From the Division of Obstetrics and Gynecology, Department of Clinical Sciences, Danderyd Hospital, Karolinska Institutet, Stockholm, Sweden

PELVIC FLOOR DYSFUNCTION DEPENDING ON MODE OF DELIVERY
CLINICAL AND EPIDEMIOLOGICAL ASPECTS

Åsa Leijonhufvud

Stockholm 2012
ABSTRACT

Objective: To study pelvic floor disorders in relation to mode of delivery using clinical and epidemiological methods; to compare the prevalence and risk of lower urinary tract symptoms (LUTS) in healthy primiparous women in relation to vaginal (VD) or elective cesarean (CD) delivery nine months after delivery; to estimate the effect of delivery on urinary and anal incontinence 10 years after first childbirth in relation to mode of delivery and to assess the influence of parity and obstetrical events; to estimate the risks of stress urinary incontinence (SUI) and pelvic organ prolapse (POP) surgery related to delivery mode at long-term follow-up; and to evaluate the influence of age at first childbirth on the risks of surgically managed SUI and POP.

Methods: Paper I is a clinical study of 435 subjects, with prospectively collected data based on self-reported questionnaires and medical charts. Paper II is a cross-sectional comparative study of 395 subjects, and Paper III and IV are nationwide cohort studies including over 90,000 subjects, based on data from the Swedish Medical Birth Register and the Swedish Inpatient Register. Statistical analysis was performed on the clinical cohorts, fulfilling a power criteria of $\alpha<0.05$, $\beta=0.8$, using non-parametric statistics, correlation coefficients and logistic regression. Incidence rates, Hazard Ratios (HR) and NNH were calculated on the population-based cohorts.

Results: VD was associated with a significantly increased prevalence and risk of LUTS nine months after childbirth when compared to elective CD (RR$_{SUI}$ 8.9 95%CI 1.9-42). De Novo SUI was likewise more prevalent after VD. The protective effect of CD was absent in subjects reporting SUI before pregnancy, symptoms before pregnancy or at three months follow-up (RR$_{SUI}$ 3.9 95%CI 1.7-8.5) were independent risk factors for persistent symptoms at nine months follow-up, with a higher prevalence of SUI after VD. At 10 years follow-up were urinary and anal incontinence symptoms significantly more common following spontaneous VD. Women with an obstetrical history of anal sphincter injury carried a substantially increased risk of gas incontinence (OR 3.1 95%CI 1.5-8.9). However, CD is not associated with a major reduction of urinary incontinence symptoms and an association between delivery mode and anal incontinence could not be confirmed. A significantly increased risk of SUI and POP surgery later in life was seen in women with only VD compared to only having had CD (HR$_{SUI}$ 2.9 95%CI 2.4-3.6, HR$_{POP}$ 9.2 95%CI 7.0-12.1). The increased risk of surgically managed pelvic floor disorders persisted for the three decades of follow-up and was especially pronounced in multiparous women. An age dependent effect was seen with higher age at first delivery associated with higher risk and incidence rate of subsequent pelvic floor surgery in both delivery groups. The protective effect of CD remained in all age categories, predominantly for POP in women $\geq$ 30 years of age at first childbirth.

Conclusions: The studies in this thesis provides clinical and epidemiological evidence that obstetrical intervention at the time of childbirth may to some extent prevent SUI and POP later in life, particularly in multiparous women and women over 30 years of age at first delivery. However, the protective effects of CD with regard to pelvic floor disorders must be weighed against postpartum maternal and neonatal morbidity associated with the procedure.

Keywords: cesarean, delivery, incontinence, prolapse, maternal age.
LIST OF PUBLICATIONS

This thesis is based on the following papers, referred to in the text by their roman numerals:

I. Planned Cesarean Section versus Planned Vaginal Delivery: Comparison of Lower Urinary Tract Symptoms.

   **Ekström Å, Altman D, Wiklund I, Larsson C, Andolf E.**


II. Symptoms of anal and urinary incontinence following cesarean section or spontaneous vaginal delivery.

   Altman D, **Ekstrom A**, Forsgren C, Nordenstam J Zetterstrom J.


III. Risks of stress urinary incontinence and pelvic organ prolapse surgery in relation to mode of childbirth.

   **Leijonhufvud A**, Lundholm C, Cnattingius S, Granath F, Andolf E, Altman D.


IV. Risk of surgically managed stress urinary incontinence and pelvic organ prolapse in relation to delivery mode and age at first childbirth.

   **Leijonhufvud A**, Lundholm C, Cnattingius S, Granath F, Altman D.

   *Manuscript*
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<th>Description</th>
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<tbody>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>CCIS</td>
<td>Cleveland Clinic Incontinence Score</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CS</td>
<td>Cesarean Section</td>
</tr>
<tr>
<td>CD</td>
<td>Cesarean Delivery</td>
</tr>
<tr>
<td>HR</td>
<td>Hazard Ratio</td>
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<tr>
<td>ICD</td>
<td>International Classification of Diseases</td>
</tr>
<tr>
<td>ICS</td>
<td>International Continence Society</td>
</tr>
<tr>
<td>ISD</td>
<td>Intrinsic Sphincter Deficiency</td>
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<tr>
<td>LUTS</td>
<td>Lower Urinary Tract Symptoms</td>
</tr>
<tr>
<td>MBR</td>
<td>Medical Birth Register</td>
</tr>
<tr>
<td>NOMESCO</td>
<td>Nordic Medico-Statistical Committee</td>
</tr>
<tr>
<td>NNH</td>
<td>Numbers Needed to Harm</td>
</tr>
<tr>
<td>NS</td>
<td>Not statistically Significant</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>POP</td>
<td>Pelvic Organ Prolapse</td>
</tr>
<tr>
<td>POP-Q</td>
<td>Pelvic Organ Prolapse Quantification system</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SUI</td>
<td>Stress Urinary Incontinence</td>
</tr>
<tr>
<td>RR</td>
<td>Relative Risk</td>
</tr>
<tr>
<td>TVT</td>
<td>Tension free Vaginal Tape</td>
</tr>
<tr>
<td>TVT-O</td>
<td>Tension free Vaginal Tape-Obturator</td>
</tr>
<tr>
<td>UI</td>
<td>Urinary Incontinence</td>
</tr>
<tr>
<td>UU</td>
<td>Urinary Urgency</td>
</tr>
<tr>
<td>UUI</td>
<td>Urge Urinary Incontinence</td>
</tr>
<tr>
<td>VB</td>
<td>Vaginal Birth</td>
</tr>
<tr>
<td>VD</td>
<td>Vaginal Delivery</td>
</tr>
<tr>
<td>%</td>
<td>Percent</td>
</tr>
</tbody>
</table>
1 INTRODUCTION

Childbirth is a life event associated with risks for both mother and child. The crude mortality rate when nothing is done to avert maternal death during childbirth has been estimated to 1,000 - 1,500 deaths per 100,000 births.\textsuperscript{1,2} Modern medicine has greatly decreased the risk and in many western countries the current maternal mortality rate is now around 14 deaths per 100,000 births (USA: 24/100,000, Sweden 5/100,000 in 2008).\textsuperscript{3}

A cesarean delivery was initially used a last resort in an attempt to save the child of a deceased mother. Today, cesarean section is generally considered to be a safe procedure in industrialized countries and associated with successful perinatal outcomes for both mother and child. In parallel with the decreased complication rates the number of women giving birth by cesarean section is rapidly increasing. This trend may also be driven by the common perception that cesarean delivery preserves pelvic floor function and sexual function. Cesarean deliveries, however, remain associated with a higher frequency of complications compared to vaginal delivery and women delivered by repeat cesarean sections are at particular risk of intraoperative adverse events. Obstetricians play an important role at antenatal counseling but the evidence on which to base recommendations on choice of delivery mode is still ambiguous.

1.1 CESAREAN AND VAGINAL DELIVERY

1.1.1 Cesarean delivery; an historical overview

Cesarean delivery has been part of human culture since antiquity and there are ancient tales of the procedure being performed in both western and non-western cultures. Despite rare references to the operation on living women, the purpose was initially to retrieve the infant from a dead or dying mothers womb. This was performed either in the rather vain hope of saving the baby's life, or required by religious edicts, so the infant might be buried separately from the mother. Above all, it was a measure of last resort and the operation was not intended to preserve the mother's life. It was not until the 19th century that such a possibility became realistic within obstetric care.

The early history of cesarean delivery remains shrouded in myth and is of dubious accuracy. The origin of "cesarean" is commonly believed to derive from the surgical birth of Julius Caesar, however, this is unlikely since his mother Aurelia is reputed to have survived the birth of his son. The first incidence in Europe of a woman surviving a cesarean delivery was recorded in the 15th century. The maternal mortality risk remained very high until the 20th century when life-threatening complications like hemorrhage and infections became available for treatment, along with advances in anesthesiology, changes in surgical techniques, improved management of dystocia and eclampsia and training of midwives. In 1955, the mortality rate in Sweden associated with a cesarean delivery had decreased to < 0.5% and today the mortality rate attributed to cesarean delivery in Sweden is close to nil.\textsuperscript{4,5,6}

In parallel with the improved safety of cesarean deliveries in modern obstetrics the number of women delivered by cesarean section has increased steadily with a steeper
rise in incidence the last three decades. The cesarean section rate in Sweden has risen substantially from 5.3 percent in 1973 to 17.7 percent in 2008.\textsuperscript{7} A similar and even more evident increase has been observed in many European countries, as well as, in the United States, Latin America and Asia.\textsuperscript{8,9} The underlying reason for this increase is complex and many factors contribute to the increasing cesarean rates, e.g. increasing number of successful at-risk pregnancies, improved fetal monitoring, repeat cesarean delivery, increasing maternal and fetal weight, increasing age at first delivery, medico-legal concerns, as well as, an increased number of women demanding elective cesarean delivery without a clear medical indication.\textsuperscript{10,11}

One explanation for the increasing section rates is the steadily increasing fetal birth weight although maternal pelvic diameters have remained the same. It has been suggested that since the introduction of successful cesarean birth, mothers with a small pelvis having large babies have survived and contributed to these traits increasing in the population. Such a hypothesis is based upon the idea that even without fears of malpractice, without maternal obesity and diabetes, and without other widely quoted factors, the cesarean section rate would continue to rise simply due to slow changes in population genetics.\textsuperscript{12}

**Figure 1.** Cesarean section rates in Sweden 1975 - 2009.

www.socialstyrelsen.se/ medicinskafodelseregistret/ inenglish.

### 1.1.2 Elective cesarean delivery

The rate of elective cesarean delivery is proportionally increasing and in Sweden the rate has doubled from 4 percent in 1991 to 8 percent in 2006 corresponding to approximately 50\% of all cesarean deliveries.\textsuperscript{7} Women requesting a cesarean delivery without a clear medical indication are an increasing proportion of this group but to which extent, and the underlying reason for this trend, is a controversial issue. Existing data from both retrospective and prospective studies are limited, “maternal-request” lacks definition, and rates vary between 1\% and 48\% in the public sector health care systems, whereas 60\% is reported in the private sector.\textsuperscript{13} At a tertiary hospital (Karolinska Universitetssjukhuset) in Sweden, with almost 10,000 deliveries per year,
the main indication for an elective cesarean delivery in 1992 was a pathological fetal presentation or a uterine factor. The dominant indication for an elective cesarean in 2005 was “psychosocial” reasons defined as maternal fear of childbirth or maternal request without any co-existing medical indication. Women’s previous birth experience, fear of delivery, need for control, and the common notion that a cesarean delivery protects the mother from pelvic floor and sexual dysfunction later in life may all influence the decision-making.

1.1.3 Cesarean delivery and associated risks

The mortality rate for both cesarean delivery and vaginal birth has dropped steadily in the western world. The risk of maternal death associated with cesarean delivery in Sweden in the 1970s has been estimated to twelve times as high as that from vaginal parturition. Other studies have reported risks of maternal death between 3 and 25 times that of a vaginal delivery, with the lower figures correlating to elective cesarean sections. A review article from 2006 concluded, however, that there were no publications with an ideal trial design and adequate power to establish the relationship between maternal mortality and method of delivery and that the studies with the highest evidence levels suggest there may not be an increased risk of maternal death with cesarean delivery as compared with vaginal delivery.

Maternal complications

Assessing the effects of cesarean section on maternal and fetal health is complex due to difficulties to separate out the effects of the procedure itself versus effects of the underlying indication for the procedure. In general, first time elective cesarean section performed on a healthy woman is considered a “safe” procedure, however, repeat cesarean sections are associated with increased risks for the mother and thereby also for the child. Studies suggest that women who deliver their first child by cesarean delivery have increased risks for placenta previa, placenta accreta, antepartum hemorrhage, prolonged labor, uterine rupture, preterm birth, low birth weight, malpresentation and stillbirth in their second delivery.

Rates of maternal complications in a prospective observational study of 30,132 subjects delivered by cesarean section without previous labor in 19 academic centers are presented in Table 1.

Like all types of abdominal surgery, a cesarean delivery is associated with risks of post-operative adhesions, incisional hernias, wound infections, thromboembolism, hemorrhage and anesthetic complications. A large prospective multicenter study within the 2005 WHO global survey on maternal and perinatal death came to the conclusion that cesarean delivery independently reduces overall risk in breech presentations and risk of intrapartum fetal death in cephalic presentations but increases the risks of severe maternal and neonatal morbidity and mortality in cephalic presentations (ORadj 2.3 95%CI 1.7-3.1 for elective CD; ORadj 2.0 95% CI 1.6-2.5 for intrapartum CD).
Table 1. Maternal morbidity in women delivered by elective cesarean delivery.

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>1st CD</th>
<th>2nd CD</th>
<th>3rd CD</th>
<th>4th CD</th>
<th>5th CD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>6,201</td>
<td>15,808</td>
<td>6,324</td>
<td>1,452</td>
<td>258</td>
<td>-</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>6.4%</td>
<td>1.3%</td>
<td>1.1%</td>
<td>2.3%</td>
<td>2.3%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Placenta accreta</td>
<td>0.2%</td>
<td>0.3%</td>
<td>0.6%</td>
<td>2.1%</td>
<td>2.3%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>0.7%</td>
<td>0.4%</td>
<td>0.9%</td>
<td>2.4%</td>
<td>3.5%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Cystotomy</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.3%</td>
<td>1.2%</td>
<td>1.9%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Ureteral injury</td>
<td>0.03%</td>
<td>0.01%</td>
<td>0.02%</td>
<td>0.07%</td>
<td>0.39%</td>
<td>.01</td>
</tr>
<tr>
<td>Bowel injury</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.0%</td>
<td>.02</td>
</tr>
<tr>
<td>Ileus</td>
<td>0.7%</td>
<td>0.5%</td>
<td>0.7%</td>
<td>0.9%</td>
<td>1.6%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>ICU admission</td>
<td>1.9%</td>
<td>0.6%</td>
<td>0.5%</td>
<td>1.6%</td>
<td>1.9%</td>
<td>.007</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>4.1%</td>
<td>1.5%</td>
<td>2.3%</td>
<td>3.7%</td>
<td>4.3%</td>
<td>.61</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>0.3%</td>
<td>0.2%</td>
<td>0.1%</td>
<td>0.2%</td>
<td>-</td>
<td>.42</td>
</tr>
<tr>
<td>Pulmonary emboli</td>
<td>0.2%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.4%</td>
<td>.85</td>
</tr>
<tr>
<td>Maternal death</td>
<td>0.2%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>-</td>
<td>.02</td>
</tr>
</tbody>
</table>


Fetal complications

A cesarean delivery necessitated by a fetal or maternal medical condition is clearly advantageous for the child. A more delicate issue is the risks associated with a cesarean delivery on maternal request where the medical consequences for the infant needs to be considered when planning birth. A large epidemiological study in Sweden has shown that elective cesarean delivery (performed without medical indication at full term) doubles the risk of admission at a neonatal care unit (6.7% vs. 3.3%) compared to vaginal delivery. Most cases of diagnosis for admission were neonatal respiratory distress syndrome. Elective cesarean delivery increases the risks of respiratory problems more than three times (4.1% vs. 1.2%) compared to vaginal delivery.27 Cases of respiratory distress are often mild and transient but may in rare cases turn severe with complications such as pneumothorax or persistent pulmonary hypertension.28 Performing the elective cesarean delivery after 39 gestational weeks may reduce the risk of neonatal respiratory distress.29

Potential beneficial effects of elective cesarean deliveries include a decrease in perinatal death, shoulder dystocia, severe intrapartum hypoxia and neonatal encephalopathy.30

1.1.4 Vaginal delivery and associated risks

Some of the serious and life-threatening complications that may occur during labor and delivery without previous warning signs includes placenta abruption, cord prolapse and shoulder dystocia. The risk of labor related infant death in the UK in
1997 was estimated to 1 in 1,500 deliveries. With regard to the mother, the risks of hemorrhage, peripartum hysterectomy, endometritis, and thrombo-embolic complications exist although at a lower level than for cesarean deliveries. The absolute risk difference in severe maternal morbidity rates between cesarean and vaginal delivery is, however, limited.

A large register based study including nearly 33,000 women reported a frequency of third to fourth degree anal sphincter disruption in 7.8\% of women with spontaneous vaginal delivery and in 22.3\% who had operative vaginal delivery. Studies of women with anal sphincter rupture reports symptoms of anal, urine or double incontinence in over 50\%, and one of four women with subsequent deliveries reports aggravated symptoms with additional childbirths. Although long-term effects of vaginal childbirth on the pelvic floor remain uncertain vaginal delivery is considered an established risk factor for stress urinary incontinence.

1.2 ANATOMY OF THE FEMALE PELVIC FLOOR

The pelvic floor, with its intricate architecture of striated muscles, smooth muscle, connective tissue, blood vessels and nerves, is a complicated system. The section below provides a brief summary of clinically relevant anatomical structures.

**Pelvic floor musculature**

The skeletal muscles of the pelvic floor include the levator ani muscles, the coccygeus, the external anal sphincter, the striated urethral sphincter, and the deep and superficial perineal muscles. The muscles of the pelvic floor, particularly the levator ani muscles, have a critical role in supporting the pelvic visceral organs and play an integral role in urinary, defecatory, and sexual function.

**Figure 2.** The levator ani muscles of the female pelvic floor.

In women with normal pelvic floor function, the levator ani muscle has a three-dimensional structure in which its anterior portion (pubococcygeus and puborectalis) is oriented vertically as a sling around the mid-urethra, vagina, and anorectum and its
posterior portion (the iliococcygeus) has a horizontal upwardly biconvex shape. Thus, the anterior portion of the levator ani complex serves to close the urogenital hiatus and pull the urethra, vagina, perineum, and anorectum toward the pubic bone, whereas the horizontally oriented posterior portion, the levator plate, serves as a supportive diaphragm.

**Fascias of the pelvic floor**

The endopelvic fascia is a loose connective tissue network between the peritoneum and the levator muscles, which envelops the pelvic organs and connects them loosely to the supportive musculature and bones of the pelvis. This connective tissue network tethers the vagina and uterus in their normal anatomic location while allowing for the mobility of the viscera to permit storage of urine and stool, coitus, parturition, and defecation. The rectovaginal fascia is the part of the endopelvic fascia that continues down the posterior wall to provide support to the distal rectum. The mid-vagina rests on the rectovaginal fascia posteriorly and is anteriorly separated from the bladder and urethra by a part of the endopelvic fascia called the pubocervical fascia, supporting the bladder and urethra.

**Figure 3a.** Fascias and ligaments of the female pelvic floor.

**Figure 3b.** Fascias and ligaments of the female pelvic floor.

Images reprinted with permission from Ethicon US.
Innervation of the pelvic floor

The pudendal nerve innervates the striated urethral and anal sphincters, as well as, the deep and superficial perineal muscles and provides sensory innervation to the external genitalia. This nerve follows a complex course that originates from S2–S4 of the sacral plexus, travels behind the sacrospinous ligament just medial to the ischial spine, exiting the pelvis through the greater sciatic foramen, then re-enters through the lesser sciatic foramen and travels through the pudendal canal on the medial aspect of the obturator internus muscles before separating into several terminal branches that terminate within the muscles and skin of the perineum.

Figure 4. The female pudendal nerve.

Image reprinted with permission from Ethicon US.

Urinary bladder and urethra

The urinary bladder is an elastic muscular organ located on the anterior surface of the uterus and its base rests on the pubocervical fascia, the cervix and the anterior vaginal wall. The middle layer of the bladder wall consists of smooth musculature, forming the detrusor muscle, whereas the inner and outer muscle layers consists of striated muscle fibers.

The female adult urethra is an approximately 3.5 cm long and 6 mm wide fibro muscular tube. The urethra passes through the endopelvic fascia and lies embedded in the anterior vaginal wall. The urethral wall consists of an outer muscularis layer containing both smooth and striated musculature, and an inner mucous membrane. The internal sphincter consists of smooth muscle and mucosa all along the length of the urethra. The external sphincter of striated muscle is situated at the proximal and mid urethra with its broadest part anteriorly at the midurethra.
The perineum

The perineum and the perineal body play an important role in support of the distal vagina and in normal anorectal function. It stabilizes the lower pelvic floor and is attached to the pelvic sidewall by the transverse perineal muscles. The perineum is anatomically defined by the distal borders of the pelvic bony structures consisting of the ischiopubic ramus, ischial tuberositas, the pubic bone and the coccyx.

Interactions between muscular and connective tissue supports

Normal pelvic organ support and function depends on the dynamic interaction between the pelvic floor musculature and the endopelvic fascia. In a standing woman, the endopelvic fascia suspends the upper vagina, the bladder, and the rectum over the levator plate while the pelvic floor muscles close the urogenital hiatus and provide a stable platform on which the pelvic viscera rests.

Pelvic floor muscles have a constant resting tone except during voiding, defecation, and the Valsalva maneuver. This activity serves to close the urethral and anal sphincters, narrow the urogenital hiatus, and provide a constant support for the pelvic viscera. The levator muscles and the skeletal components of the urethral and anal sphincters have the ability to contract quickly at the time of suddenly increased abdominal pressure, such as a cough or sneeze, in order to maintain continence and to relax during evacuation. With pelvic floor weakness, there is loss of the horizontal orientation of the levator plate with increased laxity of the urogenital hiatus, and the pelvic floor assumes a more bowl-like configuration. Over time, this may lead to pelvic organ prolapse and lower urinary tract symptoms.

1.3 EFFECTS ON THE PELVIC FLOOR OF PREGNANCY AND DELIVERY

The underlying mechanisms for the development of pelvic floor dysfunction related to pregnancy and delivery can basically be divided into hormonal factors and injury to supportive structures during pregnancy and childbirth. Alterations in collagen structure during pregnancy suggest that pregnancy is associated with a decrease in connective tissue tensile strength. As the fetus grows, the weight of the fetus and the gravid uterus results in anatomical changes of the bladder and urethra by shear pressure and mechanical force. Studies using ultrasound-imaging techniques have shown that the angle between the bladder neck and the urethra increases, producing an increased opening of the bladder neck. During pregnancy there is also an increased mobility of the bladder due to the hormonal changes, which may alter normal urinary tract function.

1.3.1 Vaginal delivery

The ability of the pelvic floor to sustain urinary and anal continence is undoubtedly endangered by the process of vaginal delivery. As the fetus emerges through the birth canal, the widest part of the fetal head stretches the pelvic floor muscles, fascia and nerves and may cause reversible or permanent damage by direct laceration or ischemia. Pudendal nerve denervation has been demonstrated in 80% of women following their first vaginal delivery with denervation occurring primarily during the second stage of labor. Pudendal nerve injury usually results in demyelination and, although axonal disruption may occur in severe cases, recovery usually occurs with time but may be cumulative with successive deliveries. Pudendal nerve damage is often occult but
may lead to the gradual development of symptoms later in life (delay of onset). Pelvic floor denervation has been implicated in the etiology of urinary incontinence, pelvic organ prolapse, chronic constipation and defecatory difficulty. Stretching and disruption of the pelvic floor muscles, as well as, fascial tears have the ability to heal but the resulting connective tissue may not be of the same tensile strength as the original. Overt or occult perineal trauma during delivery may deteriorate further and progress over time.

1.3.2 Perineal tears

Rupture of the pelvic floor during childbirth is divided into four categories based on morphological severity.

- 1st degree is a tear in the vaginal mucosa or superficial perineal skin but not in the underlying tissue.
- 2nd degree is a tear that extends beyond perineal skin and vaginal mucosa to perineal muscles and fascia.
- 3rd degree is a tear that involves the muscles of the anal sphincter complex.
- 4th degree is a complete rupture of the anal sphincter muscles including the anal or rectal mucosa.

1.3.3 Instrumental delivery

Use of vaginal instrumental delivery (ventouse and forceps) have also been increasing in frequency over time, but not as rapidly as the cesarean section rates. More than nine percent of Swedish women are delivered by vacuum or forceps delivery, and the frequency of instrumental delivery among primiparous has been estimated to almost 20%. During instrumental delivery, especially forceps delivery, there is an increased risk of perineal tears. Rupture of first and second degrees are common, they usually heal quickly and rarely cause long-term problems. Damage to the anal sphincter, grade III and IV, increases the risks of anal incontinence and perineal pain.

1.3.4 Maternal age at first delivery

There is a trend towards women being gradually older at the time of giving birth, especially first birth. It is a common notion that younger women are less likely to suffer pelvic-floor tissue trauma but the evidence to support this is lacking. It is also unknown whether or not a younger age at delivery is beneficial with regard to both short and long-term sequelae. Mean age at first delivery in Sweden has risen steadily during the last decades: from 24 years of age in 1973, to 28 in 2009. If increasing age at first childbirth is a risk factor for pelvic floor disorders later in life, the presumed number of women affected by incontinence and pelvic organ prolapse will increase even further over the coming decades.
Figure 5. Maternal age at first delivery 1975 - 2009.

Postponing first childbirth has not only been shown to increase the incidence of breast cancer, it has also been associated with cardiovascular disease and an increased risks of unfavorable obstetrical outcomes including fetal death.\textsuperscript{53} Increased age at delivery is correspondingly associated with a higher percentage of cesarean deliveries.\textsuperscript{54} Figures showing cesarean section rates by age in the Nordic countries are presented in Table 2, derived from a report by the Nordic Medico-Statistical Committee (NOMESCO).

Table 2. Cesarean section rates (per 1000 deliveries) by age in the Nordic countries.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sweden</th>
<th>Denmark</th>
<th>Norway</th>
<th>Finland</th>
<th>Iceland</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>124</td>
<td>159</td>
<td>110</td>
<td>121</td>
<td>135</td>
</tr>
<tr>
<td>25-34</td>
<td>179</td>
<td>202</td>
<td>151</td>
<td>157</td>
<td>174</td>
</tr>
<tr>
<td>35-44</td>
<td>268</td>
<td>273</td>
<td>253</td>
<td>219</td>
<td>215</td>
</tr>
<tr>
<td>45+</td>
<td>-</td>
<td>365</td>
<td>586</td>
<td>250</td>
<td>-</td>
</tr>
<tr>
<td>Overall</td>
<td>190</td>
<td>210</td>
<td>163</td>
<td>161</td>
<td>172</td>
</tr>
</tbody>
</table>


1.4 URINARY INCONTINENCE

1.4.1 Classification of urinary incontinence

The nomenclature of urinary incontinence can be confusing, as different classifications and definitions have used been over time. For this reason the International Continence Society (ICS) founded a cross-disciplinary standardization committee to present updated and uniform definitions of urinary incontinence and its’ subtypes, as well as, other forms of pelvic floor disorders. The latest revision was presented in 2010 by Haylen et al.\textsuperscript{55} of which a condensation is presented below:

- Urinary incontinence is the complaint of any involuntary loss of urine.
• **Stress urinary incontinence** is the complaint of involuntary leakage of urine on effort or exertion, or on sneezing or coughing.

• **Urgency** is the complaint of sudden compelling desire to pass urine, which is difficult to defer.

• **Urgency incontinence** is the complaint of involuntary leakage accompanied by or immediately preceded by urgency.

### 1.4.2 Pathophysiological mechanisms of urinary incontinence

Urinary continence requires normal storage function, urethral sphincter contraction and relaxation, anatomic support of the lower urinary tract and urethral mucosa pressure. Deficiencies in any of these mechanisms will cause symptoms depending on origin; urgency, urgency incontinence, stress urinary incontinence, postural incontinence (involuntary loss of urine associated with change of body position), overflow incontinence, nocturia (when the individual has to wake at night one or more times to void) or mixed urinary incontinence.

Continence and micturition involve a balance between urethral sphincter closure and detrusor muscle activity. By contraction and closure of the urethral sphincter complex, the urethral pressure normally exceeds bladder pressure, resulting in urine remaining in the bladder. The sphincter complex has a constant resting tone, which increases progressively during the filling phase. The striated component of the urethral sphincter has the ability to further contract quickly at the time of suddenly increased abdominal pressure, such as a cough or sneeze, in order to maintain continence and to relax during evacuation. In previous studies, childbirth has mainly been associated with stress urinary incontinence (SUI) and the correlation to other forms of incontinence has been less evident. For this reason SUI is the focus of this section.

Intrinsic sphincter deficiency (ISD) is characterized by low urethral closing pressures, often defined as maximum urethral closure pressure of 20 cm H2O or less, and/or abdominal/valsalva leak point pressure of 60 cm H2O or less. As a consequence of low urethral closing pressures, increases in abdominal (and subsequently detrusor) pressure may result in urinary incontinence. This type of SUI increases with age and is a less likely cause for SUI among premenopausal women. Advanced age, estrogen deficiency, previous delivery or surgery, radiation therapy and certain neurologic lesions are considered risk factors for ISD and poor urethral sphincter function. The diagnosis of ISD requires a typical history of stress incontinence and is confirmed by urodynamics.

Another underlying abnormality causing SUI is urethral hypermobility caused by a failure of the normal anatomic supports of the urethrovesical junction and the mid urethra. The mid-urethra is normally supported by the pubouretral and pubovesical ligament and contraction of the levator ani muscles may contribute further support to the mid-urethra (utilized at Kegel exercise). Loss of bladder neck and mid-urethral support leads to displacement of the sphincter at time of increased abdominal pressure and thereby inhibits urethral sphincter closure. This deficiency is often attributed to nerve, muscle and connective tissue injury, frequently linked to vaginal delivery but the risk factors for ISD mentioned above also predisposes to urethral
hypermobility. Lifestyle factors predisposing for SUI includes obesity, chronic constipation, and chronic bronchitis.

### 1.4.3 Treatment of stress urinary incontinence

There are five main principles of treatment for SUI: physiotherapy and behavioral changes, vaginal pessaries, medication, bulking agents, and surgery.

#### Physiotherapy and behavioral changes

Conservative options are often the first line of treatment with pelvic floor physiotherapy being the initial step. Pelvic floor training is often efficient if performed on regular basis with a physiotherapist when symptoms of SUI are mild to moderate.\(^5\) To reach optimal results with conservative treatment, physiotherapy often needs to be combined with behavioral changes (weight loss, fluid restriction, scheduled toilet visits, smoking cessation). Pelvic floor training should be evaluated after 2-3 months of training and if results are unsatisfactory further measures should be taken. Conservative options may also include electric stimulation and acupuncture but the level of evidence for these strategies is often low.\(^6\)

#### Medication

Estrogen and α-adrenergic pharmaceuticals can theoretically help by improving the urethral mucosa and increase urethral sphincter tonus. However, in clinical studies results of these therapies have been disappointing. A Cochrane review from 2005 concluded that treatment with serotonin-noradrenaline reuptake inhibitors (SNRI) can improve the quality of life of patients with SUI, but it is unclear whether or not benefits are sustainable, and adverse effect are frequent.\(^6\) Because of troubling side effects, SNRI are warranted only in special cases.

#### Vaginal pessaries

Mechanical aid to improve urethral support using vaginal pessaries can be efficient for some patients but studies performed in this area are few with small study populations and short-term follow-up.\(^6\) In cases where surgery is not warranted, if the patient suffers from co-morbidity limiting surgical options, or if the patient prefers conservative treatment, pessaries may be a valid alternative.

#### Transurethral injection therapy

Newly developed urethral injection treatments, administered under cystoscopic control, are now available for the treatment of SUI in the form of polyacrylamide gel or collagen. The techniques are still under evaluation and results from long-term clinical studies are awaited. Until then transurethral injection treatment of SUI should be limited to special cases.

#### Surgery

Surgical treatment is recommended after conservative treatment has been evaluated and failed. Surgery can efficiently improve SUI symptoms but may be less suitable if there is a prominent component of urinary urgency incontinence, residual urine or outlet obstruction. In the past, several surgical techniques have been tried with varied
success. Today, the tension-free vaginal tape (TVT), a mid-urethral sling, is considered gold standard in most countries due to the low morbidity, high efficiency and long-term durability of results. The mid-urethral slings are placed loosely under the urethra like a girdle in the retro-pubical space and support the mid-urethra.

**Figure 6. TVT in place.**

1.5 PELVIC ORGAN PROLAPSE

1.5.1 Classification of pelvic organ prolapse

Pelvic organ prolapse (POP), a condition characterized by the downward descent of the pelvic organs causing the vagina to protrude, afflicts millions of women worldwide and is increasingly recognized as a global burden on women’s health. More than 50% of parous women over 50 years of age have signs of POP. POP includes several types of loss of pelvic floor support. What should be considered “normal” pelvic organ support varies with age and childbirth and no universal definition of disease exists.

In 1996, the ICS standardization committee presented a system to quantify and characterize POP according to vaginal topography, the POP-Q. According to the POP-Q, predefined measures of vaginal and perineal anatomic points are used to assign an ordinal stage of prolapse in relation to the hymen. Absence of prolapse is defined as stage 0 and stage IV represents total prolapse with complete procidentia/eversion. The POP-Q remains the only validated tool for prolapse grading and quantification. In 2001, the National Institutes of Health (NIH) Terminology workshop defined POP as POP-Q stage II or greater (vaginal descent within one cm ± of the hymen). Using this criterion nearly half of women presenting for routine gynecological care have stage II or greater POP, but the definition has been contested.
1.5.2 Pathophysiological mechanisms of pelvic organ prolapse

It is widely accepted that POP arise as a result of multifactorial interactions but the precise mechanisms are still a matter of debate. Identified risk factors have the common features that they may cause harm to the soft tissue pelvic floor, including direct injury to the muscles, connective tissue and nerves, as well as, degenerative effects of estrogen depletion, smoking, ageing and musculoskeletal diseases. 73

A dysfunctional levator ani muscle complex with secondary distension of the endopelvic fascia can cause prolapse of the vagina and surrounding organs. 74 Delancey described three levels of normal vaginal support and depending on the location and
degree of disruption of the supporting fascia and ligaments, various types of prolapse might occur. Level I support the proximal part of vagina by vertical fibers of the paracolpium, a continuation of the cardinal ligaments or sacrouterina. Insufficient suspension on this level leads to prolapse of the uterus. Disruption of level II support, the pubocervical and rectocervical fascia supporting the mid-vagina, results in anterior vaginal wall prolapse (cystocele) or posterior vaginal wall prolapse (recto-, entero-, sigmoideo-, or peritoneocele). Level III attaches the distal vagina densely to the medial margins of the levator ani muscles to secure the lower portion of the vaginal wall.

**Figure 9.** Levels of vaginal support as described by DeLancey.

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The majority of patients with clinically significant prolapse will have at least two or more risk factors for the disorder. Potential risk factors for POP include: parity, obesity, advanced age, estrogen deficiency, neurogenic dysfunction of the pelvic floor, genetic predisposition, connective tissue disorders, prior pelvic surgery with disruption of natural support (hysterectomy), and chronically increased intra abdominal pressure (e.g. from strenuous physical activity, constipation, or upper respiratory disorders). However, the long-term effects of vaginal childbirth and whether or not cesarean delivery truly decreases the risk of POP has not been adequately investigated.

### 1.5.3 Treatment of pelvic organ prolapse

Women with POP may present with a variety of complaints: bowel and bladder emptying difficulties, urinary or anal incontinence, recurrent lower urinary tract infections, pain or lack of sensation during sex. However the symptoms most strongly correlated to the presence of prolapse is the sensation of a vaginal bulge or vaginal globus feeling with associated pelvic heaviness. The degree of prolapse is often not correlated to the degree of subjective complaints. Many women with clinically diagnosed POP have mild or even no symptoms.
Conservative treatment

Minor cases of POP can be treated with life style changes and exercises to strengthen the pelvic floor muscles. A Cochrane review from 2004 concluded that physiotherapy does not prevent or treat POP, but the up-date from 2011 showed that there is now some evidence available indicating a positive effect of pelvic floor muscle training for prolapse symptoms. One third of women with POP also experience urinary incontinence, and pelvic floor exercise can be extra beneficial for this group of women. Local estrogen treatment may be relevant in postmenopausal women for the treatment of prolapse with pessaries, or as mucosal preparation before surgery. Use of pessaries remains common in clinical practice but is traditionally limited to patients awaiting surgical intervention or when surgery is contraindicated or not wanted by the patient.

Surgical treatment

Surgery remains the mainstay of treatment for POP. Surgical treatment for POP can be categorized as reconstructive or obliterator surgical techniques. Reconstructive surgery for POP aims to anatomically correct the prolapsed vagina while maintaining its function and relieve the symptoms while obliterator surgery is mainly performed on the elderly, where normal function of the vagina becomes secondary to the reduction of severe prolapse symptoms. Successful reconstructive surgery relieves the sensation of vaginal bulge and globus feeling with associated pelvic heaviness but is not clearly effective in curing related urinary and defecatory problems.

There are a wide variety of surgical techniques but no consensus on which is the gold standard surgical procedure. Traditionally, anterior and posterior colporraphy, and vaginal hysterectomy are among the most frequently performed operations for POP, of which anterior colporraphy for anterior vaginal wall prolapse (cystocele) is the single most common operation. The introduction of site-specific repair and biological and synthetic implants are widening the surgical options and changing surgical routines. A randomized multicenter trial of 389 women has shown that use of a standardized, trocar-guided mesh kit for cystocele repair results in higher short-term rates of successful treatment as compared with anterior colporrhaphy, but is also associated with higher rates of surgical complications and postoperative adverse events.

Data from the 1997 US National Hospital Discharge Survey reported a low mortality rate associated with POP surgery (0.03%) but 15.5% of women who underwent POP surgery had some kind of complication. Bleeding and infections accounted for the majority of complications. Serious complications including pulmonary embolism, brain infarction and sepsis accounted for 1% of all complications.

1.6 ANAL INCONTINENCE

1.6.1 Classification of anal incontinence

Anal incontinence (AI) is the involuntary loss of flatus, liquid or solid stool causing a social or hygienic problem. The ICS has recommended that the term fecal incontinence (FI) to be used specifically for loss of liquid or solid stool. Incidence and prevalence
estimates of AI vary depending on the population being studied and if flatus is included in the definition.

AI is affecting 2-20% of community dwelling women,\textsuperscript{87,88,89,90} and up to 40% of institutionalized women in the USA.\textsuperscript{91} Among women with urinary incontinence, approximately 25% are estimated to also suffer from AI.\textsuperscript{92} The etiological background is multifactorial but vaginal delivery is one of the most important risk factors. Other obstetrical risk factors includes common risk factors for pelvic floor disorders; parity, prolonged second stage of labor, birth weight >4.5 kg, instrumental delivery and anal sphincter laceration.

1.6.2 Treatment of anal incontinence

A variety of treatments are available for AI, depending on the severity of the symptoms. Treatment may include dietary changes, medications, bowel training and physiotherapy, sacral nerve stimulation or surgery.\textsuperscript{93}

1.7 PELVIC FLOOR DISORDERS – A GLOBAL HEALTH CONCERN

Benign pelvic floor disorders are increasingly recognized as a global health concern affecting millions of women throughout the world.\textsuperscript{67}

The prevalence of SUI has been estimated to affect approximately 30% of community dwelling women,\textsuperscript{94} with prevalence figures reaching 70% in elderly women.\textsuperscript{95} POP is also highly common, affecting over 50% of parous women over 50 years of age.\textsuperscript{68} It has been estimated that one in nine women in the United States will undergo pelvic floor surgery in their lifetime, and 30% of these women will require additional surgery for the same condition.\textsuperscript{96} The number of women having surgery for urinary incontinence and POP annually in the USA is 135,000 and 200,000 respectively,\textsuperscript{97} making prolapse one of the most common surgical indications in women (at the cost of more than 1 billion USD).\textsuperscript{98} In Sweden, the corresponding figures are approximately 7,000 procedures per year for POP and 2,500 for SUI.\textsuperscript{99}

The peak incidence of POP surgery occur in individuals 60-69 years of age, however, almost 58% of procedures are undertaken in women younger than 60 years of age.\textsuperscript{86} Given the demographic distribution of the US population and the increasing prevalence of pelvic floor dysfunction with age, it has been projected that the demand for treatment of pelvic floor disorders will increase by at least 45% over the next 30 years.\textsuperscript{100} Wu et al. used population projections from the U.S. Census Bureau to estimate the number of women who will have symptomatic pelvic floor disorders in the United States from 2010 to 2050. They came to the conclusion that the number of American women with at least one pelvic floor disorder will increase from 28.1 million in 2010 to 43.8 million in 2050. During this time period, the number of women with UI will increase 55% from 18.3 million to 28.4 million. For FI, the number of affected women will increase 59% from 10.6 to 16.8 million, and the number of women with POP will increase 46% from 3.3 to 4.9 million. The highest projections for 2050 estimate that 58.2 million women will have at least one pelvic floor disorder, with 41.3 million with UI, 25.3 million with FI, and 9.2 million with POP.\textsuperscript{101}
Pelvic floor disorders are strongly correlated to psychological distress and a decrease in quality of life.\textsuperscript{102} Despite its commonness, pelvic floor disorders are not often discussed openly (even with health care professionals) and far from all women with pelvic floor disorders seek medical care for further examination and treatment.\textsuperscript{103} Many women never speak to their health care providers because of embarrassment and a perception that pelvic floor disorders are a normal part of ageing and a normal “side effect” of giving birth. In a study of middle-aged women with daily UI, only half had ever spoken to their health care provider.\textsuperscript{104} Pelvic floor disorders can have a major impact and limit lifestyles activities, daily function and social interactions. This also includes refraining from sexual intercourse and coping with the unpredictability of UI or FI.

Incontinence and other pelvic floor disorders are expensive both for the afflicted individuals, as well as, society health care systems. In the US, more than 50\% of nursing home facility admissions are related to incontinence and personal hygiene.\textsuperscript{105} Society costs for lifetime treatment of SUI reaches the same level as lifetime treatment for cardiovascular diseases and in Sweden the annual costs for drug treatment of urinary urgency incontinence alone exceeds 250 million SEK. The lifetime medical cost for a woman with SUI is 1.8 times more than the cost for a woman with no SUI.\textsuperscript{106}

1.8 CHILDBIRTH AND PELVIC FLOOR DISORDERS

The ability of the pelvic floor to maintain continence and pelvic organ support is undoubtedly influenced by the process of vaginal delivery. Evidence from various experimental and observational studies imply that vaginal delivery has a detrimental effect on the pelvic floor with increased risks of subsequent pelvic floor disorders. However, whether and to what degree cesarean delivery may protect women from developing pelvic floor disorders is an unresolved issue.

Although childbirth generally is acknowledged as a major risk factor for pelvic floor dysfunction, retrospective and cross-sectional population based studies of pelvic floor disorders in relation to delivery mode have shown inconsistent results.\textsuperscript{94,107,35,108,109} Many previous studies have methodological limitations, including small sized cohorts, lack of controls, heterogeneous population samples, short-term follow-up periods and studies do generally not differentiate between cesarean sections performed with or without trial of labor. Most studies are also limited by lack of standardized definitions and precise reproducible methods for assessing the presence of SUI or POP. Prevalence and incidence rates of pelvic floor disorders vary with study populations and according to how the diagnosis is made. The reported prevalence of urinary incontinence in the postpartum period varies between 3 to 40\%.\textsuperscript{56}

A randomized trial is required to fully answer the question on the role of elective cesarean delivery to protect against pelvic floor dysfunction, but for obvious reasons, this study will never be performed.
Table 3. Studies on pelvic organ prolapse in relation to mode of delivery.

<table>
<thead>
<tr>
<th>Reference (year)</th>
<th>Number of subjects</th>
<th>Years post partum or age</th>
<th>OR (95% CI)</th>
<th>% POP</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Handa\textsuperscript{10} (2011)</td>
<td>1,011</td>
<td>5-10 y pp</td>
<td>5.6 (2.2-14.7)</td>
<td>3-7%</td>
<td>Elective CD protective.</td>
</tr>
<tr>
<td>Larsson\textsuperscript{111} (2009)</td>
<td>1.400,000</td>
<td>0-31 y pp</td>
<td>0.18 (0.16-0.2)</td>
<td>1%*</td>
<td>CD protective.</td>
</tr>
<tr>
<td>Lukacs\textsuperscript{112} (2006)</td>
<td>4,458</td>
<td>25-84 y</td>
<td>1.82 (1.04-3.19)</td>
<td>7%</td>
<td>Elective CD protective as nulliparity.</td>
</tr>
</tbody>
</table>

POP denotes pelvic organ prolapse  
CD denotes cesarean delivery  
*Diagnosis from inpatient register, majority surgically managed pelvic organ prolapse

Cesarean delivery has been shown to reduce the risk of postpartum urinary incontinence compared to vaginal delivery at short-term follow up.\textsuperscript{113,114,50} On the other hand, little is known about the long-term effects of delivery mode on urinary incontinence and POP. Some epidemiological studies suggest that cesarean delivery significantly decreases the risk of postpartum urinary incontinence.\textsuperscript{94,107} However, results from one epidemiological study indicate a diminution of the effect of obstetrical parameters, e.g. parity, when entering menopause.\textsuperscript{115}

Whether or not cesarean delivery provides a long-lasting protection against SUI or POP surgery must be considered an unresolved issue. With this thesis we aim to evaluate different aspects of the risk of pelvic floor dysfunction in women delivered by either vaginal birth or cesarean delivery, at 9 months, 10-years and 30-years after first delivery.
2 AIMS

The overall aim of this thesis is to study pelvic floor disorders in relation to mode of delivery using clinical and epidemiological methodology.

The specific aims were to:

1. compare the prevalence and risk of lower urinary tract symptoms in healthy primiparous women in relation to vaginal birth or elective cesarean delivery nine month after delivery (Paper I).

2. estimate the effect of first delivery on urinary and anal incontinence 10 years after first childbirth in relation to mode of delivery and to assess the influence of subsequent deliveries and obstetrical events (Paper II).

3. estimate the risks of stress urinary incontinence and pelvic organ prolapse surgery related to vaginal birth or cesarean delivery at long-term follow-up (Paper III).

4. evaluate the risks of surgically managed stress urinary incontinence and pelvic organ prolapse in relation to age at first childbirth and delivery mode (Paper IV).
3 PATIENTS

Ethical approval from the Research Ethics Committee at Karolinska Institutet was obtained prior to initiation of all studies (ethical permit numbers 02-301 Paper I, 04-754/1 Paper II, 2005/450-31/3 Paper III and IV). All patients and controls gave their informed consent to participate in the clinical studies after receiving written information (Paper I and II). In Paper III and IV, the analyses were performed deidentified on a statistical group level and no specific patients could be identified.

3.1 PAPER I

The study population comprised consecutive women either scheduled for elective cesarean delivery or vaginal birth, between January 2003 and June 2005 at Danderyd Hospital, Stockholm, Sweden. 545 women fulfilled the inclusion criteria and agreed to participate in the study. Inclusion criteria included healthy women with first time delivery, singleton fetus, 37-42 completed gestational weeks, BMI< 30 at start of pregnancy, non-smoking and fluent in the Swedish language. Sixty women underwent emergency cesarean delivery after trial of labor and were excluded from the study, 50 women were excluded from the study due to maternal complications or lack of data, leaving 435 subjects (80%) available for follow-up. The elective cesarean delivery cohort had a significantly higher maternal age, lower infant birth weight, and lower gestational week compared to the vaginal delivery cohort but there were no significant differences in pretrial lower urinary tract symptoms.

3.2 PAPER II

Patients in a vaginal cohort were prospectively recruited at the Department of Obstetrics and Gynecology, Danderyd Hospital between April and June 1995. The cohort consisted of 309 consecutive women giving birth to their first child by vaginal delivery. Using hospital inpatient records, we identified a control group of 422 consecutive women giving birth to their first child by cesarean delivery between September 1994 and December 1995. Final analysis was restricted to women giving vaginal birth to their first child and with all subsequent deliveries performed vaginally without forceps or vacuum extraction, and women with the first and all subsequent deliveries performed by cesarean delivery. Mean age at time of the study was 41.5 years (±4.0 SD) in the CD group compared with 39.9 years (±4.6 SD) in the vaginal delivery group (NS). Median parity was two (range 1-4) for both groups (NS).

3.3 PAPER III AND IV

From the Swedish Medical Birth Register, we included all women who gave birth to their first child by cesarean delivery from January 1973 through December 1982, and thereafter (if multiparous) only gave birth by cesarean delivery. To each woman in this cesarean delivery cohort we randomly selected two control women, individually matched by birth year of the mother, county and calendar time of birth to women with their first and all subsequent deliveries by vaginal delivery (if multiparous). Exclusion criteria implemented for both cohorts included: i) diagnosis of both vaginal and cesarean delivery (274); ii) multiple births (2,060); iii) if SUI or POP surgery preceded
or were performed in the same year as first birth (6); iv) death before December 31st of the year of the first birth (36); v) lack of control subjects after exclusion were performed (3,018). 30,880 women in the cesarean cohort and 60,122 women in the vaginal delivery cohort were eligible for analyses. Using individually unique national registration numbers, assigned to all Swedish residents at birth or immigration, we linked both cohorts to the nationwide Inpatient and Cause of Death Registers. Women contributed person-time to the study from the 1st of January the calendar year after the first delivery until the occurrence of SUI surgery, POP surgery, death or the end of the observation period (December 31st 2004).
4 METHODS

4.1 STUDY DESIGN

4.1.1 Paper I

*Prospective cohort study.*

The cohort study is a type of longitudinal, observational study where subjects are selected based on a common characteristic (= their exposure status). It is an analysis of risk factors and follows a group of people over time that do not have the disease at study entry until they develop an outcome of interest, and uses correlations to determine the absolute risk of subject contraction. Cohort studies can either be conducted prospectively or retrospectively from archived records. The cohort study is frequently contrasted with case-control studies, in which subjects with a specific medical condition (the cases) are compared with patients who do not have the condition but are otherwise similar (the controls), to identify factors that may contribute to the medical condition.

Paper I is a clinical cohort study with prospectively collected data based on self-reported questionnaires and medical charts. The exposure was defined as vaginal delivery and the unexposed cohort consisted of women having elective cesarean delivery at the same antenatal clinic.

4.1.2 Paper II

*Cross sectional comparative study.*

Cross-sectional studies form a class of research methods that involve observation of a population, or a representative subset of a population, at a defined time. They can be used to describe absolute and relative risks and to describe some features of the population, such as prevalence of an illness, or they may support inference of cause and effect.

Paper II is a cross-sectional comparative study based on a self-reported questionnaire on lower urinary tract and anorectal symptoms, administered 10 years after first delivery. A single cohort of women delivered by their first child in 1995 has previously been analyzed regarding the natural incidence of incontinence symptoms. To be able to compare the prevalence of urinary and anal incontinence 10 years after first delivery in a subgroup of those women delivered by vaginal birth and all subsequent deliveries performed vaginally, a control group was identified including women giving birth to their first child by cesarean delivery in 1995 and who had all subsequent deliveries performed by cesarean delivery. The outcomes were urinary and anal incontinence symptoms at 10 years after first delivery.

4.1.3 Paper III

*Register based cohort study*

Paper III is a nationwide cohort study based on data from the Swedish Medical Birth Register and the Swedish Inpatient Register to assess the risk of pelvic floor surgery in
relation to mode of delivery at long-term follow up. The exposure was defined as cesarean section and the exposed cohort included all women who delivered their first child by cesarean section between 1973 and 1983, and who thereafter only gave birth by cesarean section. To each patient in the cesarean section cohort were randomly selected two control women, who gave birth to their first child by delivery at the same inclusion period, with all subsequent deliveries performed vaginally. The cohorts were linked to the Inpatient Register, from which information were retrieved on the two main outcome measures, SUI and POP surgery up to 30 years after first delivery.

4.1.4 Paper IV

Paper IV is a nested cohort study, which focuses on the age-specific risks and rates for SUI and POP surgery after cesarean and vaginal delivery. A nested case control study is a variation of a case-control study wherein a number of controls are selected for each case from that case's matched risk set. In a nested cohort (or case control) study, confounder information available in the cohort data is often used to select controls that closely match cases. The advantages of nesting a case–control study in a cohort include efficiency, cost-effectiveness, high validity, and analytic flexibility. The present study was therefore based on age-dependent analyses of the above-mentioned cohorts.

All studies conform to the STROBE guidelines for reporting observational studies.

4.2 DATA SOURCES

4.2.1 Paper I

We used self-reported questionnaires and medical charts to collect data about the patients in order to compare lower urinary tract symptoms (LUTS) up to nine months after delivery in relation to mode of delivery. The first of three questionnaires were distributed to the participants before childbirth. The baseline questionnaire included questions on socio-demographic background, medical and surgical history, and questions on LUTS before pregnancy and during the preceding week. An identical questionnaire on LUTS was distributed to all subjects, three and nine months after delivery. Obstetrical variables including gestational age, infant birth weight, perineal tears, instrumental delivery, induction of labor, and maternal weight were retrieved from the hospital obstetrical charts. Perineal tears were classified according to the International Classification of Disease (ICD) 10th revisions nomenclature.117

In compliance with the definitions set forth by the International Continence Society, SUI was defined by the question “Have you experienced involuntary loss of urine during physical exertion during the last week?” whereas urge urinary incontinence was defined by the question “Do you experience sudden desires to void urine followed by urinary leakage?” Other questions included were: “Do you experience sudden desires to void?”, “Do you use protective pads due to urinary leakage?”, “How many times do you go to the toilet to urinate in a day?”, “How many times do you go to the toilet to urinate in a night?” Symptoms were graded on an ordinal scale: ”no”, “less than once per week”, “more than once per week” and “daily” For the purpose of this study, a response of less than once per week” was considered mild symptoms, whereas “more than once per week” and “daily” were considered moderate to severe symptoms.
The questionnaire on LUTS (Appendix) has previously been used by our research team and has been found reliable, and sensitive to change.

4.2.2 Paper II

In this study all women received an identical self-administered questionnaire on lower urinary tract and anorectal symptoms 10 years after first delivery (Appendix). Questions from the validated Cleveland Clinic Incontinence Score\textsuperscript{118} was used for anal incontinence symptoms. The CCIS is based on the sum of different parameters which are scored on a scale from 0 (=absent) to 4 (daily), determining the frequency of; incontinence of gas, liquid or solid stool and the need to wear protective pads. A score of 0 means perfect control, a score of 20 means complete incontinence. Questions on urinary incontinence symptoms were modeled from the CCIS, using an identical ordinal frequency scale including the questions: “Do you experience sudden urges to void urine that are difficult to hold back?”, “Do you experience sudden desires to void urine followed by involuntary loss of urine?” , “Do you experience involuntary loss of urine at physical activities?” , “Do you experience bladder emptying difficulties?”, “Do you need to use protective pads because of urinary incontinence” A response of “less than once per week” were considered mild symptoms, whereas response alternatives “more than once per week” and “daily” were considered moderate to severe symptoms for both urinary and anal incontinence symptoms. Questions on general medical history, obstetrical history, and subsequent deliveries were added to the questionnaire.

4.2.3 Paper III and IV

Study III and IV are based on cohorts from national registries. The exposed (cesarean delivery) and unexposed (vaginal delivery) cohorts were identified in the Swedish Medical Birth Register (MBR). The nationwide Swedish MBR, kept by the National Board of Health and Welfare, contains prenatal, obstetrical, and neonatal data from almost 99 percent of all women giving birth in Swedish hospitals from 1973 and thereafter.\textsuperscript{119} Using individually unique national registration numbers, assigned to all Swedish residents at birth or immigration, we linked both cohorts to the nationwide Inpatient and Cause of Death Registers. The Swedish Inpatient Register contains data for individual hospital discharges. The register was established in 1964 and covered in 1973 more than 60% of the population, in 1983 coverage was 85%, and from 1987 complete national coverage was achieved. Every inpatient discharge record contains: (1) dates of hospital admission and discharge; (2) up to eight discharge diagnoses, coded according to the International Classification of Diseases (ICD-8 from 1973 to 1986, ICD-9 from 1987 to 1996, and ICD-10 thereafter); and (3) up to 12 operation codes from the Swedish Classification of Operations and Major Procedures. Correct coding for surgical procedures is achieved in 98% of records in the register, with a less than 1% yearly loss to registration (when cross checked with hospital charts).\textsuperscript{120} From the Inpatient Register we identified all women in the vaginal delivery and cesarean cohorts having had SUI or POP surgery. Women contributed person-time to the study from the 1\textsuperscript{st} of January the calendar year after their first delivery until the first occurrence of SUI surgery, POP surgery, death, or the end of the observation period (December 31, 2004).
We used codes from the Swedish Classification of Operations and Major Procedures for 1973-1996 and 1997-2005 to identify SUI and POP surgery in the Swedish Inpatient Register. Surgical procedures for SUI included: Kelly sutures, Kennedy sutures, abdominal and laparoscopic Burch colposuspensions, Stamey procedures, Ingelman-Sundberg plasty, intravaginal slingplasty, suburethral slings, and tension-free vaginal tapes (operation codes 6355, 6356, 6358, 7470, 7471 for 1973-1996, and LEG00, LEG10, LEG20, LEG96 and KDG10-40 for 1997-2004). POP surgery was categorized as: anterior repair, posterior repair, Manchester procedure, abdominal sacrocolpopexy, vaginal sacrospinous fixation, abdominal and vaginal enterocele obliteration, colpocleisis and hysterectomy (operation codes 4840, 4841, 4844, 4935, 7120, 7121, 7460-7464, 7466, 7469 and 1 7541 for 1973-1996 and LEF00, LEF03, LEF10-50, LEF53, LEF96, LFE20, JHB 40, JHB96, JFJ00, JGC00, JGC01 for 1997-2004). We retrieved information on potential confounders and effect modifiers including: age at first and last birth, parity, pre-gestational and gestational diabetes, instrumental delivery, gestational age and infant’s weight and head circumference at birth from the MBR. From the Swedish Inpatient Register, we derived time to surgery, and from the Cause of Death Register, we obtained information on deaths occurring before the end of the observational period.

**Figure 10.** Schematic view of record linkage of Swedish health care registers used in Paper III and Paper IV.
5 STATISTICAL ANALYSES

5.1 PAPER I

All statistical analyses were restricted to women delivered by either elective cesarean section or by vaginal birth. Women planned for vaginal birth but eventually delivered by cesarean section after trial of labor were excluded from analyses (per protocol). A pretrial power calculation determined that a sample of at least 150 subjects in each arm was necessary to demonstrate a 20% increase in prevalence of SUI symptom with \( \alpha < 0.05 \) and \( \beta = 0.8 \) based on the assumption that the prevalence of SUI is about 10% in premenopausal women. The Mann–Whitney \( U \) test for inter-cohort comparisons and the Wilcoxon signed rank test for intra-cohort were used for comparisons on non-parametric ordinal and continuous numerical data. Variables showing statistical significance at univariate regression were tested in a stepwise multivariate regression model to assess the interaction of co-variables on the risk of LUTS. Selection of co-variables tried in the multivariate model was based on factors associated with urinary incontinence in existing literature including: maternal weight, maternal age, instrumental delivery, perineal laceration infant birth weight, and level of education. Level of education was classified as: compulsory school, high school, or college-university education. Relative risks (RRs) were estimated with 95% confidence intervals (CIs). A \( p \) value <0.05 was considered significant for all analyses. Statistical analyses were performed using STATISTICA software (StatSoft Inc, Tulsa, OK).

5.2 PAPER II

The final analyses were restricted to either women with the first and all subsequent deliveries performed vaginally without forceps or vacuum extractor or women with the first and all subsequent deliveries performed by cesarean section. A pretrial power calculation determined that a sample of at least 200 subjects in each arm was necessary to detect a 10-30% increase in SUI with \( \alpha < 0.05 \) and \( \beta = 0.8 \), calculated on the assumption that the prevalence of SUI is about 10% in premenopausal women. Mann–Whitney \( U \) test was used to compare ordinal and continuous numerical data between the independent samples. A multivariate logistic regression analysis was used to evaluate the association between symptoms of urinary and anal incontinence 10 years after index delivery and covariates: delivery mode, age at first delivery, number of deliveries, and anal sphincter injury (in the vaginal delivery group). The multivariate analysis also included an interaction analysis between symptoms of anal and urinary incontinence. Odds ratios (ORs) were estimated with 95% CIs. A \( p \) value <0.05 was considered significant for all analyses. Statistical analysis was performed using STATISTICA software (Statsoft Inc, Tulsa, OK).

5.3 PAPER III

Crude and parity-specific incidence rates for SUI and POP surgery were calculated as the number of events per 10,000 person years with 95% CIs based on the Poisson distribution. The risks of SUI and POP surgery related to delivery mode and parity was estimated using Cox proportional-hazards models, adjusted for maternal age and obstetrical covariates. Only first surgery for either prolapse or incontinence was
included in the analysis after which patients were censored if secondary procedures were performed. Parity was categorized as one, two, or three and more childbirths and maternal age at first delivery was categorized in 5-year bands. Possible confounders and effect modifiers were dichotomized (yes/no) in ever given birth to a child with: a birth weight $\geq 4$ kg; head circumference $\geq 38$ cm; gestational week $\geq 40$ pregnancy; or ever having a recording of pre-gestational or gestational diabetes. Effect modification of variables was evaluated by type 3-test prior to being entered in the Cox proportional hazard model. The results of the different Cox’s regression hazard models are presented as hazard ratios (HRs) with 95% CIs. To address potential confounding of instrumental vaginal delivery, sub-analyses were performed with risk estimates for women ever delivered by vacuum extraction or forceps presented separately. Parity-specific risks were estimated through stratification. Effects of delivery mode in relation to time from first delivery until pelvic floor surgery are presented as incidence rates. As a secondary outcome measure we calculated the number needed to harm (NNH). NNH is an epidemiological measure that estimates how many patients need to be exposed to a specific risk factor during a time period to cause harm in one patient that would not otherwise have been harmed during that period. Statistical analyses were undertaken with SAS software (version 9.1; Cary, NC, USA) and performed by the principal investigator in cooperation with a biostatistician.

5.4 PAPER IV

Crude and age-specific incidence rates for SUI and POP surgery were calculated separately as the number of events per 10,000 person years with 95% CIs based on the Poisson distribution. The risks of SUI surgery or POP surgery related to delivery mode and age at first delivery was estimated with Cox’s proportional-hazards model, adjusted for obstetrical parameters and age. Age-specific HRs were estimated through stratification in 5-year bands, as well as, for further analyses, dichotomized in 29 years and younger versus 30 years and older when giving birth to their first child. Parity as well as other possible confounders and effect modifiers were categorized or dichotomized in the same way as in study III. Effect modification of variables was evaluated by type 3-test prior to being entered in the Cox proportional hazard model. Age at last delivery showed neither effect modification of clinical interest, nor confounding of the results and was thereby not included in the final model. To address potential confounding of instrumental vaginal delivery, subgroup analyses were performed with exclusion of women ever delivered by vacuum extraction or forceps delivery. Statistical analyses were undertaken with SAS software (version 9.1; Cary, NC, USA) and performed by the principal investigator in cooperation with a biostatistician.
6 RESULTS

6.1 PAPER I

6.1.1 Subject characteristics

After exclusion, a total of 220 subjects delivered by elective cesarean section and 215 subjects delivered by vaginal birth were eligible for analyses. Following childbirth, the second questionnaire was completed by 389 of 435 subjects (89%) and the third questionnaire by 376 of 435 subjects (86%).

Indications for elective cesarean delivery were breech presentation (49%) or patient request (51%). In the vaginal cohort, the prevalence for perineal rupture grade I-II was 75%; grade III 13% whereas none experienced grade IV sphincter rupture. The cesarean delivery cohort had a significantly higher maternal age, lower fetal birth weight and lower gestational week when compared to the vaginal delivery cohort but there were no significant differences in pretrial LUTS. Detailed cohort characteristics are presented in Table 4.

Table 4. Cohort characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Vaginal birth</th>
<th>Cesarean section</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 215</td>
<td>n = 220</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>30.4 year (±3.6)</td>
<td>32.6 year (±4.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Maternal weight</td>
<td>64.1 kg (±9.7)</td>
<td>64.3 kg (±10.1)</td>
<td>0.79</td>
</tr>
<tr>
<td>Infant weight</td>
<td>3,605 gr (±424)</td>
<td>3,353 gr (±418)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>College education</td>
<td>142 (66)</td>
<td>131 (60)</td>
<td>0.16</td>
</tr>
<tr>
<td>Gestational week</td>
<td>40.0 (±1.1)</td>
<td>38.2 (±0.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Instrumental delivery</td>
<td>42 (20)</td>
<td>0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Urgency</td>
<td>13 (6)</td>
<td>16 (7)</td>
<td>0.54</td>
</tr>
<tr>
<td>UUI</td>
<td>4 (2)</td>
<td>5 (2)</td>
<td>0.71</td>
</tr>
<tr>
<td>SUI</td>
<td>17 (8)</td>
<td>17 (8)</td>
<td>0.92</td>
</tr>
<tr>
<td>Pads</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>0.99</td>
</tr>
<tr>
<td>Daytime micturition</td>
<td>4.5 t/d (±1.8)</td>
<td>4.3 t/d (±1.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Nighttime micturition</td>
<td>0.2 t/n (±0.5)</td>
<td>0.3 t/n (±0.5)</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Figures are mean± standard deviation or number of subjects (%). Statistical comparison using Mann-Whitney U-test.
SUI = stress urinary incontinence, symptoms ≤1/w to daily at baseline.
UUI= urgency urinary incontinence, symptoms ≤1/w to daily at baseline.

6.1.2 Prevalence of lower urinary tract symptoms

In the vaginal delivery cohort, the prevalence of all LUTS increased significantly at three and nine months follow-up compared to baseline (Table 5). There was no significant difference in the prevalence of SUI symptoms (or any other LUTS) when
Table 5. Prevalence of lower urinary tract symptoms at 9 months follow-up compared to baseline.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months follow-up</th>
<th>9 months follow-up</th>
<th>Pᵃ</th>
<th>Pᵇ Vag</th>
<th>Pᵇ Ces</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaginal</td>
<td>Cesarean</td>
<td>Vaginal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n=215</td>
<td>n=220</td>
<td>n=197</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cesarean</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n=190</td>
<td>n=186</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>178 (83)</td>
<td>172 (80)</td>
<td>176 (82)</td>
<td>164 (76)</td>
<td>172 (78)</td>
<td>0.045</td>
</tr>
<tr>
<td>&lt;1/week</td>
<td>8 (4)</td>
<td>11 (5)</td>
<td>10 (5)</td>
<td>5 (2)</td>
<td>11 (5)</td>
<td>9 (4)</td>
</tr>
<tr>
<td>&gt;1/week</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td>6 (3)</td>
<td>1 (1)</td>
<td>11 (5)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Daily</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>3 (1)</td>
<td>0 (0)</td>
<td>4 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>UUI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>189 (88)</td>
<td>183 (83)</td>
<td>187 (87)</td>
<td>186 (85)</td>
<td>176 (82)</td>
<td>176 (80)</td>
</tr>
<tr>
<td>&lt;1/week</td>
<td>4 (2)</td>
<td>5 (2)</td>
<td>6 (3)</td>
<td>4 (2)</td>
<td>10 (5)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>&gt;1/week</td>
<td>0 (-)</td>
<td>0 (-)</td>
<td>1 (1)</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Daily</td>
<td>0 (-)</td>
<td>0 (-)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>SUI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>177 (82)</td>
<td>171 (78)</td>
<td>155 (72)</td>
<td>184 (84)</td>
<td>160 (74)</td>
<td>176 (80)</td>
</tr>
<tr>
<td>&lt;1/week</td>
<td>17 (8)</td>
<td>17 (8)</td>
<td>32 (15)</td>
<td>7 (3)</td>
<td>21 (10)</td>
<td>9 (4)</td>
</tr>
<tr>
<td>&gt;1/week</td>
<td>0 (-)</td>
<td>0 (-)</td>
<td>7 (3)</td>
<td>1 (1)</td>
<td>7 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Daily</td>
<td>0 (-)</td>
<td>0 (-)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Use of pads</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>193 (90)</td>
<td>187 (85)</td>
<td>188 (87)</td>
<td>191 (87)</td>
<td>184 (86)</td>
<td>185 (84)</td>
</tr>
<tr>
<td>&lt;1/week</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>2 (1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>&gt;1/week</td>
<td>0 (-)</td>
<td>0 (-)</td>
<td>7 (3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Daily</td>
<td>0 (-)</td>
<td>0 (-)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nighttime micturition</td>
<td>0.2/t/n</td>
<td>0.3/t/n</td>
<td>0.6/t/n</td>
<td>0.6/t/n</td>
<td>0.5/t/n</td>
<td>0.4/t/n</td>
</tr>
</tbody>
</table>

Pᵃ P-value between groups comparing prevalence of symptoms at baseline with 9 months follow-up using Mann-Whitney test for independent samples.
Pᵇ P-value within groups comparing prevalence of symptoms at baseline with 9 months follow-up using Wilcoxon matched pairs test.
SUI denotes stress urinary incontinence. UUI denotes urgency urinary incontinence.
Figures are number of subjects (%). Numbers not adding up to 100 percent indicate missing values.
comparing women delivered by instrumental delivery and women with unassisted natural birth. In the cesarean delivery cohort, the prevalence of SUI changed significantly at three months ($p=0.03$) but did not remain significantly changed at nine months ($p=0.10$) follow-up when compared to baseline. There were no other significant changes in LUTS at three and nine months follow-up in relation to symptoms at baseline.

When comparing the cesarean and vaginal delivery cohorts, there was a significantly increased prevalence of SUI in women after vaginal delivery both at three ($p<0.001$) and nine months ($p=0.001$) follow-up, as well of urinary urgency at nine months follow-up ($p=0.045$). Subjects with symptoms of SUI at baseline had a significantly increased frequency of SUI at three ($p<0.001$) and nine months ($p<0.001$) follow-up after a vaginal delivery when compared to subjects with a cesarean delivery.

The incidence of new onset of SUI after delivery (for women who were continent prior to pregnancy) was significantly more frequent in the vaginal group at both three ($p=0.001$) and nine months ($p=0.005$) follow-up compared to the cesarean delivery group. 33/197 women experienced new onset of SUI after vaginal delivery compared to 4/192 women after cesarean delivery, which corresponds to 82.5% (VD) vs. 50% (CD) of the total number of women with symptoms at three months in each delivery group.

**Figure 11.** Incidence of stress urinary incontinence after delivery (%), in women continent prior to pregnancy.

6.1.3 Risk of lower urinary tract symptoms

Nine months after first childbirth, vaginal delivery was the only statistically significant obstetrical predictor for SUI (RR 8.9, 95%CI 1.9-42) as well as for urinary urgency (RR 7.3, 95%CI 1.7-32) at multivariate risk analysis (Table 6). We found no association between other obstetrical covariates and a subsequent risk of lower urinary tract dysfunction. Regarding non-obstetrical covariates, we found that symptoms of either: SUI, urge urinary incontinence or urinary urgency at three months were independently associated to an increased risk of enduring symptoms at nine month follow-up, with the strongest association for SUI (RR_{VD} 6.2, 95%CI 2.2-18).

Subjects with late pregnancy symptoms of SUI were at decreased risk of aggravated SUI symptoms at nine months follow-up if delivered by elective cesarean delivery (RR 0.3 95% CI 0.1-0.9) when compared to women with antenatal symptoms and
subsequent spontaneous vaginal birth. Further analysis with information of breastfeeding added to the final model did not alter the conclusions.

Table 6. Predictors for urinary incontinence at nine months follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Stress urinary incontinence</th>
<th>Urge urinary incontinence</th>
<th>Urinary urgency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
<td>RR</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>1.0</td>
<td>Ref</td>
<td>1.0</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>8.9</td>
<td>1.9 – 42</td>
<td>4.1</td>
</tr>
<tr>
<td>Instrumental delivery</td>
<td>0.7</td>
<td>0.2 – 2.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Fetal birth weight*</td>
<td>2.1</td>
<td>0.7 – 5.8</td>
<td>3.2</td>
</tr>
<tr>
<td>Perineal tear (I-III)</td>
<td>0.7</td>
<td>0.3 – 1.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Symptoms at baseline</td>
<td>5.2</td>
<td>1.5 – 19</td>
<td>4.7</td>
</tr>
<tr>
<td>Symptoms at 3m FU</td>
<td>3.9</td>
<td>1.7 – 8.5</td>
<td>11</td>
</tr>
</tbody>
</table>

Multivariable logistic regression analysis adjusted for maternal age, maternal weight and level of education.
* Fetal birth weight >3.5 kg.

6.2 PAPER II

6.2.1 Subject characteristics

In the vaginal delivery group, 246 of 309 subjects (81%) responded to the questionnaire. Of the participating subjects, 232 of 246 women (94%) reported having had only vaginal deliveries, 29 subjects were excluded due to instrumental vaginal deliveries. Three subjects were excluded due to urinary incontinence surgery, leaving 200 women eligible for analyses. In the cesarean delivery group 270 of 422 subjects (64%) responded to the questionnaire, and 195 of 270 women (72%) reported having had only cesarean deliveries. No subjects reported incontinence surgery, leaving 195 women eligible for analyses.

Four subjects in both delivery groups reported conservative treatment of urinary incontinence (including physiotherapy and pelvic floor exercise) but none reported anticholinergic overactive bladder treatment. None of the subjects in either delivery group had undergone POP surgery 10 years after index delivery.

Mean age at the time of the study was 41.5 (±4.0) in the cesarean delivery group compared to 39.9 (±4.6) in the vaginal delivery group (NS). Median parity was two for both groups. In the vaginal delivery group, a cumulative prevalence of obstetrical perineal tears ICD grade I-II was reported by 86% of the patients, whereas grade III-IV anal sphincter injury was reported by 14%.
6.2.2 Prevalence of lower urinary tract and anorectal symptoms

There was a significantly increased frequency of SUI episodes ($p=0.01$) and an increased usage of protective pads ($p=0.04$) in the vaginal delivery group when compared to the cesarean delivery group. Regarding symptoms of urinary urgency or urge incontinence, there was no significant difference between the groups. When comparing anal incontinence symptoms, there was a significantly increased frequency of fecal urgency ($p=0.48$) but no significant differences in flatus or stool incontinence.

**Table 7.** Prevalence of severe stress and urge urinary incontinence with concurrent anal incontinence.

<table>
<thead>
<tr>
<th></th>
<th>Vaginal delivery group</th>
<th>Cesarean delivery group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>SUI</td>
<td>UUI</td>
</tr>
<tr>
<td>n= 24</td>
<td>%</td>
<td>n= 23</td>
</tr>
<tr>
<td>Anal urgency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>&lt;1/ week</td>
<td>4 (17)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>&gt;1/ week</td>
<td>0 (0)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Daily</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Gas incontinence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>&lt;1/ week</td>
<td>5 (21)</td>
<td>7 (30)</td>
</tr>
<tr>
<td>&gt;1/ week</td>
<td>7 (29)</td>
<td>5 (22)</td>
</tr>
<tr>
<td>Daily</td>
<td>2 (8)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Loose stool incontinence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>&lt;1/ week</td>
<td>3 (12)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>&gt;1/ week</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Daily</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Solid stool incontinence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>&lt;1/ week</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>&gt;1/ week</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Daily</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Severe stress and urge urinary incontinence defined as symptoms ≥ 1/ week or daily.
SUI denotes stress urinary incontinence. UUI denotes urge urinary incontinence.

Distributions of severe stress and urge urinary incontinence defined as symptoms one or more times per week or daily are presented in Table 7. The majority of patients with severe urinary incontinence symptoms also experienced flatus incontinence, independent of mode of delivery.
6.2.3 Risks of lower urinary tract and anorectal symptoms

In an adjusted multivariate analysis, vaginal delivery was associated with an increased risk of SUI ten years after index delivery (Table 8). Mode of delivery showed no other interactions at statistically significant levels with urinary or anal incontinence symptoms. A history of obstetrical anal sphincter tear at vaginal delivery was independently associated with an increased risk of gas incontinence. SUI was a significant predictor for an increased risk of concurrent gas and loose stool incontinence. Other covariates tried in the multivariate model, such as maternal age and number of deliveries showed no significant association with the development of urinary or anal incontinence symptoms.
Table 8. Multivariate analysis on interactions and risk factors for incontinence disorders.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Fecal urgency</th>
<th>Gas incontinence</th>
<th>Loose stool incontinence</th>
<th>Stress urinary incontinence</th>
<th>Urge urinary incontinence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>1.0 Reference</td>
<td>1.0 Reference</td>
<td>1.0 Reference</td>
<td>1.0 Reference</td>
<td>1.0 Reference</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>1.0 0.3-2.9</td>
<td>0.7 0.2-2.3</td>
<td>0.96 0.1-9.9</td>
<td>3.1 1.6-5.9</td>
<td>1.4 0.6-3.3</td>
</tr>
<tr>
<td>Age at first delivery</td>
<td>1.0 0.9-1.1</td>
<td>1.0 0.8-1.2</td>
<td>1.0 0.9-1.2</td>
<td>1.2 0.9-1.1</td>
<td>1.1 0.9-1.2</td>
</tr>
<tr>
<td>Number of deliveries</td>
<td>0.9 0.5-1.9</td>
<td>0.6 0.2-1.7</td>
<td>1.0 0.8-1.2</td>
<td>1.1 0.7-1.8</td>
<td>0.7 0.5-1.4</td>
</tr>
<tr>
<td>History of sphincter injury</td>
<td>1.2 0.5-3.4</td>
<td>3.9 1.5-9.9</td>
<td>3.2 0.8-13.0</td>
<td>0.9 0.4-2.2</td>
<td>0.6 0.2-2.1</td>
</tr>
<tr>
<td>Stress urinary incontinence</td>
<td>1.1 0.7-1.7</td>
<td>2.1 1.3-3.3</td>
<td>2.6 1.3-5.0</td>
<td>- -</td>
<td>0.5 0.2-1.0</td>
</tr>
<tr>
<td>Urge urinary incontinence</td>
<td>1.3 0.8-2.0</td>
<td>1.6 1.0-2.4</td>
<td>1.4 0.8-2.6</td>
<td>7.3 3.3-16</td>
<td>- -</td>
</tr>
</tbody>
</table>

OR = odds ratio, CI = confidence interval.
6.3 PAPER III

6.3.1 Subject characteristics

Mean follow-up time was 26.9 years in the cesarean cohort and 25.9 years in the vaginal cohort. In the cesarean cohort (n= 30,880), 194 cases (0.6%) of SUI or POP surgery were observed. In the vaginal cohort (n= 60,122), the corresponding figure was 2,029 cases (3.4%). Table 9 shows the cohort characteristics.

Table 9. Cohort characteristics with number of events for obstetrical parameters.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Vaginal delivery cohort n= 60,122</th>
<th>Cesarean delivery cohort n= 30,880</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons with SUI surgery, No. (%)</td>
<td>723 (1.2%)</td>
<td>136 (0.4%)</td>
</tr>
<tr>
<td>Persons with POP surgery, No. (%)</td>
<td>1,306 (2.2%)</td>
<td>58 (0.2%)</td>
</tr>
<tr>
<td>Parity, mean (SD)</td>
<td>2.1 (± 1.0)</td>
<td>1.8 (± 0.9)</td>
</tr>
<tr>
<td>Diabetes diagnosis, No. (%)</td>
<td>330 (0.6%)</td>
<td>862 (2.8%)</td>
</tr>
<tr>
<td>Instrumental vaginal delivery, No. (%)</td>
<td>8,622 (14.3%)</td>
<td>*</td>
</tr>
<tr>
<td>Fetal birth weight ≥ 4 kg, No. (%)</td>
<td>16,194 (26.9%)</td>
<td>5,492 (17.8%)</td>
</tr>
<tr>
<td>Head circumference ≥ 38 cm, No. (%)</td>
<td>3,165 (5.3%)</td>
<td>2,108 (6.8%)</td>
</tr>
</tbody>
</table>

SUI denotes Stress Urinary Incontinence
POP denotes Pelvic Organ Prolapse
No. = number of events, refers to any occurrence during the first or subsequent pregnancies.
*No cases available for analysis.

6.3.2 Rates of stress urinary incontinence and pelvic organ prolapse surgery

Crude absolute incidence rates of surgery after cesarean delivery were 1.7 and 0.7 per 10,000 person-years for SUI and POP, respectively, while for vaginal delivery, the corresponding incidence rates were 4.5 and 8.1 per 10,000 person-years, respectively. Table 10 shows the incidence rates for SUI and POP surgery in relation to mode of delivery and number of childbirths. Among women only having had vaginal deliveries, rates of SUI and POP surgery increased with number of childbirths. On the contrary, in the cesarean delivery cohort, rates of both SUI and POP surgery slightly decreased with increasing parity number. The overall number needed to harm was 357 for SUI and 135 for POP surgery; i.e. if 357 and 135 women respectively are exposed to vaginal delivery, one will develop surgically managed SUI or POP that they would not have if delivered by cesarean section.
**Table 10.** Incidence rates per 10,000 person-years for SUI and POP Surgery in relation to mode of delivery and number of childbirths.

### Stress Urinary Incontinence Surgery

<table>
<thead>
<tr>
<th>Parity</th>
<th>1</th>
<th>2</th>
<th>≥3</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of events</td>
<td>Rate (95% CI)</td>
<td>No. of events</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>172/15,140</td>
<td>4.2 (3.6-4.9)</td>
<td>333/27,936</td>
<td>4.4 (4.0-4.9)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>61/12,807</td>
<td>1.9 (1.4-2.4)</td>
<td>59/12,115</td>
<td>1.9 (1.4-2.4)</td>
</tr>
<tr>
<td>Total</td>
<td>233/27,947</td>
<td>3.2 (2.8-3.6)</td>
<td>392/40,051</td>
<td>3.7 (3.3-4.0)</td>
</tr>
</tbody>
</table>

### Pelvic Organ Prolapse Surgery

<table>
<thead>
<tr>
<th>Parity</th>
<th>1</th>
<th>2</th>
<th>≥3</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of events</td>
<td>Rate (95% CI)</td>
<td>No. of events</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>311/15,140</td>
<td>7.6 (6.8-8.5)</td>
<td>614/27,936</td>
<td>8.1 (7.5-8.8)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>29/12,807</td>
<td>0.9 (0.6-1.3)</td>
<td>24/12,115</td>
<td>0.8 (0.5-1.1)</td>
</tr>
<tr>
<td>Total</td>
<td>340/27,947</td>
<td>4.6 (4.2-5.1)</td>
<td>638/40,051</td>
<td>6.0 (5.5-6.4)</td>
</tr>
</tbody>
</table>

Rate refers to incidence rates per 10,000 person-years with 95% Confidence Intervals.
Table 11. Hazard ratios for SUI and POP surgery in relation to mode of delivery and number of childbirths.

<table>
<thead>
<tr>
<th></th>
<th>Parity</th>
<th>1</th>
<th>2</th>
<th>≥3</th>
<th>Overall†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Stress Urinary Incontinence Surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td></td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Vaginal deliverycrude</td>
<td></td>
<td>2.1 (1.6-3.0)</td>
<td>2.5 (1.8-3.4)</td>
<td>4.5 (2.6-7.9)</td>
<td>2.7 (2.2-3.2)††</td>
</tr>
<tr>
<td>Vaginal deliveryadjusted*</td>
<td></td>
<td>2.5 (1.7-3.5)</td>
<td>2.8 (2.0-3.9)</td>
<td>4.9 (2.7-8.6)</td>
<td>2.9 (2.4-3.6)</td>
</tr>
<tr>
<td>Pelvic Organ Prolapse Surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td></td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Vaginal del_{crude}</td>
<td></td>
<td>7.6 (5.0-11.3)</td>
<td>9.0 (5.9-13.8)</td>
<td>20.7 (8.4-51.1)</td>
<td>10.1 (7.7-13.2)††</td>
</tr>
<tr>
<td>Vaginal del_{adjusted}*:</td>
<td></td>
<td>7.7 (5.1-11.6)</td>
<td>8.7 (5.7-13.4)</td>
<td>19.8 (8.0-49.3)</td>
<td>9.2 (7.0-12.1)</td>
</tr>
</tbody>
</table>

*Adjusted for age (in 5-year bands), diabetes at pregnancy, head circumference ≥ 38 cm, gestational length ≥ 40 weeks, and infant birth weight ≥ 4 kg.
† Overall hazard ratios adjusted for variables above and childbirth category.
††Unadjusted overall Hazard Ratios.
6.3.3 Risks of stress urinary incontinence and pelvic organ prolapse surgery

Table 11 presents the crude and adjusted HRs for SUI and POP surgery in relation to mode of delivery. Compared to the cesarean cohort, the unadjusted HR for SUI surgery among women with vaginal deliveries increased from 2.1 (95% CI 1.6-3.0), after the first child to 4.5 (95% CI 2.6-7.9) in women with three or more deliveries. The corresponding unadjusted HRs for POP surgery was 7.6 (95% CI 5.0-11.3) after the first vaginal delivery and 20.7 (95% CI 8.4-51.1) after three vaginal deliveries or more. After adjusting for maternal age and obstetric covariates, the risk estimates turned even stronger for SUI surgery, but stayed largely unaffected for POP surgery.

HRs for SUI and POP surgery in relation to vacuum extraction or forceps delivery are presented in Table 12. Compared to a cesarean delivery, the risk of SUI was more than doubled (HR 2.4, 95%CI 1.7-3.3) for vaginal delivery with vacuum extraction and tripled (HR 3.1, 95%CI 2.5-3.8) for a vaginal non-instrumental delivery. The lower risks of a vacuum extraction delivery could in part be explained by an overall lower birth rate among women with a vacuum extraction compared to women with no instrumental delivery (mean birth rates were 2.0 and 2.2, respectively). Compared to a cesarean delivery, the risks of POP surgery was nine-fold increased both after non-instrumental vaginal delivery and after vacuum extraction delivery, while a 20-fold increase in risk was observed among women with forceps delivery.

Table 12. Hazard Ratios for SUI and POP surgery in relation to delivery mode and exposure to instrumental vaginal delivery.

<table>
<thead>
<tr>
<th></th>
<th>SUI Surgery</th>
<th>POP Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events (%)</td>
<td>HR* (95%CI)</td>
</tr>
<tr>
<td><strong>CD (n = 30,880)</strong></td>
<td>136 (0.4)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td><strong>VD- no instrument (n = 51,500)</strong></td>
<td>638 (1.2)</td>
<td>3.1 (2.5-3.8)</td>
</tr>
<tr>
<td><strong>VD- vacuum ext (n = 8335)</strong></td>
<td>84 (1.0)</td>
<td>2.4 (1.7-3.3)</td>
</tr>
<tr>
<td><strong>VD- forceps (n = 287)</strong></td>
<td>1 (0.3)</td>
<td>**</td>
</tr>
</tbody>
</table>

CD denotes cesarean delivery
VD denotes vaginal delivery
*Hazard ratios adjusted for age, diabetes at pregnancy entry, head circumference≥38cm, gestational length≥40 weeks, infant birth weight≥4kg and parity
**Analysis not permissible due to insufficient numbers
Events refers to number of events of any occurrence during the first or subsequent deliveries.

Figures 12a and 12b show the incidence rates for SUI and POP surgery in relation to mode of delivery and time elapsed from first childbirth. After vaginal delivery the incidence rates for both SUI and POP surgery steadily increased, reaching their peaks close to three decades after first delivery, at 9 and 27 cases per 10,000 person-years.
**Figure 12a.** Stress urinary incontinence surgery in relation to mode of delivery and time from first childbirth.

![Graph showing stress urinary incontinence surgery](image)

**Figure 12b.** Pelvic organ prolapse surgery in relation to mode of delivery and time from first childbirth.

![Graph showing pelvic organ prolapse surgery](image)
respectively. For cesarean delivery, the incidence rate for SUI surgery increased more slowly and started to diverge from the curve for vaginal delivery very early during follow-up. For POP surgery, however, the incidence rate in women with cesarean deliveries showed very little variation over time, starting to diverge more notably from the vaginal delivery cohort 10 years after first birth, remaining around 1-2 cases per 10,000 person-years throughout the observational period.

6.4 PAPER IV

6.4.1 Subject characteristics

Cohort characteristics are presented in Table 13. Mean age at last delivery did not differ between the cohorts, nor did time from last childbirth to POP surgery. Time from last birth to SUI surgery was, however, almost three years shorter in the vaginal birth cohort. These women were also three years younger at the time of stress urinary surgery compared to women who had SUI surgery in the cesarean cohort.

Table 13. Cohort characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Vaginal birth cohort</th>
<th>Cesarean delivery cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons included in analysis, No.</td>
<td>59,585</td>
<td>30,880</td>
</tr>
<tr>
<td>Parity, mean (SD)</td>
<td>2.1 (±1.0)</td>
<td>1.8 (±0.9)</td>
</tr>
<tr>
<td>Persons with SUI surgery, No. (rate*)</td>
<td>718 (4.5)</td>
<td>136 (1.7)</td>
</tr>
<tr>
<td>Persons with POP surgery, No. (rate*)</td>
<td>1,295 (8.1)</td>
<td>58 (0.7)</td>
</tr>
<tr>
<td>Age at first delivery, years (SD)</td>
<td>25.8 (±5.0)</td>
<td>27.1 (±5.6)</td>
</tr>
<tr>
<td>Age at last delivery, years (SD)</td>
<td>30.4 (±5.1)</td>
<td>30.6 (±5.4)</td>
</tr>
<tr>
<td>Time from last birth to SUI surgery, years (SD)</td>
<td>14.3 (±7.5)</td>
<td>17.1 (±6.3)</td>
</tr>
<tr>
<td>Time from last birth to POP surgery, years (SD)</td>
<td>15.8 (±8.0)</td>
<td>15.5 (±7.4)</td>
</tr>
<tr>
<td>Age at SUI surgery, years (SD)</td>
<td>46.3 (±7.5)</td>
<td>49.0 (±7.3)</td>
</tr>
<tr>
<td>Age at POP surgery, years (SD)</td>
<td>49.0 (±8.4)</td>
<td>47.9 (±8.6)</td>
</tr>
</tbody>
</table>

No denotes number of subjects
SD denotes Standard Deviation
Rate denotes incidence rates per 10,000 person-years
SUI denotes stress urinary incontinence
POP denotes pelvic organ prolapse

6.4.2 Risk and rates of stress urinary incontinence and pelvic organ prolapse surgery

Table 14 show incidence rates and hazard ratios in relation to delivery mode and age at first childbirth. For both delivery groups, the incidence rates of SUI surgery were higher in the older than in the younger age category. Women who were 30 years or
older at first vaginal birth experienced a clearly increased incidence rate for POP surgery (rate 13.9 95% CI 12.8-15.2) compared to younger women (rate 6.4 95% CI 6.0-6.8).

In the age category 13-29 years, women with vaginal childbirths had a threefold increased risks of SUI surgery compared to women delivered by cesarean (HR 3.0, 95% CI 2.3-4.0). Among women 30 years or older at first childbirth, corresponding risk for SUI surgery was more than doubled among vaginally delivered women (HR 2.4, 95% CI 1.8-3.4). For POP, the risk of having surgery after vaginal childbirth was more than seven times that of cesarean delivery among women 13-29 years (HR 7.4, 95% CI 5.2-10.5) and among women aged 30 or older the risk was eleven times increased (HR 11.0, 95% CI 7.1-16.9) after vaginal birth. When we excluded women with vaginal instrumental deliveries, the age categorized risk estimates for incontinence and prolapse surgery among vaginally delivered women were not substantially changed (data not shown).

**Table 14.** Incidence rates and hazard ratios in relation to delivery mode and age at first childbirth.

<table>
<thead>
<tr>
<th></th>
<th>Stress urinary incontinence surgery</th>
<th>Pelvic organ prolapse surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age category 13 – 29 years</td>
<td>≥ 30 years</td>
</tr>
<tr>
<td></td>
<td>Rate* 95%CI HR 95%CI</td>
<td>Rate* (95%CI) HR (95%CI)</td>
</tr>
<tr>
<td>C-section</td>
<td>1.4 1.1-1.7 1.0 (ref)</td>
<td>2.4 1.9-3.1 1.0 (ref)</td>
</tr>
<tr>
<td>Vaginalcrude</td>
<td>4.0 3.6-4.4 3.0 2.3-3.9</td>
<td>6.1 5.4-7.0 2.4 1.8-3.3</td>
</tr>
<tr>
<td>Vaginaladjust**</td>
<td>– 3.0 2.3-4.0</td>
<td>– 2.4 1.8-3.4</td>
</tr>
</tbody>
</table>

---

*Incidence rates per 10,000 person-years with 95% confidence intervals.

**HRs adjusted for parity (1, 2, ≥3), diabetes at pregnancy entry, head circumference ≥ 38cm, gestational length ≥40w and infant birth weight ≥4kg.

Analyses of SUI and POP surgery stratified by age at first childbirth are shown in Table 15. Compared with cesarean delivery, vaginal delivery among women below 35 years was associated with at least a three-fold increased risk of SUI surgery. For POP surgery, there was an even stronger effect of vaginal delivery, and a markedly increased risk was especially obtained among women aged 30-34 years (HR 18.1 95%CI 9.1-35.6) and 35-38 years (HR 15.9 95%CI 7.1-35.4) at first childbirth.
Table 15. Hazard ratios for SUI and POP surgery in relation to age at first childbirth and delivery mode.

### Stress Urinary Incontinence Surgery

<table>
<thead>
<tr>
<th>Age category</th>
<th>19</th>
<th>20-24</th>
<th>25-29</th>
<th>30-34</th>
<th>35-38</th>
<th>≥ 39</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean section</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Vaginal del crude</td>
<td>3.6 (1.3-9.4)</td>
<td>2.9 (1.9-4.6)</td>
<td>3.2 (2.2-4.6)</td>
<td>3.4 (2.2-5.2)</td>
<td>1.4 (0.8-2.5)</td>
<td>2.6 (0.6-10.2)</td>
<td>2.7 (2.2-3.2)</td>
</tr>
<tr>
<td>Vaginal del adjusted*</td>
<td>3.6 (1.3-9.6)</td>
<td>3.0 (1.9-4.7)</td>
<td>3.2 (2.2-4.7)</td>
<td>3.3 (2.1-5.2)</td>
<td>1.5 (0.8-2.7)</td>
<td>2.4 (0.6-9.8)</td>
<td>2.9 (2.3-3.5)**</td>
</tr>
</tbody>
</table>

*Adjusted for parity, diabetes at pregnancy entry, head circumference ≥ 38 cm, gestational length ≥ 40w and infant birth weight ≥ 4kg.

**Analysis adjusted for variables above including age category.

P-values for interactions: stress urinary incontinence 0.33 (crude), 0.29 (adjusted); pelvic organ prolapse 0.64 (crude), 0.69 (adjusted).
Using the youngest age category as reference, we also analyzed the interplay between age at first childbirth and mode of delivery with respect to risks of SUI (Figure 13a) and POP surgery (Figure 13b). In both the cesarean and the vaginally delivered cohort, risk estimates increased with age, with a more distinct increase for POP surgery in the vaginal delivery cohort. Among vaginally delivered women, women aged 35 to 38 years at first childbirth experienced a seven times increased risk to undergo POP surgery compared women younger than 20 years at first birth, and a more than doubled risk compared to women aged 25 to 29 years. The trend of increasing HRs in the cesarean delivery cohort need to be interpreted with caution due to statistically insignificant results in most age categories.
Figure 13a. HR with 95% CI for stress urinary incontinence surgery in relation to women aged 20 years or younger at first childbirth.

Figure 13b. HR with 95% CI for pelvic organ prolapse surgery in relation to women aged 20 years or younger at first childbirth.
7 DISCUSSION

7.1 STRESS URINARY INCONTINENCE AT SHORT TERM FOLLOW-UP

In Paper I, all aspects of lower urinary tract dysfunction (most notably symptoms of SUI) increased nine months after a vaginal delivery when compared to elective cesarean delivery. Thus, the main findings of this prospective controlled cohort study further substantiates the notion that vaginal delivery is associated with a significantly increased short-term risk of SUI when compared to elective cesarean delivery.\(^{42,114,124,125}\) When adjusting for obstetrical parameters, as well as, subject characteristics a vaginal delivery mode remained independently associated with an increased risk of SUI. Anal sphincter rupture, perineal tears or instrumental delivery used as a proxy for severe obstetric trauma to the pelvic floor did not correlate with the presence of urinary incontinence at nine months follow-up. This is in agreement with the results of prospective and cross-sectional studies with short term follow up.\(^{122,126}\) Both an increased risk,\(^{35}\) and decreased risk,\(^{107}\) of SUI after instrumental delivery has otherwise been reported from large retrospective studies.

We recognize that the self reported prevalence of symptoms in the present study is in the higher range of what previously has been reported among nulliparous women. In the present study, any leakage was defined as urinary incontinence and subsequently graded as mild to severe based on frequency. The majority of patients in our study experienced mild to moderate symptoms, but the bother frequency turned more pronounced after vaginal delivery, as did the need for protective pads. Between 3 to 40\% of women have been reported to be affected of urinary incontinence up to one year after delivery.\(^{127,128,56}\) This wide range may be explained by differences in the cut-off level of symptoms, in the heterogenous definitions of SUI used in various studies, as well as, large discrepancies in maternal age and study population characteristics. The prevalence of instrumental deliveries, as well as, number of grade III perineal tears, can be considered high in our study population but correlates well to other homogenous groups of primiparous women from similar industrialized populations.\(^{44,129,130}\)

SUI symptoms during pregnancy have been associated with an increased risk of postpartum SUI in women delivered by cesarean section.\(^{131}\) Our study could not confirm this finding. Instead, we found that women with late pregnancy symptoms of SUI were at decreased risk of aggravated symptoms if delivered by elective cesarean section when compared to women with prenatal symptoms and subsequent spontaneous delivery. However, in women reporting presence of SUI already before pregnancy, there were no significant differences in risk of any LUTS with regard to delivery mode. Thus, in this (small) subgroup of patients the seemingly overall protective effect of cesarean section noted in our study was absent. This may be attributed to their prenatal symptoms having a different, and perhaps more complex, etiology than what can be explained by tissue disruption or denervation injury at delivery.

The incidence of new onset SUI after delivery in women who were continent prior to pregnancy was significantly more frequent in the vaginal group at both three and nine
months follow-up compared to the cesarean delivery group. 19% of women experienced de novo SUI after vaginal delivery compared to 2% of women after cesarean delivery, which corresponds to 82.5% (VD) vs. 50% (CD) of the total number of women with symptoms at three months in each delivery group.

When considering possible predictors of SUI in a multivariable analysis, delivery mode was the only obstetrical predictor of SUI at a significant level. Instrumental delivery, degree of perineal tears and fetal birth weight did increase the risk of SUI at univariable analysis but did not remain significant when added to the multivariable model. When subsequently adding non-obstetrical co-variables to the multivariable model, presence of SUI symptoms before pregnancy and at three months follow-up remained significant predictors for stress urinary symptoms at nine months follow-up.

7.2 STRESS URINARY INCONTINENCE SYMPTOMS AT 10 YEARS FOLLOW-UP

Paper II comprised healthy women with normal full-term pregnancies delivered by either vaginal births or cesarean deliveries (if multipara). In this study, we found an increased overall prevalence of symptoms associated with SUI 10 years after index delivery in the vaginal delivery group when compared to the cesarean delivery group. As in study I, most symptoms were in the range of mild to moderate bother. However, approximately 10% of patients in both delivery groups presented urinary incontinence frequency scores that we classified as severe. Among these subjects a majority also experienced flatus incontinence, regardless of delivery mode, an association confirmed by the adjusted multivariate analysis.

When considering possible predictors of outcomes in a multivariate analysis, vaginal delivery was associated with an increased risk of SUI. Delivery mode showed no other significant associations with anal or urinary incontinence symptoms. We were unable to confirm a positive association between parity and increased prevalence of UI symptoms. This finding is consistent with several observational studies, suggesting that the first vaginal delivery is associated with the highest risk of loss of urethral support, and urinary incontinence. The number of subjects having undergone urinary incontinence surgery was few in both groups and did not suffice for a valid statistical comparison. We could, however, see that women only having had vaginal deliveries following birth of their first child did not show a dramatic increase in incontinence surgery when compared with women only delivered by cesarean section at 10 years follow-up.

In summary, our main findings implies that cesarean delivery is not associated with a major reduction in long term pelvic floor morbidity during the first decade after childbirth, an assumption supported by large population based cross-sectional studies. Although vaginal delivery seems to increase the prevalence of mild to moderate incontinence symptoms when compared to cesarean delivery 10 years after first delivery, the prevalence of severe incontinence was similar in the two groups.
7.3 STRESS URINARY INCONTINENCE SURGERY AT 30 YEARS FOLLOW-UP

Paper III focuses on surgically managed pelvic floor dysfunction, presumably associated with more severe bother. In this study, women having had only cesarean deliveries had substantially lower risks for both SUI and POP surgery later in life compared to women having had only vaginal deliveries. The increased risk of surgically managed pelvic floor disorders after vaginal delivery persisted for over three decades of follow-up and was especially pronounced in multiparous women. This suggests that the association between pelvic floor dysfunction and multiple childbirths, lacking in Paper II, may not become apparent unless the duration of follow-up is sufficiently long. Studies (as well as our study II) have suggested that the first vaginal delivery is pivotal with regard to the risk of developing pelvic floor disorders and that subsequent deliveries are of lesser importance. Our long-term data do not support this notion. In women with only vaginal deliveries, risks of SUI surgery consistently increased with number of deliveries: compared to women with only one vaginal delivery, women with at least three vaginal deliveries had a nearly doubled risk of SUI surgery. Compared to women only having had cesarean deliveries, an obstetrical history of only having vaginal deliveries considerably increased the risks for surgically managed SUI and POP. The risk difference became greater with additional childbirths, and, after having at least three vaginal deliveries there was a nearly fivefold increased risk of SUI surgery compared to women having at least three cesarean deliveries. These results indicate that additional vaginal deliveries add overt or occult trauma to the lower urinary tract and pelvic floor. This finding supports results from other Swedish nationwide cohort studies, showing a dose-response relationship between number of deliveries and the risk of SUI surgery. Adjusting for maternal age and a number of potential obstetrical confounders resulted in marginal changes of the risk estimates, which points to a biological rationale for the observation.

In women only having cesarean deliveries, the incidence rate of SUI surgery was unaffected after additional childbirths and even decreased after more than two cesarean deliveries. This finding indicates that childbearing itself, which has been implicated in the pathogenesis of pelvic floor disorders, are of lesser importance than the actual process of giving birth. Support for this notion can be found both in epidemiological and experimental studies.

In Paper III, vacuum extraction was associated with a somewhat lower risk of SUI surgery compared to non-instrumental birth. Although the underlying mechanism for this observation is uncertain, we speculate that the operator controlled delivery of the baby’s head during vacuum extraction may result in less injury to the pubocervical ligaments and urethral innervation compared to non-guided pushing during the final stage of labor. In the present analysis we could not adjust for obstetrical factors not accounted for in the register, such as external fundal pressure, perineal protection, and oxytocin infusion which may be related to pelvic floor trauma and could have influenced the association. Analysis of the association between forceps delivery and surgically managed SUI was not permissible due to insufficient number of cases.
7.4 PELVIC ORGAN PROLAPSE SURGERY AT 30 YEARS FOLLOW-UP

POP usually develops progressively over time and has a prolonged onset of symptoms after exposure. This notion is substantiated in Paper II and III where none of the subjects in either delivery group had undergone POP surgery ten years after index delivery, whereas 2.4% of the subjects had undergone surgery at 30 years follow-up.

Similar to SUI surgery, the increased risk of surgically managed POP after vaginal delivery compared to women having had only cesarean deliveries persisted for over three decades of follow-up and reached its peak more than 25 years after first childbirth. In women with only vaginal deliveries, risk of POP surgery consistently increased with number of deliveries: compared to women with only one vaginal delivery, women with at least three vaginal deliveries had a three-fold risk increase for POP surgery. This finding confirms data from the Women's Health Initiative, showing that additional childbirths increase the risk of POP compared with only having one child. Compared to women only having had cesarean deliveries, an obstetrical history of only having vaginal deliveries considerably increased the risk of surgically managed POP. The risk difference became greater with additional childbirths, and, after having at least 3 vaginal deliveries there was a twenty-fold increased risk of POP surgery compared to the corresponding number of cesarean deliveries. As for SUI, adjusting for maternal age and a number of potential obstetrical confounders resulted in marginal changes of the risk estimates. In women only having cesarean deliveries, the rate of POP surgery decreased after additional childbirths and no woman with > three cesarean deliveries have undergone surgery for POP in this population. We recognize however that the number of women with four cesarean deliveries or more were comparably few (=1241).

The risk of having POP surgery was more than doubled after forceps delivery compared to both vacuum and non-instrumental delivery, and more than 20 times that of cesarean delivery. Most studies agree that instrumental delivery has detrimental effects on pudendal nerve, and particularly the use of forceps is associated with higher rates of perineal and anal sphincter lacerations. Using magnetic resonance imaging, use of forceps (but not vacuum extractor) has also been shown to considerably increase the risk of levator muscle injury. As described in the section above, we could not adjust for obstetrical factors not accounted for in the register, such as external fundal pressure, perineal protection, episiotomy and oxytocin infusion which may be related to pelvic floor trauma and could have influenced the association.

7.5 ANAL INCONTINENCE AT 10 YEARS FOLLOW-UP

Anal incontinence symptoms in relation to childbirth, 10 years after index delivery, were assessed in Paper II. Similar to SUI, the change in symptom frequency after childbirth was rather limited and consisted mostly of symptoms in the range of mild to moderate bother. At 10 years follow-up, only fecal urgency and gas incontinence were significantly more prevalent in women with vaginal deliveries only. Frank fecal incontinence was uncommon in the present study regardless of delivery mode, and in agreement with Bek et al. the predominant problem associated with anal incontinence in both groups was flatus incontinence. In this context it is worth remembering that approximately 10% of patients in both delivery groups presented a
urinary incontinence frequency score that we classified as severe of which a majority also experienced flatus incontinence. In clinical practice, possible double incontinence should be kept in mind when patients present with severe urinary incontinence regardless of delivery history.

When considering possible predictors of outcomes in a multivariate analysis, delivery mode showed no significant associations with anal incontinence symptoms. Not surprisingly, women with an obstetrical history of anal sphincter injury carried a substantially increased risk of gas incontinence, an association repeatedly demonstrated by our and other research teams.\textsuperscript{44,50,137} Symptoms of SUI were associated with increased risks of both gas and loose stool incontinence confirming the importance to question the patients about the presence of double incontinence when they present with SUI symptoms.

Previous results are more divergent when considering the association between parity and anal incontinence. While some describe that the risk is not affected by parity,\textsuperscript{138,139} others suggest that multiple childbirth is associated with aggravated symptoms.\textsuperscript{140} In the present study, we found no dose-response relationship between increasing parity and prevalence of anal incontinence symptoms.

### 7.6 Maternal Age at First Delivery

The ability of the pelvic floor to efficiently maintain both continence and pelvic organ support is undoubtedly influenced by the processes of pregnancy and vaginal delivery. Accumulating evidence from experimental and observational studies has demonstrated that vaginal delivery has a detrimental effect on the pelvic floor and increases the risk of subsequent pelvic floor disorders.\textsuperscript{34,141,142,94} It is a common belief that younger women are less likely to suffer pelvic-floor tissue trauma at childbirth but robust epidemiological evidence to support this notion is lacking and it is debated whether or not age at first delivery influences long-term pelvic floor sequelae.

In Paper IV we found that maternal age at first delivery influenced the risks of SUI and POP surgery later in life regardless of delivery mode. The age related increase in incidence rate was most pronounced for POP surgery among vaginally delivered women. Regardless of age at first birth, vaginal delivery was associated with increased risks of pelvic floor surgery, and risks were higher for POP than for SUI surgery.

Our data corroborates findings from other large scale epidemiological studies suggesting that cesarean delivery convey a decreased risk of both SUI symptoms and surgically managed SUI. Rortveit et al.\textsuperscript{94} found that the risk of urinary incontinence was higher among women who have had cesarean sections when compared to nulliparous women, and was even higher among women who have had a vaginal delivery. A nested case control study, also using data from Swedish health care registries found that cesarean delivery decreased the risk of POP inpatient diagnosis in comparison to vaginal delivery by a five-fold.\textsuperscript{111} This study was adjusted for maternal age and parity but not for important confounders such as diabetes, fetal head circumference, gestational age or infant birth weight.

Stratifying maternal age at first childbirth into five-year-bands further illustrates the effects of age at first delivery in relation to delivery mode. For SUI the risk estimates
showed minor variations throughout the age strata and generally remained at least three times higher for the vaginal delivery group compared to cesarean delivery. However, in the age categories 35-38 and 39 years or older at first birth, there was notable drop in the risk estimates for incontinence surgery and vaginal delivery was no longer associated with a statistically increased risk of SUI surgery. These findings indicate that the protective effect of cesarean delivery on SUI is limited in this age group and that the etiological mechanisms underlying SUI may change as women grow older and become less dependent on obstetrical trauma to the pelvic floor and lower urinary tract.

The risk of POP surgery showed a less consistent risk pattern in relation to age at first delivery, with rather large fluctuations in the risk magnitudes, although remaining at significant levels throughout. The relatively few cases of POP in some age strata resulted in wide confidence intervals and limited statistical precision. However, similar to the results for SUI surgery, the lowest risk of POP surgery after having had only vaginal deliveries was observed in the oldest age group. Again, this finding suggests that among women who delay childbearing, the development of POP may be less related to obstetrical trauma compared to younger women.

There was a clear trend between age at first childbirth and risks of SUI and POP surgery within the delivery groups, when estimating the risks of SUI and POP surgery with the youngest age category as reference. Both birth cohorts showed increasing risk estimates for pelvic floor surgery with increasing age. However, for the cesarean delivery cohort the results should be interpreted with caution since most confidence intervals were at a non-significant level. In the vaginal delivery cohort younger age at first delivery was protective against both SUI and POP surgery when compared to older age groups. As such our results conflict with the notion that younger age at first delivery is a potential risk factor for POP later in life, and also studies suggesting that increasing age has no association with SUI.

Some of the obstetrical parameters haphazardly differed between the cesarean delivery and the vaginal delivery cohort, such as mean parity, pregnancy length, fetal birth weight, diabetes, and head circumference. However, these possible confounders were controlled for in the adjusted Cox’s model. After adjusting for these possible confounders, risk associations were largely unaffected for SUI surgery but decreased in magnitude for POP surgery in all age categories. Thus, in the present study obstetrical parameters that often clinically are thought to influence the development of surgically managed SUI had little clinical impact on our risk estimates. This is in accordance with one large epidemiological study on surgically managed SUI in relation to delivery mode where crude risk estimates were largely unaffected when adjusting for obstetrical parameters.

When comparing the two delivery cohorts, there was a similar average time from last delivery to POP surgery whereas women in the vaginal cohort underwent SUI surgery three years earlier than if delivered by cesarean section. In the vaginal delivery cohort women were also nearly three years younger at the time of stress incontinence surgery. Use of surgical procedures as measures of SUI and POP represents an obvious underestimation of the true disease incidence and the actual number of women experiencing symptoms. However, it indicates that vaginal delivery may be associated with more severe urinary incontinence since it has been shown that women with more
severe symptoms are more likely to have surgery.\textsuperscript{144,145} Menopause and advancing age are often cited risk factors for pelvic floor dysfunction. The Norwegian EPINCONT study showed that women 25 years or younger at their first delivery had a lower risk of urinary incontinence than older women but the risk attenuated with increasing actual age and disappeared in the age group 50 – 64 years.\textsuperscript{146} Our study, including women of a fairly homogenous age with a clear majority being premenopausal at the end of the observational period, is likely to be more closely related to obstetrical factors than to predisposing events occurring later in life. We therefore cannot say if the associations and trends we have observed apply to postmenopausal women.

In conclusion, our study provides longitudinal epidemiologic evidence that age at first delivery influences the risks of SUI and POP surgery later in life. The current trend in industrialized countries to postpone childbearing may increase the incidence of surgically managed pelvic floor and lower urinary tract disorders in decades to come and have important women’s health implications.

In Study I to III, adjusting for maternal age and a number of potential obstetrical confounders resulted in marginal changes of the risk estimates and a vaginal delivery mode remained independently associated with an increased risk of SUI. However, at the follow-ups performed 9 months and 10 years after first delivery, nearly all subjects had mild to moderate symptoms and the rather minor differences in incontinence symptoms according to age at first delivery might be masked by the strong influence of mode of delivery. A study design focusing on age at first delivery is necessary to detect a more true correlation.

7.7 TIME ASPECTS

In the aftermath of childbirth, injury to the pelvic organ innervation and pelvic floor support tissue may be reversible in some women, while in others injury may manifest itself soon after delivery or with a delayed onset of symptoms. The prevalence of SUI in the nine months follow-up study was 14\% (VD) vs. 4\% (CD) and in the 10 years follow-up study the corresponding figures were 41\% (VD) vs. 24\% (CD). Most women in both Paper I and Paper II presented SUI with mild to moderate symptoms. Symptom severity deteriorated over time regardless of delivery mode, with more women experiencing severe SUI at ten years follow-up, as well as, more women being in need of protective pads. In Paper III, we found that the incidence rates of surgically managed SUI and POP increased over time for both the vaginal and cesarean delivery cohort, and reached their peak more than 25 years after first childbirth thus confirming the theory that there is a delay of onset to consider which may be influenced by other life events. Given that the analyses were adjusted for age at childbirth, the effects of time cannot be explained by ageing per se.

In our studies we could see a clearly increased risk (OR 8.9, 95\% CI 1.9-42) for SUI after vaginal delivery at nine months follow-up (Paper I), whereas at ten years after first delivery (Paper II) the risk estimate was more moderately increased (OR 3.1, 95\% CI 1.6-5.9). However, in Paper III, the increasing incidence rates of surgically managed SUI over time were more or less parallel for both delivery groups and a risk reduction between the groups could not be confirmed. Thus, our long-term results differ partly from the cross-sectional Norwegian data. Part of the reason for the divergent results is
likely to be found in differences in study population and study methodology such as using surgical interventions vs. self-reported questionnaires.

Mean time since last delivery to POP surgery was equal in the two groups, whereas women in the vaginal cohort in general underwent SUI surgery three years sooner than if delivered by cesarean section, possibly explained by more severe SUI symptoms in the vaginal delivery group. Mean age for POP surgery in our study were 48 years, whereas the 1997 National Hospital Discharge Survey stated mean age in the United States to be 54 years with a peak incidence in individuals of 60-69 years of age.86 Menopause, as well as, advancing age is often cited as risk factors for pelvic floor dysfunction. Our study, including women of a fairly homogenous age with a clear majority being premenopausal at the end of the study, is likely to be more closely related to obstetrical factors than to predisposing events occurring later in life. Further studies regarding postmenopausal pelvic floor disorders and the influence of obstetrical parameters are necessary for a conclusion to be drawn.

7.8 METHODOLOGICAL ASPECTS

The questionnaire used in Paper I has previously been used by our research team and has been found reliable and sensitive to change. The validated CCIS118 was used in Study II for anal incontinence symptoms and questions on UI symptoms were modeled from the same score. Using prospectively collected data prevents recall bias but self-reported symptoms may be both under and over reported. It is a weakness of our studies that symptoms could not be correlated to clinical findings or objective examinations. However, given the lack of correlation between for example objective findings at urodynamic and subjective symptoms of SUI, we believe that use of self-reported questionnaires is a valid approach to capture the degree of bother.

Strengths of our studies include the large prospective consecutive population samples, a well-defined source populations, the homogeneity of the groups, a low loss to follow-up (Paper I and II) and the long-term follow-up from first exposure to assessment (Paper II to IV). In order to further increase the internal validity of our observations in Paper I we discarded women delivered by emergency cesarean section following trial of labor from the analysis and in Paper II women delivered by both delivery modes were not included in the final analysis. Due to the strict inclusion criteria’s in Paper I and II, our data may not be generalized to women with maternal or fetal complications during pregnancy and also limits our ability to generalize our findings to non-healthy women, women delivered by cesarean section after trial of labor, or to women delivered with both delivery modes. Even though fulfilling the power criteria, some rather large confidence intervals may be explained by a broad variance, which would be reduced in a larger study population. However, Paper I is according to our knowledge the first study to enroll equal number of cesarean and vaginal deliveries by design. Other studies encompassing women without restriction by type of delivery have been based on cesarean section populations between 9 and 25% of the total study population.

When assessing our main results one should also consider the limitations associated with the observational study designs used in this thesis. Although cohort studies based on women attending hospital or identified from national health care registries are
efficient from a sampling perspective, the design has limited abilities to draw conclusions on a causal inference but rather indicates an association, or an estimated risk, when comparing exposed to unexposed. When it comes to Paper III and IV, the independent prospective data ascertainment, a study group identified from the general population, and the near complete registration of subjects, are some of the strengths of our study. The standardized classification of both exposures and outcomes, our ability to control for important obstetrical confounders, as well as, an unprecedented observational period extending over three decades are further merits. Since all Swedish citizens have access to publicly funded health care, few procedures are performed outside of the system and loss to registration should be negligible.

Nevertheless, we recognize that studies based on health care registers have limitations. Behavioral and life-style factors possibly associated with SUI and POP, such as body mass index, exercise habits and strenuous work remain unaccounted for. Furthermore, using surgical procedures as our main outcome measure should be considered a surrogate for the actual number of women experiencing symptoms of SUI and POP. Women with more severe symptoms are more likely to seek medical treatment compared to those with mild to moderate symptoms and our results therefore represent a clear underestimation of the true prevalence of these conditions and the problem at hand. The data extracted from the birth register in the present study do not distinguish between cesarean sections performed before or after onset of labor. The labor process in emergency cesarean deliveries performed in the second or third stage of labor may to some extent already have affected the pelvic organ innervation and morphology and is a potential source of bias. However, the lack of distinction between emergency and elective cesareans would, if anything, tend to underestimate the overall risk difference between cesarean and vaginal deliveries.

7.9 CLINICAL IMPLICATIONS

The studies in this thesis provides clinical and epidemiological evidence that obstetrical intervention at the time of childbirth may to some extent prevent SUI and POP later in life, particularly in multiparous women and women over 30 years of age at first delivery.

In view of the vast number of women afflicted by pelvic floor disorders worldwide our results may have important clinical and public health implications. However, the protective effects of cesarean delivery with regard to pelvic floor disorders on a population-based level must be weighed against postpartum maternal and neonatal morbidity associated with the procedure. In order for primary prevention strategies to be clinically relevant for both the general public and individuals at risk, further undertakings are needed to target individuals who will benefit the most from a cesarean section at the time of childbirth.
8 CONCLUSIONS

The specific aims are repeated with the conclusions for the convenience of the reader:

1. **Aim:** To compare the prevalence and risk of lower urinary tract symptoms in healthy primiparous women in relation to vaginal or elective cesarean delivery nine months after delivery (Paper I).

   **Conclusion:** Vaginal delivery was associated with a significantly increased prevalence and risk of lower urinary tract symptoms nine months after childbirth when compared to elective cesarean delivery.

2. **Aim:** To estimate the effect of first delivery on urinary and anal incontinence 10 years after first childbirth in relation to mode of delivery and to assess the influence of subsequent deliveries and obstetrical events (Paper II).

   **Conclusion:** Urinary and anal incontinence symptoms are significantly more common following spontaneous vaginal delivery and women with an obstetrical anal sphincter injury carries a substantially increased risk of gas incontinence.

3. **Aim:** To estimate the risks of stress urinary incontinence and pelvic organ prolapse surgery related to vaginal birth or cesarean delivery at long-term follow-up (Paper III).

   **Conclusion:** Having only had vaginal deliveries was associated with significantly increased risks of stress urinary incontinence and pelvic organ prolapse surgery later in life compared to only having had cesarean deliveries which persisted over three decades.

4. **Aim:** To evaluate the risks of surgically managed stress urinary incontinence and pelvic organ prolapse in relation to delivery mode and age at first childbirth (Paper IV).

   **Conclusion:** Increasing age at first delivery was associated with greater risk of subsequent pelvic floor surgery regardless of delivery mode.
Urininkontinens är betydligt vanligare bland kvinnor än män och förekommer i någon form hos ca en tredjedel av alla vuxna kvinnor samt ökar i frekvens med stigande ålder. De bakomliggande faktorerna är endast delvis klarlagda men en av de faktorer som ofta kopplas ihop med utvecklingen är urinläckage är barnafödande.


Idag anses i allmänhet ett kejsarsnitt vara en säker procedur i industriländerna, särskilt ett planerat kejsarsnitt hos en förstafödelse. Kejsarsnitt är dock fortfarande associerat med en högre frekvens komplikationer jämfört med vaginal förlössning och kvinnor som förlöses upppepade gånger med kejsarsnitt löper särskild risk. Obstetriker spelar en viktig roll vid rådgivning av förlössningssätt men de underlag som finns för ett evidensbaserat beslut är fortfarande tvetydiga. Huvudsakligt med denna avhandling är att utvidga denna kunskap genom att i fyra olika studier undersöka hur förlossningssätt påverkar urininkontinens samt studera hur stort inflytande förlossningsrelaterade faktorer såsom antal förlössningar, barnets födelsevikt, moderns ålder, graviditetslängd m.m. har på utfallet.

Den första studien i denna avhandling är en undersökning av hur många kvinnor som har urininkontinens nio månader efter förlossning och se på sambandet med förlossningssätt samt obstetriska riskfaktorer. 435 förstafödende kvinnor som förlösts på Danderyd Sjukhus eller BB Stockholm med antingen planerat kejsarsnitt eller vaginal förlössning svarade på en enkät angående urininkontinensymtom före förlossning samt vid tre och nio månader efter förlossning. Undersökningen visade att de kvinnor som förlösts vaginalt till större utsträckning besväras av urinläckage, (fla ansträngningsutlöste urinläckage) jämfört med de kvinnor som förlösts med kejsarsnitt. Kejsarsnitt skyddade däremot inte de kvinnor som redan besvärades av urinläckage innan graviditeten. Studien visade även att de kvinnor som besvärades av urinläckage före förlossning samt vid tre månaders uppföljning hade en ökad risk att fortfarande besväras av urinläckage vid nio månaders uppföljning oberoende av förlossningssätt.


9 POPULÄRVETENSKAPLIG SAMMANFATTNING
svåra urinläckagesymtom varav en majoritet även besvärades av gas-inkontinens. Antalet förlossningar påverkade inte utfallet i denna studie.


Studierna i den här avhandlingen visar att förlossningssätt har en tydlig inverkan på uppkomsten av urininkontinens och framfall senare i livet. Sambandet var extra framträdande hos omföderskor samt de kvinnor som var över 30 år vid första förlossningen. När en kvinna i samråd med sin läkare diskuterar risken och fördelar med olika förlossningssätt är det viktigt att väga det skydd som en kejsarsnittförlossning delvis ger mot uppkomsten av bäckenbottenbesvär mot de risken som föreligger för både moder samt barn med en operativ förlossning. Läkaren bör sträva efter att identifiera riskfaktorer för bäckenbottenbesvär hos den enskilda kvinnan för att kunna ge råd om förebyggande insatser, däribland bäckenbottenträning, för att i möjligaste mån individualisera vården.
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My truly wonderful and amazing husband Greger, for standing by my side, supporting and taking care of me. Thank you for patiently letting me be absorbed by the computer on a Saturday when we could have had a nice walk in the sun. My darling boys, Filip and Hugo, for being the greatest joy of my life. I am looking forward to giving you my undistracted attention.

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## 11 APPENDIX

### 11.1 QUESTIONS REGARDING URINARY INCONTINENCE SYMPTOMS

Have you during the last week experienced any of the following symptoms?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No</th>
<th>&lt;1/week</th>
<th>&gt;1/week</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involuntary leakage of urine?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sudden desires to void that are difficult to hold back?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sudden desires to void followed by involuntary leakage?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Involuntary loss of urine during physical exercise?</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bladder emptying difficulties</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you use protective pads due to urinary leakage?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How many times do you go to the toilet to urinate in a day?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How many times do you go to the toilet to urinate in a night?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 11.2 QUESTIONS REGARDING ANAL INCONTINENCE SYMPTOMS

Have you during the last week experienced any of the following symptoms?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No</th>
<th>&lt;1/week</th>
<th>&gt;1/week</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involuntary leakage of gas?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Involuntary leakage of soft stool?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Involuntary leakage of firm stool?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you use protective pads due to leakage of stools?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgency for bowel emptying that are difficult to hold back?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Been unable to distinguish between flatus and fecal contents?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How many times do you go to the toilet to defecate in a week?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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