intracranial injuries
S06.9	Unspecified intracranial injury
NOMESCO classification code of surgical procedure	
Procedure code	Definition
AAA 20	Insertion of intraventricular pressure monitoring device
AAA 25	Insertion of epidural pressure monitoring device
AAA 27	Insertion of intracerebral pressure monitoring device
AAD 00	Evacuation of epidural haematoma
AAD 05	Evacuation of acute subdural haematoma
AAD 15	Evacuation of traumatic intracerebral haematoma
AAD 30	Revision of penetrating or perforating injury of skull
AAF 00	Ventriculostomy
AAK 80	Partial excision of skull cap

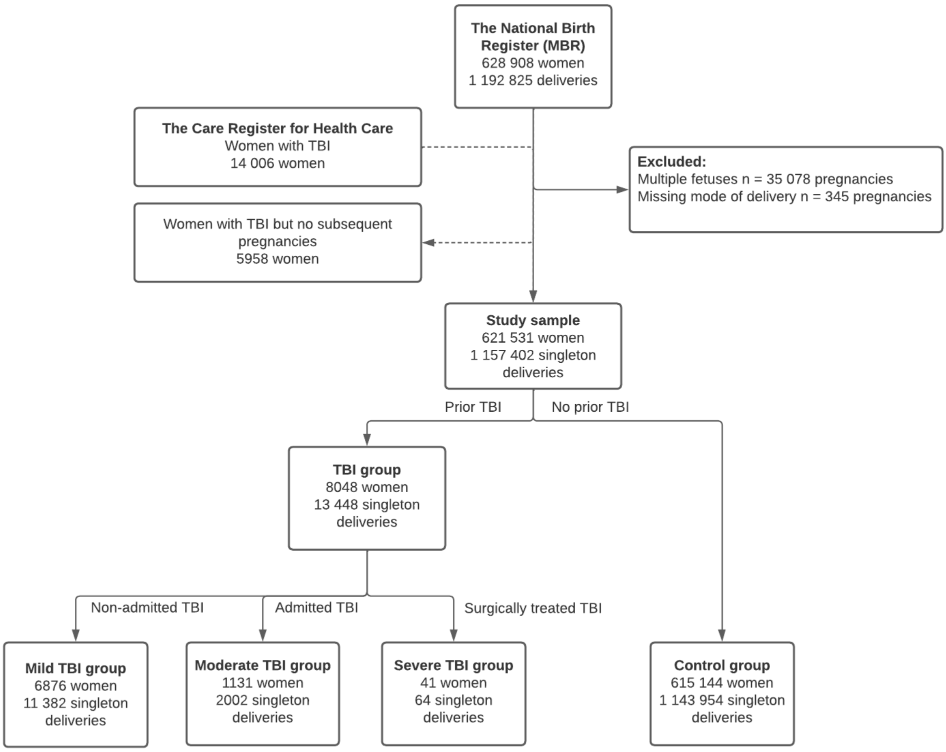

Figure 9. Flowchart of the study population in study III. Data from the MBR were combined with data on the diagnosed TBI and TBI-related surgical operations in the Care Register for Health Care.

4.3.4 Study IV

In this study, all fertile-aged women who underwent TBI, spine fracture, pelvic fracture, hip or thigh fracture, or palmar fracture hospitalization during the study period were identified from the Care Register for Health Care. Women hospitalized with palmar fractures were used as a reference group. These women were selected as the reference group as we anticipated them to have a similar background and risk-taking behavior as the women in the major trauma groups, as opposed to women in the general population without any injuries. Additionally, since palmar fractures typically have a quick healing time and are not expected to have an important impact on fertility, they were considered an appropriate reference group. However, due to the required 5-year follow-up needed for the survival analysis in this study, only those women under the age of 45 who had trauma occurring before 2014 were included in the study groups for the survival analysis. During the years 1998-2014, a total of 34 953 women (aged 15-44 years) had one of the trauma hospitalizations included in this study. There was a total of 22 780 women found in the TBI group, 3627 in the spine fracture group, 1820 in the pelvic fracture group, 1769 in the hip or thigh fracture group, and 4957 in the palmar fracture group. The specific ICD-10 codes for each trauma group are shown in Table 8. The primary outcome analysed in the study was the first pregnancy ending in delivery after a major trauma. Forming of the study groups is shown in Figure 10. In the evaluation of pregnancy outcomes after different traumas, every pregnancy following trauma in our data from 1998 to 2018 was included.

Table 4. ICD-10 (International Classification of Diseases 10th revision) codes with definitions for each major trauma group and reference group included in this study in study IV.

TBI	
ICD-10 code	Definition
S06.0	Concussion
S06.1	Traumatic cerebral edema
S06.2	Diffuse traumatic brain injury
S06.3	Focal traumatic brain injury
S06.4	Epidural hemorrhage
S06.5	Traumatic subdural hemorrhage
S06.6	Traumatic subarachnoid hemorrhage
S06.8	Other specified intracranial injuries
S06.9	Unspecified intracranial injury
Spine traumas	
ICD-10 code	Definition
S12.0	Fracture of first cervical vertebra
S12.1	Fracture of second cervical vertebra
S12.2	Fracture of third cervical vertebra
S12.7	Multiple fractures of cervical vertebra
S12.8	Fracture of other parts of neck
S12.9	Fracture of neck, unspecified
S22.0	Fracture of thoracic vertebra
S22.1	Multiple fractures of thoracic vertebra
S32.0	Fracture of lumbar vertebra
Pelvic traumas	
ICD-10 code	Definition
S32.1	Fracture of sacrum
S32.3	Fracture of ilium
S32.4	Fracture of acetabulum
S32.5	Fracture of pubis
S32.7	Multiple fractures of lumbar spine and pelvis
S32.8	Fracture of other parts of pelvis
S32.9	Fracture of unspecified parts of lumbosacral spine and pelvis
Hip or thigh traumas	
ICD-10 code	Definition
S72.0	Fracture of head and neck of femur
S72.1	Pertrochanteric fracture
S72.3	Fracture of shaft of femur
S72.4	Fracture of lower end of femur
S72.7	Multiple fractures of femur
S72.8	Other fracture of femur
S72.9	Unspecified fracture of femur

Palmar bone traumas	
ICD-10 code	Definition
S62.0	Fracture of navicular bone of wrist
S62.1	Fracture of other and unspecified carpal bone
S62.2	Fracture of first metacarpal bone
S62.3	Fracture of other and unspecified metacarpal bone
S62.4	Multiple fractures of metacarpi

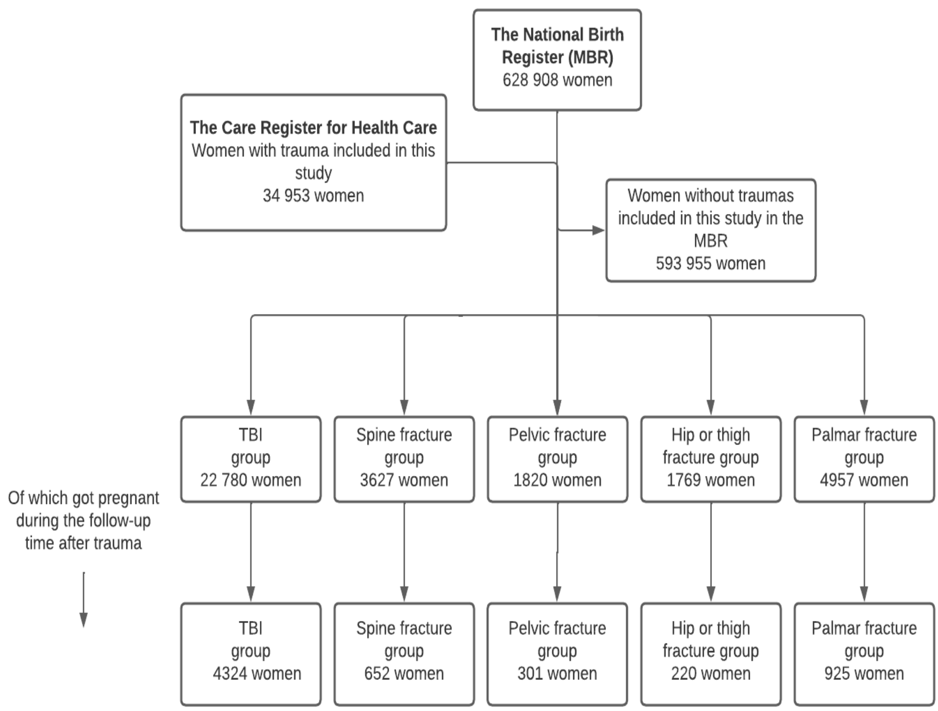

Figure 10. Flowchart of the study populations in study IV. Data from the MBR were combined with data on the diagnosed major trauma hospitalizations in the Care Register for Health Care.

4.3.5 Study V

In study V, all women who smoked during pregnancy found in the MBR were separated from women who did not smoke during pregnancy. These non-smoking women were subsequently used as a reference group. We included all pregnancies between 1998 and 2013 leading to birth in women aged 15-44 years from the MBR.

Smokers were identified using the smoking status variable found in the MBR. In the MBR, smoking is categorized into 4 alternatives: Non-smoker, smoking during 1st trimester, smoking also after 1st trimester, and unknown. Women who smoked during the 1st trimester or in the later trimester were included in the smoking group. Information on maternal smoking status during pregnancy is routinely collected during visits to maternity clinics. Women with an unknown smoking status were excluded from the analysis. According to a study conducted in 1993, the reliability of the smoking status found in the MBR has been found to be good (Gissler et al., 1993). Both the smoking group and the non-smoking group were linked with the data found in the Care Register for Health Care, which contained the data on fracture hospitalization between the years 1998 and 2014.

The risk for fracture hospitalization after giving birth was evaluated for both groups. The study included fractures of the lower arm, upper arm, spine, pelvis, hip or thigh, knee, lower leg, and ankle. The specific ICD-10 codes with definitions for each fracture included in the study are shown in Table 9. According to our hypothesis, the potential risk of fractures among smokers could have two possible causes, either weakened bone health or riskier behavior among women with lower SES, which may make them more prone to accidents. Based on this hypothesis, we categorized women into four socioeconomic (SES) classes: low, middle, high, and undefinable using the SES information available in the MBR. The categorization of the SES is shown in Table 10. Women with missing SES (16.7%) were excluded from the analysis. A total of 110 675 women were found to have smoked during pregnancy.

In the reference group, 618 085 pregnancies were found in which the mother was a non-smoker. Forming of the study groups is shown in Figure 11.

Table 9. ICD-10-codes (International Classification of Diseases 10th revision) with definitions for each fracture included in study V The fractures are categorized based on the anatomic location of the fracture.

Fractures of lower arm	
ICD-10 code	Definition
S52.0	Fracture of upper end of ulna
S52.1	Fracture of upper end of radius
S52.2	Fracture of shaft of ulna
S52.3	Fracture of shaft of radius
S52.5	Fracture of lower end of radius
S52.6	Fracture of lower end of ulna
S52.9	Unspecified fracture of forearm
S62.0	Fracture of navicular bone of wrist
S62.1	Fracture of other and unspecified carpal bone
S62.2	Fracture of first metacarpal bone
S62.3	Fracture of other and unspecified metacarpal bone
S62.4	Multiple fractures of metacarpi
Fractures of upper arm	
ICD-10 code	Definition
S42.0	Fracture of clavicle
S42.1	Fracture of scapula
S42.2	Fracture of upper end of humerus
S42.3	Fracture of shaft of humerus
S42.4	Fracture of lower end of humerus
S42.9	Fracture of shoulder girdle, part unspecified
Fractures of spine	
ICD-10 code	Definition
S12.0	Fracture of first cervical vertebra
S12.1	Fracture of second cervical vertebra
S12.2	Fracture of third cervical vertebra
S12.7	Multiple fractures of cervical vertebra
S12.8	Fracture of other parts of neck
S12.9	Fracture of neck, unspecified

S22.0	Fracture of thoracic vertebra
S22.1	Multiple fractures of thoracic vertebra
S32.0	Fracture of lumbar vertebra
Fractures of pelvis	
ICD-10 code	Definition
S32.1	Fracture of sacrum
S32.3	Fracture of ilium
S32.4	Fracture of acetabulum
S32.5	Fracture of pubis
S32.7	Multiple fractures of lumbar spine and pelvis
S32.8	Fracture of other parts of pelvis
S32.9	Fracture of unspecified parts of lumbosacral spine and pelvis
Fractures of hip or thigh	
ICD-10 code	Definition
S72.0	Fracture of head and neck of femur
S72.1	Pertrochanteric fracture
S72.3	Fracture of shaft of femur
S72.4	Fracture of lower end of femur
S72.7	Multiple fractures of femur
S72.8	Other fracture of femur
S72.9	Unspecified fracture of femur
	Fractures of knee and lower leg including ankle
ICD-10 code	Definition
S82.0	Fracture of patella
S82.1	Fracture of upper end of tibia
S82.2	Fracture of shaft of tibia
S82.3	Fracture of lower end of tibia
S82.4	Fracture of shaft of fibula
S82.5	Fracture of medial malleolus
S82.6	Fracture of lateral malleolus
S82.8	Other fractures of lower leg
S82.9	Unspecified fracture of lower leg
S92.0	Fracture of calcaneus
S92.1	Fracture of talus

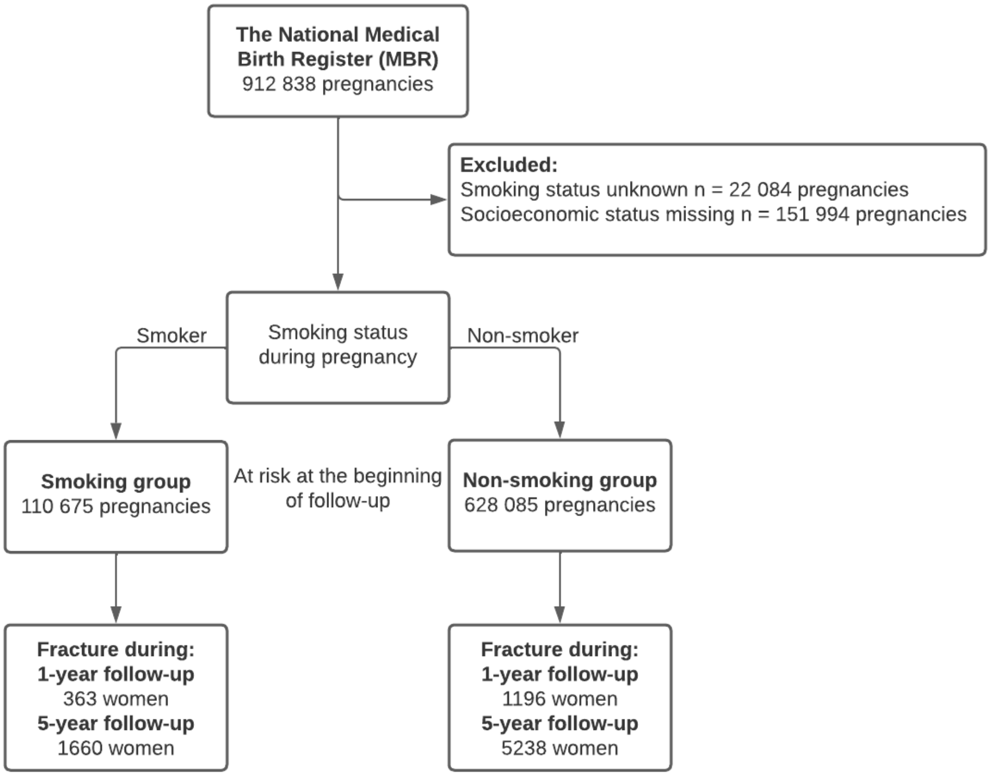

Figure 11. Flowchart of the study population in study V. Data from the MBR were combined with data on the diagnosed fracture hospitalizations recorded in the Care Register for Health Care.

Table 10. Categorization of the socioeconomic status (SES) and total number of patients with each SES found in the Medical Birth Register.

Class	Specific SES	Total number (%)
Low		**145 581 (19.7%)**
	Agricultural sole proprietors or workers	12 640
	Industrial workers	35 162
	Other production workers	31 574
	Distribution and service representatives	53 297
	Indefinite workers	7214
	Other self-employed persons or sole proprietors	816
	Unemployed (no profession)	969
	Unemployed (profession coded separately)	357
	Long-term unemployed	3126
	Retired persons	426
Middle		**307 905 (41.7%)**
	Junior employees in work management position	21 087
	Junior employees in independent office work	96 789
	Junior employees in unindependent office work	12 211
	Other indefinite junior employees	177 818
High		**146 143 (19.8%)**
	Senior employees in leadership position	19 144
	Senior employees in design and research assignments	30 246
	Senior employees working in teaching positions	52 842
	Other indefinite senior employees	43 911
SES unknown or categorization impossible		**138 937 (18.8%)**
	Homemaker (full-time taking care for children)	45 993
	Students	85 110
	Entrepreneurs	7321
	Status coded as unknown	513

4.4 Statistical methods

4.4.1 Statistics overall

The statistical analyses were conducted on R version 4.0.3 for Windows, developed by the R Foundation for Statistical Computing in Vienna, Austria. In all of the analyses, a P-value below 0.05 was deemed to be statistically significant. For continuous variables, the mean with standard deviation or median with interquartile range was reported based on the distribution of the data. Categorized variables were presented as absolute numbers and percentages. To compare groups, Student's t-test, Mann-Whitney U-test, and Chi-squared tests were utilized. The findings of each study adhere to the STROBE guidelines (Elm et al., 2008).

4.4.2 Incidences (I, II, III, IV)

The reference population for the incidence of various trauma-related hospitalizations comprised females aged between 15 to 49 years who resided in Finland at the end of a specific year. The population figures were sourced from Statistics Finland (stat.fi). The annual number of fertile-aged women living in Finland decreased during our study period from 1 389 409 in 1998 to 1 285 100 in 2018 (Figure 12). Due to the different natures of different traumas, the criteria for calculating the annual incidences of the traumas differ between studies. In study I and study II, only each first fracture diagnosis was defined as a separate fracture, as the control appointments for spine or pelvic fractures can occur after a long period, and thus make it impossible to identify any new fractures during the subsequent hospitalization periods recorded in the Care Register for Healthcare. Following a one-year wash-out period, each TBI diagnosis in study III was considered a distinct and separate TBI. This was due to the fact that hospital follow-up appointments for TBI generally do not occur beyond one-year post-injury in most cases. For study IV, to ensure the best possible comparability between major trauma groups, we utilized the same criteria for calculating the annual incidences during our study period. This was done despite the diverse nature of the various traumas that were included in the study. Hence, only the initial hospitalization period with a trauma diagnosis for each patient was identified as a distinct trauma for each trauma group in this study.

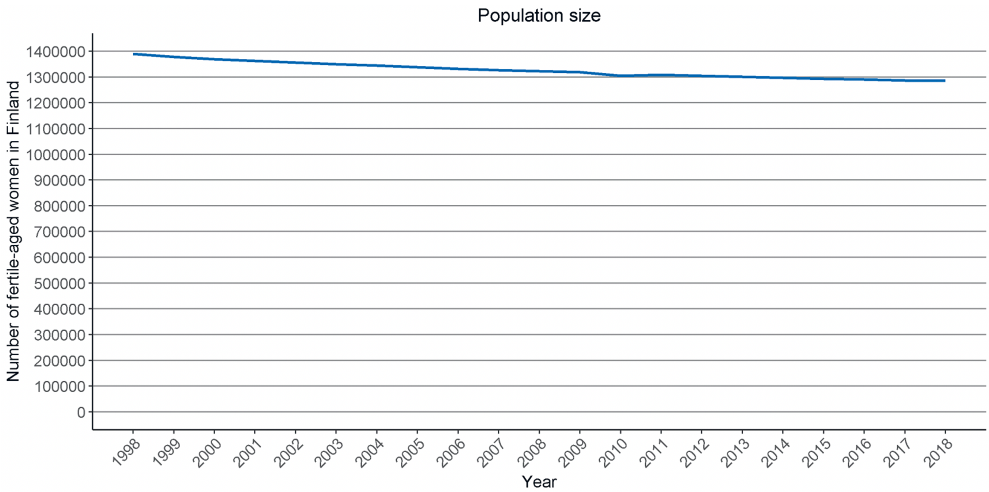

Figure 12. The annual number of fertile-aged (15-49) women living in Finland at the end of particular year (31.12). The numbers were obtained from the statistic Finland (Stat.fi).

4.4.3 Trauma and pregnancy outcomes (I, II, III)

A logistic regression model was used to access the primary outcomes. The exposure variable was the specific trauma or surgery included in each study (pelvic fracture, spine fracture or surgery, TBI). Primary outcomes were preterm deliveries, the risk for CS, and the need for neonatal intensive care. Both exposure and outcome variables were dichotomous. Adjusted odds ratios with 95% CI were compared between groups. Maternal age, maternal smoking during pregnancy, maternal GDM, and previous CS, were used as adjusting variables. Advanced maternal age is known to affect the risk for CS (Bergholt et al., 2020), maternal smoking during pregnancy is known to increase the risk for CS, preterm delivery, and adverse neonatal health outcomes (Knopik, 2009; Lurie et al., 2014; Wisborg et al., 1996). GDM is associated with increased risk for preterm deliveries, CS, and adverse neonatal health outcomes (Jain et al., 2021; Ye et al., 2022). Pregnancies for women with a history of CS have a higher risk of another CS (Kietpeerakool et al., 2019). Adjustments were made by choosing the variables for the multivariate model using directed acyclic graphs (DAGs) constructed using the free online software DAGitty (dagitty.net), which are shown in section 4.5.

In study I, a logistic regression model was used to evaluate the primary outcomes, including gestational age at birth, mode of delivery, and neonatal health. In the logistic regression model assessing the mode of delivery, the outcome of CS (including elective and urgent) was compared to vaginal delivery (including spontaneous and assisted vaginal deliveries). The neonate's need for intensive care before discharge from the hospital was used as an indicator of neonatal health. Adjusting variables such as maternal age, maternal smoking during pregnancy, maternal GDM, previous CS, and preterm delivery (in the model evaluating the need for intensive care) were used as adjustment variables.

In study II, the logistic regression model was applied separately for fracture patients and patients who underwent fusion surgeries for other reasons. The primary outcomes evaluated using the model were the mode of delivery and neonatal health. To prevent distortion in the results, the other group was excluded from the data when utilizing the model, as it would otherwise be incorporated into the control group. Given that the lumbar spine is situated in close proximity to the reproductive system, understanding the effects of traumas and surgeries on pregnancy and delivery in this area is of great interest. For this reason, we conducted a separate analysis of fractures and surgeries in the lumbar spine compared to the thoracic and cervical spine. In the logistic regression analysis, the neonate's requirement for intensive care was utilized as an indicator of neonatal health. Adjusting variables such as maternal age, maternal smoking during pregnancy, maternal GDM, and previous CS were included in the analysis.

In study III, multivariable logistic regression was used to assess the primary outcomes, which were preterm delivery, mode of delivery, and neonatal health. The neonate's requirement for intensive care was utilized as an indicator of neonatal health in the logistic regression analysis. Adjusting variables, including maternal age, maternal smoking during pregnancy, maternal gestational diabetes mellitus (GDM), and previous cesarean section, were also considered in the analysis.

As we have no information on previous pregnancy outcomes (such as previous preterm delivery, which is known to be a risk factor for another preterm delivery (Tingleff et al., 2022)), additional analyses for the main outcomes with only nulliparous women were conducted. However, we had information on previous CS, as it is routinely collected in the MBR. In addition, as we had all pregnancies with prior trauma included in the patient group, meaning that a single woman can have multiple pregnancies in the patient group, additional analysis with only the first pregnancy after major trauma included was conducted.

4.4.4 Birth rate after major trauma (IV)

To calculate the annual birth rate, the number of yearly newborns was divided by the size of the base population of women of fertile age (15-49 years) living in Finland at the end of a specific year (31.12). Data on both sizes of base population and the number of yearly newborns were obtained from Statistics Finland (stat.fi). To assess the risk of pregnancy leading to birth in women after major trauma in comparison to reference individuals with palmar fracture, the Cox regression model was utilized. The results were interpreted by utilizing hazard ratios (HRs) and 95% confidence intervals, and the proportional hazards assumption was tested using Schoenfeld residuals. In all models, this supposition was not violated. Moreover, Kaplan-Meier survival curves were generated for each group. To make the groups as comparable as possible in the analysis, women with trauma were divided into the following three categories based on their age at the time of trauma: 15-24 years, 25-34 years, and 35-

44 years. The beginning of the follow-up period was set as the date of the recorded trauma in the Care Register for Health Care. The endpoint of the follow-up was defined as either the first live-born child after the trauma or the common closing date, which was 5 years after the trauma. Because the follow-up period of those women who sustained a trauma after 2013 was less than 5 years, they were excluded from the survival analysis. Additionally, as the maximum age for fertile-aged women is defined as 49 years, only those women who experienced trauma before the age of 45 met the required 5-year follow-up condition of fertile years.

4.4.5 Association between smoking and fractures (V)

The Cox regression model was used to evaluate the risk for the first major trauma in women after giving birth. Smoking women were compared with non-smoking women. The results were interpreted with age-adjusted hazard ratios (HRs) and 95% CIs. The proportional hazards assumption was assessed by examining Schoenfeld residuals, and no violation was found in any of the models. To handle competing risks, Efron's method was used. Additionally, the model was adjusted for the age of the mother during pregnancy, as it is known to impact fracture risk, and for the mother's categorized SES to reduce the impact of differences in background and behavior.

Also, Kaplan-Meier survival curves were created for both groups. The start of the follow-up was the date of giving birth recorded in the MBR. The follow-up times we chose were 1 and 5 years, starting from the day of giving birth found in the MBR. The follow-up times selected were based on our interest in examining the risk of fractures during specific periods, including the lactation period, the stay-at-home phase (around 1 year after delivery), and the post-lactation period. The endpoint of the follow-up was the first fracture after giving birth, the following pregnancy, or the common closing date, which was 5 years after giving birth. Because the follow-up period of those women who sustained a trauma after 2013 was less than 5 years, they were excluded from the survival analysis. Additionally, as the maximum age for fertile-aged women is defined as 49 years, only those women who experienced trauma before the age of 45 met the required 5-year follow-up condition of fertile years.

We analyzed the risk for polytraumas, for hospitalization periods longer than one day (presumably more severe trauma), and the risk for non-admitted fractures requiring a hospitalization period of less than one day (including day surgery) with fracture diagnoses in only one anatomic region of the body (presumably non-severe trauma). Polytrauma was defined as the presence of two or more fracture ICD-10 diagnosis codes from at least two different anatomical regions of the body during the same hospitalization period.

Due to a moderate number of excluded patients due to missing socioeconomic status, sensitivity analyses with the excluded patients were conducted for the main results and are shown in Table 37 and Table 38 directly below the main analysis. In the initial analysis, women with no information on SES were grouped in their own category, labeled as "missing SES", and included in the main analysis. Furthermore, sensitivity analyses were conducted using multiple imputation techniques. Modified Rubin's rule was used to calculate grand means based on the best-best case, best-worst case, worst-best case, and worst-worst case imputations, as well as the observed data (Héraud-Bousquet et al., 2012).

4.5 Directed acyclic graphs

The use of directed acyclic graphs (DAGs) can aid in the selection of covariates to include in conventional statistical methods, with the aim of reducing the extent of bias in the resulting estimate (Shrier & Platt, 2008). According to a methodological review in 2021, recent orthopedic studies published in top-quality journals have encountered notable challenges in confounder selection and the interpretation of multivariable model results. (Ponkilainen et al., 2021).

Adjustments were made by choosing the variables for a multivariate model using DAGs constructed using the free online software DAGitty (dagitty.net). The variables included in the DAGs were chosen based on known risk factors and hypothesized causal pathways. DAGitty automatically suggests possible adjustment variable sets that can influence the main outcome. There are variables included in the DAGs that were not available in the data, but the adjustment variable set containing only variables that were included in our data was chosen for the analyses. In the DAGs, the exposure variable is placed in the bottom left corner and the outcome in the right corner. The yellow variables are called an ancestor of exposure (affecting the exposure variable), the blue variables as an ancestor of outcome (affecting the outcome variable), and the red variables as an ancestor of outcome and exposure variable. The pathways between different variables can be either green, red, or black. Green pathway means causal pathway, and it is located between the exposure variable and outcome variable. The red pathway means biasing pathway, and the black pathway is between the outcome and variables which affect solely the outcome.

The specific DAGs used in each study for each main outcome are presented in the following chapters.

4.5.1 Study I

In study I, the possible effect of pelvic fractures on the main outcomes, which were preterm deliveries, CS, and weakened health of neonates, was analyzed. The hypothesized causal pathway for the main outcomes is shown below in DAGs (Figure 13)

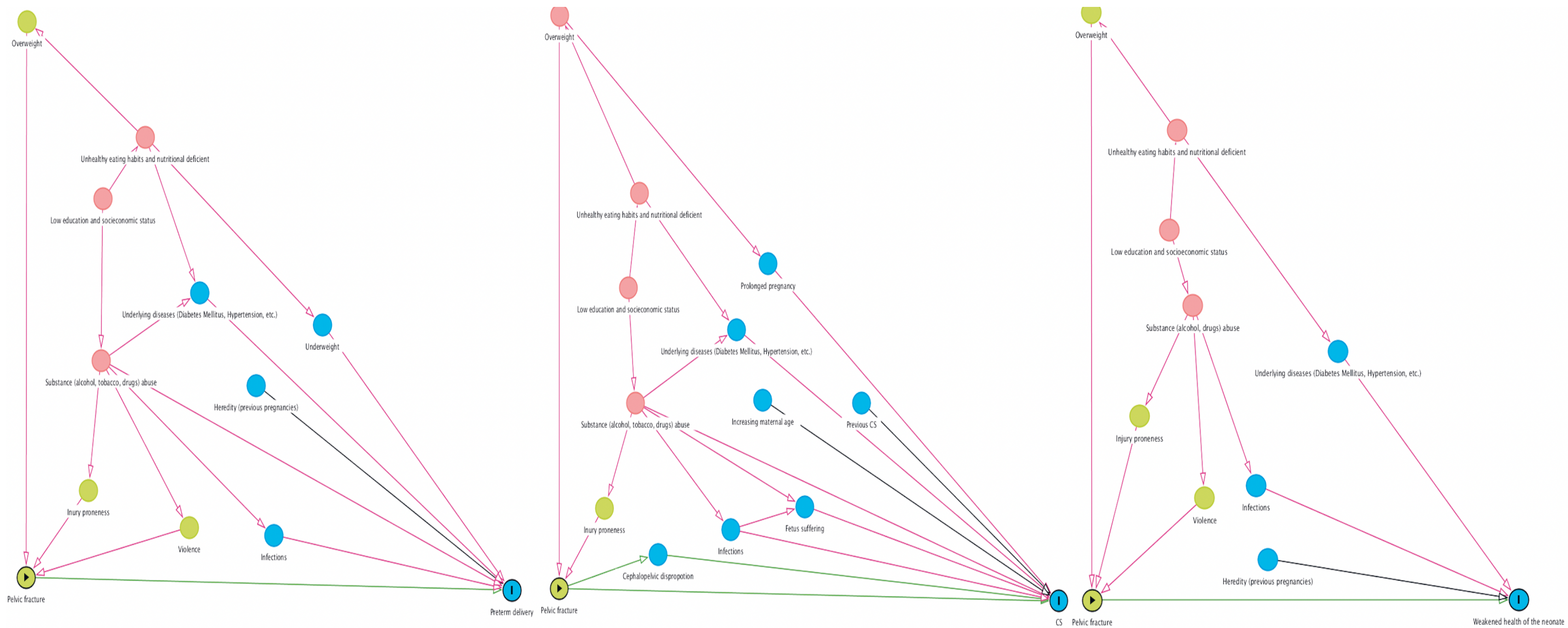

Figure 13. DAG, the risk for preterm delivery, cesarean section (CS), and weakened health of the neonate as a dependent variable, and pelvic fracture as an exposure variable.

4.5.2 Study II

In study II, the possible effect of spine fractures or surgeries on the main outcomes, which were CS, and weakened health of neonates in this study were analysed. The hypothesised causal pathway for main outcomes is shown below in DAGs (Figure 14)

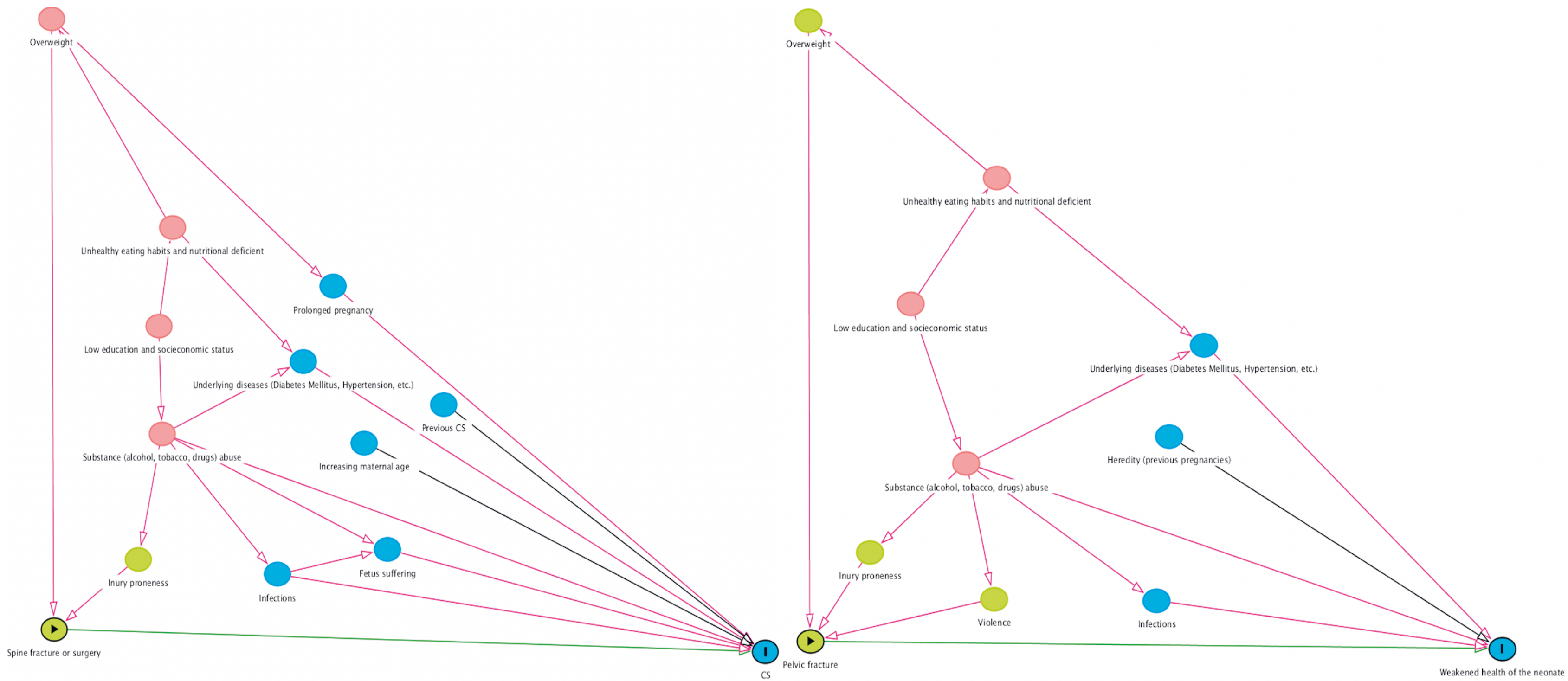

Figure 14. DAG, the risk for cesarean section (CS), weakened health of the neonate as a dependent variable, and spine fracture or surgery as an exposure variable.

4.5.3 Study III

In study III, the possible effect of pelvic fractures on main outcomes, which were preterm deliveries, CS, and weakened health of neonates was analysed. The hypothesized causal pathway for main outcomes is shown below in DAGs (Figure 15).

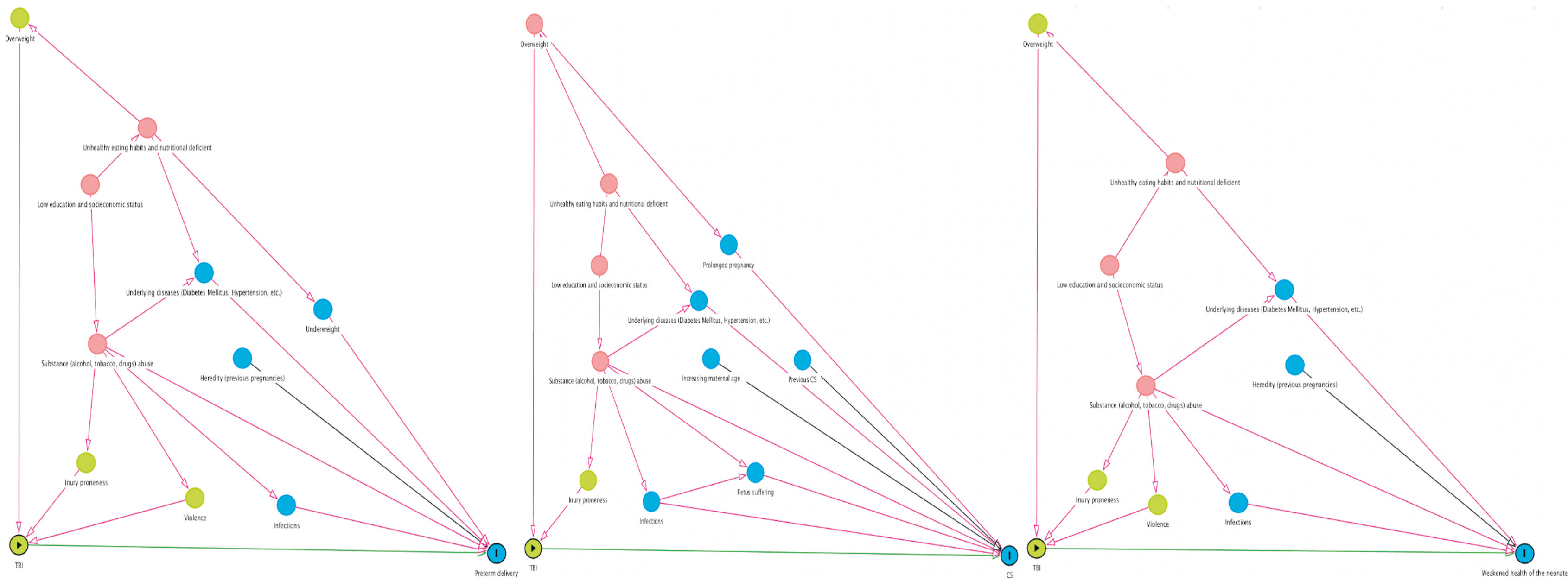

Figure 15. DAG, the risk for preterm delivery, cesarean section (CS), and weakened health of the neonate as a dependent variable, and traumatic brain injury (TBI) as an exposure variable.

4.6 Ethics and permissions

4.6.1 Ethics of the study

Following the regulations in Finland, ethical approval was not required for our register-based cohort study, and therefore, it did not undergo ethical evaluation by the local ethical committee. The utilization of routinely collected healthcare data in all retrospective studies was exempted from ethical committee evaluation by the Ethical Committee of Tampere University hospital, in accordance with the law of medical research 488/1999 and the law of patient rights 785/1992. Since this study was retrospective and register-based, informed written consent was not required in accordance with the Finnish regulations (the law of secondary use of routinely collected healthcare data 552/2019), and patients were not contacted.

4.6.2 Research permission

The MBR and the Care Register for Health Care utilized an identical unique pseudonymized identification number for each patient, which was generated by the Finnish data authority, Findata. The pseudonymization process was not accessible to the authors, as Findata maintained the pseudonymization key. Findata granted permission to use the data following an evaluation of the study protocol (Permission number: THL/1756/14.02.00/2020), and the data was made available in a secure remote access environment provided by Findata.

5 SUMMARY OF THE RESULTS

5.1 Epidemiology of traumas and surgeries (I, II, III, IV)

During the study period, a total of 2878 women sustained a pelvic fracture, a total of 6374 women sustained a spine fracture, a total of 40 028 women sustained a TBI, and a total of 3100 women sustained a fracture of hip or thigh. A total of 4.4% of the pelvic fractures were treated surgically, a total of 3.2% of the spine fractures were treated surgically, and a total of 0.4% of the TBIs were treated surgically.

Of the women who sustained a pelvic fracture, a total of 19.0% suffered also a spine fracture, 16.0%% suffered also a TBI, and 8.4% suffered also a fracture of the hip or thigh. Of the women who sustained a spine fracture, a total of 8.6% suffered also a pelvic fracture, 14.8% suffered also a TBI, and 2.5% suffered also a fracture of the hip or thigh. Of the women who sustained a TBI, a total of 1.2% suffered also a pelvic fracture, 2.4% suffered also a spine fracture, and 0.8% suffered also a fracture of the hip or thigh. Of the women who sustained a fracture of the hip or thigh, a total of 7.8% suffered also a pelvic fracture, 5.1% suffered also a spine fracture, and 9.9% suffered also a TBI. (Table 11)

Table 11. Overview of major traumas occurring during years 1998-2018 in fertile-aged women. Surgeries of hip or thigh fractures are not included in this study.

Type of trauma			**Suffered also**							
			Pelvic fracture		Spine fracture		TBI		Hip or thigh fracture	
	n	%	n	%	n	%	n	%	n	%
Pelvic fracture	2878		-	-	546	19.0	461	16.0	242	8.4
conservatively treated	2752	95.6								
surgically treated	126	4.4								
Spine fracture	6374		546	8.6	-	-	943	14.8	159	2.5
conservatively treated	6175	96.8								
surgically treated	199	3.2								
TBI	40 028		461	1.2	943	2.4	-	-	306	0.8
conservatively treated	39 879	99.6								
surgically treated	149	0.4								
Hip or thigh fracture	3100	-	242	7.8	159	5.1	306	9.9	-	-

During our study period, the incidence of pelvic fracture hospitalizations among fertile-aged women increased from 8.9 per 100 000 person-years in 1998 to 13.2 per 100 000 person-years in 2018. However, the highest peak for pelvic fractures occurred in 2013 (14.1 per 100 000 person-years) (Figure 16).

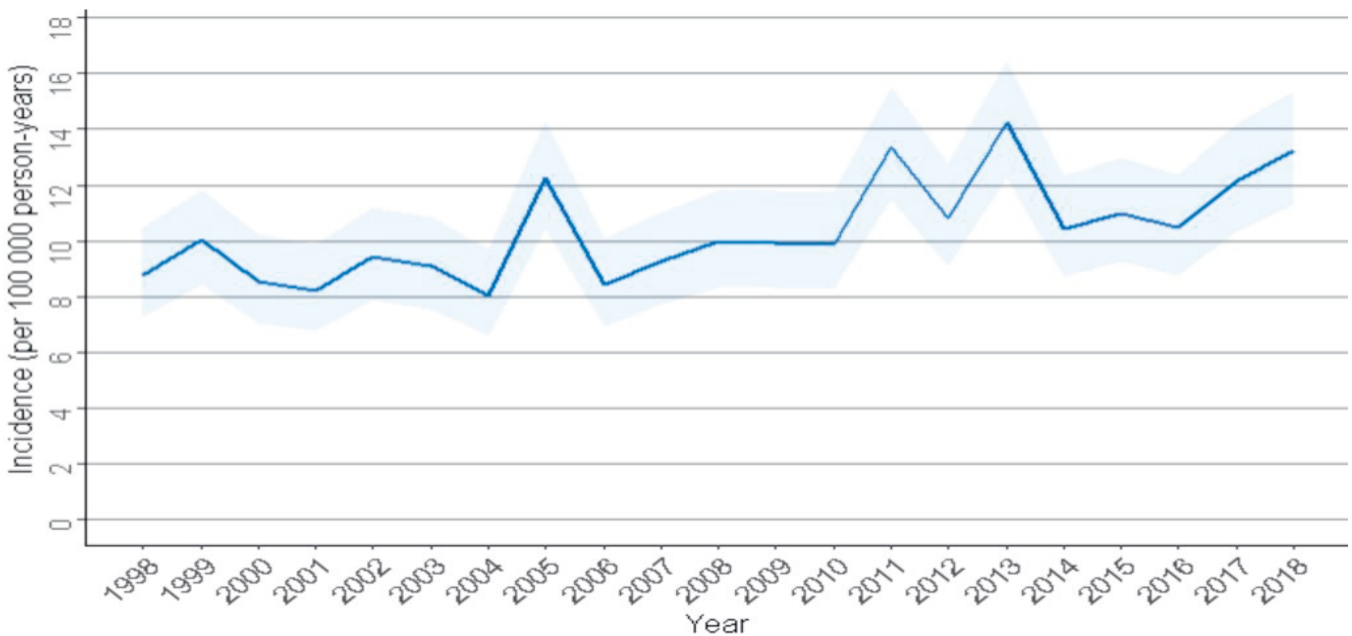

Figure 16. The annual incidence per 100 000 fertile-aged (15-49 years) women of pelvic fracture hospitalizations during the study period (1998-2018).

During the period of our study, there was a slight increase in the hospitalization incidence for spine fractures from 24.3 per 100,000 person-years in 1998 to 28.7 per 100 000 person-years in 2018. However, the incidence of surgery for spine fractures remained constant, with a range of 3.0 to 7.1 per 100 000 person-years during the same period (Figure 17).

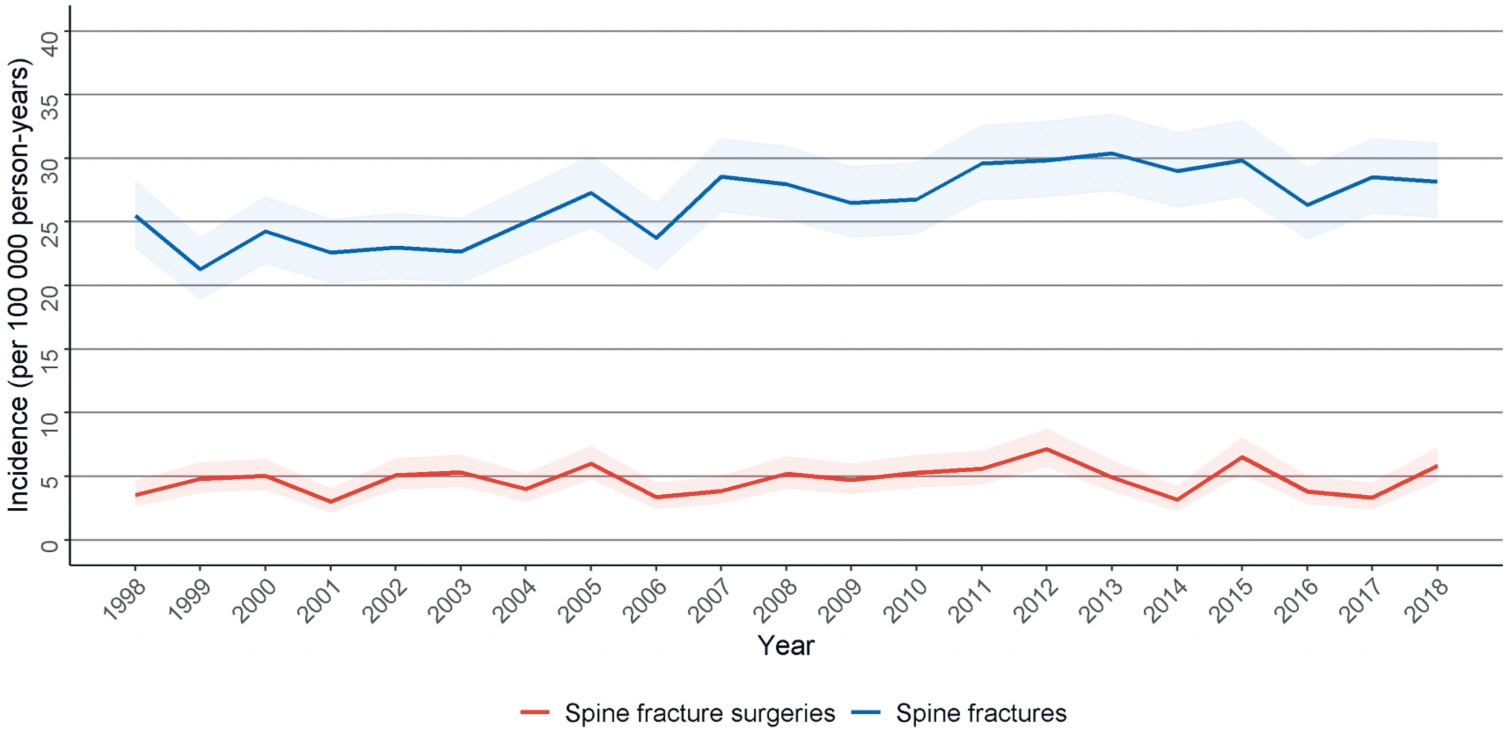

Figure 17. The annual incidence per 100 000 fertile-aged (15-49 years) women of spine fracture hospitalizations and spine fracture surgeries with 95% confidence intervals during the study period (1998-2018).

During the study period, the incidence of spine fusion surgeries not related to fractures increased by over two-fold, rising from 17.6 per 100 000 person-years to 46.3 per 100 000 person-years (Figure 18).

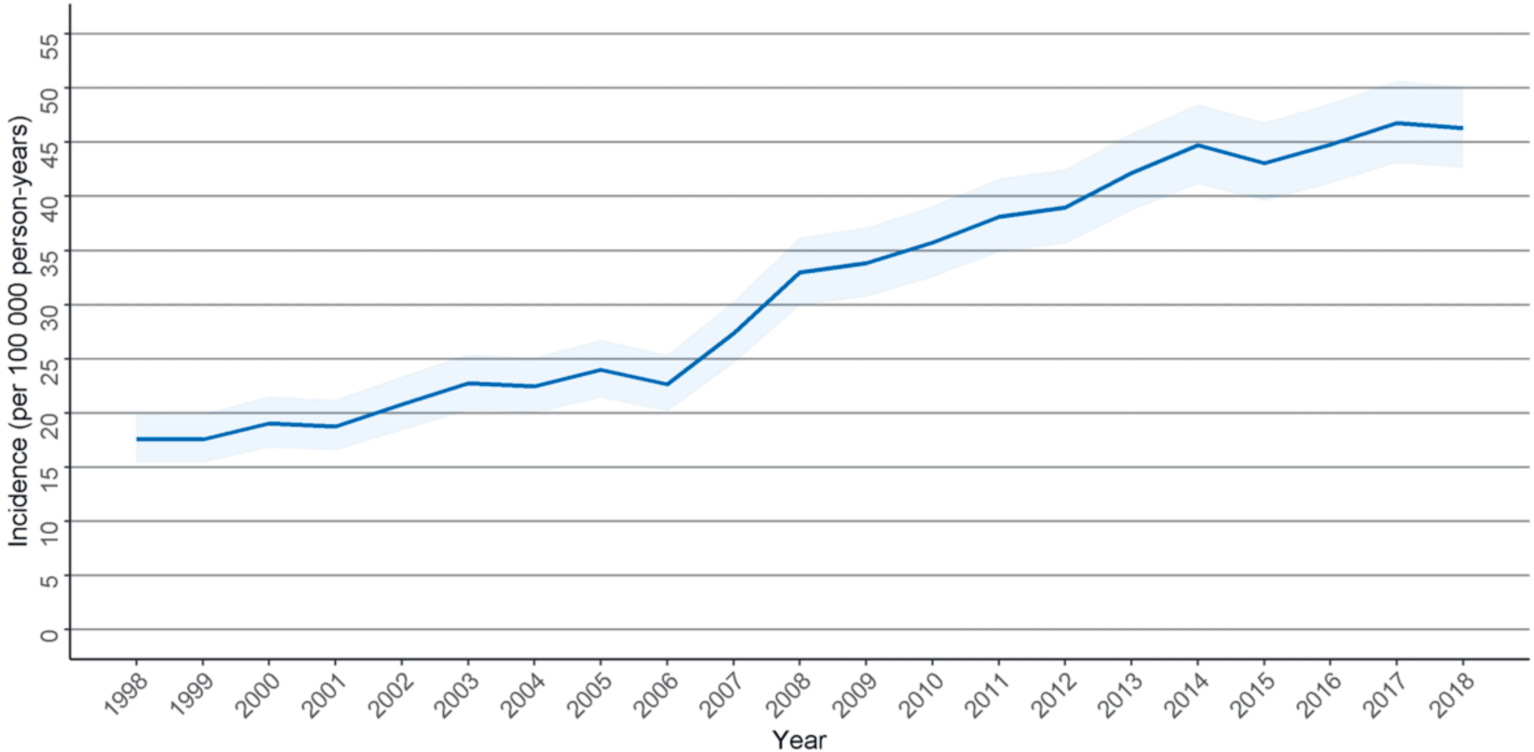

Figure 18. The annual incidence per 100 000 fertile-aged (15-49 years) women of fusion surgeries for other reasons with 95% confidence intervals during the study period (1998-2018).

In our study period, there was an over two-fold increase (149.5%) in the incidence of traumatic brain injury (TBI) hospitalization among women of reproductive age. The incidence rose from 103 per 100 000 person-years in 1998 to 257 per 100 000 person-years in 2018 (Figure 19).

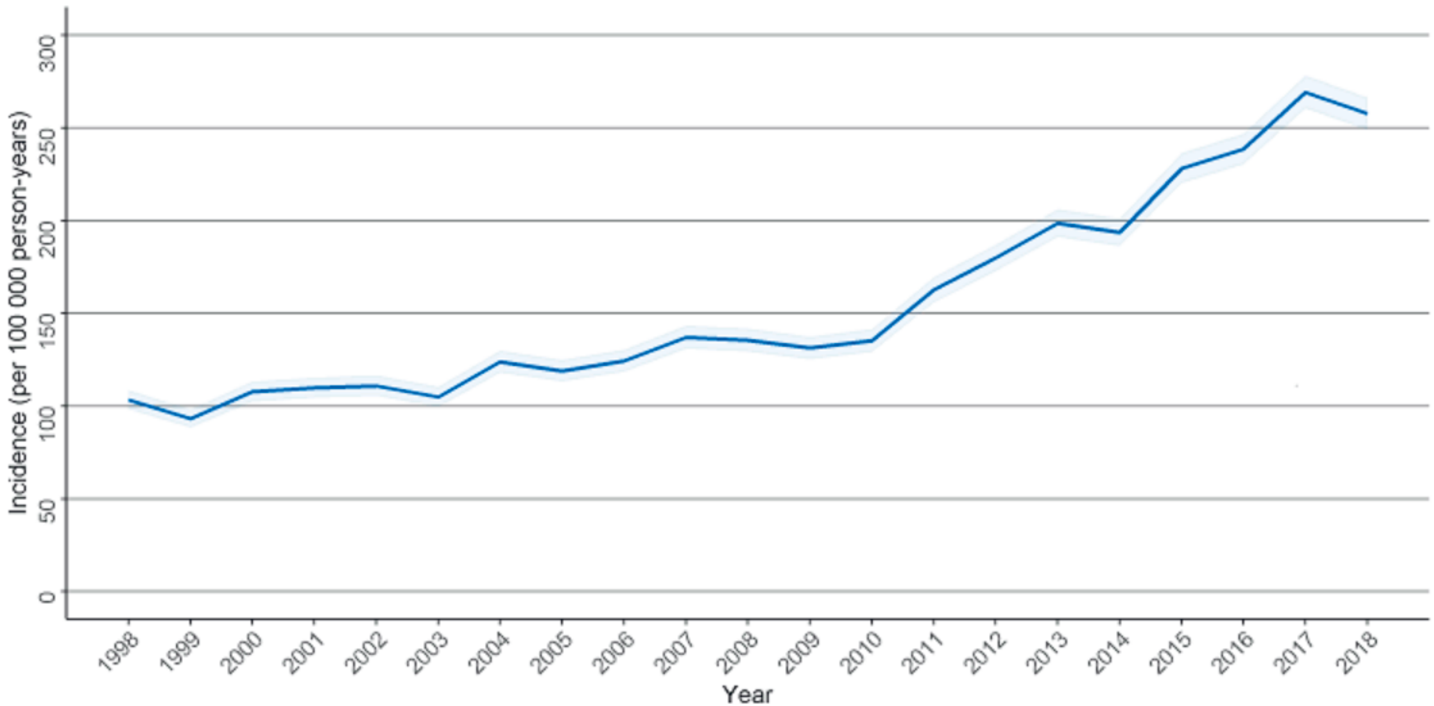

Figure 19. The annual incidence per 100 000 fertile-aged (15-49 years) women of traumatic brain injury during the study period (1998-2018).

During our study period, the rate of TBIs that required surgical intervention decreased slightly from 2.5 (1998) to 1.5 (2018) per 100 000 person-years (Figure 20).

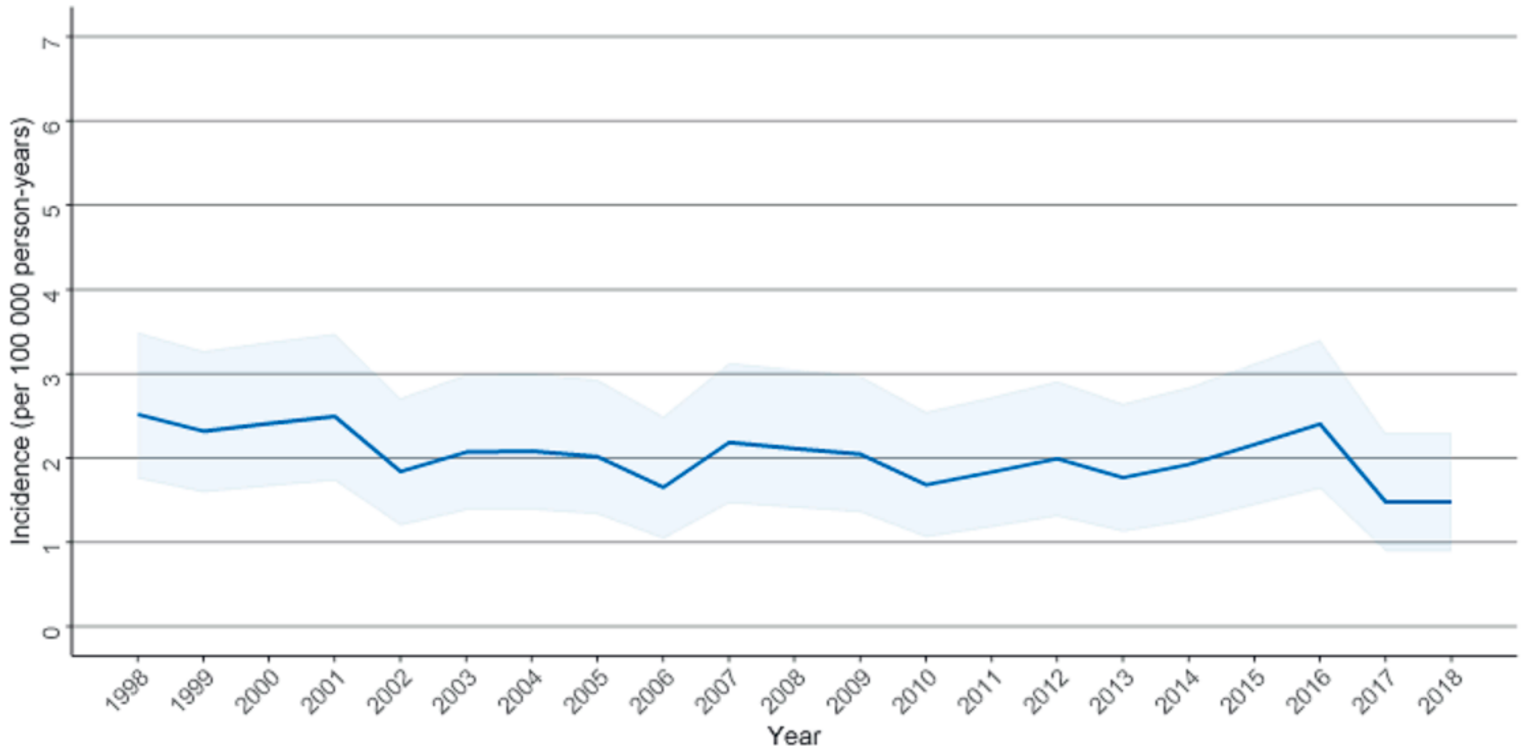

Figure 20. Incidence of traumatic brain injury surgeries among fertile-aged (15-49 years) women during the study period (1998-2018).

The incidence of fracture hospitalizations of the hip or thigh remained stable during our study period, ranging between 7.9 and 12.8 per 100 000 person-years (Figure 21).

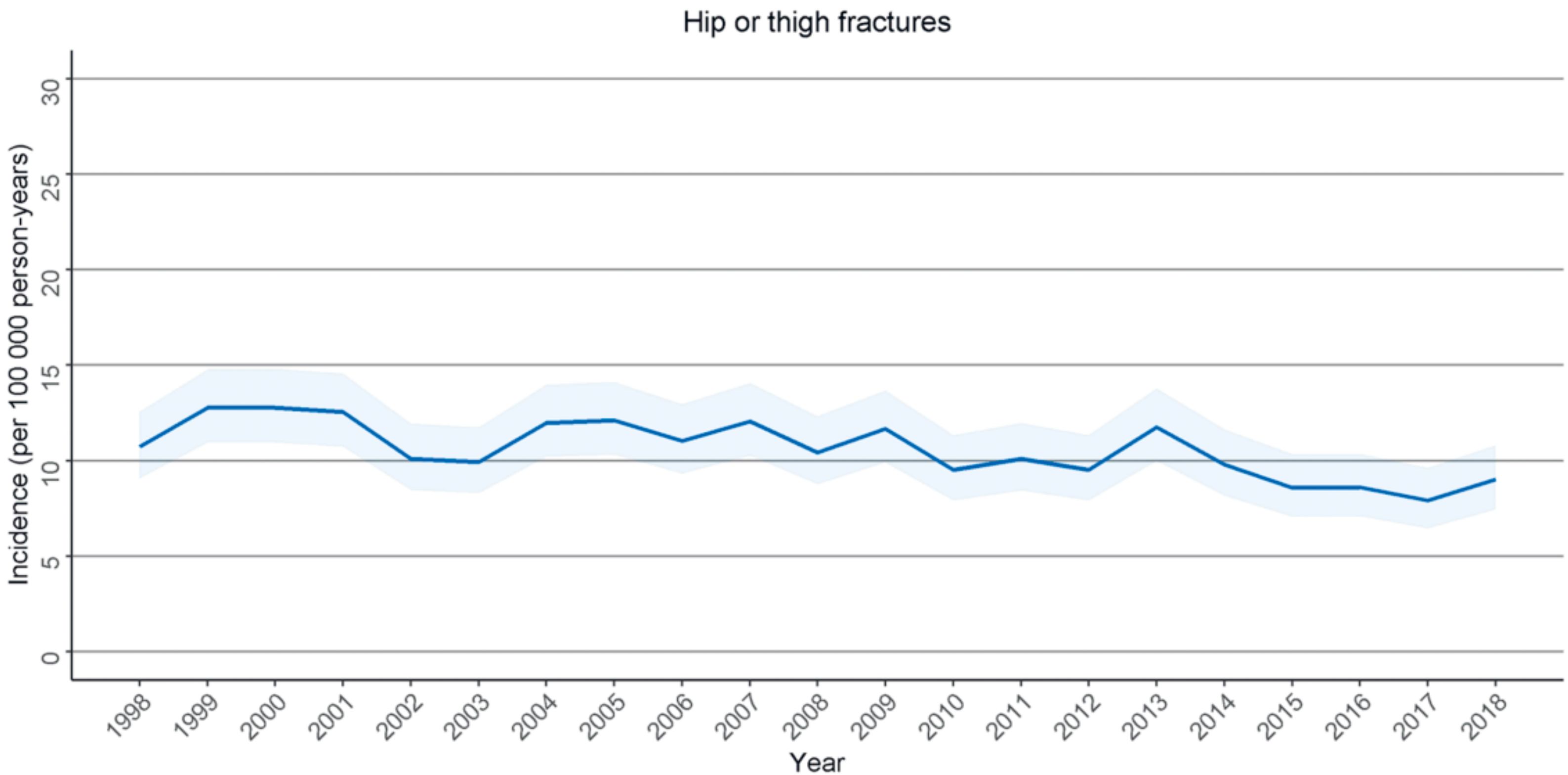

Figure 21. The annual incidence per 100 000 fertile-aged (15-49 years) women of fracture hospitalizations of hip or thigh during the study period (1998-2018).

5.2 Pelvic fractures and reproductive health (I)

In study I, the fracture group consisted of 596 women who had 1024 singleton deliveries and the no-fracture group consisted of 621 141 women who had 1 156 378 singleton pregnancies no-fracture group. During delivery, the average age of women who became pregnant after sustaining a pelvic fracture was 29.0 (SD 5.3) years, while the average age in the no-fracture group was 29.7 (SD 5.4) years. The pelvic fracture group had a higher proportion of nulliparous women compared to the no-fracture group (44.6% vs 41.4%, $p < 0.001$). Compared to the no-fracture group, a greater percentage of fetuses in the pelvic fracture group were exposed to maternal smoking during pregnancy (23.1% vs 14.6%, $p < 0.001$). (Table 12)

Table 12. Background characteristics of deliveries in the pelvic fracture group and no-fracture group. CS = Cesarean section

	Fracture-group		No-fracture group	
Total number	1024		1 156 378	
	n	%	n	%
Age at birth (mean SD)	29.0 (5.3)		29.7 (5.4)	
Nulliparous	457	44.6	478 472	41.4
Previous CS	120	11.7	124 235	10.7
Maternal smoking during pregnancy				
confirmed smoker *	237	23.1	169 135	14.6
Diagnosed maternal gestational diabetes	110	10.7	106 724	9.2
not registered**	65	6.3	326 030	28.2

* Refers to women who smoked during either the first trimester and/or later trimesters of pregnancy

** The registering of gestational diabetes started in 2004, meaning that we have no information about gestational diabetes in pregnancies occurring during the years 1998-2003

Among neonates in the fracture group, 6.2% were born preterm (gestational age at birth $<37^{+0}$ weeks of gestation) and 3.5% had low birthweight (< 2500g), whereas 4.6% of neonates in the no-fracture group were born preterm, and 3.0% had low birthweight ($p < 0.001$ for both). Neonates in the pelvic fracture group had higher percentages of health-related problems, such as neonatal deaths, Apgar scores after 1 minute, phototherapy, and neonatal intensive care unit admission, compared to the no-fracture group. (Table 13)

Table 13. Perinatal characteristics in the diagnosed fracture group and the no-fracture group.

	Fracture group		No-fracture group	
Total number	1024		1 156 378	
	n	%	n	%
Neonatal sex boy	526	51.4	591 788	51.2
Birth length (cm) (mean; SD)	50.0	2.5	50.1	2.5
Birthweight (grams) (mean; SD)	3474	546	3531	548
LBW < 2500g	36	3.5	34 470	3.0
Preterm < 37 + 0 weeks	63	6.2	53 117	4.6
Perinatal mortality*	7	0.7	6165	0.5
Neonatal deaths**	5	0.5	2708	0.2
1-minute Apgar score ≤ 6	150	14.6	157 399	13.6
Delivery related asphyxia	26	2.5	34 707	3.0
Phototherapy	65	6.3	68 752	5.9
Neonatal intensive-care unit	138	13.5	115 787	10.0
Neonatal status 7 days postpartum				
at home	956	93.4	1 086 765	94.0
at hospital	68	6.6	69 613	6.0

* Includes both stillbirths and neonatal deaths occurring during the first seven days after birth.

** Includes neonates who were born alive but did not survive beyond the first seven days

Compared to the no-fracture group, women in the pelvic fracture group had higher rates of elective CS (11.3% vs 6.6%, p < 0.001) and urgent CS (12.7% vs 9.9%, p < 0.001). In addition, the use of labor analgesia was more common among women with previous pelvic fractures, but there were no major differences found in the rate of obstetrical interventions such as amniotomy, use of oxytocin to induce or augment labor, or episiotomy compared to no-fracture group. (Table 14)

Table 14. Intended and occurred mode of delivery, labor analgesia, and delivery-related procedures in the trial of labors in the pelvic fracture group and the no-fracture group. CS=Cesarean section.

	Fracture group		No-fracture group	
Total number	1024		1 156 378	
	n	%	n	%
Intendent mode of delivery				
Elective CS	116	11.3	76 663	6.6
Trial of labor	908	88.7	1 079 715	93.4
Total number (without elective CS)	908	100	1 079 715	100
Mode of delivery				
spontaneous vaginal delivery	698	76.8	874 824	81.0
breech delivery	4	0.4	7009	0.6
vacuum or forceps delivery	91	10.0	90 840	8.4
urgent CS	115	12.7	107 042	9.9
Labor analgesia				
epidural	455	50.1	469 968	43.5
spinal	154	17.0	123 064	11.4
paracervical	148	16.3	188 597	17.5
Amniotomy	446	49.1	533 128	49.4
Use of oxytocin	431	47.5	489 282	45.3
Episiotomy	214	23.6	278 782	25.8
Manual placental removal	12	1.5	16 075	1.5
Uterine curettage	6	0.7	9419	0.9

Compared to the no-fracture group, women in the fracture group had higher odds of preterm deliveries (aOR 1.32, CI 1.01 - 1.69), CS (including elective and urgent CS) (aOR 1.57, CI 1.34 - 1.83), and neonates requiring treatment in the intensive care unit (aOR 1.31, CI 1.07 - 1.58). Also, the odds of urgent CS was higher among in the fracture group (aOR 1.29, CI 1.06 - 1.57) when compared to the no-fracture group. (Table 15) When analyzing only nulliparous pregnancies, the odds for CS were higher among women with prior pelvic fractures, when compared to the no-fracture group (aOR 1.51, CI 1.22-1.88). (Table 16) When only the first pregnancy following the pelvic fracture was included, the odds for CS (aOR 1.57, CI 1.34-1.83), and the odds for neonatal intensive care were (aOR 1.47, CI 1.14-1.84) were higher, when compared to no fracture group. (Table 17)

Table 15. Absolute numbers, percentages, univariable and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for main outcomes. Pregnancies after pelvic fractures were compared to the no-fracture group consisting of pregnancies without prior pelvic fractures. The cesarean section includes all cesarean sections.

	Fracture group		No-fracture group		Univariable	Adjusted
Total number	1024		1 156 378			
	n	%	n	%	OR (95% CI)	aOR (95% CI)
Preterm delivery	63	6.2	53 117	4.6	1.36 (1.04-1.74)	1.32 (1.01-1.69) *
Cesarean section	231	22.6	183 705	15.9	1.51 (1.33-1.78)	1.57 (1.34-1.83) **
Neonatal intensive care	138	13.5	115 787	10.0	1.40 (1.17-1.67)	1.31 (1.07-1.58) ***

* Adjusted by maternal smoking status and maternal diabetes during pregnancy
** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and previous CS
*** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

Table 16. Additional analysis with only nulliparous women included. Absolute numbers, percentages, univariable and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for main outcomes. Pregnancies after pelvic fractures were compared to the no-fracture group consisting of pregnancies without prior pelvic fractures. The cesarean section includes all cesarean sections.

	Fracture group		No fracture-group		Univariable	Adjusted
Total number	457		478 472			
	n	%	n	%	OR (95% CI)	aOR (95% CI)
Preterm delivery	29	6.3	26 158	5.5	1.17 (0.79-1.67)	1.15 (0.77-1.65) *
Cesarean section	124	27.1	95 637	20.0	1.54 (1.33-1.78)	1.51 (1.22-1.88) **
Neonatal intensive care	73	16.0	59 843	12.5	1.32 (1.03-1.70)	1.29 (0.98-1.68) ***

* Adjusted by maternal smoking status and maternal diabetes during pregnancy
** Adjusted by maternal age, maternal smoking status, and maternal gestational diabetes
*** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

Table 17. Additional analysis with only the first pregnancy following the major trauma included in the fracture group. Absolute numbers, percentages, univariable and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for main outcomes. Pregnancies after pelvic fractures were compared to the no-fracture group consisting of pregnancies without prior pelvic fractures. The cesarean section includes all cesarean sections.

	Fracture group		No fracture-group		Univariable	Adjusted
Total number	596		1 156 378			
	n	%	n	%	OR (95% CI)	aOR (95% CI)
Preterm delivery	39	6.5	53 117	4.6	1.17 (0.79-1.67)	1.15 (0.77-1.65) *
Cesarean section	162	27.2	183 705	15.9	1.98 (1.65-2.36)	1.57 (1.34-1.83) **
Neonatal intensive care	89	14.9	115 787	10.0	1.58 (1.25-1.96)	1.47 (1.14-1.84) ***

* Adjusted by maternal smoking status and maternal diabetes during pregnancy
** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and previous CS
*** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

In the subgroup analyses, among women with multiple pelvic fractures (ICD-10 diagnosis S32.7), the proportion of elective CS (17.6%) was higher than with any other diagnosis (3.3%-13.9%). However, when compared to the other fracture groups, neonatal health was at a similar level in this subgroup, when compared to other subgroups. (Table 18) The perinatal mortality rate was low for all fracture diagnoses. Vaginal delivery was possible in all groups with pelvic fractures, and the rates of labor analgesia and modes of delivery were similar when patients undergoing elective CS were excluded. However, women with multiple pelvic fractures had lower rates of spontaneous vaginal deliveries (69.9%) than women with other fractures (76.6%-82.0%). A higher rate of urgent CS among women with multiple pelvic fractures was observed (17.6%), but the rate of breech, vacuum or forceps deliveries remained similar, when compared to other subgroups. However, the relatively low number of patients in the subgroup analyses might have caused imprecision for the subgroup analysis. (Table 19)

Table 18. Perinatal characteristics and outcomes in the subgroups based on the type of fracture diagnosis among conservatively and operatively treated pelvic fracture patients.

Type of fracture	Sacrum (S32.1)		Ilium (S32.3)		Acetabulum (S32.4)		Pubis (S32.5)		Multiple fractures (S32.7)		Other or undefined (S32.8)	
Total number	179		92		128		214		262		149	
	n	%	n	%	n	%	n	%	n	%	n	%
Intended mode of delivery												
Elective CS*	25	13.9	3	3.3	14	10.9	16	7.5	46	17.6	12	8.1
Trial of labor	154	86.1	89	96.7	114	89.1	198	92.5	216	82.4	137	91.9
Preterm < 37 + 0 weeks	17	9.5	4	4.3	11	8.6	6	2.8	14	5.3	11	7.4
1 minute Apgar score ≤ 6	27	15.1	13	14.1	21	16.4	27	12.6	42	9.2	20	13.4
Neonatal intensive care unit	25	14.0	12	13.0	21	16.4	33	15.4	27	10.3	20	13.4
Neonatal status 7 days postpartum												
at home	164	91.6	85	92.4	115	89.8	201	93.9	247	94.3	138	92.6
at hospital	15	8.4	7	7.6	13	10.2	13	6.1	15	5.7	11	7.4

* CS=Cesarean section.

Table 19. Proportions of selected obstetric variables in attempted vaginal deliveries in the subgroups based on the type of fracture diagnosis among conservatively and operatively treated pelvic fracture patients.

Fracture diagnosis (ICD-10)	Sacrum (S321)		Ilium (S323)		Acetabulum (S324)		Pubis (S325)		Multiple fractures (S327)		Other or undefined (S328)	
Total number	154		89		114		198		216		137	
	n	%	n	%	n	%	n	%	n	%	n	%
Mode of delivery												
spontaneous vaginal delivery	126	81.8	73	82.0	90	78.9	153	77.3	151	69.9	105	76.6
breech, vacuum, or forceps delivery*	7	4.5	13	14.6	11	9.6	22	11.1	27	12.5	15	10.9
urgent CS**	21	13.6	3	3.4	13	11.4	23	11.6	38	17.6	17	12.4
Labor analgesia												
epidural	75	48.7	47	52.8	60	52.6	99	50.0	105	48.6	69	50.4
spinal	29	18.8	12	13.5	16	14.0	40	20.2	36	16.7	21	15.3
paracervical	16	10.4	16	18.0	24	21.1	33	16.7	33	15.3	26	19.0

* Due to the low number of breech and forceps deliveries these are combined as the Finnish legislation prevents reporting the exact event rate if the rate is lower than three.
** CS=Cesarean section.

5.3 Spine fractures, spine surgeries, and reproductive health (II)

A total of 14 006 women with a spine fracture or who underwent fusion surgery unrelated to fracture were identified from the Care Register for Health Care. During the study period, 6374 women sustained a spine fracture, and 7630 women underwent spine fusion surgery for other reasons. In total, there were 1329 women with 2224 singleton deliveries after spine fracture and 416 women with 632 singleton deliveries after spine fusion surgery unrelated to fracture. The control group consisted of 620 093 women with 1 154 469 singleton deliveries without prior spine fracture or fusion surgery.

The percentage of nulliparous women was higher in both the spine fracture group (46.1%) and spine fusion surgery group (43.4%) compared to those without a previous spine fracture or fusion surgery (41.4%) ($p < 0.001$ for both groups). A lower rate of women in the spine fracture group (49.9%) and the fusion surgery for other reasons group (51.7%) had been married before the particular pregnancy ($p < 0.001$ for both) than in the control group (59.5%). A high rate of fetuses was exposed to the smoking of the mother in the fracture group (27.1%, $p < 0.001$) and the fusion surgery for other reasons group (18.0%, $p < 0.001$), whereas only 14.2% of the fetuses in the control group were exposed. (Table 20)

Table 20. Background characteristics of women having singleton pregnancies in the patient groups (pregnancies with prior spine fractures, or spine fusion surgeries), and control group (no prior spine fractures or spine fusion surgeries). CS=Cesarean section.

	Fracture group		Fusion surgery group		Control group	
Total number	2301		632		1 154 469	
	n	%	n	%	n	%
Age at birth (years, mean SD)	29.4 (4.7)		30.6 (6.2)		29.7 (5.4)	
Nulliparous	1060	46.1	274	43.4	477 595	41.4
Previous CS	241	10.5	99	15.7	124 013	10.7
Ever married	1148	49.9	327	51.7	687 288	59.5
Smoking during pregnancy*	625	27.2	114	18.0	168 633	14.6
Diagnosed maternal gestational diabetes	287	12.5	102	16.1	106 445	9.2
not registered**	134	5.8	45	7.1	325 916	28.2

* Refers to women who smoked during either the first trimester and/or later trimesters of pregnancy.
** The registering of gestational diabetes started in 2004, meaning that we have no information about gestational diabetes on pregnancies occurring during the years 1998-2003

Patients who had spine fracture or undergone spine fusion surgery unrelated to fracture had a higher rate of elective CS (9.5% and 13.1%, respectively, $p < 0.001$ for both) when compared to the control group (6.6%). After excluding elective CS, the proportion of urgent CS was higher in the fracture group (11.3%, $p = 0.032$) and higher in the spine fusion surgery for other reasons group (14.0%, $p < 0.001$), compared to the control group (9.9%). In the same analysis, when only primiparous women and women without a history of previous CS were included, the rates of urgent CS were 15.5% in the spine fracture group, 17.2% in the spine fusion surgery group, and 14.2% in the control group ($p < 0.001$ for both the fracture and fusion surgery groups when compared to the control group). Epidural and spinal anesthesia were more common among patients in the spine fracture group (48.0% and 14.4%) and the fusion surgery for other reasons group (46.8% and 14.4%) than in the control group (43.5% and 11.4%, p < 0.001 for both). In addition, in the fracture and fusion surgery for other reasons groups, pudendal (9.2% and 8.7%) and paracervical (19.9% and 23.3%) analgesia were slightly more common when compared to the control group (6.2% for pudendal and 17.5% for paracervical, p < 0.001 for both). (Table 21)

Table 21. Proportions of obstetric variables in attempted vaginal deliveries (without elective CS) of the spine fracture or spine fusion surgery patient groups and the control group. Elective CS was the intended mode of delivery in 218 (9.5%) of all deliveries in the fracture group, 83 (13.1%) in the fusion surgery for other reasons group, and 76 478 (6.6%) in the control group.

	Fracture group		Fusion surgery group		Control group	
Total number pregnancies	2083		549		1 077 991	
	n	%	n	%	n	%
Mode of delivery						
spontaneous vaginal delivery	1630	78.3	411	74.9	873 485	81.0
instrumental vaginal delivery	217	10.4	61	11.1	97 666	9.1
urgent CS	236	11.3	77	14.0	106 844	9.9
Labor analgesia						
epidural	1000	48.0	257	46.8	469 166	43.5
spinal	342	16.4	79	14.4	122 797	11.4
spinal + epidural	58	2.8	14	2.6	13 600	1.3
paracervical	414	19.9	128	23.3	188 203	17.5
pudendal	192	9.2	48	8.7	67 331	6.2

* CS=Cesarean section.

There was a higher rate of fetuses born with LBW in the fracture group (3.5%) and fusion surgery for other reasons group (3.8%) than in the control group (3.0%, p < 0.001 for both). Perinatal mortality rates or problems related to the health of the neonate, such as 1-minute Apgar score below 6, delivery-related asphyxia, and need for phototherapy, were not found to be more common in the fracture group or the fusion surgery for other reasons group compared to the control group. However, a higher proportion of neonates born to women in the spine fracture and fusion surgery for other reasons groups required intensive care when compared to the control group (12.3% and 13.4% vs 10.0%, respectively, p < 0.001). (Table 22)

Table 22. Perinatal characteristics and outcomes in the patient groups and the control group.

	Fracture group		Fusion surgery group		Control group	
Total number	2301		632		1 154 469	
	n	%	n	%	n	%
LBW* < 2500g	80	3.5	24	3.8	34 402	3.0
Preterm < 37 + 0 gestational weeks	115	5.0	46	7.3	53 019	4.6
Perinatal mortality**	9	0.4	5	0.8	6158	0.5
1 minute Apgar score ≤ 6	333	14.5	85	13.4	157 131	13.6
Neonatal intensive-care unit	281	12.2	86	13.6	115 558	10.0
Discharged from the hospital during the first week	2143	93.1	589	93.2	1 084 983	94.0

* LBW=low birthweight

** Perinatal mortality includes stillbirths and deaths before the age of seven days

In the logistic regression model, women in the spine fracture group had a higher rate of CS (aOR 1.30, CI 1.17 - 1.45) and a higher need for intensive care treatment for the neonate (aOR 1.19, CI 1.05 - 1.34) when compared to the control group. The same comparison of the fusion surgery for other reasons group to the control group showed a higher rate of CS (aOR 1.63, CI 1.34 - 1.96) and a higher need for intensive care treatment for the neonate (aOR 1.35, CI 1.07 - 1.68). When comparing only patients with fracture or fusion surgery for other reasons in the lumbar spine, the odds for CS after fracture of the lumbar spine (aOR 1.42, CI 1.23 - 1.64) or fusion surgery of the lumbar spine (aOR 1.80, CI 1.38 - 2.34) was higher. The odds for neonatal intensive care were higher after a fracture of the lumbar spine (aOR 1.21, CI 1.02 - 1.94), and after fusion surgery of the lumbar spine (aOR 1.43, CI 1.02 - 1.94). (Table 23)

When only nulliparous women were included, the odds for CS were higher especially after spine fusion surgeries (aOR 1.57, CI 1.12-2.04), when compared to the control group without prior spine fractures or fusion surgeries. The odds for CS after fusion surgery in the lumbar spine were also higher (aOR 1.80, CI 1.38-2.34). A high rate for CS after fusion surgery of the lumbar spine was observed (aOR 1.94, CI 1.32-2.81) when compared to the control group. (Table 24)

When only first pregnancies following spine fracture or spine fusion surgery were included, the odds for CS were higher, especially after spine fusion surgeries overall (aOR 2.40, CI 1.93-2.98), or spine fusion surgeries in the lumbar spine (aOR 2.75, CI 2.02-3.70), when compared to the control group without prior spine fractures or fusion surgeries. The odds for neonatal intensive care were also higher in first pregnancies following the spine fracture or spine fusion surgery, when compared to the control group. (Table 25)

Table 23. Absolute numbers, percentages, and both univariable (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for the primary outcomes. Pregnancies after spine fractures and spine fusion surgeries were compared to the control group consisting of pregnancies without prior spine fractures or fusion surgeries. L means only patients with fractures or fusion surgery for other reasons in the lumbar spine. The cesarean section includes all cesarean sections.

	Patient group n	%	Control group n	%	Univariable OR (95% CI)	Adjusted aOR (95% CI)
Spine fractures						
Total number of patients	2301		1 154 469			
Cesarean section	454	19.7	183 322	15.9	1.30 (1.17-1.44)	1.30 (1.17-1.45) *
Neonatal intensive care	281	12.2	115 558	10.0	1.25 (1.10-1.41)	1.19 (1.05-1.34) **
Total number of patients (L)	1198		1 154 469			
Cesarean section (L)	254	21.2	183 322	15.9	1.42 (1.24-1.63)	1.42 (1.23-1.64) *
Neonatal intensive care (L)	149	12.4	115 558	10.0	1.28 (1.07-1.51)	1.21 (1.02-1.44) **
Spine fusion surgeries						
Total number of patients	632		1 154 469			
Cesarean section	160	25.3	183 322	15.9	1.80 (1.50-2.14)	1.63 (1.34-1.96) *
Neonatal intensive care	86	13.6	115 558	10.0	1.42 (1.12-1.77)	1.35 (1.07-1.68) **
Total number of patients (L)	309		1 154 469			
Cesarean section (L)	88	28.5	183 322	15.9	2.11 (1.64-2.69)	1.80 (1.38-2.34) *
Neonatal intensive care(L)	44	14.2	115 558	10.0	1.49 (1.07-2.03)	1.43 (1.02-1.94) **

* Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and previous cesarean section

** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

Table 24. Additional analysis with only nulliparous women included. Absolute numbers, percentages, and both univariable (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for the primary outcomes. Pregnancies after spine fractures and spine fusion surgeries were compared to the control group consisting of pregnancies without prior spine fractures or fusion surgeries. L means only patients with fractures or fusion surgery for other reasons in the lumbar spine. The cesarean section includes all cesarean sections.

	Patient group		Control group		Univariable	Adjusted
	n	%	n	%	OR (95% CI)	aOR (95% CI)
Spine fractures						
Total number of patients	1060		477 595			
Cesarean section	255	24.1	95 212	19.9	1.27 (1.10-1.46)	1.22 (1.06-1.41) *
Neonatal intensive care	162	15.3	59 607	12.5	1.26 (1.06-1.49)	1.21 (1.02-1.42) **
Total number of patients (L)	577		477 595			
Cesarean section (L)	134	23.2	95 212	19.9	1.27 (1.04-1.54)	1.21 (0.99-1.48) *
Neonatal intensive care(L)	81	7.6	59 607	12.5	1.19 (0.93-1.50)	1.14 (0.89-1.44) **
Spine fusion surgeries						
Total number of patients	274		477 595			
Cesarean section	82	29.9	95 212	19.9	1.71 (1.31-2.21)	1.57 (1.12-2.04) *
Neonatal intensive care	40	14.6	59 607	12.5	1.20 (0.84-1.65)	1.13 (1.05-1.57) **
Total number of patients (L)	124		477 595			
Cesarean section (L)	43	34.7	95 212	19.9	2.13 (1.46-3.06)	1.94 (1.32-2.81) *
Neonatal intensive care(L)	21	16.9	59 607	12.5	1.43 (0.87-2.23)	1.37 (0.83-2.14)**

* Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and previous cesarean section
** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

Table 25. Additional analysis with only the first pregnancy following the major trauma included. Absolute numbers, percentages, and both univariable (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for the primary outcomes. Pregnancies after spine fractures and spine fusion surgeries were compared to the control group consisting of pregnancies without prior spine fractures or fusion surgeries. L means only patients with fractures or fusion surgery for other reasons in the lumbar spine. The cesarean section includes all cesarean sections.

	Patient group n	%	Control group n	%	Univariable OR (95% CI)	Adjusted aOR (95% CI)
Spine fractures						
Total number of patients	1371		1 154 469			
Cesarean section	314	22.9	183 322	15.9	1.57 (1.39-1.78)	1.90 (1.66-2.16) *
Neonatal intensive care	198	14.4	115 558	10.0	1.52 (1.30-1.76)	1.44 (1.24-1.67) **
Total number of patients (L)	713		1 154 469			
Cesarean section (L)	170	23.8	183 322	15.9	1.66 (1.39-1.97)	2.00 (1.67-2.38) *
Neonatal intensive care(L)	103	14.4	115 558	10.0	1.52 (1.22-1.86)	1.45 (1.17-1.78) **
Spine fusion surgeries						
Total number of patients	416		1 154 469			
Cesarean section	125	30.0	183 322	15.9	2.28 (1.84 – 2.80)	2.40 (1.93-2.98) *
Neonatal intensive care	66	15.9	115 558	10.0	1.70 (1.29-2.19)	1.59 (1.21-2.06) **
Total number of patients (L)	206		1 154 469			
Cesarean section (L)	69	33.5	183 322	15.9	2.67 (1.99-3.55)	2.75 (2.02-3.70) *
Neonatal intensive care(L)	35	17.0	115 558	10.0	1.84 (1.26-2.61)	1.74 (1.19-2.47) **

* Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and previous cesarean section
** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

5.4 TBIs and reproductive health (III)

The Care Register for Health Care identified 40 028 women who had a hospitalization related to TBI. During our study period, 8048 women had 13 448 deliveries after TBI. In the control group, 615 144 women had 1 143 954 deliveries. The mean age at the time of pregnancy among women with previous TBI was lower than for women in the control group without previous TBI (28.7 years vs 29.7 years). Among women with prior TBI, a notably greater proportion of fetuses were exposed to maternal smoking during pregnancy compared to the control group (27.7% vs 14.5%, $p < 0.001$). Women with previous TBI had a higher rate of deliveries requiring induction when compared to the control group (25.4% vs 18.9%, $p < 0.001$). (Table 25) Compared to the control group, a higher proportion of neonates born to women with TBI before pregnancy were born with LBW (3.8% vs 3.0%, $p < 0.001$) and preterm (5.6% vs 4.6%, $p < 0.001$). However, the rates for very preterm deliveries and extremely preterm deliveries were similar between the groups. Perinatal mortality was similar between women with previous TBI and the control group, but the TBI group had a higher proportion of neonates requiring neonatal intensive care compared to the control group (13.1% vs 9.9%, $p < 0.001$). (Table 26)

Table 26. Background information on the deliveries and perinatal characteristics in the traumatic brain injury (TBI) group and the control group. GW = gestational weeks

	TBI group		Control group	
Total number of pregnancies	13 448		1 143 954	
	n	%	n	%
Age at birth (years, mean SD)	28.7 (5.5)		29.7 (5.4)	
Nulliparous	5 963	44.3	472 966	41.3
Previous cesarean section	1 566	11.6	122 789	10.7
Maternal smoking during pregnancy	3 722	27.7	165 650	14.5
Diagnosed gestational diabetes	1896	14.1	104 938	9.2
Not registered*	740	5.5	325 355	28.4
Low birth weight (< 2500 g)	515	3.8	33 991	3.0
Induction of labor	3412	25.4	216 715	18.9
Preterm**				
Preterm < 37 + 0 GW	755	5.6	52 425	4.6
Very preterm 28+0 – 31+6 GW	75	0.6	4710	0.4
Extremely preterm ≤ 27+6 GW	37	0.3	3268	0.3
Perinatal mortality***	72	0.5	6100	0.5
1-minute Apgar score ≤ 6	1948	14.5	155 601	13.6
Neonatal intensive-care unit	1756	13.1	114 160	10.0
Discharged from the hospital during the first week	12 458	92.6	1 075 257	94.0

* The registering of gestational diabetes started in 2004, meaning that we have no information about gestational diabetes on pregnancies occurring during the years 1998-2003

** The analysis considered preterm births both overall (before 37 + 0 gestational weeks) and according to the World Health Organization's classification, which distinguishes between very preterm (between 28+0 and 31+6 gestational weeks) and extremely preterm (≤ 27+6 gestational weeks) pregnancies.

*** Includes stillbirths as well as deaths occurring before the seventh day of life.

The rate of elective CS as a mode of delivery was higher in women with TBI compared to the control group (7.7% vs 6.6%, p < 0.001). Among attempted vaginal deliveries, the rate of urgent CS was higher in the TBI group (12.5% vs 9.9%, p < 0.001) than in the control group. Also, the rate for vacuum and forceps deliveries was higher after TBI (9.5% vs 8.4%), when compared to the control group. The proportion of epidural analgesia use was higher in the TBI group compared to the control group (50.8% vs 43.4%, p < 0.001). (Table 27)

Table 27. Proportions of obstetric variables in attempted vaginal deliveries in the traumatic brain injury (TBI) group and control group. Elective CS in the TBI group n 1039 (7.7%) and in the control group n 75 740 (6.6%) were excluded.

	TBI group		Control group		
Total number (without elective CS)	12 409		1 068 214		
	n	%	n	%	P-value
Mode of delivery					
spontaneous vaginal delivery	9613	77.5	865 909	81.1	<0.001
breech delivery	75	0.6	6938	0.6	0.035
vacuum of forceps delivery	1174	9.5	89 757	8.4	0.060
urgent CS*	1547	12.5	105 610	9.9	<0.001
Labour analgesia					
epidural	6306	50.8	464 117	43.4	<0.001
spinal	1962	15.8	121 256	11.4	0.292
spinal + epidural	232	1.9	13 440	1.3	0.915
paracervical block	2301	18.5	186 444	16.3	<0.001
pudendal block	1082	8.7	66 489	6.2	0.044

In subgroup analysis, patients who underwent operative TBI had a markedly higher rate of instrumental vaginal deliveries compared to the non-admitted and admitted TBI groups (21.9% vs 9.3% and 8.8%, p = 0.015). Also, the rate for elective CS was higher among women with previous TBI (10.9%). No perinatal mortality during or after delivery was reported among women with previously operated TBI. However, the number of patients in the previously operated TBI group was relatively low. (Table 28)

Table 28. The distribution of obstetric variables and perinatal characteristics among the traumatic brain injury (TBI) group categorized into three subgroups based on TBI severity. CS=Cesarean section.

	Non-admitted TBI group		Admitted TBI group		Operated TBI group	
Total number	11 382		2002		64	
	n	%	n	%	n	%
Mode of delivery						
elective CS	884	7.8	148	7.4	7	10.9
spontaneous vaginal	8127	71.4	1446	72.2	40	62.5
instrumental delivery	1059	9.3	176	8.8	14	21.9
urgent CS	1312	11.5	232	11.6	3	4.7
Perinatal mortality *	63	0.6	9	0.4	0	0.0
Neonatal intensive care unit	1484	13.0	266	13.3	6	9.3

* Perinatal mortality includes stillbirths and deaths before the age of seven days

The probability for preterm deliveries in the TBI group was also slightly higher (aOR 1.19, CI 1.11 to 1.28) when compared to the control group. The odds for all CS, including both elective and urgent CS, were slightly higher in the TBI group when compared to the control group (aOR 1.25, CI 1.19 to 1.31). The odds for neonatal intensive care showed a small increase in the TBI group compared to the control group (aOR 1.26, CI 1.19 to 1.33). (Table 29) When analyzing only nulliparous women, the odds for CS (aOR 1.25, CI 1.19-1.31), and neonatal intensive care (aOR 1.26, CI 1.19-1.33) were higher after TBI. (Table 30) When only the first pregnancy following the TBI was included in the patient group, the odds for preterm delivery (aOR 1.29, CI 1.17-1.41), odds for CS (aOR 1.72, CI 1.63-1.82), and odds for neonatal intensive care unit (aOR 1.46, CI 1.46-1.56) were higher, when compared to the control group. Of the CS occurring in first pregnancies following TBI 59.8% were urgent CS. (Table 31)

Table 29. Absolute numbers, percentages, and both univariable (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for the primary outcomes. Pregnancies after TBIs were compared to the control group consisting of pregnancies without TBIs.

	TBI group		Control group		Univariable	Adjusted
Total number	13 348		1 143 954			
	n	%	n	%	OR (95% CI)	aOR (95% CI)
Preterm delivery	755	5.7	52 425	4.6	1.24 (1.14-1.33)	1.19 (1.11-1.28) *
Cesarean section *	2586	19.4	181 350	15.8	1.26 (1.21-1.32)	1.25 (1.19-1.31) **
Neonatal intensive care	1756	13.2	114 160	9.9	1.35 (1.29-1.42)	1.26 (1.19-1.33) ***

* Adjusted by maternal smoking status and maternal diabetes during pregnancy
** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and previous CS
*** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

Table 30. Additional analysis with only nulliparous women included. Absolute numbers, percentages, and both univariable (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for the primary outcomes. Pregnancies after TBIs were compared to the control group consisting of pregnancies without TBIs. The cesarean section includes all cesarean sections.

	TBI group		Control group		Univariable	Adjusted
Total number	5963		472 966			
	n	%	n	%	OR (95% CI)	aOR (95% CI)
Preterm delivery	361	6.1	25 826	5.5	1.12 (1.00-1.24)	1.10 (0.99-1.23) *
Cesarean section	1341	22.5	94 420	20.0	1.16 (1.09-1.24)	1.20 (1.13-1.28) **
Neonatal intensive care	910	15.3	59 006	12.5	1.26 (1.18-1.36)	1.22 (1.13-1.32) ***

* Adjusted by maternal smoking status and maternal diabetes during pregnancy
** Adjusted by maternal age, maternal smoking status, and maternal gestational diabetes
*** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

Table 31. Additional analysis using only the first pregnancy following the major trauma was included. Absolute numbers, percentages, and both univariable (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) for the primary outcomes.. Pregnancies after TBIs were compared to the control group consisting of pregnancies without TBIs. The cesarean section includes all cesarean sections.

	TBI group		Control group		Univariable	Adjusted
Total number	8048		1 143 954			
	n	%	n	%	OR (95% CI)	aOR (95% CI)
Preterm delivery	488	6.0	52 425	4.6	1.34 (1.22-1.47)	1.29 (1.17-1.41) *
Cesarean section	1740	21.6	181 350	15.8	1.46 (1.39-1.54)	1.72 (1.63-1.82) **
Neonatal intensive care	1198	14.9	114 160	9.9	1.58 (1.48-1.68)	1.46 (1.37-1.56) ***

* Adjusted by maternal smoking status and maternal diabetes during pregnancy
** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and previous CS
*** Adjusted by maternal age, maternal smoking status, maternal gestational diabetes, and preterm delivery

5.5 Birth rate after major traumas (IV)

The annual birth rate for the entire population of fertile-aged women initially exhibited an upward trend over the study period, with an increase from 41.1 newborns per 1000 fertile-aged women in 1998 to 46.8 newborns per 1000 fertile-aged women in 2010. However, the birth rate experienced a strong decline and reached 37.0 newborns per 1000 fertile-aged women in 2018. The average yearly birth rate from 1998 to 2018 was 42.9 newborns per 1000 fertile-age women (Figure 22).

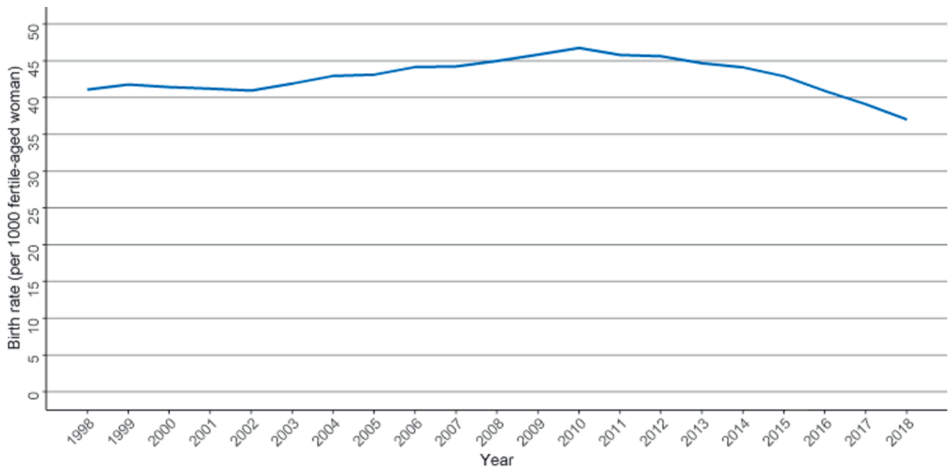

Figure 22. Annual birth rate with 95% confidence intervals per 1000 for the whole Finnish population of fertile-aged (15-49 years) women during years 1998-2018 in Finland.

Generally, women in the spine fracture group (mean age 28.5 years), hip or thigh fracture group (mean age 28.4 years), and palmar fracture group (28.4 years) were the oldest at the time of trauma. Women in the TBI group (mean age 27.6 years) and pelvic fracture group (27.4 years) were the youngest at the time of trauma. During the 5-year follow-up period after the fracture, women in the hip or thigh fracture group had the lowest birth rate (12.4%). Notably, the TBI group had the highest birth rate during the same period (19.0%), which was even higher than the reference group's birth rate (18.7%). (Table 32)

Table 32. Background information on the study groups and the reference group (palmar fractures) for the survival analysis. TBI=Traumatic brain injury

	TBI group	Spine fracture group	Pelvic fracture group	Hip or thigh fracture group	Palmar fracture group
Total number of women included*	22 780	3627	1820	1769	4957
Age at the start of follow-up					
15-24 years	10 273 (45.1%)	1476 (40.7%)	852 (46.8%)	707 (40.0%)	2004 (40.4%)
25-34 years	5965 (26.2%)	1018 (28.1%)	481 (26.4%)	437 (24.7%)	1430 (28.8%)
35-44 years	6542 (28.7%)	1133 (31.2%)	487 (26.8%)	625 (35.3%)	1523 (30.7%)
Birth rate during the 5-year follow-up (%)	4324 (19.0%)	652 (18.0%)	301 (16.5%)	220 (12.4%)	925 (18.7%)
Age at the time of trauma (mean; sd)	27.6 (9.2)	28.5 (9.1)	27.4 (9.2)	28.4 (9.1)	28.4 (9.1)
Age at the time of delivery (mean; sd)	28.0 (5.6)	28.5 (5.5)	27.9 (5.4)	28.7 (5.4)	28.7 (5.4)
Follow-up period in weeks (mean; sd)	237.6 (55.6)	237.8 (56.3)	240.9 (52.3)	246.4 (44.6)	237.9 (55.6)

* To ensure a 5-year follow-up period, only women who had experienced trauma before 2014 and were younger than 45 years at the time of trauma were included in the Cox survival analysis.

The Kaplan-Meier survival curves showed an evenly increasing line for each trauma for the risk of having a pregnancy leading to birth. The curve showed the smallest increase in the risk of another pregnancy leading to birth after hip or thigh traumas (Figure 23). Women in the hip or thigh fracture group had a decreased risk for pregnancy leading to birth during the 5-year follow-up period in the age groups of 15 to 24 years (HR 0.72, CI 0.58 - 0.88) and 25 to 34 years (HR 0.65, CI 0.52 - 0.82) compared to the palmar fracture group. In addition, women in the pelvic fracture group aged 25 to 34 had a lower risk of having a pregnancy leading to birth during the 5-year follow-up period (HR 0.79, CI 0.64 - 0.97). Spine fractures and TBIs did not show an impaired risk for a pregnancy leading to birth when compared to palmar fractures. (Table 33)

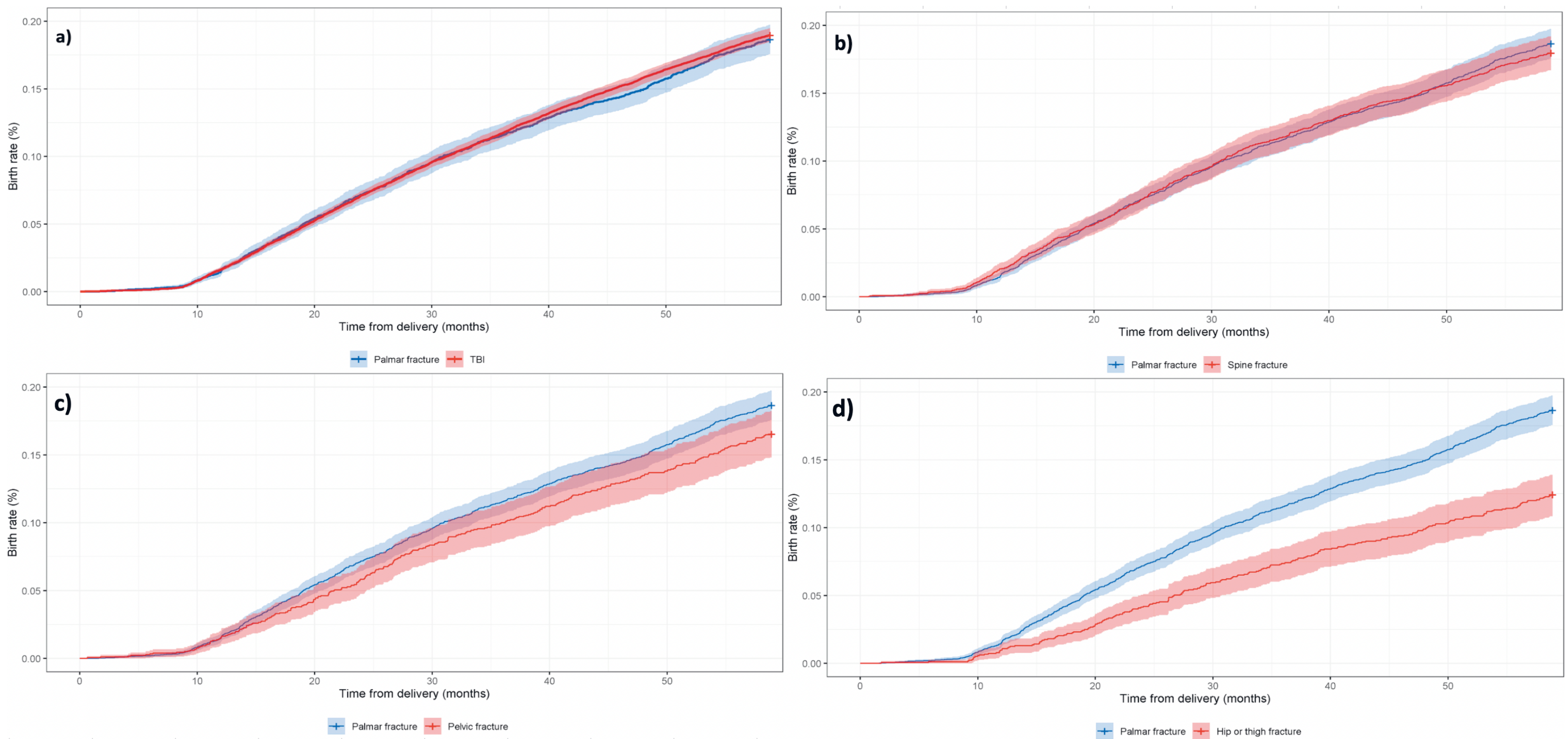

Figure 23. Kaplan–Meier survival curves (with 95% confidence intervals) of fertile-aged women for an event of getting pregnant after suffering a TBI (**a**), spine fracture (**b**), pelvic fracture (**c**), or hip or thigh fracture (**d**) when compared to palmar fracture.

Table 33. Age-stratified hazard ratios (HR) with 95% confidence intervals (CI) for women giving birth in the major trauma groups of this study. The major trauma groups were compared with all fertile-aged women with palmar fractures during the same study period. The results are presented separately for 15-24 years old, 25-34 years old, and 35-44 years old.

Age	15-24 years	25-34 years	35-44 years
TBI group*			
Hazard ratio (CI)	1.09 (0.98 – 1.21)	0.92 (0.83 – 1.02)	0.99 (0.76 – 1.29)
Spine fracture group			
Hazard ratio (CI)	1.02 (0.88 – 1.17)	0.91 (0.78 – 1.06)	1.06 (0.74 – 1.51)
Pelvic fracture group			
Hazard ratio (CI)	0.91 (0.77 – 1.09)	0.79 (0.64 – 0.97)	0.67 (0.39 – 1.18)
Hip or thigh fracture group			
Hazard ratio (CI)	0.72 (0.58 – 0.88)	0.65 (0.52 – 0.82)	0.60 (0.35 – 1.01)

* TBI = Traumatic brain injury

5.6 Smoking and fractures (V)

The annual proportion of smokers among pregnant women remained relatively stable during the years 1998-2012, ranging from 12.2% to 14.4%. However, after reaching a peak in 2012, the rate decreased to 10.2% in 2018 (Figure 24).

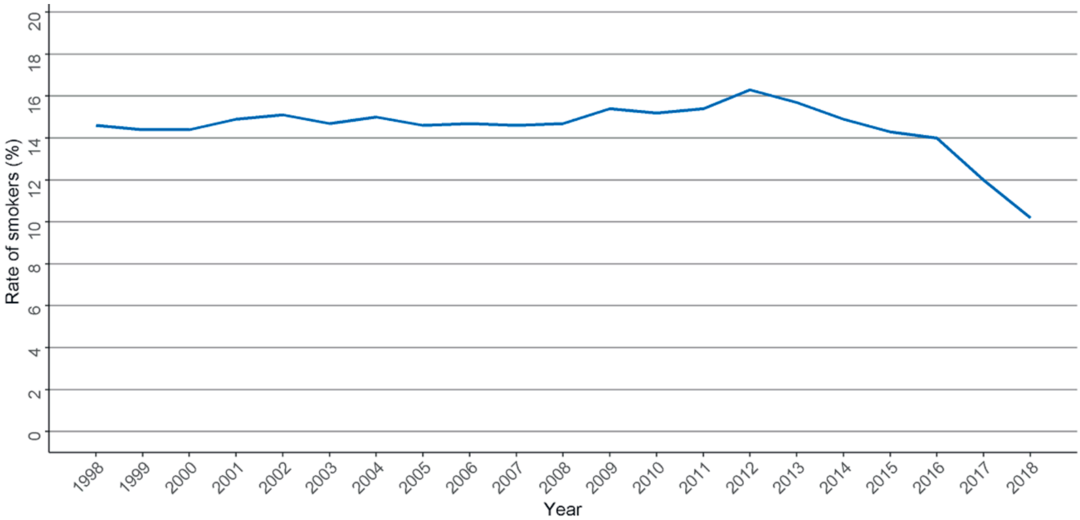

Figure 24. The annual rate of smokers during pregnancy of all pregnancies in Finland during the years 1998-2018. In this study, women who smoked during the 1st semester or in later trimesters were considered smokers.

We identified a total of 110 675 pregnancies with a mother who smoked in the MBR. In a total of 628 085 pregnancies there was no maternal smoking during pregnancy. Those who smoked were found to be younger than their non-smoking counterparts at the time of delivery, with a mean age of 27.5 years compared to 30.0 years ($p < 0.001$). There was a notably lower proportion of women married during or before pregnancy among those who smoked during pregnancy (37.0% vs 65.5%, $p < 0.001$), when compared to non-smoking women. In the smoking group, there was also a notably higher rate of women with low SES (32.6% vs 17.4%) and a lower rate of women with high SES (6.0% vs 22.2%, $p < 0.001$ for both), when compared to the non-smoking group. A higher rate of women who smoked suffered a fracture 1 year

(0.3% vs 0.2%, $p < 0.001$) and 5 years (1.5% vs 0.8%, $p < 0.001$) after pregnancy, when compared to non-smokers. (Table 34)

Table 34. Background information on the smoking and non-smoking groups formed in this study.

	Smoker group		Non-smoker group	
Total number of pregnancies	110 675		628 085	
	n	%	n	%
Age during pregnancy (mean; sd)	27.5 (5.8)		30.0 (5.2)	
Marital status during pregnancy				
ever married	40 930	37.0	411 367	65.5
never married	65 807	59.5	203 190	32.4
unknown	3938	3.6	13 528	2.2
Socioeconomic status				
low	36 106	32.6	109 475	17.4
middle	56 477	51.0	336 538	53.6
high	6647	6.0	139 496	22.2
undefinable	11 445	10.3	42 576	6.8

The Kaplan-Meier survival curve showed that smokers already had more fractures from the beginning, than non-smokers. As illustrated in Figure 33, the curve exhibited a less pronounced increase for women who did not smoke (Figure 33).

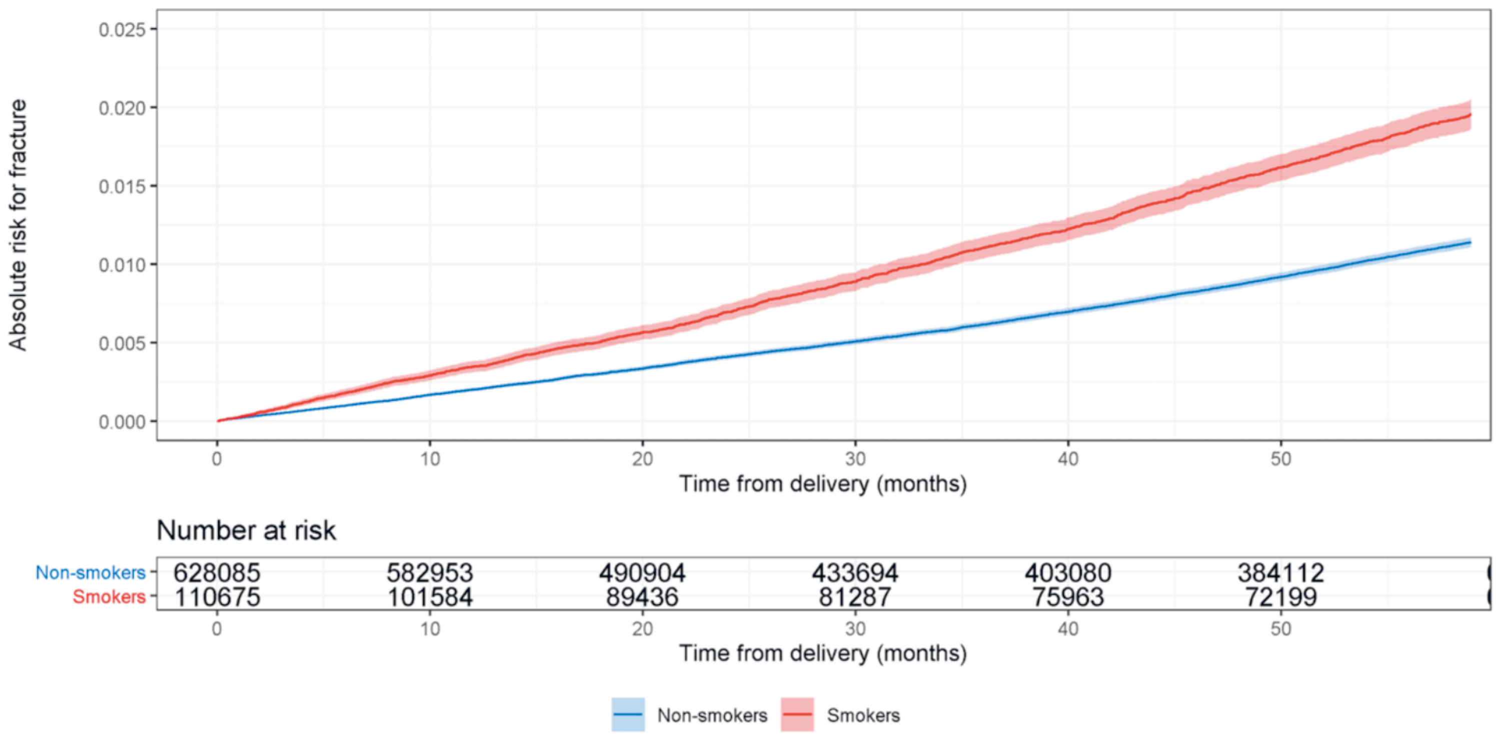

Figure 25. Cumulative incidence plot (with 95% confidence intervals) of fertile-aged women for an event of suffering a fracture after delivery and the total number of patients at-risk at different time points during the follow-up time. Smokers were compared to non-smokers.

Fractures of the lower arm were the most common types of traumas in both the smoker (35.2%) and non-smoker groups (44.0%), followed by fractures of the lower leg (41.7% and 36.4%) and the upper arm (11.9% and 11.5%). Fractures of the pelvis and hip or thigh were the least common types of fractures in both groups (3.7% and 2.7%). (Table 35)

Table 35: Absolute numbers and rates of fractures in total and in different anatomic regions among patients included in the Cox regression model.

	Smoker group		Non-smoker group	
Total number of pregnancies*	110 675		628 085	
	n	%	n	%
Fracture during 1-year follow-up	363	0.3	1196	0.2
Fracture during 5-year follow-up	1660	1.5	5238	0.8
Fracture location (after 5-year follow-up)*				
Lower arm	584	35.2	2305	44.0
Upper arm	197	11.9	604	11.5
Spine	115	6.9	247	4.7
Pelvis	49	3.0	101	1.9
Hip or thigh	53	3.2	110	2.1
Lower leg including ankle	693	41.7	1907	36.4

* As those patients who had fractures in multiple anatomic regions appear in multiple groups, the total number of pregnancies doesn't match with the subgroups.

The total risk for fractures was higher among smoking women when compared to non-smoking women during the 1-year follow-up (aHR 1.73, CI 1.53 - 1.96) and 5-year follow-up (aHR 1.74, CI 1.64 - 1.84). After one year of follow-up, the fracture rate for all anatomical regions except for hip fractures showed a higher fracture rate among smokers when compared to non-smokers. The highest fracture rates were observed for the pelvic region (aHR 2.15, CI 1.11 - 4.18) and spine (aHR 2.10, CI 1.32 - 3.35). After 5-years, the fracture rate was found to be higher for all anatomic regions, with hip or thigh fractures having the highest fracture rate (aHR 2.38, CI 1.69 - 3.35), followed by spine fractures (aHR 2.30, CI 1.82 - 2.90) and pelvic fractures (aHR 2.10, CI 1.47 - 3.01) in comparison to non-smokers. When different types of traumas were considered, smoking women had highest risk for polytraumas after a 5-year follow-up (aHR 2.29, CI 1.42 - 3.69), when compared to non-smoking women.

Furthermore, smoking women had a higher risk for fractures requiring hospitalization for longer than one day after the 1-year follow-up (aHR 2.13, CI 1.55 - 2.92) and 5-year follow-up (aHR 2.04, CI 1.74 - 2.39) when compared to non-smokers. Smoking women had a higher risk for non-severe fractures (less than one day hospitalization period) than non-smoking women, with an aHR of 1.78 (CI 1.58 - 2.02) after 1-year follow-up and 1.75 (CI 1.65 -1.85) after 5-year follow-up. (Table 36) In all sensitivity analyses conducted, smoking was consistently associated with a markedly increased risk of fractures. (Table 37 and Table 38)

Table 36. Comparison of fracture risk in smoking and non-smoking women after giving birth during 1-year and 5-year follow-up periods. The results are interpreted as hazard ratios (HR) and adjusted hazard ratios (aHR) with 95% confidence intervals (CI).

Follow-up time	1-year		5-year	
Fracture	HR (CI)	aHR (CI)*	HR (CI)	aHR (CI)*
Total	1.74 (1.54 – 1.96)	1.73 (1.53 – 1.96)	1.73 (1.64 – 1.83)	1.74 (1.64 – 1.84)
Location of fracture				
Lower arm	1.41 (1.14 – 1.73)	1.43 (1.15 – 1.77)	1.38 (1.26 – 1.52)	1.42 (1.29 – 1.56)
Upper arm	1.85 (1.33 – 2.56)	1.75 (1.25 – 2.45)	1.79 (1.52 – 2.10)	1.70 (1.44 – 2.01)
Spine	2.59 (1.66 – 4.04)	2.10 (1.32 – 3.35)	2.55 (2.04 – 3.18)	2.30 (1.82 – 2.90)
Pelvis	2.50 (1.34 – 4.69)	2.15 (1.11 – 4.18)	2.66 (1.89 – 3.75)	2.10 (1.47 – 3.01)
Hip or thigh	1.76 (0.92 – 3.36)	1.76 (0.90 – 3.44)	2.65 (1.91 – 3.68)	2.38 (1.69 – 3.35)
Lower leg including ankle	1.87 (1.55 – 2.26)	1.92 (1.58 – 2.33)	1.99 (1.82 – 2.17)	2.04 (1.86 – 2.23)
Type of fracture				
Polytrauma	0.76 (0.17 – 3.34)	0.51 (0.11 – 2.30)	3.06 (1.93 – 4.86)	2.29 (1.41 – 3.69)
Severe fracture **	2.10 (1.55 – 2.85)	2.13 (1.55 – 2.92)	2.02 (1.74 – 2.34)	2.04 (1.74 – 2.39)
Less severe fracture ***	1.78 (1.56 – 2.00)	1.78 (1.58 – 2.02)	1.73 (1.64 – 1.83)	1.75 (1.65 – 1.85)

* The models were adjusted for the age of the mother at the time of pregnancy and with categorized socioeconomic status

** Fractures with a hospitalization period lasting more than one day were considered severe traumas

*** Fractures with less than one day hospitalization period (including day surgeries) and non-polytraumas were considered less severe fractures

Table 37. Sensitivity analysis was conducted with excluded women included by placing them in the unknown socioeconomic status class. Comparison of fracture risk in smoking and non-smoking women after giving birth during 1-year and 5-year follow-up periods. The results are interpreted as hazard ratios (HR) and adjusted hazard ratios (aHR) with 95% confidence intervals (CI).

Follow-up	1-year		5-year	
Fracture	HR (CI)	aHR (CI)*	HR (CI)	aHR (CI)*
Total	1.71 (1.54 – 1.90)	1.72 (1.54 – 1.92)	1.71 (1.63 – 1.80)	1.73 (1.65 – 1.83)
Location of fracture				
Lower arm	1.44 (1.20 – 1.74)	1.47 (1.21 – 1.79)	1.42 (1.30 – 1.54)	1.46 (1.34 – 1.59)
Upper arm	1.85 (1.39 – 2.47)	1.79 (1.32 – 2.41)	1.74 (1.50 – 2.01)	1.68 (1.45 – 1.95)
Spine	2.50 (1.70 – 3.69)	2.07 (1.38 – 3.11)	2.61 (2.15 – 3.16)	2.32 (1.90 – 2.84)
Pelvis	2.13 (1.18 – 3.87)	1.72 (0.92 – 3.21)	2.54 (1.87 – 3.44)	2.00 (1.46 – 2.76)
Hip or thigh	2.24 (1.28 – 3.94)	2.14 (1.19 – 3.85)	2.43 (1.80 – 3.29)	2.20 (1.61 – 3.03)
Lower leg including ankle	1.75 (1.47 – 2.08)	1.82 (1.52 – 2.18)	1.91 (1.77 – 2.07)	1.98 (1.83 – 2.15)
Type of fracture				
Polytrauma	0.65 (0.15 – 2.83)	0.42 (0.10 – 1.88)	2.95 (1.94 – 4.49)	2.22 (1.44 – 3.43)
Severe fracture **	2.19 (1.68 – 2.85)	2.20 (1.67 – 2.89)	1.97 (1.72 – 2.25)	2.03 (1.77 – 2.33)
Less severe fracture ***	1.75 (1.57 – 1.95)	1.77 (1.58 – 1.98)	1.75 (1.57 – 1.95)	1.77 (1.58 – 1.98)

* The models were adjusted by maternal age during pregnancy and with categorized socioeconomic status

** Fractures with a hospitalization period lasting more than one day were considered severe trauma

*** Fractures with less than one day hospitalization period (including day surgeries) and non-polytraumas were considered less severe fractures

Table 38. Sensitivity analysis was performed using the multiple imputation technique for the socioeconomic status variable, with Best-best Case, best-worst case, worst-best case, worst-worst case imputation, and data as observed methods used to calculate grand means using the modified Rubin's Rule. Comparison of fracture risk in smoking and non-smoking women after giving birth during 1-year and 5-year follow-up periods. The results are interpreted as hazard ratios (HR) and adjusted hazard ratios (aHR) with 95% confidence intervals (CI).

Follow-up	1-year		5-year	
Fracture	HR (CI)	aHR (CI)*	HR (CI)	aHR (CI)*
Total	1.74 (1.54 – 1.96)	1.73 (1.52 – 1.98)	1.73 (1.64 – 1.81)	1.72 (1.59 – 1.81)
Location of fracture				
Lower arm	1.41 (1.14 – 1.73)	1.40 (1.21 – 1.82)	1.38 (1.26 – 1.52)	1.39 (1.34 – 1.59)
Upper arm	1.85 (1.33 – 2.56)	1.83 (1.34 – 2.54)	1.79 (1.52 – 2.10)	1.68 (1.42 – 2.01)
Spine	2.59 (1.66 – 4.04)	2.14 (1.27 – 3.41)	2.55 (2.04 – 3.18)	2.31 (1.76 – 2.88)
Pelvis	2.50 (1.34 – 4.69)	2.21 (1.08 – 4.32)	2.66 (1.89 – 3.75)	2.12 (1.54 – 3.01)
Hip or thigh	1.76 (0.92 – 3.36)	1.83 (0.88 – 3.54)	2.65 (1.91 – 3.68)	2.14 (1.52 – 3.04)
Lower leg including ankle	1.87 (1.55 – 2.26)	1.94 (1.59 – 2.32)	1.99 (1.82 – 2.17)	2.01 (1.89 – 2.21)
Type of fracture				
Polytrauma	0.76 (0.17 – 3.34)	0.51 (0.14 – 2.82)	3.06 (1.93 – 4.86)	2.19 (1.41 – 3.62)
Severe fracture **	2.10 (1.55 – 2.85)	2.08 (1.64 – 2.93)	2.02 (1.74 – 2.34)	2.04 (1.67 – 2.39)
Less severe fracture ***	1.78 (1.56 – 2.00)	1.79 (1.59 – 2.04)	1.73 (1.64 – 1.83)	1.69 (1.66 – 1.86)

* The models were adjusted for the age of the mother at the time of pregnancy and with categorized socioeconomic status

** Fractures with a hospitalization period lasting more than one day were considered severe traumas

*** Fractures with less than one day hospitalization period (including day surgeries) and non-polytraumas were considered less severe fractures

6 DISCUSSION

6.1 Epidemiology of traumas

The incidence of pelvic fractures showed a slightly increasing trend during our study period. According to the latest epidemiologic study on pelvic fractures in Finland, the incidence of pelvic fracture hospitalization of the whole adult population in Finland increased during the years 1997-2014, which is the same trend we observed (Rinne et al., 2020). The study drew the conclusion that the aging of the population is likely partly responsible for this increase (Rinne et al., 2020). However, we observed that the incidence also increased in fertile-aged women, meaning that the aging of the population does not fully explain this increase. Indeed, based on our data, the exact reason behind the increase remains unclear. A similar increasing trend has also been reported in Sweden (Lundin, Huttunen, Enocson, et al., 2021).

The incidence of spine fracture hospitalizations and fracture surgeries remained nearly unchanged during the study period. Interestingly, the incidence of spine fusion surgeries unrelated to fracture increased strongly (156%) in fertile-aged women. According to a previous study in Finland with study period during the years 1998-2017, there was an approximately 65% increase in spine fracture hospitalizations and spine fusion surgeries in all patients older than 20 years of age (Ponkilainen et al., 2020). The proportional increase of elective fusion surgeries among fertile-aged women observed in this study was higher than in this previous study. Although the exact reason for this increase is unknown, one possible explanation could be an increase in surgical activity and a potential rise in scoliosis incidence. (Heideken et al., 2018). Also, the indications for spine fusion surgeries have broadened over time (Mj et al., 2020).

The incidence of TBIs had a strongly increasing trend during our study period in fertile-aged women. These findings could be attributed to indirect temporal factors and phenomena, such as the widespread use of CT imaging (STUK, 2020), and improved awareness of mild TBIs, especially concussions, leading to a decrease in the threshold for seeking medical attention (Laker, 2011; Langer et al., 2020). Additionally, the establishment of a joint emergency service in 2011 may have contributed to advancements in the diagnosis of acute head trauma. In addition, the threshold for admission to the hospital most likely decreased during the study period, as the knowledge, management, and imaging of TBIs have improved during the last decades (Dash & Chavali, 2018; Lee, 2020).

Interestingly, the incidence of hip or thigh fractures decreased during our study period. A previous study in Finland found that the incidence of hip fractures has had a strongly increasing trend for the whole Finnish adult population (Lönnroos et al., 2006). Moreover, the increase was observed for both men and women (Lönnroos et al., 2006). Hip fractures are known to be more common among the older population (Kannus et al., 1996), suggesting that the differing results of our study compared to the previous study might be partly explained by the aging of the population in Finland, as it appears that the annual number of fractures is decreasing in the fertile-aged population.

6.2 Pregnancy and neonate outcome after major traumas

The main finding of the study I was the high rate of successful vaginal deliveries after pelvic fracture. Nevertheless, there was a higher proportion of CSs observed among women with pelvic fractures. This can be attributed to the greater frequency of elective CSs performed in the fracture group when compared to the no-fracture group. Similar findings were observed in study II, as elective and urgent CS were more common in the spine fracture and spine fusion surgery for other reasons groups, but vaginal delivery was still the most common mode of delivery in both groups. Especially after fusion surgery in the lumbar spine, the odds for CS were notably higher. In addition, the need for a neonatal intensive care unit for neonates born to mothers with prior spine fractures or spine fusion surgeries was higher, but the clinical importance of this remains unclear. In study III, women with a history of TBI had a higher rate of CS, instrumental vaginal deliveries, preterm deliveries, and labor analgesia. Interestingly, in the first pregnancies following the TBI, the odds for CS were relatively high. Furthermore, the need for a neonatal intensive care unit was increased in this group.

6.2.1 Intended mode of delivery after major traumas

In studies I and II, a high rate of CS, especially elective CS were observed after pelvic fractures, spine fractures, or spine fusion surgeries. Especially in the first pregnancies after pelvic fracture, spine fracture, or spine fusion surgery CS was more common. However, vaginal delivery was still possible in most cases despite the higher rate of CS. Our results show that even after multiple fractures of the pelvic circle, vaginal delivery was still successful in the majority of cases. The elective CS rate was nearly two times higher in the pelvic fracture group and spine fracture group, and over two times higher in the spine fusion surgery for other reasons group. This is a noteworthy increase, as in Finland, the decision to perform a cesarean section is made after careful consideration and discussion between the patient and the physician.

According to THL, the combined CS rate (elective + urgent CS) in Finland is reported to be 16% (THL, 2018b), and it has remained consistent over the last two decades (Betrán et al., 2016; THL, 2018b). Even though the elective CS rate was notably higher after fractures of the pelvis or spine, or spine fusion surgeries for other reasons in Finland, the CS rate is not as high as in many of the other countries. Indeed, in a previous systematic review concerning level-1 trauma centers, the rate of elective CS was reported to be over 40% after pelvic fractures (Riehl, 2014), which is over threefold the rate of elective CS in the patient groups seen in our study. Also, in a study in the United States, the incidence of elective CS after spine surgery was reported to be 37% (Lavelle et al., 2009), which is over three times higher than the rate after spine fractures or surgeries in our results. However, the rate of elective CS was not importantly higher after TBIs.

CS procedures were more common in the pelvic fracture, spine fracture, and spine fusions surgery group, but vaginal delivery was still successful in most cases. CSs have been associated with reduced mortality among neonates and mothers in selected cases. These findings raise questions about the reasons behind the high rate of elective CS among women with previous pelvic fractures, spine fractures, or spine fusion surgery. While CS is generally considered a relatively safe and efficient operation, that has played a remarkable role in decreasing mortality in neonates, it has been reported to be associated with many disadvantages for the mother and neonate following the operation. Studies have shown that neonates delivered via CS have a higher likelihood of developing asthma, obesity, and poor cardiorespiratory health later in life (Ekstrom et al., 2020; Li et al., 2013; Mueller et al., 2019). Mothers who undergo CS have been found to experience shorter breastfeeding duration and may also be at risk of future subfertility and complications in subsequent pregnancies (Hobbs et al., 2016; Keag et al., 2018; S. Liu et al., 2007; M. Ometti Bettinelli, G. ,. Candiani, M. ,. &. Salini, V., 2020). Further, our results suggest that the necessity for elective CS after pelvic fracture, spine fracture, or fusion surgery should be considered carefully by the patient, the obstetrician, and the orthopaedic consultant, who might be consulted about the capability to deliver vaginally such major traumas. Our findings should alleviate any concerns that women, obstetricians, or orthopedic consultants may have regarding vaginal delivery as a viable delivery method following pelvic or spinal fractures or spinal fusion surgery.

Also, based on our results, the incidence of pelvic fractures, and spine fusion surgeries among fertile-aged women is strongly increasing in Finland, and similar findings have been reported in other Nordic countries too (Grotle et al., 2019b; Lundin, Huttunen, Berg, et al., 2021). As a result, there may be a rise in childbirths following these traumas or surgical procedures in the future, further emphasizing the significance of the study's findings.

In summary, as the incidence of pelvic fractures and spine fusion surgeries have had an increasing trend during the last decades, there will most likely be an increase in deliveries after these major traumas in the future. Therefore, the results of the present study should be considered when obstetricians, the orthopedic consultant, and pregnant women who have had a prior pelvic fracture, spine fracture, or spine fusion surgery discuss the mode of delivery during pregnancy, as delivery vaginally appears to be possible and could be attempted for these women.

6.2.2 Pregnancy outcomes after major traumas

A higher rate of urgent CS was found among women with prior pelvic fractures and spine fusion surgeries in studies I and II. Interestingly, no such increase was found in the spine fracture group. In study III, women with a TBI history had a higher rate of instrumental vaginal deliveries and urgent CS.

The precise cause of the increased rate of urgent CS remains uncertain, as it is not documented in the registry. However, a prior history of pelvic or spine fracture or surgery may have complicated delivery, potentially leading to a higher rate of urgent CS as a result of these complications. Also, the awareness of a prior pelvic fracture, spine fracture, or spine fusion surgery might have reduced the threshold for the obstetrician to transition from a trial of labor to performing an urgent CS. Moreover, certain women who underwent an emergency CS may have initially intended to have a planned cesarean section. However, due to the early onset of labor, their planned elective CS was documented as an urgent CS. In a subgroup analysis conducted in study I, women with multiple pelvic fractures had notably higher rates of both elective and unplanned CSs in comparison to women with other pelvic fracture diagnoses and those without pelvic fractures. The overall CS rate (including both elective and urgent CS) was 32.1% among women with multiple pelvic fractures.

The reason for the lower increase in urgent CS rate for women with previous spine fractures, when compared to spine fusion surgeries remains unknown. However, a higher rate of nulliparous women, and women with a history of CS in spine fusion surgery for other reasons group when compared to the spine fracture group, could partly explain the increased rate of elective and urgent CS. The odds for CS remained higher in the spine fusion surgery group than in the spine fracture group, when only nulliparous women were included, however. In addition, the higher rate of preterm deliveries among women with spine fusion surgery could have an impact on the urgent CS rate. An alternative explanation could be that obstetricians or physicians are more cautious during delivery in cases where the patient has previously undergone spinal fusion surgery, potentially lowering the threshold for the obstetrician to convert the trial of labor to CS. Furthermore, the fusion surgery for other reasons group had a rate of instrumental vaginal deliveries, suggesting that vaginal delivery may have been more challenging following their spine fusion surgery.

In study III, women with a prior history of TBI had an increased incidence of delivery-related complications, as indicated by an increased rate of instrumental vaginal deliveries, urgent CS, and labor analgesia. Especially in first pregnancies following the TBI, the odds for CS were interestingly high, consisting mostly of urgent CS (60%). Among women with surgically operated TBI (usually indicating more severe neurotrauma), the rate of instrumental vaginal deliveries was markedly higher. The increased incidence of instrumental vaginal deliveries along with higher utilization of labor analgesia may be related to a slower progression of labor. Nevertheless, the rate of urgent CS and the need for intensive care unit treatment were lower in this group compared to the other non-surgical TBI groups. However, the limited sample size of women in the operated TBI group may have influenced these findings. Our findings suggest that women with a history of TBI face more challenges during delivery, which can be observed as a lower rate of spontaneous vaginal deliveries than in other groups. However, due to the crude nature of our data, too strong conclusions cannot be made. It remains unknown whether the higher rate of CS and instrumental vaginal deliveries are caused by TBI or by other factors. Further research is needed to clarify this issue.

Interestingly, in study II, the rates of labor analgesia administered by anesthesiologists were considerably higher in the spine fracture and the spine fusion surgery groups compared to the control group. There is limited literature on the management of labor analgesia after spinal surgery or spine fracture, with only a few studies conducted on small study populations. The main challenges faced by anesthesiologists when performing the procedure, as reported in the limited published literature, include difficulty in identifying the epidural space, multiple attempts before catheter insertion, vascular trauma, subdural local anesthetic injection, and accidental dural puncture. (Kuczkowski, 2006). Our study, however, was unable to assess any possible complications during or after anaesthesia as this information is not recorded in the MBR. Therefore, it is not possible to draw conclusions about the success rate of labor analgesia after spine fracture or surgery. It is worth noting, however, that the current understanding is that epidural analgesia does not increase the risk of CS or instrumental vaginal delivery (Daley et al., 1990; Villevieille et al., 2003). One possible explanation could be that the elevated rates of labor analgesia in the fracture or fusion surgery group could be due to reduced mobility and flexibility of the spine, which may increase the need for more effective pain relief.

In summary, a higher rate of urgent CS, instrumental vaginal deliveries, and labor analgesia were observed among women with previous spine fractures, spine fusion surgery, or TBI. Also, a higher rate of urgent CS was observed among women with previous pelvic fractures. Previous pelvic or spine surgery may have complicated the delivery leading to instrumental vaginal delivery or urgent CS and the higher rate of urgent CS might be due to complications caused by these. Also, the awareness of a previous pelvic fracture, spine fracture, or spine fusion surgery may have lowered the threshold for the obstetrician to convert the trial of labor to urgent CS. However, the clinical importance of this remains unclear and further research on this topic, studying the indications for urgent CS or instrumental vaginal deliveries after major traumas are warranted. Also, a history of TBI should be acknowledged as a possible factor affecting the course of delivery, but due to the limited nature of our data, this topic requires further research.

6.2.3 Fetal outcomes among women with prior major traumas

Overall, the perinatal and neonatal mortality rate was truly low, and no increased mortality was observed among women with previous pelvic fractures, spine fractures or fusion surgeries, or TBIs. However, the need for a neonatal intensive care unit was a little higher after pelvic fracture, spine fracture, or spine fusion surgery for other reasons group, but the clinical relevance of this finding remains unclear. In addition, the need for neonatal intensive care was increased among women with a history of TBIs.

The higher need for the intensive care unit for neonates in the pelvic or spine fracture or surgery groups can be partly explained by the higher rate of CS (Wisborg et al., 1996). Previous studies did not report an increase in rates of miscarriage or infertility after pelvic trauma, but the sample sizes were limited, and neonatal health outcomes were not reported. (Cannada & Barr, 2010; Copeland et al., 1997; Madsen et al., 1983). A study with a limited number of patients suggested that spinal cord injury did not adversely impact neonatal health (Cross et al., 1992), but there is inadequate information available regarding the impact of spinal trauma or surgery on neonatal health. Despite the higher rate of preterm deliveries observed in women who have had prior fusion surgery, our findings indicate that a prior spine fracture or fusion surgery does not appear to have a clinically relevant adverse impact on neonatal health. Indeed, the slightly higher percentages of neonates requiring intensive care may be partly due to the higher proportion of CS and preterm deliveries in these groups. The rate of preterm deliveries and the need for intensive care for the neonate was higher among women with fractures of the pelvic circle or spine, but the importance of these findings in clinical practice remains still uncertain. The higher rate of preterm deliveries among women with previous fracture of the pelvis or spine, or with previous spine fusion surgery can partly be explained by the higher prevalence of smoking among mothers with a history of pelvic or spine fracture, or spine fusion surgery, as smoking women are known to be at increased risk for preterm deliveries (Wisborg et al., 1996).

Interestingly, the proportion of neonates requiring intensive care was higher among mothers with prior TBI. One possible contributing factor to this observation is the slightly higher rate of CSs among women with prior TBIs, as CSs are often associated with an increased need for neonatal intensive care (Kamath et al., 2009; Khasawneh et al., 2020). Furthermore, while the higher rate of smokers in the TBI group may partly explain the increase, adjusted analysis with smoking status included still showed higher odds for neonatal intensive care unit in this group. To the best of our knowledge, there are no prior studies examining the impact of TBIs occurring before pregnancy on obstetric outcomes, though it is recognized that TBI during pregnancy can lead to maternal and fetal health complications (Legros et al., 2000). TBIs are known to have an impact on the menstrual cycle and severe TBIs during pregnancy are associated with an increased risk of fetal death. (Colantonio et al., 2010; Kho & Abdullah, 2018). In general, traumatic events with high energy during pregnancy were found to elevate the likelihood of placental abruption and fetal injuries, which may in part explain the increased risk of fetal mortality associated with TBI (Brown, 2009). The underlying reason behind the higher rate of neonates requiring intensive care units among women with previous TBIs remains unclear, however.

In summary, the need for a neonatal intensive care unit was a little higher after pelvic fracture, spine fracture, or spine fusion surgery for other reasons group, but the clinical importance of this finding remains unclear, and this topic should be further researched. Furthermore, women with previous TBI had a higher prevalence of preterm deliveries, cesarean sections, instrumental vaginal deliveries, and labor analgesia, and the need for a neonatal intensive care unit was increased in this group. Hence, it is important to recognize a previous TBI as a potential factor that may impact the delivery and health of the neonate. However, due to the limited nature of our data, this topic requires further research.

6.3 Birth rate

This study provides novel information on the impact of major traumas on the subsequent birth rate. The main finding of this study was that the risk of giving birth during the follow-up period was lower in younger women with hip or thigh fractures. Additionally, there was a notable difference in the proportion of women who gave birth during the follow-up period when compared to the control group consisting of women with palmar fractures. The cumulative birth rate was also slightly lower among women with a pelvic fracture at the age of 25-34. However, in comparison to women with palmar fractures, there was no substantial effect on the birth rate during the 5-year follow-up observed among women with prior TBIs or spine fractures.

When compared to palmar fractures, only hip or thigh fractures, and pelvic fractures had a negative impact on the birth rate during the five years following the injury in this study. Several studies have reported sexual dysfunction in women who have sustained proximal thigh or pelvic fractures, with the dysfunction occurring particularly in younger women (Shulman et al., 2015; Walton et al., 2021). However, according to a study on proximal femur fractures, the majority of women reported only mild or no sexual dysfunction after a one-year follow-up period (Shulman et al., 2015). Furthermore, fractures of the pelvic ring are often associated with reports of dyspareunia (Vallier et al., 2012a). The lower risk of giving birth in these two groups could plausibly be explained by these factors. However, due to the crude nature of our data, the exact reason for the lower risk remains unclear. Further research using larger datasets is needed to validate these findings, as the number of women in the hip or thigh and pelvic fracture groups was relatively small in this study.

One possible explanation could be the fear of potential adverse maternal and fetal outcomes resulting from previous trauma of the pelvic area or femur, which may result in women choosing not to get pregnant or deciding not to give birth vaginally. According to our results, spontaneous vaginal delivery was the predominant mode of delivery after major traumas, with CSs accounting for only 18% to 24% of deliveries in each trauma group. However, the rate of CSs in the trauma groups was slightly higher when compared to the overall rate in Finland, which ranges from 16-17% (THL, 2018b). The results of this study may help alleviate any concerns that mothers, treating obstetricians, or physicians may have regarding the ability to successfully go through pregnancy and delivery after experiencing major trauma. Among women with TBIs and spine fractures, the risk of giving birth during the follow-up was at a similar level to women with palmar fractures, indicating that these traumas may not have an important adverse impact on fertility or subsequent risk of giving birth. Moreover, to the best of our knowledge, no prior research has been conducted on the topic of sexual dysfunction resulting from spine fractures or TBIs.

In summary, based on our results women with thigh, hip, or pelvic fractures had a lower cumulative birth rate in 5-year follow-up. However, it appears that the outcome of pregnancies after each trauma was generally good, meaning that these results should be helpful for the patient or doctor wondering whether it is possible to go through pregnancy and give birth after major trauma. The information gained from this study should be utilized in clinical practice when women with prior major traumas are considering the possibility to become pregnant and give birth.

6.4 Smoking and fractures

The main finding of this study was that smoking during pregnancy was associated with a higher fracture risk during the 1-year and 5-year follow-up periods after giving birth compared to non-smokers. During the 5-year follow-up period, the risk of fractures in different anatomical regions, including the spine, pelvis, and hip or thigh, was markedly higher among smoking women. Furthermore, the risk of fractures considered more severe (fractures requiring longer hospitalization periods, and polytraumas) was higher compared to non-severe fractures with less than a one-day hospitalization period.

Based on previous literature, trauma populations have a higher proportion of individuals with a low SES, but the underlying cause of this association remains unclear (Geckova et al., 2002, p.). Furthermore, as per the data from the Finnish Institute for Health and Welfare (THL, 2018c), individuals with lower levels of education tend to smoke more compared to those with higher levels of education. According to our data, the group of smokers had a notably higher number of women with low SES, which is consistent with the findings in previous literature. However, even after adjusting the model by categorized SES, the fracture rate among smoking women remained higher. This suggests that risky behavior alone may not fully explain the increased incidence of fractures among smoking women. In the elderly population, polytraumas may occur with less energy due to age-related skeletal fragility (Burr, 2019) (de Vries et al., 2018). In the fertile-aged population, however, polytraumas are typically attributed to high-energy trauma mechanisms, such as falls from height or traffic collisions (van Breugel et al., 2020). Interestingly, when adjusting for the maternal age during pregnancy and SES, the aHR showed a greater decrease compared to crude HR in the model for polytraumas than for other models. This could possibly indicate that the higher incidence of injuries caused by more risky behavior may explain high-energy accidents resulting in injuries in multiple anatomical regions, but may not be as important in explaining low-energy fractures among women who smoke.

The results of this study show a higher risk for more severe fractures (polytraumas and fractures needing longer hospitalization) than for less severe fractures among smokers. This could be an indication that the increased number of injuries is a more dominant reason for the fractures than the complications and weakened bone health caused by smoking. Also, during the lactation period, it seems that mothers have a lower risk of suffering severe injuries, as the incidence of polytraumas was very low during the 1-year follow-up. According to our data, smoking women also had a higher risk of non-severe fractures, but the exact cause remains unclear as these non-severe fractures could also be related to behavioral factors. However, the results still showed a markedly higher risk for fractures among smoking women when the socioeconomic background of the women was taken into account. Based on previous literature, smoking has been found to be strongly associated with osteoporosis due to numerous mechanisms it has a negative effect on bone health and metabolism (Al-Bashaireh et al., 2018; J. S. Chen et al., 2011.) Furthermore, women are at risk for osteoporosis, particularly during premenopausal and postmenopausal age, as estrogen is the primary regulator of bone metabolism (Cauley, 2015; Keen & Reddivari, 2022; Vondracek et al., 2009). These two risk factors could potentially increase the vulnerability of smoking women to osteoporotic fractures. However, based on previous studies, age is known to be a main risk factor for osteoporosis (Jakobsen et al., 2013), and as a result, osteoporosis is relatively uncommon among women of reproductive age (Clynes et al., 2020).

In summary, the relationship between smoking and osteoporotic fractures can only be speculated, and in reality, the increased risk for fractures among smokers is likely due to a combination of factors. These may include more common risky behavior, poorer musculoskeletal health resulting from an unhealthy lifestyle, and possibly the direct detrimental effects of smoking on the musculoskeletal system. However, as the results of this study establish a nationwide association and demonstrate a great increase in fracture risk among smoking women, the results of this study should be acknowledged by the clinician and used when encouraging the patient to quit smoking. Furthermore, the findings of this study highlight the need for further research to determine the etiology of the increased fracture risk among smoking women, utilizing more refined datasets to assess whether the increased risk is related to the direct effects of smoking on bone health, more risky behavior, or other factors.

6.5 Strengths and limitations

6.5.1 Strengths of the study

The robustness of our study lies in the extensive nationwide study population and the lengthy study period, which enabled us to compare large patient cohorts. Our data consisted of a total of 628 908 women with 1 192 825 singleton deliveries, which is a notably higher number of patients than previous studies. In addition, the study period was 20 years, which is much longer than that of previous studies. To our best knowledge, no previous studies have been conducted with as comprehensive data as ours. The data utilized in our study were obtained from registers that employ structured forms with national guidelines, ensuring comprehensive coverage and minimizing the likelihood of reporting and selection bias (THL, 2018b). Additionally, the coverage of both registers used in this study is extensive (Gissler & Shelley, 2002; Sund, 2012). In a study evaluating the validity of the Care Register for Health Care, the diagnosis was correctly placed in 96% of cases, the coverage for procedural coding was 98%, and the coverage for external cause injury was found to be 95% with an accuracy of 90% (Huttunen et al., 2014). Therefore, the advantage of these studies compared to previous ones is the large national research material in a country with uniform delivery-related guidelines and attitudes.

6.5.2 Main limitations of the study

The main limitation of our study is the lack of clinical information on the TBIs and fractures examined (e.g., radiological findings, mechanism of injury), which is not documented in the registers. Therefore, we had to rely solely on ICD-10 coding, and as a result, the extent of the injuries remains unclear. This means that the severity of the traumas remains unknown and only directive variables, such as length of the hospitalization period and number of trauma diagnoses during the hospitalization period, were used to evaluate the severity of the trauma. Moreover, our ICD-10 coding was restricted to trauma-related codes, and therefore, other factors that could potentially influence the outcome during or prior to the follow-up period are also unknown. Also, in studies I, II, and III, polytraumas are not taken into account. Therefore, we cannot be certain whether the association between the exposure (e.g., spine fracture) and outcome (e.g., CS) is not caused by additional pelvic fracture among women with spine fractures included in the patient group. However, the rate of patients with major traumas in multiple categories (pelvic, spine, TBI, and hip or thigh) was relatively low, being highest among pelvic fracture patients with spine fractures (19.0%). Also, it is not possible to identify, which of the appointments are control appointments and which are new traumas. However, as the study design in studies I, II, III was taking only the first trauma for each woman into account, this shouldn't have major impact on the results. In addition, traumas occurring during pregnancy are not taken into account in this study. (Table 11)

The birth register has been updated twice, in 2004 and 2017. Information on 5-minute Apgar scores, durations of labor stages, maternal body mass index, and chronic disease diagnoses were not included in the register until after the 2004 update. Therefore, these clinical parameters were not analyzed in our study. However, the diagnosis of GDM started in 2004, but it is included as an adjustment in the analyses in studies I, II, III. However, the number of pregnancies occurring before 2004 in patient groups was relatively low, and therefore, it should not have major impact on our results. It should be noted, that as the rate of pregnancies occurring during years 1998-2003 was higher in control groups, the rate of undiagnosed GDM is also most likely higher in control groups. However, performing the analyses without GDM as an adjustment variable didn't show major differences in the results. Moreover, the classification of CS cases as either elective or urgent was done differently before 2004. Therefore, in our study, we have used the same classification instead of using the newer three-stage classification that includes emergency CSs. Additionally, the reasons behind CSs or instrumental vaginal delivery are not recorded in the MBR, making it impossible to determine the indications for these delivery methods. Thus, we cannot determine whether the patient had planned elective CS or attempted vaginal delivery before undergoing an urgent CS. Also, in study I, II, and III we had no information on the outcomes of previous pregnancies, which didn't occur during our study period, expect for previous CS, which is collected routinely in the MBR. Therefore, we couldn't adjust the models with previous outcomes, such as previous preterm delivery, which is known to be a strong risk factor for another preterm delivery (Tingleff et al., 2022). However, we performed sensitivity analyses using only nulliparous women, which showed similar risk as for all pregnancies in studies I, II, and III. In addition, sensitivity analyses using only first pregnancies following the major trauma was conducted, as some women can have multiple pregnancies after major traumas. Also, we had no information on miscarriages or induced abortion, meaning that these outcomes remain unknown in studies I, II, and III. Women who became pregnant but had a miscarriage or induced abortion was not available in study IV. In addition, it should be noted, that regional differences especially in the usage of labor analgesia exists, as the university hospitals in big cities have specialized anesthesiologists, which are not available in smaller hospitals.

In survival analyses (Study IV and V), the date of death and migration are not available in our data, making it impossible to identify those women who were lost to follow up. Furthermore, in terms of the risk for fractures, the smoking status of the women found in the MBR is only indicative, as it does not identify those women who did not admit they smoked during their visits to maternity clinics. The information on the smoking status in the MBR is collected during pregnancy in maternity clinics, but it does not tell whether the women smoked after the pregnancy or not. However, the reliability of the smoking status in the MBR was over 92% in 1991, which makes it a reliable source (Gissler et al., 1993). It is good to note though, that this reliability study is relatively old, and the societal stigma towards smoking has changed markedly during last decades, meaning that the reliability of the smoking status might have impaired or improved.

6.6 Future studies

According to our results, future research should focus on analyzing the effects of different traumas on subsequent reproductive health in a larger multinational register-based cohort study. Our results provide good baseline information, but due to the numerous limitations in our data, these topics need to be researched further using more precise and larger datasets or registers. Especially studies focusing on the indications for urgent CS, and reasons for elective CS after major traumas should be performed. Furthermore, the effects of previous TBIs sustained by the mother on the health of the neonate showed interesting results and should be researched further in future, as these are not well studied. Another study design to be considered could be that women with major traumas could be questioned about their thoughts on future reproductive health, which could give information, e.g., about the lower number of children born after traumas. In addition, future research should focus on addressing patients concerns and to provide optimal counseling.

7 SUMMARY AND CONCLUSIONS

The goal of this study was to provide new information on the effects of different major traumas on reproductive health in fertile-aged women. We conducted a nationwide register-based cohort study for the period 1998-2018 to evaluate the effect of pelvic fractures, spine fractures or fusion surgeries, and TBIs on reproductive health. In addition, we evaluated the effect of different major traumas on subsequent birth rate and the effect of smoking on the risk for fractures in fertile-aged women. The following are the principal findings and conclusions of each study:

1. Vaginal delivery was the primary mode of delivery despite the higher rate of CS among women with a previous pelvic fracture. The results suggest that vaginal delivery after fractures of the pelvic circle is generally possible for the mother and safe for the neonate. The necessity for elective CS after pelvic fracture should be considered carefully by the patient, the obstetrician, and the orthopaedic consultant, who might be consulted about the capability to deliver vaginally such major traumas.
2. The incidence of fusion surgeries unrelated to fracture increased during the study period. Women who had a prior spine fracture or fusion surgery had a higher incidence rate of CS. Although the clinical importance is unclear, there was a slightly higher requirement for neonates born to mothers who had undergone spine fracture or fusion surgery prior to pregnancy to receive intensive care. Nonetheless, our findings imply that mothers who have sustained spine fractures or undergone spine surgeries can typically have a vaginal delivery that is both possible for themselves and safe for their neonates.
3. There was a strong increase in the rate of hospitalizations for TBI during the study period. Women with a history of TBI had a higher incidence of preterm deliveries, CS, instrumental vaginal deliveries, and labor analgesia.

Additionally, a greater proportion of neonates in this group necessitated intensive care. Consequently, a history of TBI should be recognized as a potential factor impacting both delivery and neonatal health, emphasizing the need for further investigation into this topic.

4. Based on our findings, women who had sustained fractures in their thigh, hip, or pelvis had a decreased likelihood of giving birth, and a reduced risk of having a pregnancy that resulted in a live birth over a 5-year follow-up period. Information gained from this study will be important in clinical decision making when women with previous major trauma are considering becoming pregnant and giving birth. It should be acknowledged, that these patients may have anxieties and require counseling or support regarding the safety of pregnancy and the well-being of their child.
5. The risk for fractures among smoking women was higher in all anatomic regions. The risk for polytraumas and both severe and non-severe fractures was also higher. Our results show that women who smoke during pregnancy have a higher fracture rate after giving birth. Clinicians should take note of these findings and utilize them to encourage patients to quit smoking. The exact cause of the heightened fracture risk, whether it is due to direct effects of smoking on bone health or riskier behavior, remains uncertain.

8 AUTHOR'S CONTRIBUTIONS

I Vaajala wrote the initial manuscript, performed appropriate statistical analyses, and interpreted the results. Vaajala was the corresponding author in this manuscript.

II Vaajala wrote the initial manuscript, planned and performed appropriate statistical analyses, and interpreted the results. Vaajala was the corresponding author in this manuscript.

III Vaajala planned the study design, wrote the initial manuscript, performed appropriate statistical analyses, and interpreted the results. Vaajala was the corresponding author in this manuscript

IV Vaajala planned the study design, wrote the initial manuscript, performed appropriate statistical analyses, and interpreted the results. Vaajala was the corresponding author in this manuscript.

V Vaajala planned the study design, wrote the initial manuscript, performed appropriate statistical analyses, and interpreted the results. Vaajala was the corresponding author in this manuscript.

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Pregnancy and delivery after pelvic fracture in fertile-aged women: A nationwide population-based cohort study in Finland

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Pregnancy and delivery after pelvic fracture in fertile-aged women: A nationwide population-based cohort study in Finland

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ABSTRACT

Objective: Only a few small studies have assessed the effects of pelvic fractures on pregnancies, deliveries, and rates of cesarean sections. We aimed to evaluate the effect of pelvic fractures on subsequent pregnancy and delivery in Finland.
Study design: In this retrospective register-based nationwide cohort study, data on all fertile-aged (aged 15–49) women with a pelvic fracture during our study period (1998–2018) were retrieved from the Care Register for Health Care. The data were subsequently combined with data from the National Medical Birth Register. Women with pelvic fracture before pregnancy were compared with a no-fracture group consisting of 621 141 women who had had 1 156 723 singleton deliveries without a preceding pelvic fracture. We used logistic regression to analyze preterm deliveries, cesarean sections, and neonatal health. Results are reported as adjusted odds ratios (AOR) with 95% confidence intervals (CI).
Results: A total of 2 878 women with a previous pelvic fracture were identified. Of these, 596 women had 1 024 singleton deliveries after pelvic fracture. In the no-fracture group, 621 141 women had 1 156 378 singleton deliveries. Compared to the no-fracture group, women with a previous pelvic fracture had higher rates of cesarean sections (22.6% vs 15.9%) (AOR 1.55 CI 1.32–1.80), higher rate of preterm deliveries (6.2% vs 4.6%) (1.32 CI 1.01–1.69), and a higher rate of neonates requiring intensive care unit treatment (13.5% vs 10.0%) (AOR 1.35 CI 1.13–1.62).
Conclusion: Vaginal delivery was the primary mode of delivery despite the higher rate of cesarean section among women with a previous fracture of the pelvis. The rate for preterm deliveries and need for neonatal intensive care was also higher, but the clinical importance of these findings is unclear. Our results suggest that vaginal delivery after fractures of the pelvic circle is generally safe for both mother and neonate.

Introduction

The incidence of pelvic fractures in the younger population is approximately 20/100 000 person-years. [1] In younger populations, fractures of the pelvic circle are typically the result of high energy collisions, such as falls from height or traffic accidents, whereas falls from standing height are more common in older populations. [1] Among the Finnish adult population during the years 1997–2014, around 8.2% of all pelvic fractures were treated surgically [2]. The main aim for surgical treatment of pelvic fracture is to restore stability and allow for mobilization and healing. [3] Allowing faster mobilization of the patient and shortening the recovery period lowers the total treatment costs when compared with those treated conservatively. [4]

Fractures of the pelvic circle may affect the sexual health of fertile-aged women, causing pain during sexual intercourse and sexual dysfunction.[5] To date, there have only been a few small studies that have assessed deliveries and pregnancies after pelvic fractures. It seems that even though pelvic fractures have affected

Abbreviations: AOR, adjusted odds ratio; CI, confidence intervals; CS, cesarean section; MBR, the National Medical Birth Register; OR, odds ratio.

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the mode of delivery, vaginal delivery is still possible after pelvic trauma.[6–8] Indeed, even after operatively treated pelvic fractures with associated damaged pubic symphysis, vaginal delivery is still possible.[5]

According to the findings of previous studies, patients who have suffered a pelvic fracture have a notably higher proportion of cesarean section (CS) (30–60%), even though the reason for this remains unclear.[9] There are no previous studies reporting major challenges during pregnancy after pelvic fracture when delivery itself is not considered. Copeland et al. found that patients with a pelvic fracture with over 5 mm dislocation had an increased risk for CS. The same study showed that pelvic fractures did not have a notable effect on miscarriage or fertility. Currently, it is suggested that the reason behind the increased risk for CS is most likely multifactorial and requires further investigation.[10]

As previous studies have all been relatively small and have only focused on the mode of delivery, we aimed to examine the mode of delivery and neonatal health in women with pelvic fracture on a larger scale. The aim of our nationwide register study is therefore to report the incidence of pelvic fractures in fertile-aged women and to investigate the effects of pelvic factures on subsequent pregnancy and delivery.

Materials and methods

In this retrospective nationwide register-based cohort study, we linked data from two national registers: the National Medical Birth Register (MBR) and the Care Register for Health Care. Both registers are maintained by the Finnish Institute for Health and Welfare. The study period was from 1998 to 2018, as we acquired data for these years.

The MBR contains information on all pregnancies, delivery statistics, and perinatal outcomes of births with a birthweight of $\geq$ 500 g or a gestational age $\geq 22^{+0}$, but only singleton deliveries were included in our study. The MBR has high coverage and quality (the current coverage is nearly 100%).[11,12]

Pelvic fracture was defined as a hospitalization period with one of the pelvic fracture ICD-10 codes (shown in supplementary file Table 1). Each patient with a hospitalization period with one of these ICD-codes was classified as a fracture patient. When forming the fracture group, only the first pelvic fracture for each woman was noted and each subsequent pregnancy after sustaining the pelvic fracture was added to the fracture group. Our data was limited to ICD-10 codes starting with S and NOMESCO (Nordic Medico-statistical Committee, Finnish version approved by the Finnish Institute for Health and Welfare) operation codes starting with N. All fertile-aged (15–49 years) women with a pelvic fracture during our study period (1998–2018) were included. Pelvic fracture surgery patients were included based on the operations codes of the Nordic version of the NOMESCO classification (Supplementary Table 1). Data from both registers were then combined by using the pseudonymized identification number of the mother.

Women with a pelvic fracture prior to delivery formed the patient cohort, which was categorized into operated and non-operated patients. A total of 604 women with 1 054 deliveries were identified in the group of women with a previous pelvic fracture. The identification of the fracture patients with subsequent deliveries was based on the date of the fracture in the Care Register for Health Care and the date of the pregnancy in the MBR. The date of the pregnancy is calculated from the last periods or confirmed with ultrasound. Conservatively treated fracture patients (570 women with 975 singleton deliveries) and operatively treated fracture patients (26 women with 49 deliveries) were analyzed separately. For clarity, they are presented together as the fracture group in tables and only significant findings have been presented separately. The no-fracture group consisted of 621 141 women who had 1 156 723 singleton deliveries without a preceding pelvic fracture (Fig. 1). Deliveries with missing information on the mode of delivery were excluded. In this study, each non-elective CS is considered as an urgent CS. The results of this study are reported according to the STROBE guidelines.[13]

Ethics

Both the MBR and the Care Register for Health Care used the same unique pseudonymized identification number for each patient. The pseudonymization was made by the Finnish data authority FINDATA. The authors did not have access to the pseudonymization key, as it is maintained by FINDATA. In accordance with Finnish regulations, no ethical approval or informed written consent was required because of the retrospective register-based study design. [14] Permission to use the data was granted by FINDATA after evaluation of the study protocol (Permission number: THL/1756/14.02.00/2020)

Statistics

Incidences per 100 000 person-years for hip fractures in fertile-aged (15–49 years) women were calculated with 95% confidence intervals. The baseline population was the number of females aged 15 to 49 years who were living in Finland at the end of a particular year, which was obtained from Statistics Finland (Stat.fi).[15] Means with standard deviation were calculated for continuous variables with expected normal distribution, and medians with interquartile range were used for non-normally distributed variables. Categorized variables were presented as absolute numbers and percentages. Subclass analyses were performed according to fracture diagnoses. A *p*-value under 0.05 was considered statistically significant. Logistic regression model was used to access the primary outcomes (gestational age at birth, mode of delivery, and neonatal health). CS (including elective and urgent) as an outcome was compared to vaginal delivery (including spontaneous and assisted vaginal deliveries) in a logistic regression model assessing mode of delivery. The need for intensive care for the neonate before being sent home from the hospital was used as an indicator for neonatal health. Maternal smoking during pregnancy, maternal diabetes during pregnancy, previous cesarean section and preterm delivery (in the model evaluating need for intensive care) were used as adjusting variables. Maternal smoking status during pregnancy is collected in women and child welfare clinics and can be either non-smoker, smoking during 1st trimester, smoking after 1st trimester or unknown. Maternal diabetes includes women with pregestational and gestational diabetes, and gestational diabetes is defined as pathological glucose tolerance test. Odds ratios with 95% CI were compared between groups. Statistical analysis was performed using R version 4.1103. Adjustments were made by choosing the variables for a multivariate model by using directed acyclic graphs (DAGs) constructed using the free online software Dagitty.[16] The variables included in the DAGs were chosen based on known risk factors and by the hypothesized causal pathways. DAGs are presented as a supplementary file (Supplementary Figs. 1-3).

Results

A total of 2 878 women with pelvic fracture were identified from the register. The incidence of fertile-aged patients with a pelvic fracture was 8.9 per 100 000 person-years in 1998. By 2018, this figure had in increased to 13.2 per 100 000 person-years (Fig. 2).

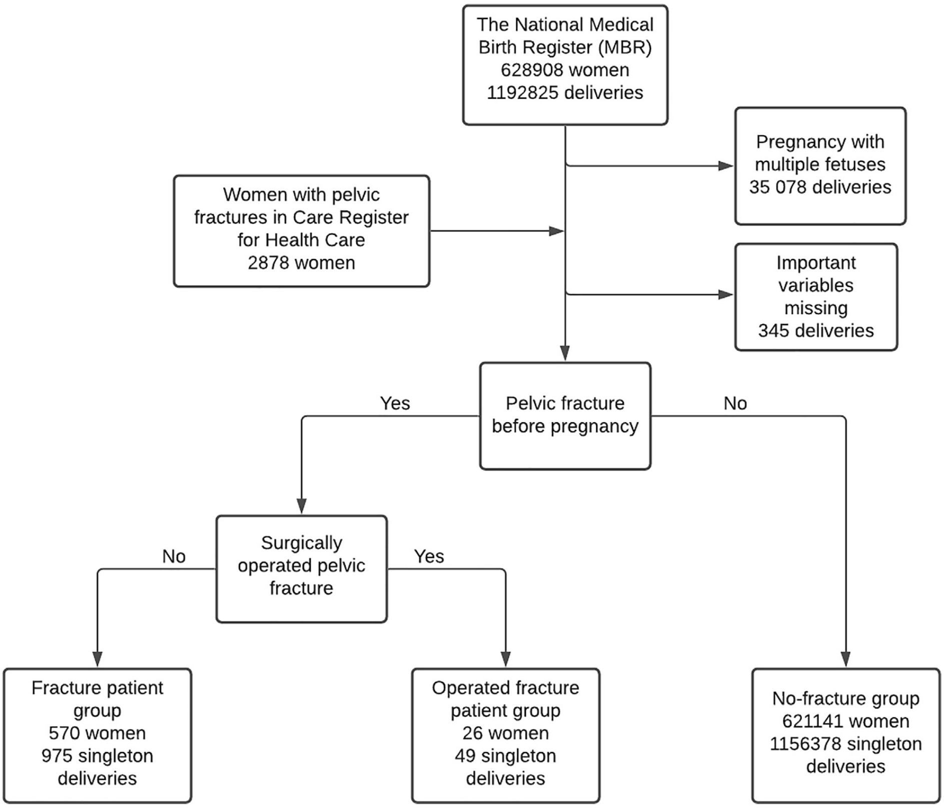

Fig. 1. Flowchart of the study population. Data from the MBR were combined with data on the diagnosed pelvic fractures in the Care Register for Health Care.

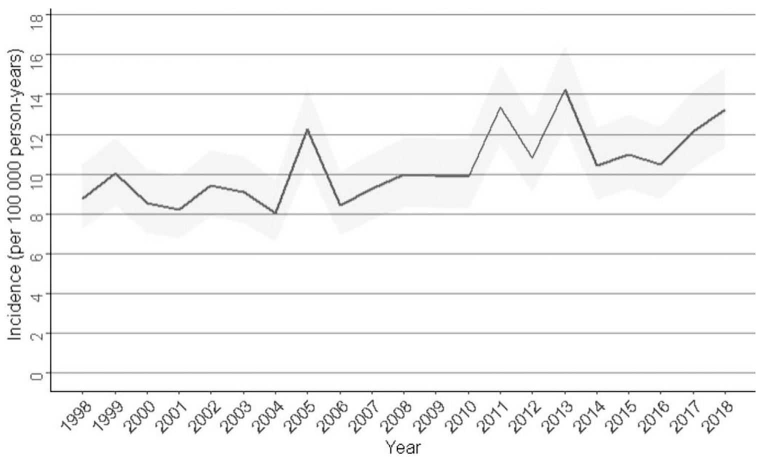

Fig. 2. Incidence of pelvic fractures among fertile-aged (15–49 years) women during the study period.

The mean age of the women in fracture group at the time of the delivery was 29.0 (SD 5.3) years and 29.7 (SD 5.4) in the no-fracture group. A higher rate of women were nulliparous in the fracture group compared to the no-fracture group (44.6% vs 41.4%). A higher percentage of fetuses in the fracture group were exposed to the smoking of the mother during pregnancy when compared to fetuses in the no-fracture group (23.1% vs 14.6%). The rate for previous CS was similar between the fracture and the no-fracture group. Basic background information on the deliveries in the fracture group and the no-fracture group is presented in Table 1.

In the fracture group, 6.2% of the neonates were preterm (gestational age at birth <37^{+0} weeks of gestation) and 3.5% had low birthweight (LBW, birthweight <2500 g), whereas 4.6% of neonates were preterm and 3.0% had LBW in the no-fracture group. Neonates had higher percentages in those variables related to the health problems of neonates (neonatal deaths, Apgar after 1 min, phototherapy, neonatal intensive care unit) in the fracture group. (Table 2).

Women in the fracture group had higher rates of elective CS when compared to the no-fracture group (11.3% vs 6.6%). However, no major differences were found in anesthetics or the rate of obstetrical interventions (amniotomy, use of oxytocin to induce or augment labor, episiotomy) (Table 3). Women in the fracture group had higher rates of preterm deliveries (AOR 1.32 CI 1.01–1.69), higher rates of cesarean sections (AOR 1.55 CI 1.32–1.80) and neonates requiring intensive care unit treatment (AOR 1.31 CI 1.07–1.58) (Table 4). The proportional amount of urgent CS was more common among the fracture group (AOR 1.29 CI 1.06–1.57).

Subgroup analyses based on given pelvic fracture diagnosis (Table 5 and Table 6) showed no major differences between groups. Among women with multiple pelvic fractures (ICD-10 diagnosis S32.7), the proportion of elective CS (17.6%) was higher than with any other diagnosis (Table 4). However, neonatal health was similar in this subgroup when compared to other fracture groups. Perinatal mortality was low with every fracture diagnosis. Vaginal delivery was possible in both fracture groups, and the rates of labor analgesia and modes of delivery were similar when elective cesarean sections were excluded (Table 5).

Discussion

The main finding of this study was the high rate of successful vaginal deliveries, despite the increased rate of CS after pelvic fracture. The rate for preterm deliveries and impaired health of the neonate was also higher after pelvic fracture.

The most important finding was the high rate of successful vaginal deliveries after pelvic fracture. Nevertheless, the proportion of CS was higher after a pelvic fracture, which is further explained by the increased rates of elective CS in the fracture group compared to the no-fracture group. In a country like Finland, where the option of CS is a matter of careful consideration between patient and physician, such a high proportional increase in a patient group is a significant finding. The rate of CS in Finland is one of the lowest in Europe (16–17%), and it has remained stable for the past two decades.[17,18] Even though the rate of elective CS was clearly higher after pelvic fracture in Finland, the rate is still lower than that in other countries. Indeed, in a previous systematic review concerning level-1 trauma centers, the rate of elective CS was over 40% after pelvic fractures[9] which is over 3-fold the rate of elective CS in the fracture group seen in our study. Our results should serve to reduce any doubts women may have regarding vaginal delivery as a mode of delivery after pelvic fracture.

Interestingly, we also found that urgent CS was more frequent in the fracture group. The exact reason for urgent CS remains

Table 1
Background characteristics of deliveries in the fracture group and no-fracture group.

	Fracture-group		No-fracture group	
Total number	1024		1 156 378	
	n	%	n	%
Age at birth (mean SD)	29.0 (5.3)		29.7 (5.4)	
Nulliparous	457	44.6	478 472	41.4
Previous cesarean section	120	11.7	124 235	10.7
Maternal smoking during pregnancy *	237	23.1	169 135	14.6

* Contains women who smoked during only the 1st trimester and/or later trimesters.

Table 2
Perinatal characteristics in the diagnosed fracture group and the no-fracture group.

	Fracture group		No-fracture group	
Total number	1024		1 156 378	
	n	%	n	%
Neonatal sex boy	526	51.4	591 788	51.2
Birth length (cm) (mean; SD)	50.0	2.5	50.1	2.5
Birthweight (grams) (mean; SD)	3474	546	3531	548
LBW <2500 g	36	3.5	34 470	3.0
Preterm <37+0 weeks*	63	6.2	53 117	4.6
Perinatal mortality**	7	0.7	6165	0.5
Neonatal deaths***	5	0.5	2708	0.2
1-minute Apgar score $\leq$ 6	150	14.6	157 399	13.6
Delivery related asphyxia	26	2.5	34 707	3.0
Phototherapy	65	6.3	68 752	5.9
Neonatal intensive-care unit	138	13.5	115 787	10.0
Neonatal status 7 days postpartum				
at home	956	93.4	1 086 765	94.0
at hospital	68	6.6	69 613	6.0

* Weeks of gestation.
** Includes stillbirths and neonatal deaths occurring during the first seven days.
*** Includes neonates born alive but died during the first seven days.

Table 3
Intended and true mode of delivery, labor analgesia, and procedures related to delivery in trials of labor in the fracture group and the no-fracture group.

	Fracture group		No-fracture group	
Total number	1024		1 156 378	
	n	%	n	%
Intendent mode of delivery				
Elective CS	116	11.3	76,663	6.6
Trial of labor	908	88.7	1,079,715	93.4
Total number (without elective CS *)	908	100	1,079,715	100
Mode of delivery				
spontaneous vaginal delivery	698	76.8	874,824	81.0
breech delivery	4	0.4	7009	0.6
vacuum or forceps delivery	91	10.0	90,840	8.4
urgent CS	115	12.7	107,042	9.9
Labor analgesia				
epidural	455	50.1	469,968	43.5
spinal	154	17.0	123,064	11.4
paracervical	148	16.3	188,597	17.5
amniotomy	446	49.1	533,128	49.4
use of oxytocin	431	47.5	489,282	45.3
episiotomy	214	23.6	278,782	25.8
manual placental removal	12	1.5	16,075	1.5
uterine curettage	6	0.7	9419	0.9

* CS = cesarean section.

Table 4
Absolute numbers, percentages, univariable and adjusted Odds ratios (OR) with 95% confidence intervals (CI) for the main outcomes. The models were adjusted using the following variables: Maternal smoking during pregnancy, maternal diabetes during pregnancy, previous cesarean section, and preterm delivery. Each of the adjusting variables were reported in the MBR during pregnancy.

Total number	Fracture group		No fracture-group		Univariable	Adjusted
	n	%	n	%	OR (95% CI)	OR (95% CI)
Preterm delivery	63	6.2	53 117	4.6	1.36 (1.04–1.74)	1.32 (1.01–1.69) **
Cesarean section *	231	22.6	183 705	15.9	1.54 (1.33–1.78)	1.55 (1.32–1.80) ***
Neonatal intensive care	138	13.5	115 787	10.0	1.40 (1.17–1.67)	1.31 (1.07–1.58) ****

* All cesarean sections, including elective CS.
** Adjusted with maternal smoking during pregnancy and maternal diabetes during pregnancy.
*** Adjusted with maternal smoking during pregnancy, maternal diabetes during pregnancy, and previous CS.
**** Adjusted with maternal smoking during pregnancy, maternal diabetes, diabetes during pregnancy, and preterm delivery.

unclear, as this information is not recorded to the register. The previous pelvic fracture may have complicated the delivery and the higher rate of urgent CS might be due to complications caused by pelvic fractures. Also, the awareness of a previous pelvic fracture may have lowered the threshold for the obstetrician to convert the trial of labor to urgent CS. Additionally, some women with a recorded urgent CS may already have planned an elective CS, but because the labor began early, the planned elective CS was recorded as an urgent CS. In the subgroup analysis, women with multiple pelvic fractures had notably higher rates of elective and urgent CS than women with other fracture diagnoses and women in the no-fracture group. The total rate of CS (including elective and urgent CS) was 32.1% in the group of women with multiple fractures.

Overall, the perinatal mortality rate was low, and no increase was observed among patients in the fracture group. However, the need for neonatal intensive care was higher in the fracture group, which can be explained by the higher CS rate. The higher rate of preterm deliveries can partly be explained by the higher rate of smoking among women with previous pelvic fracture, as smoking is known to increase risk for preterm deliveries.[19] In previous studies, no increase in rates of miscarriage or infertility after pelvic trauma has been reported either. However, the number of patients included in these studies was quite low, and the health of neonates was not reported.[5,8,10]

CS procedures were more common in the fracture group, but in majority of cases vaginal delivery was successful, and the health of the neonate was not affected. CS is linked to a decrease in mortality of neonates and parturients in selected cases. However, the downsides of CS for the neonate are the increased risk for asthma, obesity, and poorer cardiorespiratory health in later life than those born vaginally.[20,21] Additionally, breastfeeding duration is shorter after elective CS.[22] For women, CS may cause pregnancy-related complications in future pregnancies.[23] According to the results of this study, vaginal delivery is the primary mode of delivery even after multiple pelvic fractures or operated pelvic trauma. Interestingly, our results show that the incidence of pelvic fractures among fertile-aged women is increasing in Finland, and similar findings have been reported in Sweden.[1] Consequently, there may be an increase in deliveries after pelvic fracture in future. The results of our study should also be considered when obstetricians and women who have had a pelvic fracture discuss the delivery method during pregnancy, as vaginal delivery for these women appears to be safe and could be attempted.

The strength of our study is the large, nationwide study population with long study period which enabled the analysis of these relatively rare events. The data for the registers used in this study are routinely collected using structured forms with nationwide instructions, which ensures the registers have good coverage and

Table 5
Perinatal characteristics and outcomes in the subgroups based on the type of fracture diagnosis among fracture patients.

Type of fracture	Sacrum (S321)		Ilium (S323)		Acetabulum (S324)		Pubis (S325)		Multiple fractures (S327)		Other or undefined (S328)	
Total number	179		92		128		214		262		149	
	n	%	n	%	n	%	n	%	n	%	n	%
Intended mode of delivery												
Elective CS*	25	13.9	3	3.3	14	10.9	16	7.5	46	17.6	12	8.1
Trial of labor	154	86.1	89	96.7	114	89.1	198	92.5	216	82.4	137	91.9
Preterm <37+0 weeks**	17	9.5	4	4.3	11	8.6	6	2.8	14	5.3	11	7.4
1 min Apgar score $\leq$ 6	27	15.1	13	14.1	21	16.4	27	12.6	42	9.2	20	13.4
Neonatal intensive care unit	25	14.0	12	13.0	21	16.4	33	15.4	27	10.3	20	13.4
Neonatal status 7 days postpartum												
at home	164	91.6	85	92.4	115	89.8	201	93.9	247	94.3	138	92.6
at hospital	15	8.4	7	7.6	13	10.2	13	6.1	15	5.7	11	7.4

* CS = cesarean section.
** Weeks of gestation.

Table 6
Proportions of selected obstetric variables in attempted vaginal deliveries in the subgroups based on the type of fracture diagnosis among fracture patients.

Fracture diagnosis (ICD-10)	Sacrum (S321)		Ilium (S323)		Acetabulum (S324)		Pubis (S325)		Multiple fractures (S327)		Other or undefined (S328)	
Total number	154		89		114		198		216		137	
	n	%	n	%	n	%	n	%	n	%	n	%
Mode of delivery												
spontaneous vaginal delivery	126	81.8	73	82.0	90	78.9	153	77.3	151	69.9	105	76.6
breech, vacuum, or forceps delivery*	7	4.5	13	14.6	11	9.6	22	11.1	27	12.5	15	10.9
urgent CS **	21	13.6	3	3.4	13	11.4	23	11.6	38	17.6	17	12.4
Labor analgesia												
epidural	75	48.7	47	52.8	60	52.6	99	50.0	105	48.6	69	50.4
spinal	29	18.8	12	13.5	16	14.0	40	20.2	36	16.7	21	15.3
paracervical	16	10.4	16	18.0	24	21.1	33	16.7	33	15.3	26	19.0

* Due to the low number of breech and forceps deliveries, they were combined because Finnish legislation prevents the reporting of the exact event rate if the rate is lower than three.
** CS = cesarean section.

reduces possible reporting and selection bias.[24] Therefore, the coverage and validity of both registers included in this study are high.[25] The advantage of our study compared to previous studies is the large national research material in a country with uniform delivery-related guidelines and attitudes. Furthermore, another advantage compared to multinational studies is that in multinational studies, CS standards may differ between countries (for example, attitudes towards CS and threshold for elective CS), which could result in inaccuracies in the results and make these studies vulnerable to bias.

The main limitation of our study is the missing clinical information on fractures (for example, radiological findings or pelvimetric examination results). As this information is not recorded to the registers, we could only use ICD-10 coding. Further, the contents of the birth register were updated in 2004 and 2017, and ICD-codes concerning chronic diseases of the mother, pregnancy, and delivery, 5-minute Apgar scores, and durations of labor stages were only included after 2004. Therefore, these were not analyzed in our study. Furthermore, since cases of CS were classified as elective or urgent prior to 2004, we have used the same classification in the present study instead of the elective, urgent, and emergency classifications.

Conclusion:

Based on our findings, the proportion of CS was higher after pelvic fracture when compared to the no-fracture group without previous pelvic fractures. However, the rate of preterm deliveries and neonates with health problems born to women with previous pelvic fracture was affected less by previous pelvic fracture when compared to the no-fracture group. Thus, our results advocate vaginal delivery as safe for women after fractures of the pelvis or operated pelvic trauma. These findings could further encourage obstetricians and women with a previous pelvic fracture to consider the possibility of vaginal delivery.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2022.01.008.

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PUBLICATION
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Pregnancy and delivery after spine fracture or surgery: A nationwide population-based register study in Finland

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RESEARCH ARTICLE

Pregnancy and delivery after spine fracture or surgery: A nationwide population-based register study in Finland

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Abstract

Background

The incidences of spine fractures and fusion surgeries have increased. A few studies have reported an increased rate of caesarean sections (CS) in women who have undergone spine surgery but have not reported on the health of neonates.

Objective

We report the incidence of spine fractures, spine fracture surgeries and fusion surgery for other reasons and the effect of these injuries and procedures on later pregnancy outcomes in Finland.

Methods

Data on all fertile-aged women (1998–2018) who had undergone spine fracture or spine fusion surgery were retrieved from the Care Register for Healthcare and combined with data from the National Medical Birth Register. Women with spine fracture or spine surgery before pregnancy were compared with women without previous spine fracture or surgery. We calculated incidences of spine fracture, spine fracture surgery and fusion surgery for other reasons with 95% confidence intervals (CI). We used multivariable logistic regression to evaluate CS and neonatal health. Results are reported as adjusted odds ratios (AOR).

Results

The main finding of our study was the increasing incidence (156%) of spine fusion surgeries for other reasons in fertile-aged women. A total CS rate (including elective and unplanned

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CS) in the spine fracture group was 19.7% (AOR 1.26, CI 1.17–1.34), in fusion surgery for other reasons group 25.3% (AOR 1.37, CI 1.30–1.49) and 15.9% in the control group. The rate for neonates requiring intensive care in the spine fracture group was 12.2% (AOR 1.18, CI 1.08–1.29), in fusion surgery for other reasons group 13.6% (AOR 1.12, CI 1.02–1.23) and 10.0% in the control group.

Conclusions

The incidence of fusion surgery for other reasons increased during our study period. The rate of CS was higher in women with preceding spine fracture or fusion surgery. Our results suggest that vaginal delivery after fractures of the spine is both possible and safe for mother and neonate.

Introduction

Fractures of the spine are typically caused by high-energy trauma and usually occur anatomically at the junction of the thoracic and lumbar spine (Thoracic vertebrae 10–12) [1]. According to the literature, the most common cause of spine fractures in younger patients is falling from height, followed by traffic collisions/accidents and high impact sports. The majority of these high energy spine fractures in younger patients are in the thoracic or lumbar vertebrae [2].

In Finland, the incidence of spine fractures leading to hospitalisation in all patients older than 20 years increased from 57/100 000 person-years in 1998 to 89/100 000 person-years in 2017. Furthermore, a corresponding increase was also observed in the incidence of spine fracture surgeries (from 5.3/100 000 to 8.8/100 000 person-years). Among women, the rate of spine fracture surgeries increased by 147% during the same period [3]. In addition to spine fracture surgery, scoliosis surgery is a more common procedure in younger adults and teenagers. According to von Heideken et al., the annual incidence of scoliosis surgery in Sweden between 2000 and 2013 was estimated to be 12.5/100 000 person-years, with a rapidly increasing trend among women [4].

Moreover, anterior spinal surgery or scoliosis surgery affected the mode of delivery and increased the number of caesarean sections (CS) and led to more frequent preterm deliveries when compared to the population without operation [5–7]. Furthermore, patients who undergo spine surgery have been reported to sustain higher rates of complications related to pregnancy and delivery. A previous small local study reported unchanged delivery rates and neonatal health after surgically treated scoliosis [5].

In Finland, incidences of spine fractures or major surgical spine operations for the whole population have been extensively studied. There is, however, a scarcity of studies on the effects of spine fractures or surgical spine operations on reproductive health, although a few small studies have investigated the effects on delivery and the health of the neonate [5, 7]. This lack of information on the effects of spine fractures and surgeries on the reproductive health of fertile-aged women makes the study of the incidence of spine fractures and surgeries and subsequent pregnancies after spine fracture or surgery of the utmost importance.

The aim of this nationwide register study was therefore to report the incidence of spine fracture, spine fracture surgery and fusion surgery for other reasons in fertile-aged females and to investigate their impact on pregnancies and deliveries.

Methods

In this nationwide register-based study, we combined data from two national registers–the Care Register for Healthcare and the National Medical Birth Register (MBR). The quality and coverage of both registers is high [8–10]. Both registers are maintained by the Finnish Institute for Health and Welfare. Data on all deliveries and neonates were collected from the MBR, which contains information on all pregnancies, delivery statistics and the perinatal outcomes of births with a birthweight of ≥500 grams or a gestational age of $\geq 22^{+0}$ [11]. Data from both registers were then combined by using the pseudonymised identification number of the mother. The study period was from 1998 to 2018.

We differentiated three groups of problems related to the spine–spine fracture, spine fracture surgery and fusion surgery for other reasons. Spine fracture was defined as a hospitalisation period with spine fracture ICD-10 codes. All fertile-aged (15–49 years) women with a spine fracture were included. For each patient, the first spine fracture diagnosis per patient was classified as a separate spine fracture. This was important as the control appointments for the fracture could occur after a long period, and thus make it impossible to identify any new fractures during subsequent hospitalisation periods recorded in the Care Register for Healthcare. Those patients who underwent spine fracture surgery or fusion surgery for other reasons were included based on the operation codes of the Nordic version of the NOMESCO (Nordic Medico-statistical Committee, Finnish version approved by the Finnish Institute for Health and Welfare) classification. Women who underwent spine fusion surgery in a hospitalisation period with a spine fracture diagnosis were identified as fracture surgery patients. The spine fracture diagnosis codes and operation codes included in this study are presented in S1 Table.

Women with a spine fracture prior to delivery formed the fracture group, which was then categorized into operated and non-operated fracture patients. A total of 1371 women with 2301 singleton deliveries were identified in the group of women with previous spine fracture. Of these, 734 women with 1234 deliveries suffered a fracture in lumbar spine. Conservatively treated fracture patients (1329 women with 2224 singleton deliveries) and surgically treated fracture patients (42 women with 77 singleton deliveries) were analysed separately. For clarity, they are presented together as the fracture group in tables, and only remarkable findings have been presented separately. Women with fusion surgery for other reasons included 416 women with 632 singleton deliveries. Of these, 206 women with 309 deliveries had a fusion surgery for other reasons in lumbar spine. The control group consisted of 620 093 women who had 1 154 469 singleton deliveries without a preceding spine fracture, spine fracture surgery or fusion surgery for other reasons (Fig 1). Deliveries with missing information on the mode of delivery were excluded. In this study, each non-elective caesarean section (CS) is considered an unplanned CS. The results of this study are reported according to the STROBE guidelines [12].

Ethics

Both the National Medical Birth Register (MBR) and the Care Register for Healthcare had the same unique pseudonymised identification number for each patient. The pseudonymisation was made by the Finnish data authority FINDATA, and the authors did not have access to the pseudonymisation key, as it is maintained by FINDATA. In accordance with Finnish legislation, no informed written consent was required because of the retrospective register-based study design and because the patients were not contacted. Permission for the use of this data was granted by FINDATA after evaluation of the study protocol (Permission number: THL/1756/14.02.00/2020).

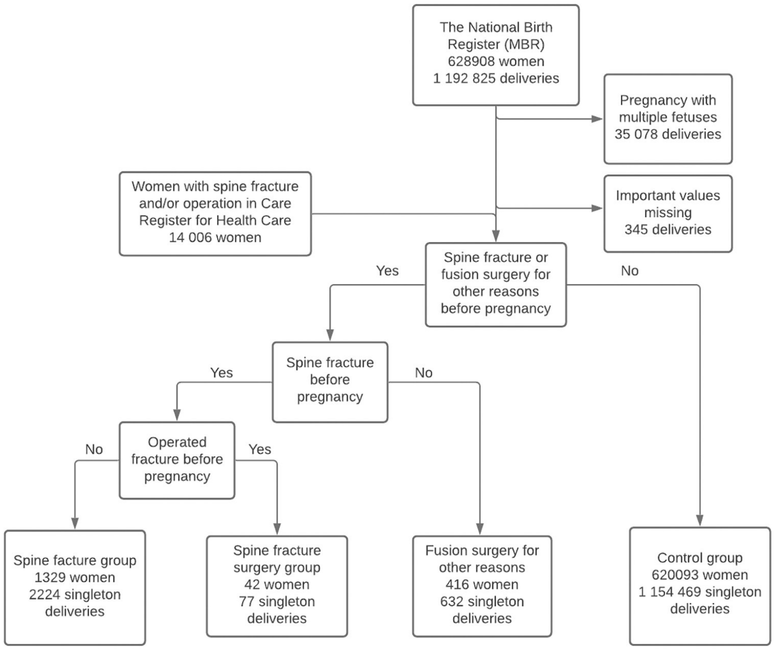

Fig 1. Flowchart of the study population. Data from the MBR were combined with data on the diagnosed spine fractures and spine operations recorded in the Care Register for Healthcare.

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Statistics

Continuous variables were interpreted as mean with standard deviation or as median with interquartile range based on distribution of the data. Categorized variables were presented as absolute numbers and percentages. Student's t-test, Mann-Whitney U-test and Chi squared tests were used for group comparisons. Statistical tests were used to compare separately patient groups (spine fracture and fusion surgery for other reasons group) to control group. P-value under 0.05 was considered statistically significant. The multivariable logistic regression model was used to access the primary outcomes (mode of delivery and neonatal health). The model was used separately for fracture patients and patients with fusion surgeries for other reasons. When using the model, the other group were excluded from the data, as it would otherwise occur as part of the control group and cause distortion in the results. As lumbar spine is anatomically located near the reproductive system and therefore the effects of traumas and surgeries on this area on pregnancy and delivery are of great interest, we analysed fractures and surgeries in lumbar spine separately from thoracical and cervical spine. The need for intensive care for the neonate was used as an indicator for neonatal health in logistic regression analysis. Maternal smoking during pregnancy and maternal diabetes during pregnancy were used as adjusting variables. Odds ratios (OR) and adjusted odds ratios (AOR) with 95 confidence intervals (CI) were calculated for the main outcomes. Crude OR were included in the study because of the unreliability of the maternal diabetes variable in the data. Adjustments were made by choosing the variables for the multivariate model using directed acyclic graphs (DAGs) constructed using the free online software DAGitty (dagitty.net). The variables included in the DAGs were chosen based on known risk factors and the hypothesised causal pathways. The DAGs are presented as a supplementary file (S1 and S2 Figs). Statistical analysis was performed using R version 4.0.3.

Results

Spine fractures and spine fracture surgery

A total of 14 006 women with a spine fracture or who underwent fusion surgery for other reasons were identified from the Care Register for Healthcare. A total of 6374 women had a spine fracture during the study period. The incidence of spine fracture hospitalisation increased slightly during our study period from 24.3 per 100 000 person-years in 1998 to 28.7 per 100 000 person-years in 2018. However, the incidence of spine fracture surgery remained stable during this period (Fig 2A).

Fusion surgery for other reasons

A total of 416 fusion surgeries for other reasons prior to delivery were identified. The incidence of fusion surgeries for other reasons increased more than twofold from 17.6 per 100 000

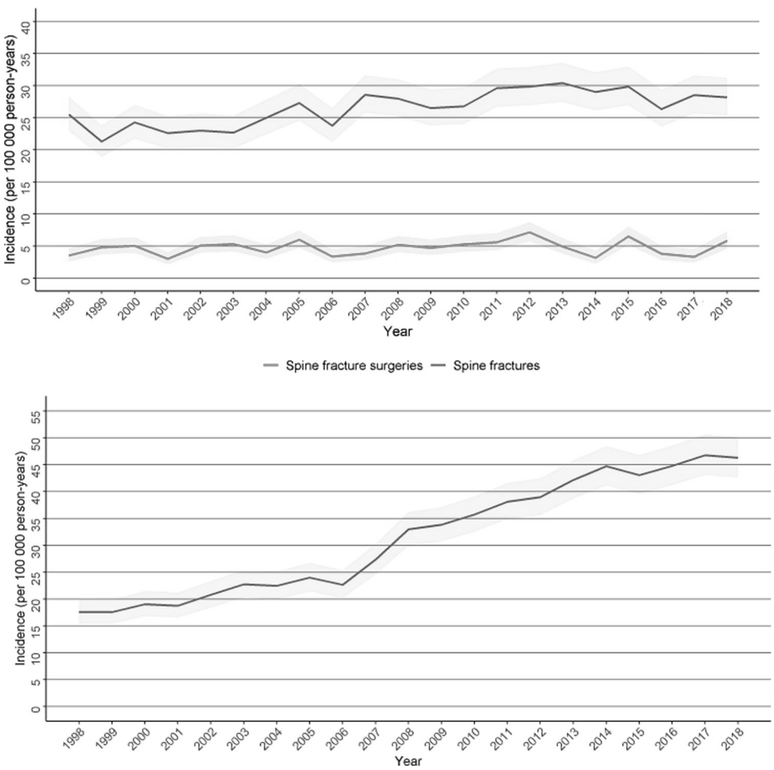

Fig 2. A. Incidence of spine fractures and spine fracture surgeries with 95% confidence intervals among fertile-aged (15–49 years) women during the study period. B. Incidence of fusion surgeries for other reasons with 95% confidence intervals among fertile-aged (15–49 years) women during the study period.

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Table 1. Background characteristics of women having singleton pregnancies in the patient groups and control group.

	Fracture group		Fusion surgery group		Control group	
Total number	**2301**		**632**		**1 154 469**	
	n	**%**	**n**	**%**	**n**	**%**
Age at birth (years, mean SD)	29.4 (4.7)		30.6 (6.2)		29.7 (5.4)	
Nulliparous	1060	46.1	274	43.4	477 595	41.4
Previous C-section	241	10.5	99	15.7	124 013	10.7
Smoking during pregnancy	625	27.2	114	18.0	168 633	14.6

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person-years to 46.3 per 100 000 person-years (Fig 2B). Anterior fusion of the cervical spine without fixation (38%) and posterior fusion of the lumbar spine with fixation (21%) were the most common operations during the study period, with scoliosis being the most typical reason for these operations. The mean age of the women undergoing the operation NAG 53 (Posterior or lateral fusion of thoracic spine with fixation, more than 3 vertebrae) had a notably lower mean age (19.1) than any other operation (S2 Table).

Pregnancies and deliveries

Compared to patients without a previous spine fracture or fusion surgery, the rate of nulliparous women was higher in the fracture group (46.1%, $p < 0.001$) and the fusion surgery group (43.4%, $p < 0.001$). In the fracture group, a higher percentage of women smoked during pregnancy (27.2%, $p < 0.001$), whereas only 14.6% of women in the control group smoked (Table 1).

AOR for CS in the spine fracture group was 1.26 (CI 1.17–1.34), and the need for intensive care treatment for the neonate was 1.18 (CI 1.08–1.29). Among women with fusion surgery for other reasons, the AOR for caesarean sections was 1.39 (CI 1.30–1.49), and the need for intensive care treatment for the neonate was 1.12 (CI 1.02–1.23). When comparing only patients with fracture or fusion surgery for other reasons in lumbar spine, the AORs were similar compared to the AORs of the whole spine. (Table 2)

Patients with spine fracture or fusion surgery without fracture had a slightly higher rate of elective CS when compared to control group (9.5% and 13.1% vs 6.6%, $p < 0.001$ for both). After excluding elective CS, unplanned CS was on the same level in the fracture group ([11].3%, $p = 0.032$) and higher in the fusion surgery group (14.0%, $p < 0.001$), when compared to the control group (9.9%). In the same analysis, including only primipara and women without previous CS, the rates of unplanned CS were 15.5% ($p < 0.001$) in the fracture group, 17.2%

Table 2. Univariable and multivariable logistic regression interpreted as odds ratios (OR) with 95% confidence intervals (CI) for the main variables. Both groups were compared with the control group. Also, patients with fracture or surgery in lumbar spine (L) were compared with control group separately. The models were adjusted by maternal smoking and diabetes during pregnancy.

	Caesarean section (fracture group)	Neonatal intensive care (fracture group)	Caesarean section (Fusion surgery group)	Neonatal intensive care (Fusion surgery group)
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Univariable	1.27 (1.17–1.36)	1.23 (1.12–1.35)	1.38 (1.28–1.48)	1.14 (1.04–01.25)
Adjusted	1.26 (1.17–1.34)	1.18 (1.08–1.29)	1.39 (1.30–1.49)	1.12 (1.02–01.23)
Univariable (L)*	1.35 (1.22–1.48)	1.27 (1.13–1.44)	1.46 (1.30–1.65)	1.27 (1.09–1.48)
Adjusted (L)	1.34 (1.21–1.48)	1.23 (1.09–1.39)	1.49 (1.32–1.68)	1.26 (1.08–1.16)

* L meaning only patients with fractures or fusion surgery for other reasons in the lumbar spine.

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Table 3. Proportions of obstetric variables in attempted vaginal deliveries (without elective CS) of the fracture patient groups and the control group. Elective CS was the intended mode of delivery in 218 (9.5%) of all deliveries in fracture group, 83 (13.1%) in fusion surgery for other reasons group and 76 478 (6.6%) in control group.

	Fracture group		Fusion surgery group		Control group	
Total number (without elective CS)	**2083**		**549**		**1 077 991**	
	n	**%**	**n**	**%**	**n**	**%**
Mode of delivery						
spontaneous vaginal delivery	1630	78.3	411	74.9	873 485	81.0
Instrumental vaginal delivery	217	10.4	61	11.1	97 666	9.1
unplanned CS	236	11.3	77	14.0	106 844	9.9
Labour analgesia						
epidural	1000	48.0	257	46.8	469 166	43.5
spinal	342	16.4	79	14.4	122 797	11.4
spinal + epidural	58	2.8	14	2.6	13 600	1.3
paracervical	414	19.9	128	23.3	188 203	17.5
pudendal	192	9.2	48	8.7	67 331	6.2

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($p < 0.001$) in the fusion surgery for other reasons group and 14.2% in the control group. Epidural and spinal anaesthesia were more common among patients with fracture or fusion surgery when compared to control group ($p < 0.001$ for both) (Table 3). In addition, pudendal and paracervical analgesia were slightly more common in these groups ($p < 0.001$). Labour analgesia showed a larger proportional increase in the fracture patients and fusion surgery patients groups when compared to the control group ($p < 0.001$). (Table 3).

Neonatal health

Perinatal mortality or problems related to the health of the neonate (1-minute Apgar under 6, delivery related asphyxia, need for phototherapy) were not more common in the fracture group or the fusion surgery for other reasons group. However, a higher proportion of neonates born to women in the spine fracture and fusion surgery for other reasons groups needed intensive care compared to the control group (12.2% and 13.6 vs 10.0%, $p < 0.001$). (Table 4).

Comment

The main finding of our study was the increasing incidence (156%) of spine fusion surgeries for other reasons in fertile-aged women. The incidence of spine fractures, however, remained

Table 4. Perinatal characteristics and outcomes in the patient groups and the control group.

	Fracture group		Fusion surgery group		Control group	
Total number	2301		632		1154469	
	n	%	n	%	n	%
LBW* < 2500g	80	3.5	24	3.8	34 402	3.0
Preterm < 37 + 0 gestational weeks	115	5.0	46	7.3	53 019	4.6
Perinatal mortality**	9	0.4	5	0.8	6158	0.5
1 minute Apgar score ≤ 6	333	14.5	85	13.4	157 131	13.6
Neonatal intensive-care unit	281	12.2	86	13.6	115 558	10.0
Discharged from hospital during the first week	2143	93.1	589	93.2	1 084 983	94.0

*LBW = low birthweight.

**perinatal mortality includes still births and deaths before the age of seven days

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nearly unchanged during the study period. Moreover, women with spine fracture or spine fusion surgery for other reasons had higher rates of elective and unplanned CS, but neonatal health was not importantly impaired in either group.

In a recent study on the incidence of spine fracture and spine fusion surgeries in all patients older than 20 years in Finland (1998–2017), the increase was evaluated to be approximately 65% [3]. When compared to this finding, the proportional increase in elective fusion surgery in fertile-aged women was higher in the present study. The exact reason for this increase is unknown, but the rapidly increasing incidence of scoliosis [4] might be one probable explanation for this finding. In addition, based on our results the incidence of spine fracture surgery remained stable in fertile-aged women, which possibly indicates that the increase observed in previous study is mostly due to increase in the older age groups. The previous study also reported that the increase in the whole population was highest in patients over 60-years of age (400%) [3].

Elective and unplanned CS were more common in the fracture and spine fusion surgery groups. In addition, the risk for elective and unplanned CS among patients with fracture or fusion surgery in lumbar spine increased slightly. However, vaginal delivery was possible in most cases. In addition, the need for intensive care for the neonates was little higher in fracture and fusion surgery for other reasons group, but the clinical importance of this remains unclear. Adjusting the models with smoking status and maternal diabetes decreased the AORs for caesarean section and impaired health of neonate, meaning that these have most likely effect on these outcomes in fracture group and fusion surgery for other reasons group, but aren't an explanation alone. Elective CS rate was two times higher in the spine fusion surgery for other reasons group. This increase is notable because in Finland the indication for CS is always considered carefully between patient and physician. The combined elective and unplanned CS rate in Finland is reported to be 16% [13]. In our study, however, the rate of CS in spine fracture and spine fusion surgery patients is lower than in most Western countries [14]. In a study in the United States, the incidence of elective CS after spine surgery was reported to be 37% [7], which is three times higher than the incidence in our results. These results raise questions about the reasons behind the higher rate of elective CS in patients with spine fracture or fusion surgery, as we did not observe neonatal health to be importantly impaired. Although CS is a fast and relatively safe operation and has played a remarkable role in decreasing mortality in neonates, many disadvantages for the mother and neonate following the operation have been reported. In neonates born by CS, an increased risk for asthma, obesity, and poorer cardiorespiratory health in later life has been reported [15–17]. For mothers, CS has been associated with shorter breastfeeding duration, future subfertility and complications related to future pregnancies [18–21]. Further, these results should be acknowledged by the patient, the obstetrician and the orthopaedic consultant when considering the necessity for elective CS, as vaginal delivery appears still to be safe delivery method. In the present study, the rate of unplanned CS was higher among patients in the fusion surgery for other reasons group. The exact reason for this remains unclear, as no such increase was found in the fracture group. However, there was a higher proportion of nulliparous women in the fusion surgery group, and the women in this group had higher rates of previous CS, which could partly explain the higher rate of elective and unplanned CS. In addition, a slightly higher rate of preterm deliveries in this group could affect the rate of unplanned CS. Another possible explanation might be the awareness of previous spine fusion surgery, which may lower the threshold for the obstetrician to convert the trial of labour to CS. Additionally, some women with a recorded unplanned CS may already have planned an elective CS, but because the labour began early, the planned elective CS was recorded as an unplanned CS. Further, the rate of instrumental vaginal deliveries was higher in the fusion surgery for other reasons group, which could possibly indicate a more challenging vaginal delivery after fusion surgery.

A study with a small number of patients concluded that spinal cord injury did not have a negative effect on the health of neonates [22], but there is little information about the effects of spinal trauma or surgery on neonatal health. Even though women who previously underwent fusion surgery had a higher rate of preterm deliveries, our results suggest that a previous spine fracture or fusion operation does not have a clinically relevant negative effect on the health of the neonate. Indeed, the slightly higher percentages of neonates in need of intensive care might partly be explained by the higher proportional number of CS and preterm deliveries in these groups. However, no clinically important difference was found between the groups in any of the neonatal health indicators.

Interestingly, the rates of labour analgesia provided by anaesthesiologists in the fracture group and the fusion surgery group were remarkably higher when compared to the control group. The literature documenting the management of labour analgesia after spinal surgery or spine fracture is limited to only a few studies with small study populations. According to this quite limited literature, the main problems for the anaesthesiologist are the difficulties associated with performing the procedure. These difficulties include the inability to identify the epidural space, multiple attempts before catheter insertion, vascular trauma, subdural local anaesthetic injection and accidental dural puncture [23]. Based on our results it appears that the rates of labour analgesia was higher in fracture group and fusion surgery for other reasons group. In our study, however, any possible complications during or after anaesthesia remain unknown, as this information is not recorded in the MBR, making it impossible to draw conclusions about the success rate of labour analgesia after spine fracture or surgery. However, current understanding is that epidural analgesia does not raise the risk for CS or instrumental vaginal delivery [24, 25]. One possible explanation for higher rates of labour analgesia in the fracture or fusion surgery group might be the decreased mobility and possible decreased flexibility of the spine, which could create the need for greater pain relief.

The strength of our study is the large nationwide study population with a long study period, enabling the proper analysis of such rare events. The register data we used in our study are routinely collected using structured forms with nationwide instructions, which ensures the good coverage and reduces possible reporting and selection bias [13]. Therefore, the coverage and validity of both registers included in this study are high [10]. The advantage of our study compared to previous studies is the large national research material in a country with uniform delivery-related guidelines and attitudes.

The main limitation of our study is the missing clinical information on fractures and other spine diseases (i.e., radiological findings or pelvimetric examination results). As this information is not recorded to the registers, we could only use ICD-10 coding. Further, the contents of the birth register were updated in 2004 and 2017, and 5-minute Apgar scores, durations of labour stages, body mass index and the chronic disease diagnosis of the mother were only included after 2004. Therefore, these were not analysed in our study. Furthermore, since cases of CS were classified as elective or urgent prior to 2004, we have used the same classifications in the present study instead of the elective, urgent and emergency classifications. Also, the indications behind CS are not registered in the MBR, which means that the indications for elective CS, such as had the patient planned an elective CS or attempted vaginal delivery before unplanned CS, remain unknown.

Conclusions

Based on the findings of the present study, the incidence of fusion surgery for other reasons had a strongly increasing trend during our study period. The proportion of CS was higher in the spine fracture or fusion surgery for other reasons group when compared to the women (in control group) without spine fracture or operated spine. Moreover, the need for intensive care for neonates born to mothers who underwent spine fracture or fusion surgery for other reasons before pregnancy was little higher, but the clinical importance of this remains unclear. However, our results suggest that vaginal delivery after fractures of the spine is both possible and safe for mother and neonate. These findings could further encourage obstetricians and women with a previous spine operation or fracture to consider the vaginal delivery approach.

Supporting information

S1 Table. Definitions for ICD-10-codes and NOMESCO classification codes for fracture-related and other major spine operations included in this study.
(PDF)

S2 Table. Frequencies of the spine operations and the mean age of the women at the time of operation in these subgroups during the study period.
(PDF)

S1 Fig. DAG: Health of neonate as a dependent variable.
(TIF)

S2 Fig. DAG Risk for caesarean section as a dependent variable.
(TIF)

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Pregnancy and delivery after traumatic brain injury: a nationwide population-based cohort study in Finland

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ORIGINAL ARTICLE

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Pregnancy and delivery after traumatic brain injury: a nationwide population-based cohort study in Finland

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ABSTRACT

Objectives: Few studies have assessed pregnancies and deliveries after traumatic brain injury (TBI). We report the incidence of TBIs and TBI-related surgeries in fertile-aged females and investigate subsequent pregnancy outcomes.

Methods: All fertile-aged (15–49) women with TBI diagnosis during our study period (1998–2018) were retrieved from the Care Register for Health Care and combined with data from the National Medical Birth Register. TBIs were categorized into three subgroups based on the length of the hospitalization period and the need for neurosurgery. Logistic regression was used to analyze preterm deliveries, cesarean sections (CS) and neonatal health. Results are reported as adjusted odds ratios (AOR) with 95% confidence intervals (CI).

Results: The incidence of TBIs increased from 103 per 100 000 person-years in 1998 to 257 per 100 000 (149.5%) in 2018. The incidence of TBI-related surgeries remained stable during our study period. The rate of preterm deliveries was 5.6% in the TBI group and 3.0% in the control group (AOR 1.23, CI 1.17–1.28). The CS rate in the TBI group was 19.2% and 15.9% in the control group (AOR 1.23, CI 1.18–1.29). The use of labor analgesia was higher among women with previous TBI. The rate of neonates requiring intensive care in the TBI group was 13.1% and 9.9% in the control group (AOR 1.30, CI 1.24–1.37).

Conclusion: The incidence of TBI hospitalizations increased during our study period, whereas the number of surgically treated TBI remained stable. Preterm deliveries, CS, instrumental vaginal deliveries and labor analgesia were more prevalent in women with previous TBI. Furthermore, more neonates required intensive care in this group. Therefore, a history of TBI should be acknowledged as a possible factor affecting the delivery and health of the neonate.

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TBI; delivery; cesarean section; epidemiology; head trauma

Introduction

Traumatic brain injury (TBI) has increasingly become an important global health problem [1]. Indeed, more than 10 million people worldwide are affected annually by TBI [2], with the most common causes being traffic accidents, falls and sports activities [3]. An international study has estimated the incidence of TBI globally to be approximately 369 per 100 000 person-years. [4] In Finland, the average incidence of hospitalized TBI for all women between 1991 and 2005 was 80 per 100 000 person-years. TBI patients are known to have higher mortality rates compared to the general population, although the mortality rate depends on the severity of injury [5,6]. In an earlier study, the mortality rate in Finland was estimated to be around 18 per 100 000 person-years, with a higher mortality rate among women [7].

To date, the effects of TBI on the reproductive health of women have been sparsely studied. For fertile-aged women, TBI is reported to cause disorders in the menstrual cycle and nearly 50% of women report amenorrhea following TBI [8,9].

Interestingly, even though women who experience menstrual and/or sexual dysfunctions after a

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Supplemental data for this article can be accessed here.

concussion are reported to have a decreasing incidence of pregnancy, previous studies have not assessed the effects of TBI on fertility [10]. Moreover, only a few case reports have discussed the effects of TBI on deliveries in acute cases, where traumatic brain injury leads to the acute cesarean section after a craniotomy is performed to lower intracranial pressure [11,12]. The long-term effects of TBI on subsequent deliveries and neonatal health have not previously been studied, however. The aim of this nationwide register study is to report the incidence of TBI and surgeries related to TBI in fertile-aged females in Finland and to investigate the impact of TBI on subsequent pregnancies and deliveries

Materials and methods

In this nationwide retrospective register-based cohort study, data were retrieved from the Care Register for Health Care and combined with data retrieved from the National Medical Birth Register (MBR). Both registers are maintained by the Finnish Institute for Health and Welfare. The study period was from January 1, 1998 to December 31, 2018.

All fertile-aged (15–49 years) women with a TBI diagnosis during our study period were retrieved from the Care Register for Health Care. TBI was defined as a hospitalization period following TBI based on ICD-10 (International Classification of Diseases 10th revision) codes. After a one-year washout period, each TBI diagnosis was classified as a new separate TBI, as hospital follow-up appointments for TBI rarely occur later than one-year post-injury in the majority of cases. In subgroup analysis, TBIs with a hospitalization period lasting more than one day were considered as admitted TBI, and TBIs with a hospitalization period lasting less than one day were considered as non-admitted TBI. Patients who underwent surgery were identified by NOMESCO (Nordic Medico-Statistical Committee) classification procedure codes. Only procedure codes with one of the TBI diagnosis codes during the same hospitalization period were included because these operations are also performed for reasons other than TBI. ICD-10 codes and NOMESCO classification procedure codes included in this study are shown in Supplementary Table 1.

The incidences of TBIs and TBI surgeries were calculated using the whole population of fertile-aged (15–49 years) women in Finland at the end of a particular year, which was obtained from Statistics Finland (Stat.fi). During our study period, the size of the study population in Finland decreased from 1 389 409 in 1998 to 1 285 100 in 2018 [13].

Data retrieved from the Care Register for Health Care were combined with data from the National Medical Birth Register (MBR) using the pseudonymised identification number of the mother. The MBR contains information on all pregnancies, delivery statistics and the perinatal outcomes of births with a birthweight of $\geq$500 grams or a gestational age $\geq 22+0$. The MBR has a coverage of nearly 100% [14,15]. In the present study, we use the standard variables used in the MBR, which are defined in the register description [16].

A flowchart of the study population is presented in Figure 1. All deliveries of women with previous TBI were compared with a control group without previous TBI, which consisted of 615 144 women with 1 143 954 singleton deliveries. In subgroup analysis, non-admitted admitted and operated TBIs were analyzed separately. The identification of women with previous TBI with subsequent deliveries was based on the date of the TBI or operation in the Care Register for Health Care and the start date of the pregnancy in the MBR. Deliveries with missing information on the mode of delivery were excluded. In the MBR, cesarean section (CS) was classified as elective or urgent until 2004, and in order to have uniform coding throughout the study period, we used this instead of the current three-stage classification (elective, urgent and emergency). This means that each emergency and urgent CS is considered as an unplanned CS in our current report. The results of this study are reported according to the STROBE guidelines (Supplementary Table 1) [17].

Ethics

Both the National Medical Birth Register (MBR) and the Care Register for Health Care have the same unique pseudonymised identification number for each patient. The pseudonymisation was made by the Finnish data authority Findata. The authors did not have access to the pseudonymisation key, as it is maintained by Findata. In accordance with Finnish regulations, no informed written consent was required because of the retrospective register-based study design and because the patients were not contacted. Permission for use of this data was granted by Findata after evaluation of the study protocol (Permission number: THL/1756/14.02.00/2020)

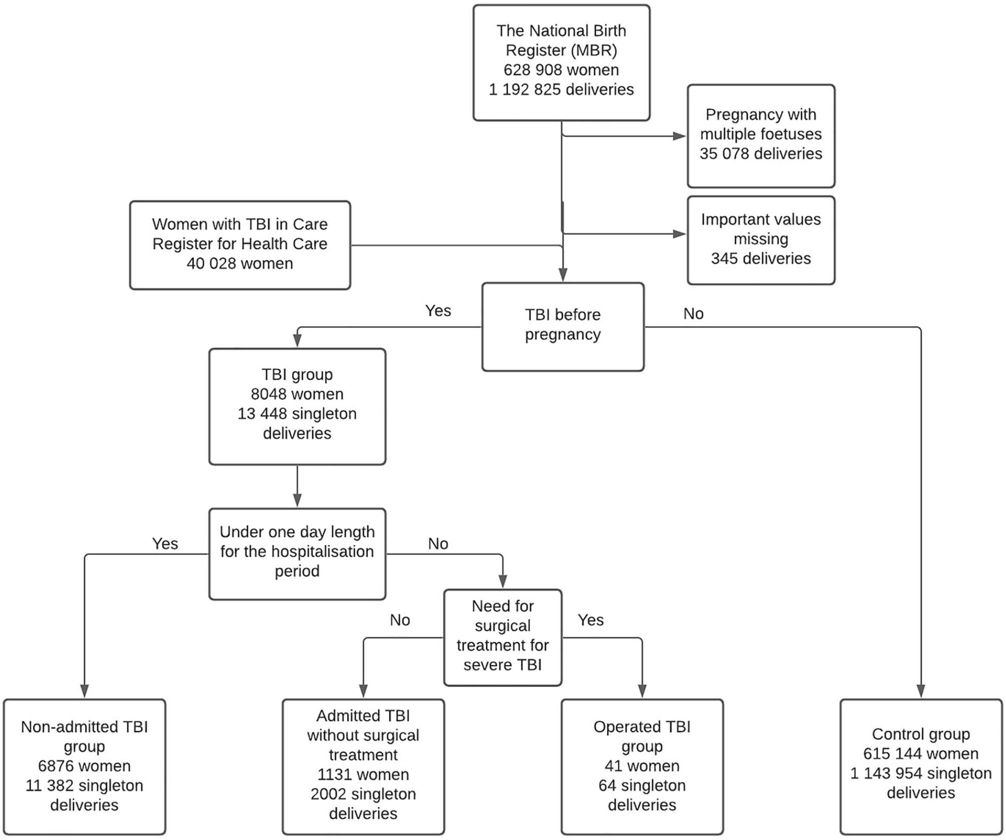

Figure 1. Flowchart of the study population. Data from the MBR were combined with data on the diagnosed TBI and TBI-related surgical operations in the Care Register for Health Care.

Statistics

Continuous variables were interpreted as mean with standard deviation or as median with interquartile range based on variable distribution. Categorized variables were presented as absolute numbers and percentages. Student's *t*-test, Mann-Whitney *U*-test and Chi-Squared tests were used for group comparisons. Multivariable logistic regression was used to assess the primary outcomes (preterm delivery, mode of delivery and neonatal health). The need for intensive care for the neonate was used as an indicator for neonatal health in logistic regression analyses. Maternal smoking during pregnancy, maternal diabetes during pregnancy and the socioeconomic status of the mother was used as adjusting variables. Details of maternal smoking status during pregnancy are collected during visits to maternity clinics and can be either non-smoker, smoking during the first semester, smoker or unknown. The socioeconomic status of the mother is recorded in the MBR during pregnancy. Odds ratios (OR) and adjusted odds ratios (AOR) with 95% confidence intervals (CI) were calculated for the main outcomes. *P*-value under .05 was considered statistically significant. Adjustments were made by choosing the variables for a multivariate model using directed acyclic graphs (DAGs) constructed using the free online software DAGitty (dagitty.net). The variables included in the DAGs were chosen based on known risk factors and by hypothesized causal pathways [18,19]. DAGs are presented as supplementary files (Supplementary Figures 1–3). Statistical analysis was performed using R version 4.0.3.

Results

A total of 40 028 women with a TBI hospitalization were retrieved from the Care Register for Health Care. During our study period, the incidence of TBI hospitalization in fertile-aged women increased over two-fold

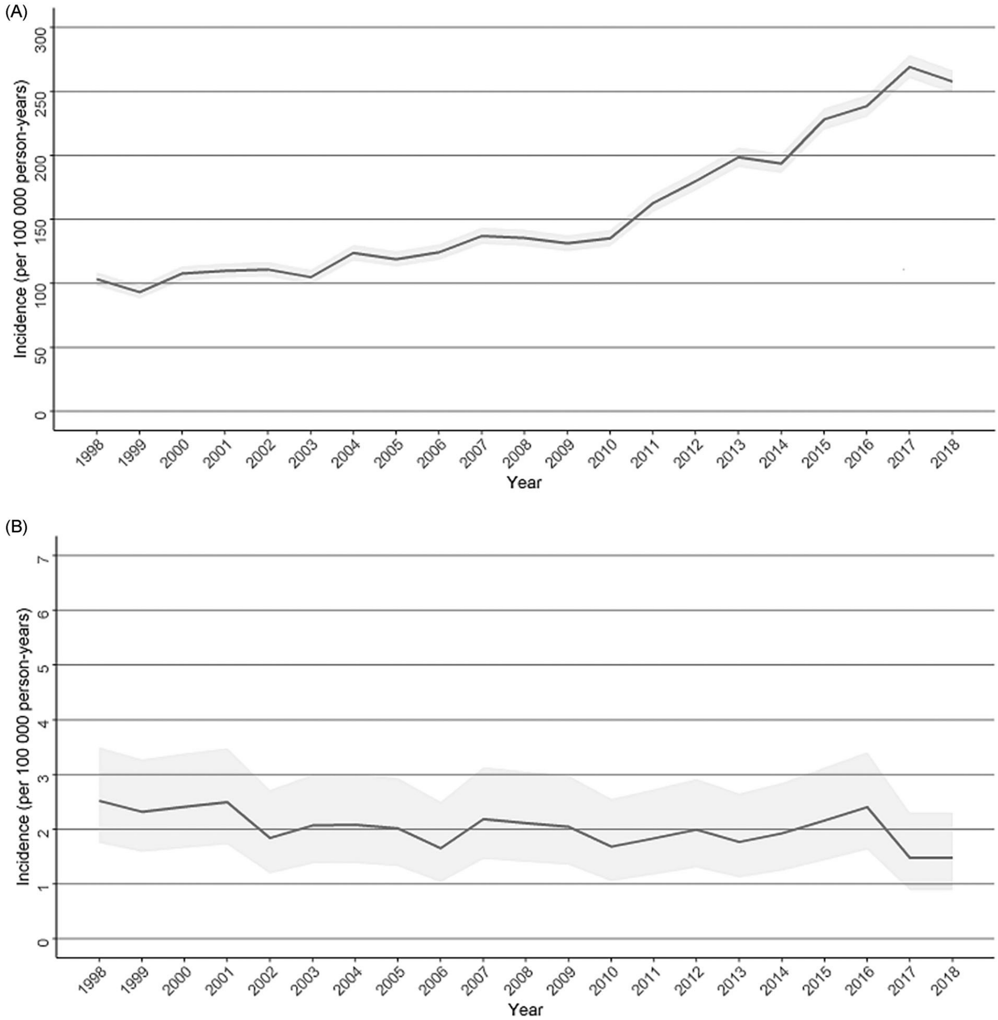

Figure 2. (A) Incidence of traumatic brain injury hospitalization among fertile-aged (15–49 years) women during the study period. (B) Incidence of traumatic brain injury surgeries among fertile-aged (15–49 years) women during the study period.

(149.5%) from 103 per 100 000 person-years in 1998 to 257 per 100 000 person-years in 2018 (Figure 2A). The incidence of TBI requiring surgical treatment, however, decreased slightly during our study period from 2.5 to 1.5 per 100 000 person-years (Figure 2B).

The majority of patients with TBI suffered concussion trauma (S06.0) ($n = 36\ 703$, 85.3%), with focal traumatic brain injury (S06.3) ($n = 1126$, 2.6%) and traumatic subdural hemorrhage (S06.5) ($n = 1119$, 2.6%) being the second most common types of trauma. The mean age of patients was highest among patients with traumatic subdural hemorrhage (S06.5) (37.6, SD 10.0). Among patients with other TBIs, the mean age was lower, ranging from 29.8 to 33.8 years. A total of 5890 women (13.4%) had a hospitalization period of more than one day (Supplementary Table 2).

During our study period, 8048 women gave birth after TBI. In the TBI group, a notably higher number of fetuses were exposed to maternal smoking during pregnancy when compared to the control group (27.7% vs 14.5%, $p < .001$). The rate for deliveries requiring induction was higher among women with previous TBI when compared to the control group (25.4% vs 18.9%, $p < .001$) (Table 1). Moreover, a higher rate of women in the TBI group underwent elective CS as a mode of delivery (7.8% vs 6.6%, $p < .001$). After elective CS was excluded, the rate of

Table 1. Background information on the deliveries and perinatal characteristics in the traumatic brain injury group and the control group.

	Traumatic brain injury group		Control group		
	13 448		1 143 954		
Total number	*n*	%	*n*	%	*p*-value
Age at birth (years, mean SD)	28.7 (5.5)		29.7 (5.4)		<.001
Nulliparous	5 963	44.3	472 966	41.3	<.001
Previous CS*	1 566	11.6	122 789	10.7	<.001
Maternal smoking during pregnancy**	3 722	27.7	165 650	14.5	<.001
LBW*** < 2500 g	515	3.8	33 991	3.0	<.001
Induction of labor	3412	25.4	216 715	18.9	<.001
Preterm****					
Preterm < 37 + 0 gestational weeks	755	5.6	52 425	4.6	<.001
Very preterm 28 + 0 − 31 + 6 gestational weeks	75	0.6	4710	0.4	<.001
Extremely preterm ≤ 27 + 6 gestational weeks	37	0.3	3268	0.3	.108
Perinatal mortality*****	72	0.5	6100	0.5	.176
1 minute Apgar score ≤ 6	1948	14.5	155 601	13.6	.326
Neonatal intensive-care unit	1756	13.1	114 160	9.9	<.001
Discharged from hospital during the first week	12 458	92.6	1 075 257	94.0	<.001

*CS: Cesarean section.
** Contains women with smoking during the only first trimester and/or in later trimesters.
***LBW: low birthweight.
**** Preterm births were calculated in overall (< 37 + 0 gestational weeks), and for very preterm (28 + 0 – 31 + 6 gestational weeks) and extremely preterm (≤ 27 + 6 gestational weeks) pregnancies, which is the classification by the World Health Organization (WHO).
*****Perinatal mortality includes stillbirths and deaths before the age of seven days.

Table 2. Proportions of obstetric variables in attempted vaginal deliveries in the traumatic brain injury group and control group.

	Traumatic brain injury group		Control group		
	12 409		1 068 214		
Total number (without elective CS)	*n*	%	*n*	%	*p*-value
Mode of delivery					
Spontaneous vaginal delivery	9613	77.5	865 909	81.1	<.001
Breech delivery	75	0.6	6938	0.6	.035
Vacuum or forceps delivery	1174	9.5	89 757	8.4	.060
Unplanned CS*	1547	12.5	105 610	9.9	<.001
Labor analgesia					
Epidural	6306	50.8	464 117	43.4	<.001
Spinal	1962	15.8	121 256	11.4	.292
Spinal + epidural	232	1.9	13 440	1.3	.915
Paracervical block	2301	18.5	186 444	16.3	<.001
Pudendal block	1082	8.7	66 489	6.2	.044

Elective CS in the TBI group n 1039 (7.7%) and in the control group n 75 740 (6.6%) were excluded.
*CS: Cesarean section.

unplanned CS was higher in the TBI group (12.5% vs 9.9%, $p < .001$) when only attempted vaginal deliveries were included. Moreover, the rates of different labor analgesia were higher in the TBI group. In particular, the proportional amount of epidural analgesia (50.8% vs 43.4%, $p < .001$) and spinal analgesia (15.8% vs 11.4%, $p = .292$) were higher in the TBI group when compared with the control group (Table 2).

Among women with TBI before pregnancy, a slightly higher proportion of neonates were born with low birthweight (birthweight < 2500 grams, LBW) (3.8% vs 3.0%, $p < .001$) and born preterm (5.6% vs 4.6%, $p < .001$). Furthermore, the need for neonatal intensive care was slightly higher in the TBI group (13.1% vs 9.9%, $p < .001$) (Table 1). The probability for preterm deliveries in the TBI group was also slightly higher (AOR 1.23, CI 1.17–1.28). The odds for all CS, including both elective and unplanned CS, were slightly higher in the TBI group when compared to the control group (AOR 1.23, CI 1.18–1.29). The odds for impaired health of the neonate showed a small increase in the TBI group when compared with the control group (AOR 1.30, CI 1.24–1.37) (Table 3). When compared to the non-admitted and admitted TBI groups in subgroup analysis, patients with operated TBI had a notably higher rate of instrumental vaginal deliveries (21.9% vs 9.3% and 8.8%, $p = .015$). (Supplementary Table 3)

Discussion

The main finding of this study was the two-fold increase in the incidence of TBI hospitalizations among fertile-aged women within the last two decades. The

Table 3. Univariable and adjusted Odds ratios (OR) with 95% confidence intervals (CI) for the main variables.

	Preterm delivery OR (95% CI)	Cesarean section OR (95% CI)	Neonatal intensive care OR (95% CI)
Univariable	1.24 (1.15–1.33)	1.26 (1.21–1.32)	1.35 (1.29–1.42)
Adjusted*	1.23 (1.17–1.28)*	1.23 (1.18–1.29)**	1.30 (1.24–1.37)***

Women in the TBI group were compared with the control group consisting of all women without TBI before pregnancy.
*The model was adjusted with the socioeconomic status of the mother, maternal smoking during pregnancy and maternal diabetes during pregnancy.
**The model was adjusted with maternal smoking during pregnancy and maternal diabetes during pregnancy.
***The model was adjusted with maternal smoking during pregnancy.

incidence of TBI-related surgeries remained stable or had decreased slightly during this period. Women with previous TBI had a lower rate of spontaneous vaginal deliveries and higher use of labor analgesia. Women in the TBI group had a higher rate of neonates requiring intensive care.

The overall increased incidence of TBI hospitalizations during our study period, combined with the stable incidence of TBI-related surgeries, indicates that the increase in incidence is predominantly among milder injuries. According to previous systematic reviews, the incidence of TBI among fertile-aged women in Finland has increased to the same level as that seen in the general European population [20–22]. The high increase in TBI hospitalizations among Finnish fertile-aged women can be partly explained by indirect temporal factors and phenomena such as (i) lower patient-based threshold to seek medical care due to mild head injuries, (ii) better access to CT imaging and (iii) improved awareness of TBIs and TBI-related health issues. Furthermore, the foundation of joint emergency service in 2011 may have led to improvements in acute TBI diagnostics. Notably, TBI hospitalizations among Finnish fertile-aged women began to increase more rapidly after 2011.

Women with a history of TBI had a higher rate of complications during delivery, which was indicated by a higher rate of instrumental vaginal deliveries, unplanned CS and labor analgesia. There are no national guidelines for pregnancies/deliveries after TBI in Finland. Most of the time, the mode of delivery after TBI is chosen based on obstetric indications, maternal preference is taken into account, without any particular recommendation from neurosurgeons. Neurosurgeons are consulted during pregnancy about the preferred mode of delivery when deemed necessary. To date, no previous studies have investigated the effects of TBI before pregnancy on obstetric outcomes, although head trauma during pregnancy is known to cause complications for the mother and for the health of the fetus [23]. Interestingly, the rate of instrumental vaginal deliveries among operated TBI patients, where the need for neurosurgery usually indicates more severe neurotrauma, was notably higher. This higher rate of instrumental vaginal deliveries accompanied by a higher rate of labor analgesia could be related to a slower progression of labor. Nevertheless, the rate of unplanned CS and the need for intensive care unit treatment was lower in this group than in the other non-surgical TBI groups. The low number of women in the operated TBI group may have affected these results. Based on our findings, it appears that women with previous TBI experience more challenges related to delivery (lower rate of spontaneous vaginal deliveries) than other groups. Due to the crude nature of the data, however, solid conclusions cannot be made. Furthermore, it remains unknown whether the higher rate of instrumental vaginal deliveries and CS is caused by TBI or by other factors. Additional research on this topic is therefore needed.

Interestingly, the rate of neonates requiring intensive care was higher in the group of mothers with previous TBI. This can partly be explained by the slightly higher rate of CS in this group, as the procedure is usually associated with an increased need for intensive care for the neonate [24,25]. Moreover, a notably higher rate of smokers in the TBI group partly explains the increase, but adjusted analysis with smoking status still showed higher odds for the need for intensive care for the neonate. We are unaware of previous studies that have examined the effects of a mother's previous TBI on her offspring. TBIs are known to affect the menstrual cycle and severe head traumas during pregnancy are related to increased risk for fetal deaths [9,26]. Overall, high-energy traumas during pregnancy increased the risk for placental abruption and direct fetal injuries, which partly explains the increased risk for fetal deaths associated with TBI [27]. The exact reason for the higher rate of neonatal intensive care in the group of mothers with previous TBI remains unknown.

The strength of our study is the large nationwide study population with a long study period, making it possible to compare large patient groups. The register data used in our study are routinely collected with structured forms with national instructions, which ensures good coverage and reduces possible reporting and selection bias [28]. Furthermore, the coverage of both registers included in this study is high [28,29]. The advantage of this study compared to previous ones is the large national research material in a country with uniform delivery-related guidelines and attitudes.

The main limitation of our study is the missing clinical information on TBIs (e.g. radiological findings and TBI severity indices). As this information is not recorded to the registers, we could only use ICD-10 coding, which means that the severity of trauma-based on the length of the hospitalization period (non-admitted and admitted TBI patients) is only directive. It has to be kept in mind that TBI management has improved during the last two decades. This improvement in turn has ultimately reflected the diagnostic threshold of especially mild MTBI. Currently, mild injuries are identified more frequently among healthcare professionals and also the public has been sensitized to the possible lingering problems related to mild head injuries. This shift in clinical practice has most likely increased the number of reported TBI cases in Finland. Thus, the increasing TBI incidence among fertile-aged women can be partly explained by the alterations in national practice. Further, the contents of the birth register were updated in 2004 and 2017, and 5-min Apgar scores, durations of labor stages, body mass index and the chronic disease diagnosis of the mother were only included after 2004. Therefore, these clinical parameters were not analyzed in our study. Furthermore, since cases of CS were classified as elective or urgent prior to 2004, we have used the same classification in the present study instead of the newer three-stage classification (elective, urgent and emergency). In addition, the indications behind CS or instrumental vaginal delivery are not registered in the MBR, which means that indications for these remain unknown. Thus, it is unknown whether the patient had planned elective CS or attempted vaginal delivery before undergoing unplanned CS.

Conclusion

The incidence of TBI hospitalizations among fertile-aged women increased during our study period, whereas the incidence of TBI-related surgical operations remained stable. Preterm birth, CS, instrumental vaginal delivery and the use of labor analgesia were more frequent among mothers with a history of TBI. Furthermore, a slightly increased rate of neonates with impaired health was observed among women with previous TBI. Therefore, maternal history of TBI should be acknowledged as a possible factor affecting the delivery and health of the neonate.

Disclosure statement

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PUBLICATION IV

Birth rate after major trauma in fertile-aged women: a nationwide population-based cohort study in Finland

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RESEARCH

Open Access

Birth rate after major trauma in fertile-aged women: a nationwide population-based cohort study in Finland

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Abstract

Background: To date, only a few small studies have assessed the effects of major orthopedic traumas on the subsequent birth rate in fertile-aged woman. We assessed the incidences of traumatic brain injury (TBI) and fractures of the spine, pelvis, and hip or thigh and evaluated their association with the birth rate in fertile-aged woman.

Methods: In this retrospective register-based nationwide cohort study, data on all fertile-aged (15–44 years of age) women who sustained a TBI or fracture of the spine, pelvis, hip or thigh between 1998 and 2013 were retrieved from the Care Register for Health Care. A total of 22,780 women were included in TBI group, 3627 in spine fracture group, 1820 in pelvic fracture group, and 1769 in hip or thigh fracture group. The data were subsequently combined with data from the National Medical Birth Register. We used Cox regression model to analyze the hazard for a woman to give birth during 5-year follow-up starting from a major trauma. Women with wrist fractures (4957 women) formed a reference group. Results are reported as hazard ratios (HR) with 95% confidence intervals (CI).

Results: During 5-year follow-up after major trauma, 4324 (19.0%) women in the TBI group, 652 (18.0%) in the spine fracture group, 301 (16.5%) in the pelvic fracture group, 220 (12.4%) in the hip or thigh fracture group, and 925 (18.7%) in the wrist fracture group gave birth. The cumulative birth rate was lower in the hip or thigh fracture group in women aged 15–24 years (HR 0.72, CI 0.58–0.88) and 15–34 years (HR 0.65, CI 0.52–0.82). Women with pelvic fracture aged 25–34 years also had a lower cumulative birth rate (HR 0.79, CI 0.64–0.97). For spine fractures and TBIs, no reduction in cumulative birth rate was observed. Vaginal delivery was the primary mode of delivery in each trauma group. However, women with pelvic fractures had higher rate of cesarean section (23.9%), when compared to other trauma groups.

Conclusions: Our results suggest that women with thigh, hip, or pelvic fractures had a lower birth rate in 5-year follow-up. Information gained from this study will be important in clinical decision making when women with previous major trauma are considering becoming pregnant and giving birth.

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Plain language summary

To date, only a few small studies have assessed the effects of major orthopedic traumas on the subsequent birth rate in fertile-aged woman. We assessed the incidences of traumatic brain injury (TBI) and fractures of the spine, pelvis, and hip or thigh and evaluated their association with the birth rate in fertile-aged woman.

Data on all fertile-aged (15–44 years of age) women who sustained a TBI or fracture of the spine, pelvis, hip or thigh between 1998 and 2013 were retrieved from the Care Register for Health Care and the data was then subsequently combined with data from the National Medical Birth Register.

A total of 22,780 women were included in TBI group, 3627 in spine fracture group, 1820 in pelvic fracture group, 1769 in hip or thigh fracture group, and 4957 in wrist fracture group, which was used as control group. Of these, 4324 (19.0%) women in the TBI group, 652 (18.0%) in the spine fracture group, 301 (16.5%) in the pelvic fracture group, 220 (12.4%) in the hip or thigh fracture group, and 925 (18.7%) in the wrist fracture group gave birth during the 5-year follow-up.

Our results suggest that women with thigh, hip, or pelvic fractures had a lower birth rate in 5-year follow-up. Information gained from this study will be important in clinical decision making when women with previous major trauma are considering becoming pregnant and giving birth.

Introduction

Traumas to the head, spine, pelvis, and femur are usually caused by high-energy impact, such as vehicle collisions and falls from height [1–4]. In particular, traumatic brain injuries (TBI) are one of the most common and socially notable traumas [5]. Moreover, the mortality rates of people suffering especially severe TBIs are higher compared to the general population [6, 7]. In the younger population, however, the incidence of spine, pelvic and hip trauma is not as high as that of head trauma [8–10]. The mortality rate following hip and pelvic trauma is known to be relatively low in the younger population, ranging between 1.3% and 3.5% among the population aged 18–49 years [10].

In Finland, there has been an increasing trend in the incidence of TBI, spine, and pelvic trauma [8]. Indeed, the average incidence of hospitalized TBI for all women during the years 1991–2005 was 80 per 100,000 person-years, an increase of 59% [7]. The incidence of spine fractures leading to hospitalization in all patients over 20 years of age in Finland increased from 57 per 100,000 person-years in 1998 to 89 per 100,000 person-years in 2017 [8]. Moreover, among Finnish adults, the incidence of pelvic fractures increased from 34 to 56 per 100,000 person-years between 1997 and 2014 [11].

Although the incidences and effects of major trauma on health have been studied extensively, there is a scarcity of studies on the effects of major trauma on fertility among women. Many earlier studies have focused mainly on trauma and abnormalities of the reproductive system, especially of the uterus and ovaries [12]. It has been reported, however, that musculoskeletal trauma around the area of the pelvic ring and the femur can cause sexual dysfunction and dyspareunia [13, 14]. Moreover, women in Finland who have undergone total hip replacement are reported to have a lower birth rate than women in the general population [15].

Our hypothesis is that major trauma can affect sexuality and sexual function and thereby increase the threshold for becoming pregnant and reduce the number of births. The aim of this nationwide register study is therefore to report the incidence of TBIs and fractures of the spine, pelvis, and hip or thigh in fertile-aged women in Finland and to investigate the effects of these injuries on the birth rate.

Materials and methods

In this retrospective nationwide register-based cohort study, data were obtained from the Care Register for Health Care, which has a coverage of more than 95% [16], and the National Medical Birth Register (MBR), which has a coverage of nearly 100% [17, 18]. The study period was from 1998 to 2018.

Data on deliveries and newborns after major orthopedic trauma were collected from the MBR, which contains information on all pregnancies, delivery statistics, and the perinatal outcomes of births with a birthweight of ≥ 500 g or a gestational age of $\geq 22^{+0}$. Our data included all pregnancies and deliveries from fertile-aged (15–49 years of age) women during our study period. The variables used in this study are defined in the MBR register description [19].

All fertile-aged (15–49 years of age) women with TBI, spine fracture, pelvic fracture, or hip or thigh fracture occurring during the study period were identified from the Care Register for Health care. We used women who were hospitalized with fracture of the wrist as a reference group. Women with fractures of the wrist were chosen as a reference group because we expected these women to be similar in background and risk-taking behavior to those women in the major trauma groups than women in the general population without any injuries. In addition, as wrist fractures generally heal quickly, we did not expect them to have a major impact on fertility, and therefore they formed a good reference group.

ICD-10 (International Classification of Diseases 10th revision) codes were used to identify the trauma patients. The specific ICD-10 codes with definitions for each major trauma group and reference group included in this study are shown in Additional file 1: Table S1. Due to challenges in distinguishing new traumas and control visits/appointments, the first trauma hospitalization for a woman in each category was included (meaning that the same woman can be included in multiple study groups). The formation of the study groups and number of women who became pregnant during the 5-year follow-up after the first trauma is described in Fig. 1. In the evaluation of pregnancy outcomes after different traumas, each pregnancy found in our data after traumas (1998–2018) was included.

Due to the best possible comparability between major trauma groups, the annual incidences during our study period were calculated using the same criteria, despite the varied nature of the different traumas included in the study. Therefore, for each trauma group, only the first hospitalization period with trauma diagnosis per patient was classified as a separate trauma, as the control appointments could occur after a long period, making it unreliable to identify subsequent traumas in the Care Register for Healthcare.

The base population used for the calculation of the birth rate and incidences of major traumas was the number of females aged 15–49 who were living in Finland at the end of a particular year. The population data were obtained from Statistic Finland. During our study period, the size of the study population decreased from 1,389,409 in 1998 to 1,285,100 in 2018. The annual number of newborns was also obtained from Statistic Finland (stat.fi) [20].

Ethics

Both the National Medical Birth Register (MBR) and the Care Register for Health Care used the same unique pseudonymized identification number for each patient. The pseudonymization was performed by the Finnish data authority Findata. The authors did not have access to the pseudonymization key as it is maintained by Findata. In accordance with Finnish legislation, no informed written consent was required because of the retrospective register-based study design and because the patients were not contacted. Permission to use this data was

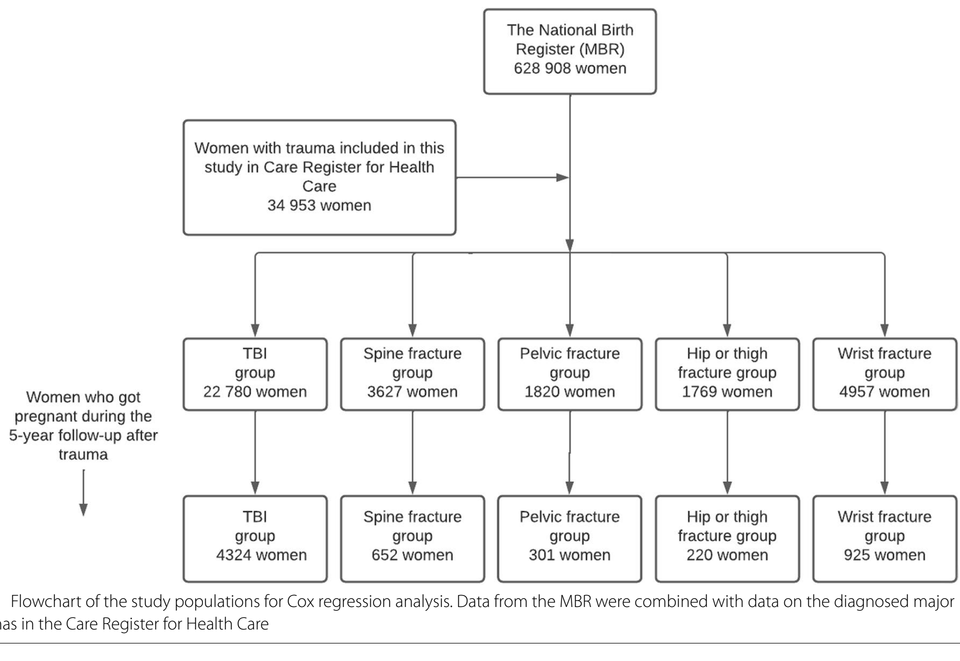

Fig. 1 Flowchart of the study populations for Cox regression analysis. Data from the MBR were combined with data on the diagnosed major traumas in the Care Register for Health Care

granted by Findata after evaluation of the study protocol (Permission number: THL/1756/14.02.00/2020).

Statistics

Continuous variables were reported as mean with standard deviation or as median with interquartile range based on distribution of the data. Categorized variables were presented as absolute numbers and percentages. The annual birth rate was calculated using the size of the base population of fertile-aged (15–49 years) women living in Finland at the end of a particular year (31.12) and the number of yearly newborns. The base population for the incidences of different traumas were all women aged 15 to 49 who were living in Finland at the end of a particular year. Base population figures were obtained from Statistic Finland (stat.fi) [20]. The Cox regression model was used to evaluate the risk for the first live-born child in women after major trauma in relation to reference individuals with wrist fracture. The results were interpreted with hazard ratios (HRs) and 95% confidence intervals. Proportional hazards assumption was tested using Schoenfeld residuals and the supposition was true. To control the confounding effect of age, women with trauma were divided into three categories based on their age at the time of trauma: the categories were 15–24, 25–34, and 35–44 years. The start of the follow-up was the date of the trauma in the Care Register for Health care. The endpoint of the follow-up was the first live-born child after the trauma, or the common closing date, which was 5 years after the trauma. Because a 5-year follow-up period is required for the Cox regression model, all women with a trauma occurring after 2013 were excluded from the survival analysis because the follow-up period after this is not fully available based on the data. Moreover, as 49 is the maximum age for fertile-aged woman in this study, the required 5-year follow-up condition of fertile years is only met by women who sustained trauma before the age of 45. Statistical analysis was performed using R version 4.0.3.

Results

Initially, the annual birth rate for the whole population of fertile-aged women showed an increasing trend during our study period, rising from 41.1 newborns per 1000 fertile-aged woman in 1998 to 46.8 per 1000 fertile-aged women in 2010, but then decreased strongly to 37.0 per 1000 fertile-aged women in 2018. The average annual birth rate between 1998 and 2018 was 42.9 (Fig. 2).

During the study period, the incidence of TBIs, which originally also had a notably higher incidence than the other traumas included in this study, showed a strongly increasing trend, increasing from 110.9 per 100,000 person-years in 1998 to 208.8 per 100,000 person-years in 2018. Furthermore, the incidence of wrist fractures increased from 26.3 per 100,000 person-years in 1998 to 35.9 per 100,000 person-years in 2018. The incidence of hip or thigh fractures, pelvic fractures, and spine fractures remained stable during our study period, ranging between 7.9 and 12.8 per 100,000 person-years for hip or thigh fractures, 8.1 and 14.0 per 100,000 person-years for pelvic fractures, and 17.5 and 23.4 per 100,000 person-years for spine fractures (Fig. 3).

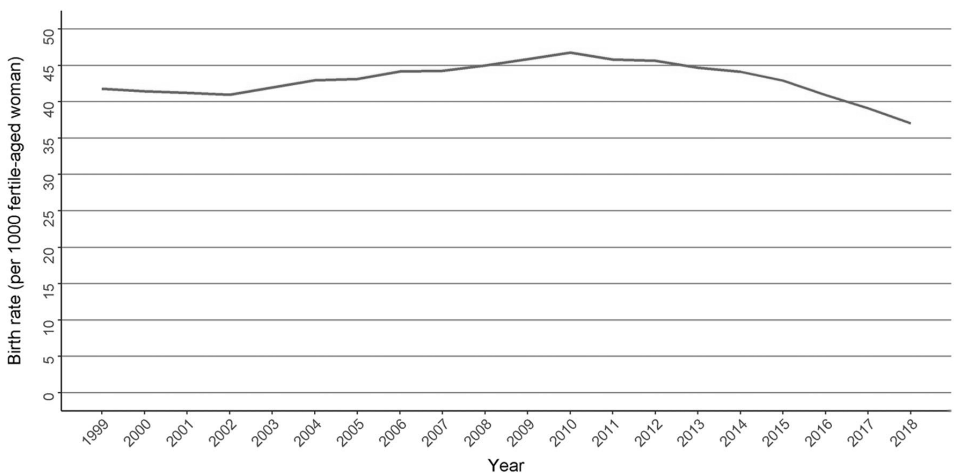

Fig. 2 Birth rate with 95% confidence intervals per 1000 for the whole Finnish population of fertile-aged (15–49 years) women during the study period

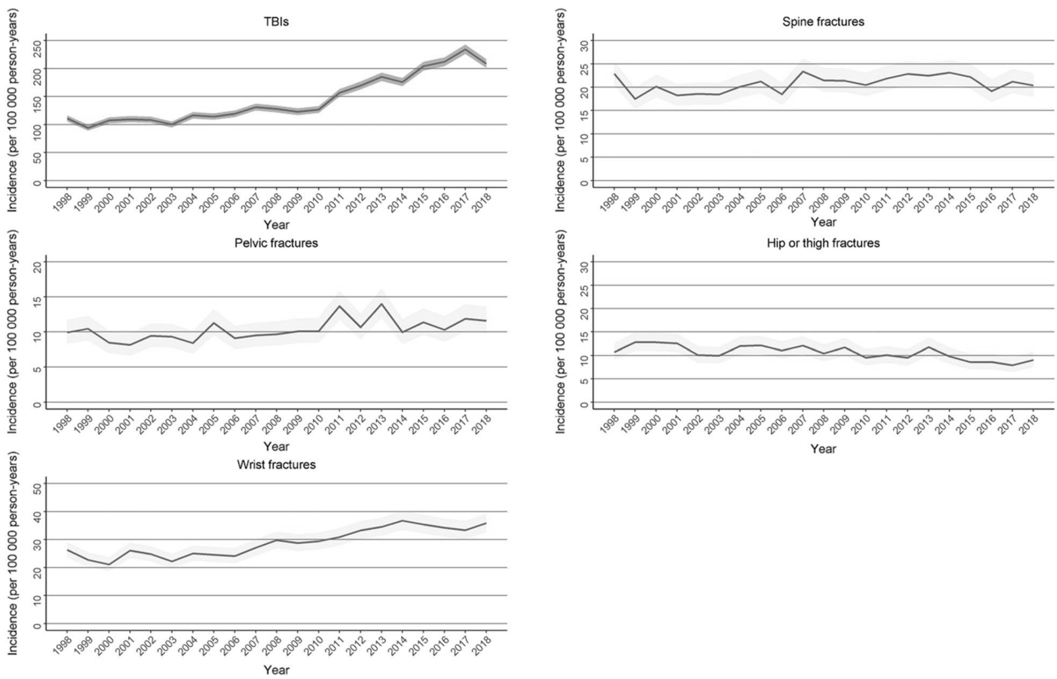

Fig. 3 Incidence with 95% confidence intervals of major traumas and the reference group (wrist fractures) in women (15–49 years) included in this study

Women in the hip or thigh fracture group had the lowest birth rate during the 5-year follow-up period after fracture (12.4%). The highest birth rate during the 5-year follow-up was in the TBI group (19.0%), which was also higher than in the reference group (18.7%) (Table 1). Women in the hip or thigh fracture group had lower hazard for the event of giving birth during the 5-year follow-up period in the 15–24 years (HR 0.72, CI 0.58–0.88) and the 25–34 years (HR 0.65, CI 0.52–0.82) age groups when compared to the wrist fracture group. Furthermore, women in the pelvic fracture group aged 25–34 had lower hazard for giving birth during the 5-year

Table 1 Background information on the study groups and the reference group (wrist fractures) for the survival analysis

	TBI group	Spine fracture group	Pelvic fracture group	Hip or thigh fracture group	Wrist fracture group
Total number of women included*	22,780	3627	1820	1769	4957
Age at the start of follow-up					
15–24 years	10 273 (45.1%)	1476 (40.7%)	852 (46.8%)	707 (40.0%)	2004 (40.4%)
25–34 years	5965 (26.2%)	1018 (28.1%)	481 (26.4%)	437 (24.7%)	1430 (28.8%)
35–44 years	6542 (28.7%)	1133 (31.2%)	487 (26.8%)	625 (35.3%)	1523 (30.7%)
Number of women giving birth during the 5-year follow-up (%)	4324 (19.0%)	652 (18.0%)	301 (16.5%)	220 (12.4%)	925 (18.7%)
Age at the time of trauma (mean; SD)	27.6 (9.2)	28.5 (9.1)	27.4 (9.2)	28.4 (9.1)	28.4 (9.1)
Age at the time of delivery (mean; SD)	28.0 (5.6)	28.5 (5.5)	27.9 (5.4)	28.7 (5.4)	28.7 (5.4)
Follow-up period in weeks (mean; SD)	237.6 (55.6)	237.8 (56.3)	240.9 (52.3)	246.4 (44.6)	237.9 (55.6)

*Because a 5-year follow-up period was required, only women with trauma occurring before 2014 and aged under 45 years at the time of trauma were included for Cox survival analysis follow-up period (HR 0.79, CI 0.64–0.97). Spine fractures and TBIs did not show an impaired cumulative birth rate when compared to wrist fractures (Table 2).

When compared to other trauma groups, the rate of cesarean sections after fractures was highest in the pelvic fracture group (23.9%), followed by TBI group (20.3%), hip or thigh fracture group (20.3%) and spine fracture group 20.2%. The wrist fracture group had the lowest rate of cesarean section (18.2%). However, despite the preceding trauma, vaginal delivery was the primary mode of delivery in all trauma groups. There was a relatively high proportion of fetuses in all trauma groups who were exposed to maternal smoking during pregnancy compared to the average rate for the whole Finnish population (23.5–27.1% vs 14.6%). Previous CS rate was similar between groups (9.7–11.7%).

Discussion

The main finding of this study was that younger women with hip or thigh fractures had (evidently) a lower hazard of giving birth during the follow-up period. In addition, there was a considerable variation in the rates of women giving birth during the follow-up period, when compared to the wrist fracture group. The cumulative birth rate was a little lower for women aged 25–34 with pelvic fracture. When compared with women with wrist fractures, spine fractures or TBIs did not have a substantial effect on the birth rate during the 5-year follow-up after major trauma. During our study period, the incidence of TBI hospitalizations in Finland increased strongly among fertile-aged women. This study is unique in that it gives baseline information on the effects of major traumas on the subsequent birth rate.

When compared to wrist fractures, hip or thigh fractures and pelvic fractures were the only major traumas included in this study that had a negative impact on the birth rate during the five subsequent years after sustaining the fracture. There are a few studies that have reported sexual dysfunction in women with proximal thigh traumas or pelvic traumas, with sexual dysfunction occurring mostly among younger women [13, 14]. However, a study on proximal thigh traumas reported that in most cases only a few women report anything other than mild or no sexual dysfunction after 1-year follow-up [14]. In addition, dyspareunia is commonly reported, especially after fractures of the pelvic ring [21]. These factors could most likely explain the lower hazard in these two groups. However, based on our data, the exact reason remains unknown. As the number of women in the hip or thigh and pelvic fracture groups was lower than in the other groups in this study, this might have influenced the results.

One likely explanation is the fear of possible negative outcomes resulting from previous trauma of the pelvic area or femur which may result in women choosing not to get pregnant or deciding not to give birth vaginally. Based on our results, however, spontaneous vaginal delivery was the primary mode of delivery after traumas, as only 18–24% of the deliveries after trauma in each trauma group were cesarean sections. However, the rate of cesarean sections in trauma groups was little higher when compared to general rate in Finland (16–17%) [19]. The findings of this study should serve to reduce any doubts mothers may have of their capability to go through pregnancy and give birth after major trauma. As for other TBIs and spine fractures, the hazard for giving birth was the same as that of wrist fractures, which suggests that these traumas do not have a negative effect on fertility or subsequent pregnancies. Moreover, we are unaware of previous studies that report sexual dysfunction caused by spine fractures or TBIs.

The incidence of TBI hospitalization increased strongly among fertile-aged women. This finding can be mostly explained by indirect temporal factors and phenomena, such as the significant increase in the amount of CT imaging (Stuk.fi [22]) and an improved awareness of mild TBIs (especially concussions [23]), which lowers the patient-based threshold to seek medical care [24]. Furthermore, the creation of a joint emergency service in 2011 may have also led to improvements in acute head trauma diagnostics.

The strength of our study is the large nationwide study population with a long study period, which made it possible to compare large patient groups. The register data used in our study are routinely collected with structured forms with national instructions, which ensures good coverage and reduces possible reporting and selection bias [25]. Furthermore, the coverage of both registers included in this study is high [16]. To our

Table 2 Age-stratified hazard ratios (HR) with 95% confidence intervals (CI) for women giving birth in the major trauma groups of this study

Age	15–24 years	25–34 years	35–44 years
TBI group			
Hazard ratio (CI)	1.09 (0.98–1.21)	0.92 (0.83–1.02)	0.99 (0.76–1.29)
Spine fracture group			
Hazard ratio (CI)	1.02 (0.88–1.17)	0.91 (0.78–1.06)	1.06 (0.74–1.51)
Pelvic fracture group			
Hazard ratio (CI)	0.91 (0.77–1.09)	0.79 (0.64–0.97)	0.67 (0.39–1.18)
Hip or thigh fracture group			
Hazard ratio (CI)	0.72 (0.58–0.88)	0.65 (0.52–0.82)	0.60 (0.35–1.01)

The major trauma groups were compared with all fertile-aged women with wrist fractures during the same study period best knowledge, this study is the first to examine the effects of a variety of major traumas on the subsequent capability of women to become pregnant and give birth using large national research material with uniform delivery-related guidelines and attitudes.

The main limitation of our study is the missing clinical information on the TBIs and fractures included in this study (e.g., radiological finding). As this information is not recorded to the registers, we could only use ICD-10 coding, which means that the severity of the traumas remains unknown. Further, our ICD-10 codes were limited to trauma-related codes, meaning that other factors possibly affecting the outcome during or before the follow-up period also remain unknown. Due to these limiting factors, the effects of trauma severity or possible polytraumas on birth-rate remains unknown.

Conclusion

Our results suggest that giving birth was more challenging for women with thigh, hip, or pelvic fractures in 5-year follow-up. However, neither TBIs nor spine fractures negatively affected the possibility of having a child during 5-year follow-up. Information gained from this study should be considered by women and physicians when a woman who has sustained major trauma is considering the possibility and possible risks of becoming pregnant and giving birth.

Abbreviations

CS: Cesarean section; TBI: Traumatic brain injury; MBR: Medical Birth Register; HR: Hazard ratio; CI: Confidence intervals.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12978-022-01387-w.

Additional file 1: Supplementary Table 1: ICD-10 codes with definitions for each major trauma group and reference group included in this study.

Authors' contributions

All authors participated in the research for this paper. MV wrote the initial draft. IK and VM designed this study. MV, VP, TH and LN planned and conducted the statistical analysis. MK provided clinical expertise. All authors participated in writing process and have approved the final version to be submitted. All authors read and approved the final manuscript.

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Availability of data and materials

Data used in this study cannot be shared without the permission of the Finnish authority Findata.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Smoking is associated with an increased risk for fractures in women after childbirth: a nationwide population-based cohort study in Finland

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Smoking is associated with an increased risk of fractures in women: a nationwide population-based cohort study in Finland

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Background and purpose — Smoking weakens bone health and increases the risk of fractures. We investigated the incidence of fractures in smoking, fertile-aged women and compared it with that of non-smoking, fertile-aged women using data from nationwide registers.

Patients and methods — We conducted a retrospective register-based nationwide cohort study from 1998 to 2018. We identified all women smoking during pregnancy from the Medical Birth Register and compared these with non-smokers. We gathered fractures for both groups from the Care Register for Health Care. Pregnancies with missing smoking or socioeconomic status were excluded. A Cox regression model was used to analyze adjusted hazard ratios (aHR) with 95% confidence intervals (CI) for fractures during the 5-year follow-up starting from delivery. The model was adjusted for the age of the mother at the time of delivery and socioeconomic status.

Results — The smoking group included 110,675 pregnancies and the non-smoking group 628,085 pregnancies. The overall fracture rate was higher in smokers after 1-year follow-up (aHR 1.7, CI 1.5–2.0) and 5-year follow-up (aHR 1.7, CI 1.6–1.8). After 5-year follow-up, the fracture rates for polytraumas (aHR 2.3, CI 1.4–3.7), inpatient admitted fractures (aHR 2.0, CI 1.7–2.4), and non-admitted fractures (aHR 1.8, CI 1.7–1.9) were all higher among smoking women.

Conclusion — Smoking in fertile-aged women was associated with a higher risk of fractures during the 1-year and 5-year follow-up after giving birth, also after adjusting for age and socioeconomic status. Whether the increased fracture risk is caused by direct effects of smoking on bone health or riskier behavior remains uncertain.

Smoking is one of the biggest health problems worldwide, contributing to approximately 5 million deaths each year (**1**). According to a recent systematic review, the current global prevalence of smoking in the general population by women is estimated to be around 17% (**2**). The pooled prevalence of women ever smoking was highest, 38%, in Europe (**2**). In Finland the rate of smokers has decreased during last 2 decades in adults from 19% (2000) to 13% (2018) (**3**). According to the Finnish Institute for Health and Welfare, the less educated smoke more than those with a higher education in Finland (**4**).

Smoking is known to be associated with numerous health problems, such as respiratory and cardiovascular disorders, cancers, and disorders in bone metabolism (**5-7**). Smoking is known to cause an imbalance in bone turnover, making smokers prone to lower bone mass and osteoporosis, putting them at a higher risk of fractures (**7**). In addition to an increased risk of fractures, smokers experience more complications with delayed bone healing, even if they have already stopped smoking, because some adverse effects persist for a prolonged period (**8**). Females, especially after menopause, are at higher risk of osteoporosis than males (**9**). However, women of premenopausal age are also known to have an increased risk of osteoporosis. Unhealthy lifestyle (e.g., nutritional deficiency, lack of exercise, high BMI, and use of alcohol or tobacco) also occurs as a high risk factor in this age group (**10,11**).

The negative effects of smoking on health are generally well studied, but, possibly due to challenges and inaccuracies in collecting data on smokers, only a limited number of studies have investigated the association between smoking and fractures on a national level. We hypothesized that smoking increases the risk of fractures directly, making bones prone to fractures, and indirectly, through increasing risk-taking behav-

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ior among smokers (**12,13**). As studies assessing fracture risk caused by smoking on the population level are lacking, studies with a large nationwide study sample should be performed. Thus, we investigated the fracture rate in smoking women of fertile-age and compared it with that of non-smoking women using data from nationwide registers.

Patients and methods

In this nationwide retrospective register-based cohort study, data from the National Medical Birth Register (MBR) was combined with data from the Care Register for Health Care. Both registers are maintained by the Finnish Institute for Health and Welfare. Data from both registers was then combined using the pseudonymized identification number of the mother. The study period was from January 1, 1998, to December 31, 2018.

Registers

The MBR contains information on pregnancies, delivery statistics, and perinatal outcomes of all births with a birthweight of ≥ 500 g or a gestational age ≥ 22 weeks, including maternal smoking habits. According to a study by Gissler et al. (**14**) the reliability of smoking status has been found to be good. The MBR has a high coverage and quality (the current coverage is nearly 100%) (**15,16**). We included every pregnancy between 1998 and 2013 leading to birth in women aged 15–44. In the MBR, smoking is categorized as either non-smoker, smoker during the 1st trimester of pregnancy but quitted, smoker throughout the pregnancy, or unknown. Women smoking during the 1st trimester of pregnancy, or in later trimesters, were included in the smoker group in our report. Women in the smoker group were compared with the non-smoker group.

The Care Register for Health Care contains information on all special healthcare visits during our study period. The coverage and quality of the Care Register for Health Care is good (**17**). Each fracture between 1998 and 2018 was included in this study. ICD-10 (International Classification of Diseases 10th revision) codes were used to identify fracture patients. Fractures of the lower arm, upper arm, spine, pelvis, hip or thigh, and lower leg were included.

Formation of study groups

Both groups, smokers and non-smokers, were linked with data found in the Care Register for Health Care. Pregnancies with unknown smoking status were excluded. Based on our hypothesis, the potential risk of fractures among smokers might be diverse, as it may be caused by weakened health of bone (osteoporosis, weakened circulation etc.) leading to a higher number of low-energy fractures (**18**), or by risky behavior, which has been found to be more common among people of lower socioeconomic status (SES) (**12,13**), leading to accident-proneness. Due to this hypothesis, we categorized

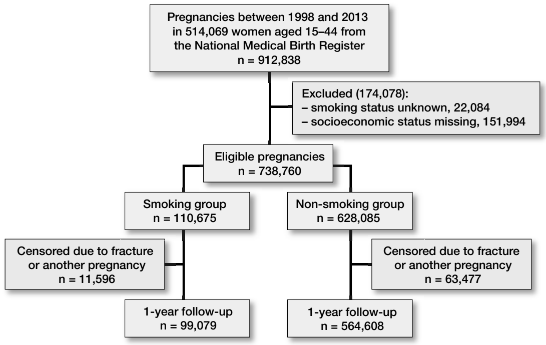

Figure 1. Flowchart of the study population. Data from the National Medical Birth Register was combined with data on the diagnosed fracture hospitalizations in the Care Register for Health Care.

women in 4 SES classes, low, middle, high, and undefinable, using the SES found in the MBR. The categorization of the SES is indicated in Table 1 (see Supplementary data). Pregnancies with missing SES (17%) were excluded from the analysis. 110,675 pregnancies with a smoking mother were found in the MBR. In 628,085 pregnancies the mother did not smoke (Figure 1).

Outcomes

The period of fracture hospitalization found in in the Care Register for Health Care was used to compare the risk of a woman suffering a fracture after giving birth. The total risk and the risk of fractures of different anatomic regions were the main outcomes. In addition, we analyzed the risk of polytraumas, for hospitalization period longer than 1 day (presumably more severe trauma), and risk of non-admitted fractures requiring a less than 1 day hospitalization period (including day surgery) with fracture diagnoses in only 1 anatomic region of the body (presumably non-severe trauma). Polytrauma was defined as 2 or more fracture ICD-10 diagnoses codes from at least 2 anatomic regions of the body during the same hospitalization period. This study is reported according to the STROBE guidelines (**19**).

Statistics

Continuous variables were reported as mean with standard deviation (SD) or as median with interquartile range (IQR) based on distribution of the data. Categorized variables were presented as absolute numbers and percentages. Kaplan¬–Meier survival curves were used to evaluate the absolute risk during the follow-up period. The Cox regression model was used to evaluate the risk of a fracture after pregnancy. Smokers were compared with non-smokers. The follow-up times were 1 and 5 years, starting from the day of giving birth found in the MBR. These follow-up times were chosen as the interests were in the risk of fractures during the lactation period and stay-at-home phase (approximately 1 year after giving birth)

Table 2. Background characteristics by smoking status. Values are number (%) unless otherwise specified

Factor	Smoker group n = 110,675	Non-smoker group n = 628,085
Age during pregnancy, mean (SD)	28 (6)	30 (5)
Marital status during pregnancy		
Ever married	40,930 (37)	411,367 (66)
Never married	65,807 (60)	203,190 (32)
Unknown	3,938 (3.6)	13,528 (2.2)
Socioeconomic status		
Low	36,106 (33)	109,475 (17)
Middle	56,477 (51)	336,538 (54)
High	6,647 (6.0)	139,496 (22)
Undefinable	11,445 (10)	42,576 (6.8)

Table 3. Absolute numbers and rates (%) of fractures in total and in different anatomic regions among patients included in the Cox regression model

Factor	Smoker group n = 110,675	Non-smoker group n = 628,085
Fracture during 1-year follow-up	363 (0.3)	1,196 (0.2)
Fracture during 5-year follow-up	1,660 (1.5)	5,238 (0.8)
Fracture location (after 5-year follow-up) [a]		
Lower arm	584 (35)	2,305 (44)
Upper arm	197 (12)	604 (12)
Spine	115 (6.9)	247 (4.7)
Pelvis	49 (3.0)	101 (1.9)
Hip or thigh	53 (3.2)	110 (2.1)
Lower leg including ankle	693 (42)	1,907 (36)

[a] More than 1 location possible.

and the post-lactation period. The endpoint of the follow-up was 1 of the following events: the 1st fracture after giving birth, start of the next pregnancy, or the common endpoint of the follow-up, which was 1 or 5 years after giving birth, depending on the chosen follow-up time. The univariable and adjusted hazard for fractures was calculated. The multivariable model was adjusted for the age of the mother during pregnancy, as it is known to affect to the risk of fractures and SES category of the mother, to minimize the effect of background and behavioral differences. The results were interpreted with unadjusted hazard ratios (HRs), adjusted hazard ratios (aHRs), and 95% confidence intervals (CI). Proportional hazards assumption was tested using Schoenfeld residuals and the assumption was not violated in any tested model. Competing risks were handled using Efron's method. Statistical significance was analyzed based on the 95% confidence intervals. Statistical analysis was performed using R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Sensitivity analyses

Sensitivity analysis with excluded patients due to missing SES was conducted for the Cox regression analysis (Table 5, see Supplementary data). In this analysis, women with missing SES were placed in their own SES category ("missing SES") and the model was as in the main analyses.

In addition, sensitivity analysis using the multiple imputation techniques was performed. Best–best case, best–worst case, worst–best case, worst–worst case imputation, and data as observed were used to calculate grand means using the modified Rubin's Rule (Table 6, see Supplementary data).

Ethics, funding, data sharing, and disclosures

Both registers, the National Medical Birth Register (MBR) and Care Register for Health Care, had the same unique pseudonymized identification number for each patient. The pseudonymization was done by the Finnish data authority Findata. The authors did not have access to the pseudonymization key as it is maintained by Findata. In accordance with Finnish regulations, no informed written consent was required because of the retrospective register-based study design and as the patients were not contacted. Permission for this data was granted by the Findata after evaluation of the study protocol (Permission number: THL/1756/14.02.00/2020). This study has not received funding. The authors declare no conflicts of interest. The data that supports the findings of this study is available from Findata, but restrictions apply to the availability of this data, which was used under license for the current study, and so is not publicly available. Data is, however, available from the authors upon reasonable request and with the permission of Findata (url: Findata.fi, email: info@Findata.fi). The corresponding author (MV) can be contacted for the data with a reasonable request.

Results

The prevalence of smokers among pregnant women stayed relatively stable during 1998–2012, ranging between 12% and 14%. However, after reaching its peak in 2012, the rate decreased to 10% in 2018 (Figure 2, see Supplementary data). Women who smoked were younger than their non-smoking counterparts at the time of delivery, with a mean age of 28 years (SD 6) among smokers and 30 years (SD 5) among non-smokers. A notably lower rate of women who smoked had been married during or before the pregnancy (37% vs. 66%). In the smoking group, there was also a notably higher rate of women of low SES (33% vs. 17%) and lower rate of high SES (6% vs. 22%) (Table 2). A higher rate of smoking women suffered a fracture in the following 1 year (0.3% vs. 0.2%) and 5 years after pregnancy (1.5% vs. 0.8%) (Table 3).

Fractures of the lower arm, lower leg, and upper arm were the most common types of traumas. In the smoker group, 35% of fractures occurred in the lower arm, 42% in the lower leg, and 12% in the upper arm. Among non-smokers, 44% of frac-

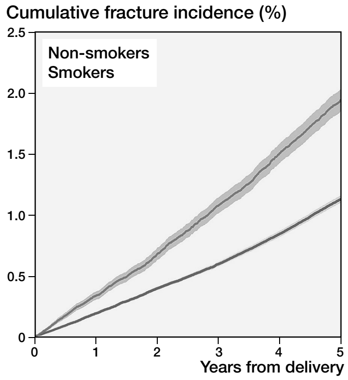

Figure 3. Cumulative incidence plot (with 95% CI) of fertile-aged women for the event of suffering a fracture after giving birth.

Table 4. Hazard ratios (HR) and adjusted hazard ratios (aHR) with 95% confidence intervals (CI) for the event of a woman suffering a fracture after giving birth during the 1-year and 5-year follow-up. Smoking women were compared with non-smoking women

Fracture	1-year follow-up HR (CI)	1-year follow-up aHR (CI) [a]	5-year follow-up HR (CI)	5-year follow-up aHR (CI) [a]
Total	1.7 (1.5–2.0)	1.7 (1.5–2.0)	1.7 (1.6–1.8)	1.7 (1.6–1.8)
Location of fracture				
Lower arm	1.4 (1.1–1.7)	1.4 (1.2–1.8)	1.4 (1.3–1.5)	1.4 (1.3–1.6)
Upper arm	1.8 (1.3–2.6)	1.8 (1.3–2.5)	1.8 (1.5–2.1)	1.7 (1.4–2.0)
Spine	2.6 (1.7–4.0)	2.1 (1.3–3.4)	2.6 (2.0–3.2)	2.3 (1.8–2.9)
Pelvis	2.5 (1.3–4.7)	2.2 (1.1–4.2)	2.7 (1.9–3.8)	2.1 (1.5–3.0)
Hip or thigh	1.8 (0.9–3.4)	1.8 (0.9–3.4)	2.7 (1.9–3.7)	2.4 (1.7–3.4)
Lower leg including ankle	1.9 (1.6–2.3)	1.9 (1.6–2.3)	2.0 (1.8–2.2)	2.0 (1.9–2.2)
Type of fracture				
Polytrauma	0.8 (0.2–3.3)	0.5 (0.1–2.3)	3.0 (1.9–4.9)	2.3 (1.4–3.7)
Severe [b]	2.1 (1.6–2.9)	2.1 (1.6–2.9)	2.0 (1.7–2.3)	2.0 (1.7–2.4)
Less severe [c]	1.8 (1.6–2.0)	1.8 (1.6–2.0)	1.7 (1.6–1.8)	1.8 (1.7–1.9)

[a] Adjusted for the age of the mother at the time of pregnancy and SES category.
[b] Fractures with hospitalization period lasting > 1 day.
[c] Fractures with < 1 day hospitalization (including day surgeries) and non-polytraumas.

tures occurred in the lower arm, 36% in the lower leg, and 12% in the upper arm (Table 3).

The cumulative incidence plot showed that smokers had a higher fracture rate from the beginning. The curve showed a smaller increase for non-smoking women (Figure 3). The total fracture rate was higher among smoking women than among non-smokers during the 1-year follow-up (aHR 1.7, CI 1.5–2.0) and 5-year follow-up (aHR 1.7, CI 1.6–1.8). After the 1-year follow-up, the fracture rate for all anatomical regions except for the hip was higher among smokers than among non-smokers. The fracture rate was highest for the pelvis (aHR 2.2, CI 1.1–4.2) and spine (aHR 2.1, CI 1.3–3.4). After 5 years, the fracture rate was higher for all anatomic regions. The fracture rate was highest for hip or thigh fractures (aHR 2.4, CI 1.7–3.4), followed by spine fractures (aHR 2.3, CI 1.8–2.9), and pelvic fractures (aHR 2.1, CI 1.5–3.0).

The risk of polytraumas among smoking women was higher after 5-year follow-up (aHR 2.3, CI 1.4–3.7). The risk of fractures requiring hospitalization for longer than 1 day was also higher after 1-year follow-up (aHR 2.1, CI 1.6–2.9) and after 5-year follow-up (aHR 2.0, CI 1.7–2.4) among smoking women. The risk of non-severe fractures (less than 1-day hospitalization period) was not as high as with severe fractures, but still higher among smoking women, the aHR being 1.8 (CI 1.6–2.0) after 1-year follow-up and 1.8 (CI 1.7–1.9) after 5-year follow-up (Table 4). All sensitivity analyses also showed a markedly increased risk of fractures among smokers (Tables 5 and 6, see Supplementary data).

Discussion

The main finding of this study was that smoking was associated with a higher fracture rate during the 1-year and 5-year follow-up time after giving birth when compared with non-smokers. After 5-year follow-up the risk was higher for all studied fractures in different anatomical regions, especially for the spine, pelvis, and hip or thigh. Also, the risk was higher for fractures considered as more severe (polytraumas and fractures requiring a longer hospitalization period) than for non-severe fractures (non-polytraumas and 1-day hospitalization period).

According to previous literature, a low SES has been over-represented in trauma populations, but the exact reason behind this is unknown (**13**). In addition, according to the Finnish Institute for Health and Welfare (**3**), people who have a lower level of education smoke more than those with a higher level of education. Based on our data, there was a notably higher number of women with low SES in the group of smokers, which supports these finding in the previous literature. However, adjusting the model with categorized SES still showed a notably higher fracture rate among smokers, possibly indicating that the riskier behavior is not the only explanation behind the increased incidence of fractures among smoking women. In the elderly population, due to age-related skeletal fragility (**20**), polytraumas require less energy to occur (**21**), but in the fertile-aged population, polytraumas are known to be caused mostly by high-energy trauma mechanisms, such as traffic accidents and falls from a height (**22**). Adjusting the model for polytraumas with the age of the mother and SES, the aHR showed a greater decrease compared with crude HR for this model than for others. This could possibly mean that the increased number of injuries caused by behavioral background is a more important explanation for high-energy accidents causing injuries in multiple anatomic regions but less important for low-energy fractures among smoking women. In addition, it appears that during the lactation period mothers are at a smaller risk of severe injuries, as the number of polytraumas was truly low during 1-year follow-up.

The risk of non-severe fractures was also higher for smoking women but, based on our data, the reason behind this remains unclear, as these fractures could also be caused by injuries related to behavioral background. However, aHRs showed a notably higher risk of fractures among smoking women when the SES was considered. Smoking is known to be a strong risk factor for osteoporosis, due to the numerous ways it negatively affects bone health and metabolism (**7,18**). In addition, estrogen is the key regulator of bone metabolism (**23**), making women (especially oft premenopausal and postmenopausal age) at risk of osteoporosis (**9,11**). These 2 risk factors could make smoking women especially vulnerable to osteoporotic fractures. However, age is known to be a dominating risk factor for osteoporosis (**24**), making osteoporosis relatively rare among the fertile-aged population (**25**).

In general, the association between smoking and osteoporotic fractures based on our data is only speculative and the increased risk of fractures among smokers is most likely caused by the combined effect of numerous factors, such as more common risky behavior, weaker health of the musculoskeletal system caused by an unhealthier lifestyle, and possibly the direct weakening effects of smoking on the musculoskeletal system. However, as the results of this study are proving the association in a nationwide setting and the results showed a great increase in the risk of fractures, these results should be acknowledged by the clinician and used when encouraging the patient to quit smoking. In addition, the results of this study should encourage research on the etiology behind the increased risk using more precise datasets (whether the increased risk is caused by direct effects of smoking on bone health, or riskier behavior).

Due to challenges and inaccuracies in gathering data on smokers, the studies researching the association between smoking and fractures are made using a relatively small population or questionnaires (**8,26,27**). The strength of our study is the large nationwide register with a smoking status variable registered for each pregnancy during the study period, making it the most comprehensive data found regarding smoking by women in Finland. The register data used in our study is routinely collected using structured forms with national instructions, which ensures good coverage and reduces possible reporting and selection bias. (**28**). Furthermore, the coverage of both registers included in this study is high (**15,17**).

The main limitation of our study is residual confounding as there is no reason to believe that smoking in itself causes more polytrauma. Residual confounding may be the bone mineral density, other comorbidities, substance (alcohol, drugs etc.) abuse, and missing clinical information on the registered fractures (e.g., radiological finding, trauma mechanisms). As this information is not reported to the registers, a level of uncertainty on the severity of the traumas remains, as it is derived from the existence of fractures in multiple anatomical sites and the length of hospital stay. Also, a relatively high proportion of pregnancies (19%) were excluded from the analysis due to missing SES or smoking status. However, the excluded population is missing at random, and, based on our sensitivity analyses, this does not have a major impact on the results. Furthermore, the date of death and migration is not available based on our data, making it impossible to identify women lost to follow-up. Also, in terms of the risk of fractures, smoking status found in the MBR is not comprehensive as it does not expose those who did not admit their smoking during maternity clinic visits or contain any information on how much the person smokes. However, the reliability of smoking status in the MBR was over 92%, which makes it a reliable source (**14**).

Conclusion

Smoking among fertile women was associated with higher risk of fractures in all anatomic regions after 5 years of follow-up. Smoking was also associated with a higher risk of polytraumas, other more severe fractures, and less severe fractures.

MV wrote the initial manuscript. IK and VM undertook the study design. VM supervised the study. VP, TH, and LN helped planning appropriate statistical analysis. Each author commented on the manuscript during the process and confirmed the final version to be submitted.

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Supplementary data

Table 1. Categorization of the socioeconomic status and total number of patients with each socioeconomic status found in the Medical Birth Register

Class/Specific socioeconomic status	Total number (%)
Low	145,581 (19.7)
Agricultural sole proprietors or workers	12,640
Industrial workers	35,162
Other production workers	31,574
Distribution and service representatives	53,297
Indefinite workers	7,214
Other self-employed persons or sole proprietors	816
Unemployed (no profession)	969
Unemployed (profession coded separately)	357
Long-term unemployed	3,126
Retired persons	426
Middle	307,905 (41.7)
Junior employees in work management position	21,087
Junior employees in independent office work	96,789
Junior employees in unindependent office work	12,211
Other indefinite junior employees	177,818
High	146,143 (19.8)
Senior employees in leadership position	19,144
Senior employees in design and research assignments	30,246
Senior employees working in teaching positions	52,842
Other indefinite senior employees	43,911
Status missing or categorization impossible	138,937 (18.8)
Homemaker (full-time taking care for children)	45,993
Students	85,110
Entrepreneurs	7,321
Status coded as unknown	513

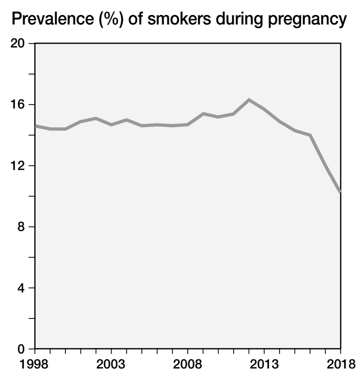

Figure 2. Prevalence of smokers during pregnancy of all pregnancies in Finland during 1998–2018. Women smoking during 1st trimester of pregnancy, or in later trimesters, were considered smokers in this study.

Table 5. Sensitivity analysis with excluded women due to missing SES (n = 151,994; 26,514 smokers and 125,480 non-smokers) included and placed in the SES category of "status missing or categorization impossible." Hazard ratios (HR) and adjusted hazard ratios (aHR) with 95% confidence intervals (CI) for the event of a woman suffering a fracture after giving birth during the 1-year and 5-year follow-up. Women smoking (n = 137,188) during the pregnancy were compared with non-smoking women (n = 753,566)

	1-year follow-up		5-year follow-up	
Fracture	HR (CI)	aHR (CI) [a]	HR (CI)	aHR (CI) [a]
Total	1.7 (1.5–2.0)	1.7 (1.5–1.9)	1.7 (1.6–1.8)	1.7 (1.7–1.8)
Location of fracture				
Lower arm	1.4 (1.1–1.7)	1.5 (1.2–1.8)	1.4 (1.3–1.5)	1.5 (1.3–1.6)
Upper arm	1.9 (1.3–2.6)	1.8 (1.3–2.4)	1.8 (1.5–2.1)	1.7 (1.5–2.0)
Spine	2.6 (1.7–4.0)	2.1 (1.4–3.1)	2.6 (2.0–3.2)	2.3 (1.9–2.8)
Pelvis	2.5 (1.3–4.7)	1.7 (0.9–3.2)	2.7 (1.9–3.8)	2.0 (1.5–2.8)
Hip or thigh	1.8 (0.9–3.4)	2.1 (1.2–3.9)	2.7 (1.9–3.7)	2.2 (1.6–3.0)
Lower leg including ankle	1.9 (1.6–2.3)	1.8 (1.5–2.2)	2.0 (1.8–2.2)	2.0 (1.8–2.2)
Type of fracture				
Polytrauma	0.8 (0.2–3.3)	0.4 (0.1–1.9)	3.1 (1.9–4.9)	2.2 (1.4–3.4)
Severe [b]	2.1 (1.6–2.9)	2.2 (1.7–2.9)	2.0 (1.7–2.3)	2.0 (1.8–2.3)
Less severe [c]	1.8 (1.6–2.0)	1.8 (1.6–2.0)	1.7 (1.6–1.8)	1.8 (1.6–2.0)

[a] Adjusted for the age of the mother at the time of pregnancy and SES category.
[b] Fractures with hospitalization period lasting > 1 day.
[c] Fractures with < 1 day hospitalization (including day surgeries) and non-polytraumas.

Table 6. Sensitivity analysis using multiple imputation technique for the SES variable. Best–best case, best–worst case, worst–best case, worst–worst case imputation, and data as observed was used to calculate grand means using the modified Rubin's Rule. Hazard ratios (HR) and adjusted hazard ratios (aHR) with 95% confidence intervals (CI) for the event of a woman suffering a fracture after giving birth during the 1-year and 5-year follow-up. Women smoking during the pregnancy were compared with non-smoking women

	1-year follow-up		5-year follow-up	
Fracture	HR (CI)	aHR (CI) [a]	HR (CI)	aHR (CI) [a]
Total	1.7 (1.5–2.0)	1.7 (1.5–3.0)	1.7 (1.6–1.8)	1.7 (1.6–1.8)
Location of fracture				
Lower arm	1.4 (1.1–1.7)	1.4 (1.2–1.8)	1.4 (1.3–1.5)	1.4 (1.3–1.6)
Upper arm	1.9 (1.3–2.6)	1.8 (1.3–2.5)	1.8 (1.5–2.1)	1.7 (1.4–2.0)
Spine	2.6 (1.7–4.0)	2.1 (1.3–3.4)	2.6 (2.0–3.2)	2.3 (1.8–2.9)
Pelvis	2.5 (1.3–4.7)	2.2 (1.1–4.3)	2.7 (1.9–3.8)	2.1 (1.5–3.0)
Hip or thigh	1.8 (0.9–3.4)	1.8 (0.9–3.5)	2.7 (1.9–3.7)	2.1 (1.5–3.0)
Lower leg including ankle	1.9 (1.6–2.3)	1.9 (1.6–2.3)	2.0 (1.8–2.2)	2.0 (1.9–2.2)
Type of fracture:				
Polytrauma	0.8 (0.2–3.3)	0.5 (0.1–2.8)	3.1 (1.9–4.9)	2.2 (1.4–3.6)
Severe [b]	2.1 (1.6–2.9)	2.1 (1.6–2.9)	2.0 (1.7–2.3)	2.0 (1.7–2.4)
Less severe [c]	1.8 (1.6–2.0)	1.8 (1.6–2.0)	1.7 (1.6–1.8)	1.7 (1.7–1.9)

[a–c] see Table 5