Pelvic floor trauma after childbirth – Risk factors, surgical treatment and prevention

Jennie Larsudd-Kåverud

Department of Obstetrics and Gynecology

Institute of Clinical Sciences

Sahlgrenska Academy, University of Gothenburg

UNIVERSITY OF GOTHENBURG

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Cover illustration: Viva la vulva by Natalie Bergschwinger.

Natalie Bergschwinger lives and works with her partner and four dogs in Berlin. In 2020, she founded Make&Believe, her own little brand, and started selling her art.

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jennie.larsudd-kaverud@gu.se

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An ounce of prevention is worth a pound of cure

-Benjamin Franklin

To my family

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Jennie Larsudd-Kåverud

Department of Obstetrics and Gynecology, Institute of Clinical Sciences
Sahlgrenska Academy, University of Gothenburg
Gothenburg, Sweden

ABSTRACT

Background: As women live longer, the long-term effects of childbirth may negatively affect their quality of life and professional careers.

Aim: The overall objective of this thesis was to examine how childbirth-related factors, such as delivery mode, number of births, and infant birth weight, affect long-term pelvic floor health in mothers, with a focus on the risks of pelvic floor disorders, surgical interventions, and the prevention of obstetric anal sphincter injury (OASI).

Material and methods: Papers I and **II** analysed cohorts of women from the Swedish National Quality Register of Gynecological Surgery who underwent prolapse or incontinence surgery. National birth registers were used in **Papers I**, **III**, and **IV** to identify women with a first and second vaginal delivery.

Results: In **Paper I,** pregnancies per se were not associated with an increased risk of surgery for pelvic organ prolapse or urinary incontinence compared with nulliparous women. Vaginal delivery increased the risk of surgery for pelvic organ prolapse or urinary incontinence, while cesarean delivery alone preserved long-term pelvic floor support, similar to that of nulliparous women. **Paper II**: Despite lower cure rates with increasing age and morbidity, most women were satisfied with mid-urethral sling surgery if incontinence episodes decreased. Women with severe incontinence were more likely to improve and report satisfaction. In **Paper III**, higher infant birthweight reduced the rate of spontaneous vaginal delivery (80.4% to 44.9%) and increased acute cesarean

rates (8.3% to 41.6%). Delivery experience declined with higher birthweight, mirroring complication patterns. In **Paper IV**, incorporating infant biometrics and intrapartum factors improved OASI risk prediction and informed clinical decision-making through an online calculator.

Conclusion: Vaginal delivery increases pelvic floor surgery risk, whereas cesarean delivery is protective. Despite lower cure rates with age and morbidity, most women were satisfied with sling surgery if incontinence symptoms improved. Accurate infant birthweight assessment is crucial for preventing birth trauma and enabling personalised obstetric care.

Keywords: delivery, vaginal; cesarean section; vaginal birth after cesarean; pelvic floor disorders; birth weight, birth injury; maternal morbidity; obstetric anal sphincter injuries, probability, bayes theorem.

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SAMMANFATTNING PÅ SVENSKA

Bakgrund

Bäckenbottendysfunktion är ett stort, globalt, hälsoproblem för kvinnor i alla åldrar. Mellan 10–20% av alla kvinnor i västvärlden genomgår en rekonstruktiv bäckenbottenkirurgi före 80 års ålder, och efterfrågan ökar fortsatt. En bakomliggande orsak är bäckenbottenskador efter vaginal förlossning och dess bidrag till långsiktig bäckenbottendysfunktion, såsom urin- och avföringsinkontinens och genitalt framfall. Den främsta riskfaktorn för avföringsinkontinens bland kvinnor är en analsfinkterskada. Kvinnor lever idag en stor del av sitt yrkesaktiva liv efter barnafödandet och många kvinnor riskerar att drabbas av allvarliga störningar i sitt sociala liv och i sin yrkesutövning. Denna avhandling undersöker riskfaktorer för bäckenbottenskador i samband med förlossning samt behovet av och resultaten efter bäckenbottenkirurgi. Eftersom förebyggande åtgärder generellt är mer effektiva än behandling syftar avhandlingen även till att belysa möjligheterna med individuellt anpassade förlossningsstrategier för att minska risken för allvarliga bäckenbottenskador.

Metod

Delarbete I och **II** identifierade kvinnor ≥ 45 år som genomgått prolaps- eller urininkontinenskirurgi och var registrerade i Nationella kvalitetsregistret inom gynekologisk kirurgi (GynOp) mellan 2010 och 2017. I **Delarbete I** kopplades kvinnans (n=60,105) uppgifter till data ur Medicinska födelseregistret samt Befolkningsregistret. Kvinnorna delades in i tre grupper; kvinnor som aldrig fött barn, ≥1 vaginal förlossning och ≥1 kejsarsnittsförlossning. Referensgruppen identifierades i Befolkningsregistret (n=2,309,765). Fördelningen avseende paritet och förlossningssätt i referensgruppen beräknades med data från Medicinska födelseregistret, begränsat till kvinnor födda år 1960. I **Delarbete II** undersöktes 5200 kvinnor som var 55–94 år och som genomgått slyngkirurgi för urininkontinens med avseende på grad av bot, nöjdhet och förbättring ett år efter operation. Från Medicinska födelseregistret hämtades studiepopulationen till **Delarbete III** och **IV**. I **Delarbete III** identifierades 520,564 kvinnor samt deras första fullgångna graviditeter och delades in efter (1) förlossningssätt och (2) födelsevikt hos barnet. Alla

förlossningsenheter i Sverige deltog i **Delarbete IV**, med totalt 609,916 första och andra förlossningar med fullgångna barn födda mellan 2009 och 2017. Totalt 25,245 analsfinkterskador förekom. Förlossningarna delades in i 3 scenarier; den första vaginala förlossningen, den första vaginala förlossningen efter tidigare kejsarsnitt samt den andra vaginala förlossningen.

Resultat

Delarbete I: Bland kvinnor som genomgått prolapskirurgi hade 97.8% ≥1 vaginal förlossning, 0.4% hade ≥1 kejsarsnitt och 1.9% hade inte fött barn. Motsvarande antal var 93.1%, 2.6% samt 4.3% hos kvinnor som genomgått inkontinenskirurgi. Den första vaginala förlossningen bidrog till den största absoluta riskökningen för kirurgi; 6 gånger ökad risk för prolapskirurgi och 3 gånger ökad risk för inkontinenskirurgi. Ingen ökning av risk för kirurgi sågs vid flera kejsarsnitt, samt hos kvinnor som inte fött barn.

Delarbete II: Graden av bot efter slyngkirurgi var 64.2% hos kvinnor ≥75 år jämfört med 88.5% hos kvinnor som var 55–64 år. Sannolikheten för bot sjönk med $aOR_{10år}$=0.51 för bot och $aOR_{10år}$=0.59 för nöjdhet med operationsresultatet. Kvinnor med ASA klass 3–4 hade lägre grad av bot och nöjdhet än kvinnor med ASA klass 1–2, (65.5% vs. 83.7% respektive 65.7% vs. 80.6%). Oavsett ålder så var kvinnorna nöjda i samma utsträckning om frekvensen av urinläckage minskat.

Delarbete III: Vid planerad vaginal förlossning minskade frekvensen av spontan vaginal förlossning från 80,4 % vid födelsevikt 3000-3999g till 44,9 % vid ≥5000g. Samtidigt ökade andelen akuta kejsarsnitt från 8,3 % till 41,6 %. Förlossning med sugklocka förekom hos 10–15 % oavsett födelsevikt hos barnet. Komplikationer drabbade mödrar sju gånger oftare än nyfödda (29,2 % vs. 4,0 %). Sugklocka och akuta kejsarsnitt gav flest maternella komplikationer (42,3 % resp. 52,7 %), särskilt vid födelsevikt ≥4500g (68,1 % resp. 66,0 %). Lägst antal maternella komplikationer sågs vid spontan vaginal förlossning upp till 4200 g, därefter vid planerat kejsarsnitt. Andelen neonatala komplikationer ökade mest vid förlossning med sugklocka (8,6–24,5 %) och akuta kejsarsnitt (6,6–9,5 %), men var lägre vid spontan vaginal förlossning (2,6–12,0 %) och planerat kejsarsnitt (1,0–6,3 %). Mödrarnas upplevelse av förlossningen försämrades i takt med att barnets födelsevikt ökade, oavsett förlossningssätt.

Delarbete IV: Prediktionsmodellens prestanda utvärderades med hjälp av Nagelkerkes R^2 (R^2_N). Födelsevikt hos barnet var den primära prediktorn och bidrog med 31%-45% av R^2_N i de respektive prediktionsmodellerna. Hos kvinnor som födde sitt andra barn utgjordes 50% av prediktionskapaciteten av uppgifter från den första förlossningen. Inkluderandet av uppgifter om interventioner under förlossningen, såsom sugklocka, ökade modellernas prestanda väsentligt (t. ex ökade R^2_N från 1,7 till 9,3% i det första scenariot).

Konklusion

Vaginal förlossning ökar risken för prolaps- och inkontinenskirurgi, medan kejsarsnitt är skyddande i samma utsträckning som att inte ha varit gravid. Även om inkontinenskirurgi hos äldre och sjukligare kvinnor var associerade med lägre grad av bot och nöjdhet med operationen, så var majoriteten nöjda om de upplevde en minskning i antalet läckage. Studien visar också att barnets födelsevikt har en betydande inverkan på förlossningssätt, på mödra- och neonatal morbiditet samt på moderns upplevelse av förlossningen. Resultaten talar starkt för att skattning av fostervikt kan förbättra utfallen genom att möjliggöra säkrare och mer individualiserad förlossningsvård. Att undvika analsfinkterskada skulle sannolikt signifikant minska förekomsten avföringsläckage.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Larsudd-Kåverud J, Gyhagen J, Åkervall S, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of pregnancy, parity, and mode of delivery on urinary incontinence and prolapse surgery-a national register study. Am J Obstet Gynecol. 2023;228:61.e1-61.e13. doi: 10.1016/j.ajog.2022.07.035.

II. Gyhagen J, Åkervall S, Larsudd-Kåverud J, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of age and health status for outcomes after mid-urethral sling surgery - a nationwide register study. Int Urogynecol J. 2023;34:939-947. doi: 10.1007/s00192-022-05364-6.

III. Larsudd-Kåverud J, Åkervall S, Molin M, Milsom I, Kuusela P, Gyhagen M. The influence of infant birthweight on mode of delivery and short-term maternal and neonatal complications in primiparous pregnancies. (Submitted)

IV. Larsudd-Kåverud J, Åkervall S, Molin M, Nilsson IE, Steyerberg EW, Milsom I, Gyhagen M. Predicting obstetric anal sphincter injury in the first and second vaginal delivery and after a cesarean delivery: development and validation of an intrapartal model. J Clin Epidemiol. 2025 Jul;183:111782. doi: 10.1016/j.jclinepi.2025.111782.

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ABBREVIATIONS

AGA	Appropriate for gestational age
AI	Anal incontinence
aOR	Adjusted odds ratio
APGAR	Appearance, Pulse, Grimace, Activity, Respiration score
AR	Absolute risk
ASA	American Society of Anesthesiologists Physical Status classification
BMI	Body mass index
BIC	Bayesian information criterion
CD	Cesarean delivery
CI	Confidence interval
DRG	Diagnosis Related Group
EAS	External anal sphincter
GynOp	The Swedish national quality register of gynecological surgery
HIE	Hypoxic ischemic encephalopathy
IAS	Internal anal sphincter
IBW	Infant birth weight
ICD-10	International Classification of Diseases, 10th revision
IPR	The Swedish national inpatient register

ISD	Intrinsic sphincter deficiency
IQR	Inter quartile range
LGA	Large for gestational age
LISA	The Longitudinal integrated database for health insurance and labour market studies
LUTS	Lower urinary tract symptoms
MBR	The Swedish medical birth register
MRI	Magnetic resonance imaging
MUI	Mixed urinary incontinence
MUS	Mid-urethral sling
NICU	Neonatal intensive care unit
NPR	National patient register
OASI	Obstetrical anal sphincter injury
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
PFD	Pelvic floor disorder
POP	Pelvic organ prolapse
PROBAST	Prediction model Risk of Bias Assessment Tool
RR	Relative risk
SD	Standard deviation
SPR	The Swedish Pregnancy Register

SUI	Stress urinary incontinence
TPR	The Total Population Register
TRIPOD	Transparent Reporting of a Multivariable Prediction Model
UI	Urinary incontinence
UUI	Urgency urinary incontinence
VD	Vaginal delivery
SAS	Statistical analysis system
SCB	Statistics Sweden
SE	Standard error
SVD	Spontaneous vaginal delivery
TVT	Transvaginal tape
VBAC	Vaginal birth after cesarean
VE	Vacuum extraction

1. INTRODUCTION

As women live longer, the long-term consequences of childbirth may negatively affect their quality of life and professional careers for many years. A major long-term complication of vaginal delivery is pelvic floor trauma which contributes to maternal pelvic floor disorders (PFDs). Swedish patient legislation mandates that care during pregnancy and childbirth respects a woman's integrity, autonomy, and active participation (1). Similarly, in the United Kingdom (UK), the legal focus has shifted towards ensuring that obstetricians provide balanced information about the risks and benefits of different delivery modes (2). Globally, patient rights and women's autonomy in decision-making are gaining recognition, underscoring the need to properly implement legislation, such as the Patient Act (3). However, practical implementation remains challenging due to the absence of consensus among obstetricians and midwives regarding the comparative risks and benefits of different delivery modes for both mother and child. Achieving this consensus is vital for providing accurate counselling to pregnant women and ensuring informed consent (4).

Personalised medicine in obstetric care offers a potential solution to these challenges by tailoring decisions to each patient's individual needs, preferences, and medical circumstances. This approach recognises the diversity of risk profiles among women and moves beyond generalised recommendations to provide care that is both evidence-based and patient-centred. Incorporating predictive models and individualised risk assessments into clinical practice could help optimise delivery planning and reduce the occurrence of severe complications.

Nonetheless, the current evidence base lacks sufficient quality to decisively favour one mode of delivery over the other (5). Advancing personalised obstetric care requires robust research to identify and integrate predictive factors into comprehensive tools that support individualised decision-making, ensuring that women receive care aligned with their unique health contexts and values.

PFD is an umbrella term encompassing conditions such as stress urinary incontinence (SUI), pelvic organ prolapse (POP), and fecal incontinence (FI)

(6). These disorders affect many women and are strongly associated with vaginal childbirth. Approximately every fourth woman reports one or more PFDs (7), and the lifetime risk of pelvic floor surgery is currently up to one in five women (8-11), although the actual need may be even higher (12). Evidence from epidemiological, imaging, and electromyography studies indicates that vaginal delivery is a primary cause of SUI and POP and, consequently, the need for related surgery (13–15).

The protective effect of cesarean delivery against PFDs is debated. While cesarean delivery may initially lower the risk of PFDs, studies suggest this benefit diminishes over time, particularly after multiple deliveries (16, 17). Health economic analyses reveal that for nulliparous women, the total cost of planned cesarean section is comparable to that of planned vaginal delivery when costs associated with pelvic floor trauma and vaginal tears are included (18). However, PFDs, particularly SUI, continue to affect a significant percentage of older women, imposing substantial individual and societal costs (19, 20).

The mid-urethral sling (MUS) is a highly effective, safe, and less invasive procedure than prior surgical techniques for SUI (21-23). Nevertheless, various factors, including comorbidity, persistent urgency urinary incontinence (UUI), and intrinsic sphincter deficiency (ISD), can influence less favourable outcomes in older women (24, 25). In the UK, the number of these procedures in older women decreased between 2000–2012, and these procedures are now prohibited (https://www.immdsreview.org.uk/Report.html), in contrast to numerous European countries. MUS procedures are still being performed in the Nordic countries, where they continue to be the evidence-based gold standard.

An obstetrical anal sphincter injury (OASI) is a major trauma to the pelvic floor sustained during the second stage of labor. In Sweden, the national rate of OASI in primiparous women rose from 2.9% in 1990 to a peak of 7.0% in 2004, before declining to 4.5% in 2020 (26). Common well-known risk factors for OASI include forceps and vacuum-assisted delivery, midline episiotomy, increased fetal birth weight, Asian ethnicity, labor induction, labor augmentation, and the first vaginal birth after one or more cesarean sections (VBAC) (27-43). Even when adequately sutured, OASI significantly increases the risk of bowel incontinence (44).

Though the cause of FI is often multifactorial (45), the prevalence of FI increases in the first 12 months after an OASI, compared to those without an OASI (46-48). A study by Nilsson et al. showed that the FI prevalence in women 20 years after delivery without sphincter injuries was 11.7%, doubling to 23.8% (odds ratio (OR) 2.27; 95% confidence interval (CI), 1.75-2.94) in those with one sphincter injury and more than tripled to 36.1% (OR 3.97; 95% CI 3.11-5.07) after two sphincter injuries (49). FI has profound consequences, including social isolation and diminished quality of life (50, 51).

There is still no generally accepted prediction model for clinical use to determine the individual risk for OASI. This could explain why OASI is still often excused as an inevitable event, impossible to foresee (52,53). Sultan and de Leeuw (54) advocate for the development of prediction models based on large national datasets to identify women at high risk of OASI. Similar predictive tools have proven effective in other areas of medicine (55, 56).

Sweden provides a unique opportunity for epidemiological research in this field due to the availability of high-quality national registers with nearly complete coverage. Since 1973, the Swedish Medical Birth Register (MBR) has prospectively recorded over 98% of all births, encompassing more than 6 million (57). Additional registers, such as the Swedish National Register of Gynecological Surgery (GynOp) (58), the Cause of Death Register, the Patient Register (59), and the Swedish Pregnancy Register (60), offer valuable data. Furthermore, Statistics Sweden provides socioeconomic information, including education, school performance, and income (61).

This thesis investigates risk factors for pelvic floor trauma and evaluates the need for and outcomes of pelvic floor surgery. Recognising that prevention is more effective than treatment, it also explores the potential for individualised labour management strategies to reduce the risk of severe vaginal trauma during childbirth. By leveraging Sweden's comprehensive national registers, this work aims to improve maternal health outcomes and advance clinical practices in obstetrics.

1.1 THE FUNCTIONAL ANATOMY OF THE PELVIC FLOOR IN WOMEN

The pelvic floor in women comprises a complex network of muscles, connective tissue, blood vessels, and nerves. These anatomical structures play a critical role in maintaining urinary and fecal continence while simultaneously preventing pelvic organ prolapse during episodes of increased abdominal pressure. At the same time, the pelvic floor must also allow the passage of waste and the passage of a fetus during childbirth (62). The functional changes in the pelvic floor associated with vaginal delivery stem primarily from injury or overstretching.

1.1.1 THE PELVIC DIAPHRAGM (LEVATOR ANI)

Functionally, the pelvic diaphragm and the endopelvic fascia interact to maintain continence and pelvic organ support. The pelvic diaphragm is a U-shaped structure composed of muscles with central defects enclosing the urethra, vagina, and rectum. The levator ani muscle is functionally the main component and consists of four muscles: the puborectalis, the pubococcygeus, the iliococcygeus, and the coccygeus (63). Through constant adjustments in contraction, the pelvic diaphragm balances the intra-abdominal pressure and maintains continence (62,64). The urogenital hiatus of the levator ani, which allows passage of the urethra and vagina, is supported anteriorly by the pubic bones and portions of the pubococcygeus and iliococcygeus muscles (collectively referred to as the pubovisceralis) (Figure 1).

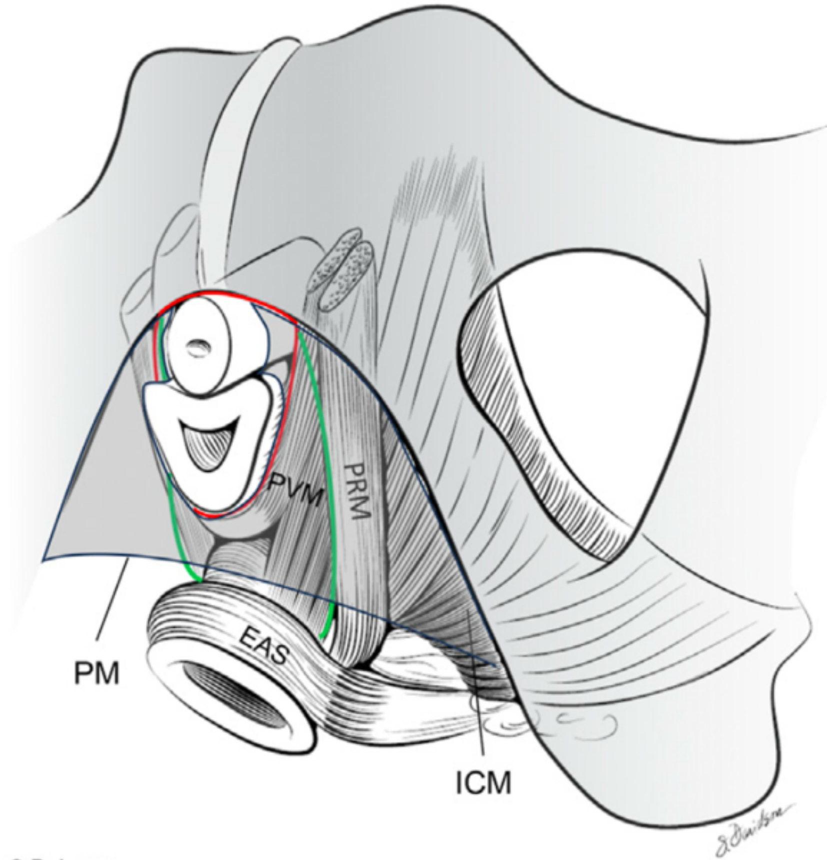


Figure 1. Hiatuses. *The urogenital hiatus is outlined in red, and the levator hiatus is outlined in green. © DeLancey Reprinted with permission from Professor DeLancey.*

These muscles attach on either side of the pubic symphysis, encircle and attach to the urethra, vagina, perineal body, and external anal sphincter (Figure 2). The pubovisceral muscles lift the perineal structures and close the hiatuses on the pelvic floor, which the puborectal muscle assists in. Posteriorly, the urogenital hiatus is supported by the perineal body and the external anal sphincter. When the levator ani contracts, it compresses the urogenital hiatus toward the pubic symphysis in a cephalic direction (65).

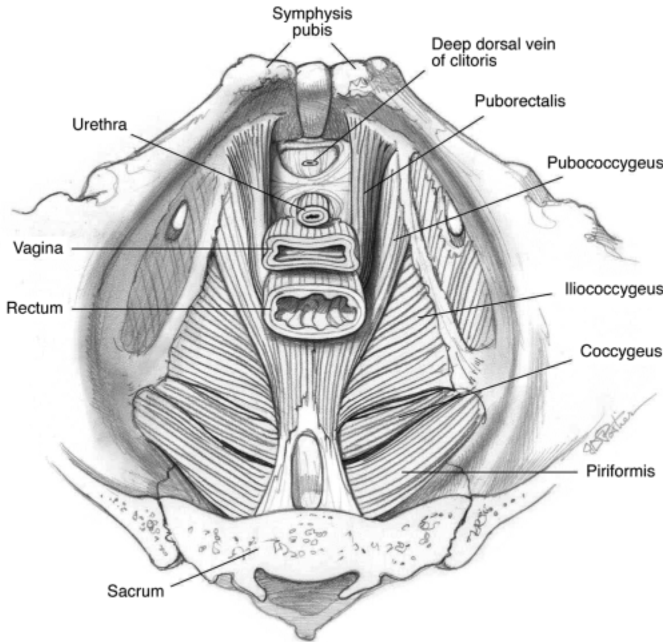


Figure 2. Pelvic view of the levator ani demonstrating its four main components: puborectalis, pubococcygeus, iliococcygeus, and coccygeus. *From Dyck PJ, Thomas PK, eds. Autonomic and somatic systems to the anorectum and pelvic floor. IN: Peripheral neuropathy, 4th ed, Philadelphia, PA: Elsevier Saunders, 2005; 37: 279-98. Used with permission of Mayo Foundation for Medical Education and Research, all rights reserved.*

1.1.2 THE PERINEAL MEMBRANE AND PERINEAL BODY

The perineal membrane is constituted by a one-layer muscle and connective tissue complex and stretches horizontally between the pubic bones and the ischiopubic rami. Laterally, it attaches the pelvic organs to the bony outlet and is connected to the levator ani muscles and the birth canal. It provides structural support, particularly to the urethra and vagina, playing a key role in maintaining continence and supporting the perineal body. The superficial layer of supporting muscles in the pelvic floor is the external anal sphincter (EAS), the superficial transverse perineal muscle, the bulbospongiosus, and the ischiocavernosus muscles (Figure 3).

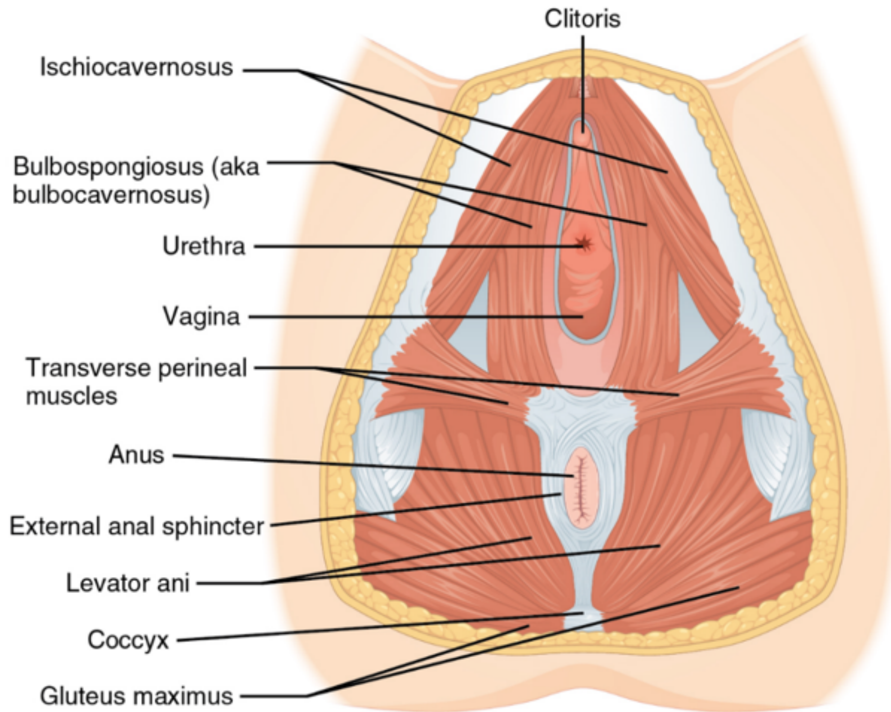


***Figure 3.**"OpenStax AnatPhys fig.11.20 - Muscles of the Female Perineum - English labels" at AnatomyTOOL.org by OpenStax, license: CC BY 4.0. Source: book 'Anatomy and Physiology', https://openstax.org/details/books/anatomy-and-physiology.*

The perineal body is a fibromuscular mass into which these muscles insert (except for the ischiocavernosus muscles), lying between the vagina and anorectum. It is bordered cephalically by the rectovaginal fascia, anteriorly by the posterior wall of the vagina, and posteriorly by the wall of the anorectum. Among many clinically important functions, the perineal body: (I) anchors the anorectum and vagina, (II) prevents expansion of the urogenital hiatus, and (III) contributes to maintaining fecal and urinary continence (66).

1.1.3 THE ENDOPELVIC FASCIA AND LEVELS OF SUPPORT

The endopelvic fascia is an enfolding connective tissue layer in the pelvis that provides structural support to the pelvic organs, in relation to the vagina, anchoring the organs to the pelvic walls and stabilising the pelvic floor (62). As described by DeLancey in 1992, the endopelvic fascia provides support at three levels (67). The first level of support consists of the cardinal and uterosacral ligaments, which connect the cervix and upper vagina to the pelvic walls and sacrum. Disruption of this support can result in uterine or vaginal vault prolapse (68). The second level is provided by the tendinous arch, extending from the pubic bone to the ischial spines, and the paravaginal fascia, which supports the middle third of the vagina. The third level of support is formed by the perineal membrane and perineal body, which stabilise the lower third of the vagina (67) (Figure 4).

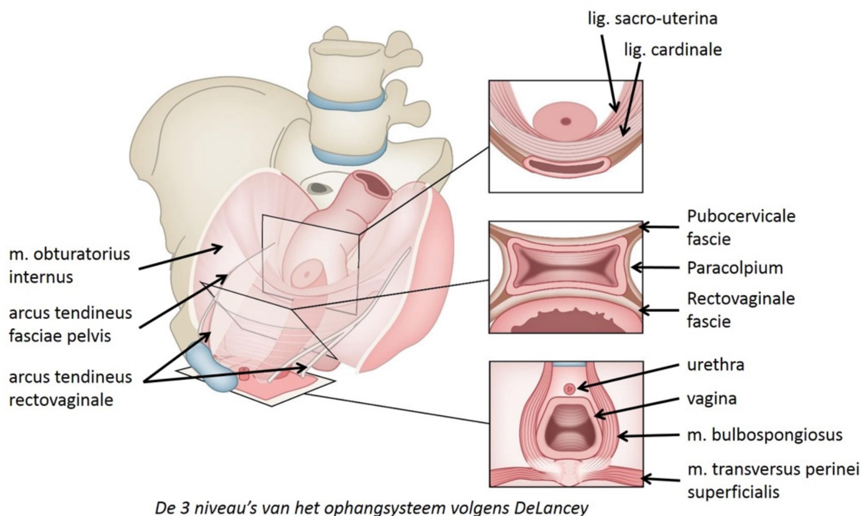


Figure 4. The endopelvic fascia's three levels of support. *Reprinted by permission by:"Delancey's three levels of pelvic support – Dutch lables" at AnatomyTOOL.org by Ron Slagter, LUMC and Marco DeRuiter, LUMC, license: Creative Commons Attribution-NonCommercial-ShareAlike.*

1.1.4 THE LOWER URINARY TRACT

The lower urinary tract comprises the bladder, bladder neck, and urethra. The female urethra, measuring 2-4 cm, extends from the bladder neck to the external urinary meatus. Initially, it passes through the bladder wall, surrounded by smooth muscle and the internal urethral sphincter. It then consists of three muscle layers and a vascular plexus and runs under an arch of striated muscle called the external urethral sphincter. The distal portion is a fibrous section lacking muscle (Figure 5). The structural layer, the pubovisceral fascia, that supports the bladder is composed of the anterior vaginal wall and its attachment through the endopelvic fascia to the pelvic wall (65).

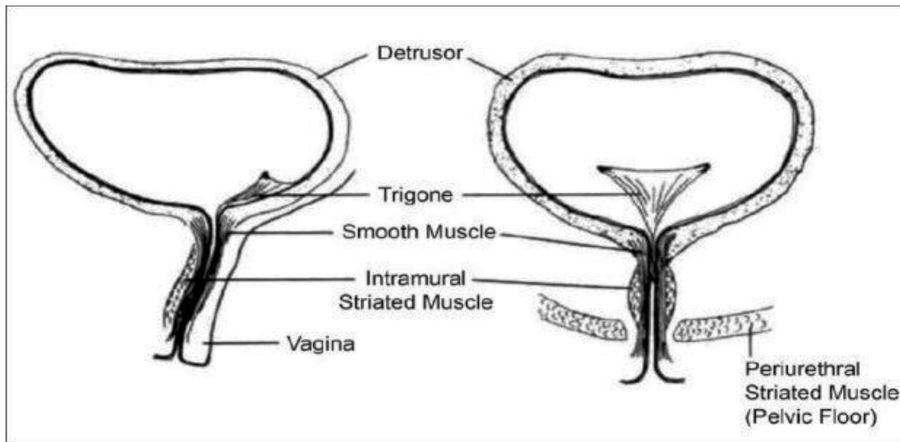


Figure 5. Anatomy of the female urethra: Linear diagram. *License by: CC BY-NC-SA 3.0.*

1.1.5 THE ANAL SPHINCTER COMPLEX

The anal sphincter complex consists of two muscles (Figure 6): (I) the internal anal sphincter (IAS), a smooth muscle that is innervated by autonomic nerves and forms the distal portion of the rectal circular smooth muscle, and (II) the EAS, a striated muscle that integrates with the puborectalis muscle of levator ani. The EAS surrounds the IAS and is innervated by the pudendal nerve (S2-S4) (69). Anal continence is maintained by the IAS, accounting for 70% of the resting tone, along with the constant activation of the EAS and the levator ani

(70). The puborectalis of levator ani, a sling-shaped muscle that forms a U-shape, around the rectum, creates the anorectal angle, where the anterior rectal wall functions as a flap valve, supporting anal continence (69,71).

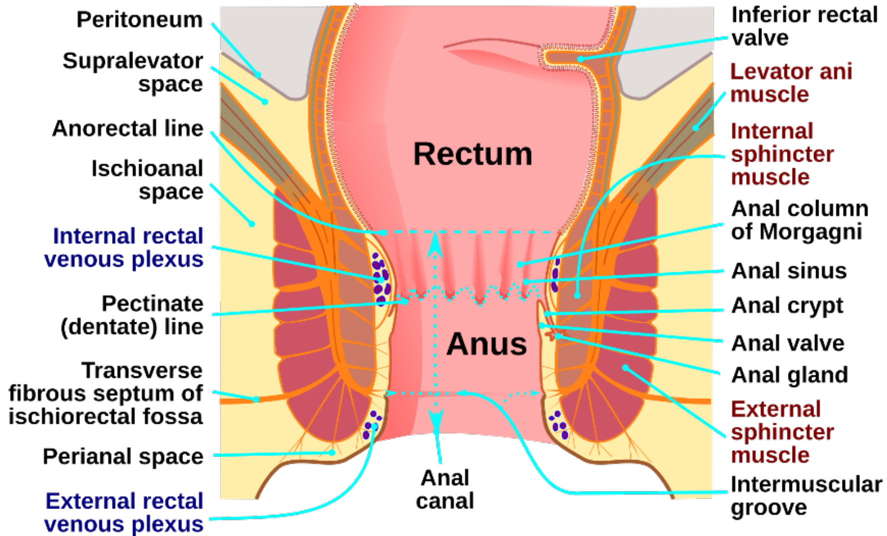


Figure 6. *"Jmarchn - Drawing Human Anus - English labels" at AnatomyTOOL.org by Jordi Marchn, license: Creative Commons Attribution-ShareAlike.*

1.2 THE EFFECT OF VAGINAL DELIVERY ON PELVIC FLOOR FUNCTION

Vaginal delivery causes significant trauma to the pelvic floor, affecting the pelvic nerves and levator ani muscle complex while also increasing the size of the levator hiatus and altering the pelvic fascial structures, bladder-neck position, mobility, and the anal sphincter (72). While most women experience some degree of pelvic floor injury during childbirth, only a portion go on to develop long-term dysfunction (14,15).

During pregnancy and childbirth, the pelvic floor undergoes physiological adaptations that facilitate the passage of the fetus from the intrauterine to the extrauterine environment. The second stage of labor, which starts at full cervical dilation and ends with the birth of the fetus, involves the levator ani muscle, which is involved in defining the dimensions and biomechanical ability of the birth canal. During the second stage, damage to the levator ani muscle is reported in 17.7% to 19.1% of cases when assessed with magnetic resonance imaging (MRI) and may result from overstretching (73-75). When evaluated by 3D/4D ultrasound, levator ani injuries after vaginal delivery range between 15-39.5%, depending on the clinical setting and mode of delivery (73,75). The most medial part of the levator ani, the pubovisceral muscle, has a stretch ratio of 3.26 during the final stages of the delivery and is most often injured at a vaginal birth (76) (Figure 7). The more lateral parts of the levator ani experience less tissue strain. Of the main pelvic floor nerves, the nerves supplying the anal sphincter undergo the greatest strain, 33% during the second stage of labor (13).

As the fetal head descends through the birth canal, it compresses and constricts intraneural vessels. Electrophysiological studies have demonstrated that neuropathic injury was observed in 42% of women after vaginal delivery. No evidence of pudendal nerve injury was seen after cesarean section. After 2 months, 40% of the vaginally delivered women still had unrecovered pudendal nerve function (77-79). While injuries to the levator ani near the perineal body are usually visible and repairable, avulsion of the levator ani from its attachment at the pubic bone is rarely diagnosed at delivery and has proven difficult to repair. Prevention of such avulsions is crucial, as they are a major risk factor for POP and recurrence of prolapse after surgical repair (80-82).

Factors significantly increasing the risk of levator ani avulsions include forceps delivery (OR 6.25, 95% CI [4.33-9.0]), OASI (OR 3.93, 95% CI [2.85-5.42]), vacuum delivery (OR 2.41, 95% CI [1.40-4.16]), and maternal age (OR 1.06, 95% CI [1.02-1.10]) (83).

Fascial trauma following vaginal delivery can impact various pelvic compartments. In the anterior compartment, disruption of the paraurethral and paravaginal structures may result in increased bladder descent after childbirth. In the posterior compartment, damage to the rectovaginal septum, the key connective tissue, can manifest as a rectocele, which is strongly associated with symptoms of POP and obstructed defecation (84,85).

The role of cesarean delivery in reducing the long-term risk of PFDs remains debated. Most epidemiological and imaging studies suggest that vaginal delivery is the primary cause of SUI and POP, including more severe cases (14,15,86,87). However, some studies indicate that the protective effect of cesarean delivery may diminish over time and even disappear after multiple deliveries (16, 17).

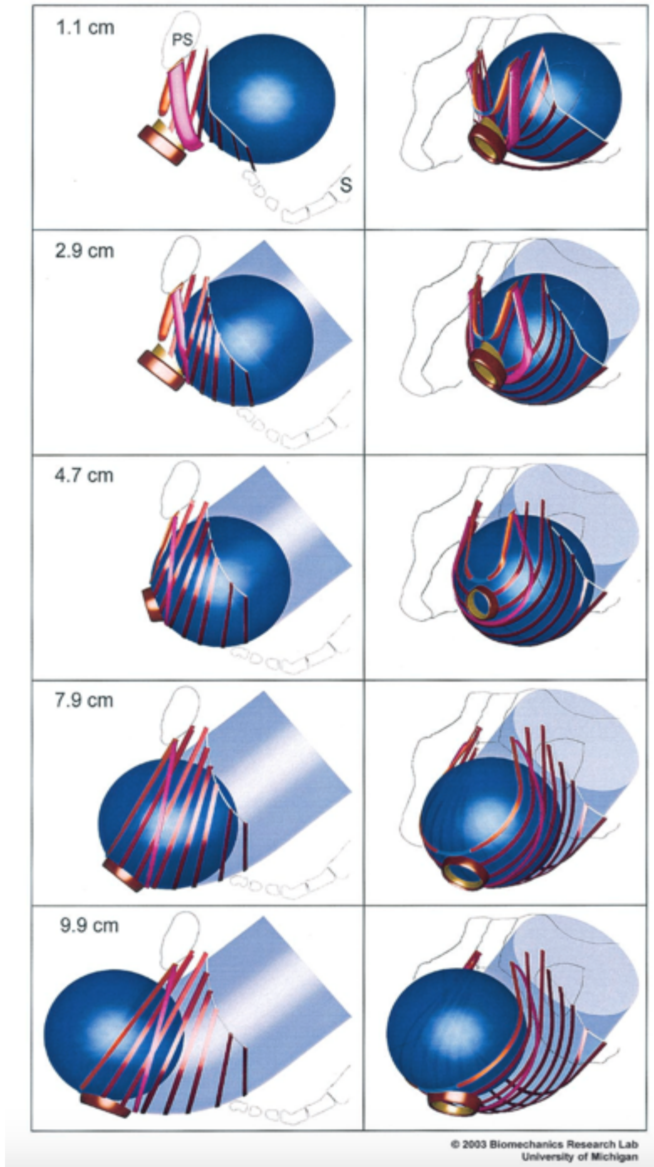


Figure 7. LAM. Simulated effect of fetal head descent on the levator ani muscles in the second stage of labor. *At top left, a left lateral view shows the fetal head (blue) located posteriorly and inferiorly to the pubic symphysis (PS) in front of the sacrum (S). The sequence of five images at left show the fetal head as it descends 1.1, 2.9, 4.7, 7.9, and 9.9 cm below the ischial spines as the head passes along the curve of Carus (indicated by the transparent, light blue, curved tube). The sequence of five images at right are front-left, three-quarter views corresponding to those shown at left. © 2003 Biomechanics Research Lab, University of Michigan, Ann Arbor*

1.3 PATHOGENESIS, PATHOPHYSIOLOGY AND SURGICAL TREATMENT

1.3.1 PELVIC ORGAN PROLAPSE AND SURGICAL TREATMENT

POP involves the descent of the anterior or posterior vaginal wall, uterus, or vaginal vault following hysterectomy. The integrity of the endopelvic fascia, the pelvic floor musculature, and an adequate nerve supply maintain the normal support of the pelvic organs. Vaginal delivery and increasing parity are known to compromise these structures and are regarded as primary causal factors in the development of POP (17,88-93). In an ultrasound study of 781 women, prolapse was observed in 83% of those with levator ani muscle avulsion, compared to 44% of women without, indicating a relative risk (RR) of 1.9 (95% CI 1.7-2.1) (94). However, DeLancey's life span model suggests that pelvic floor function is affected by three phases: predisposing factors (e.g., genetic constitution), inciting factors (e.g., vaginal delivery with muscle or nerve damage), and intervening factors (e.g., aging, obesity, chronic cough) (Figure 8) (95,96).

The hymen seems to be an important cut-off level regarding the presence of symptoms, and reporting “seeing” or “feeling” a vaginal bulge strongly correlates to symptomatic POP (sPOP) (97-99). Lower urinary tract symptoms (LUTS), bowel emptying dysfunction, and sexual dysfunction are common in POP (100). Several studies show that women seeking treatment for POP have a poorer body image and quality of life (101,102).

The treatment of sPOP depends on the severity of the condition, the patient’s health, and their preferences. Options include conservative management, such as the use of pessary devices and surgical interventions.

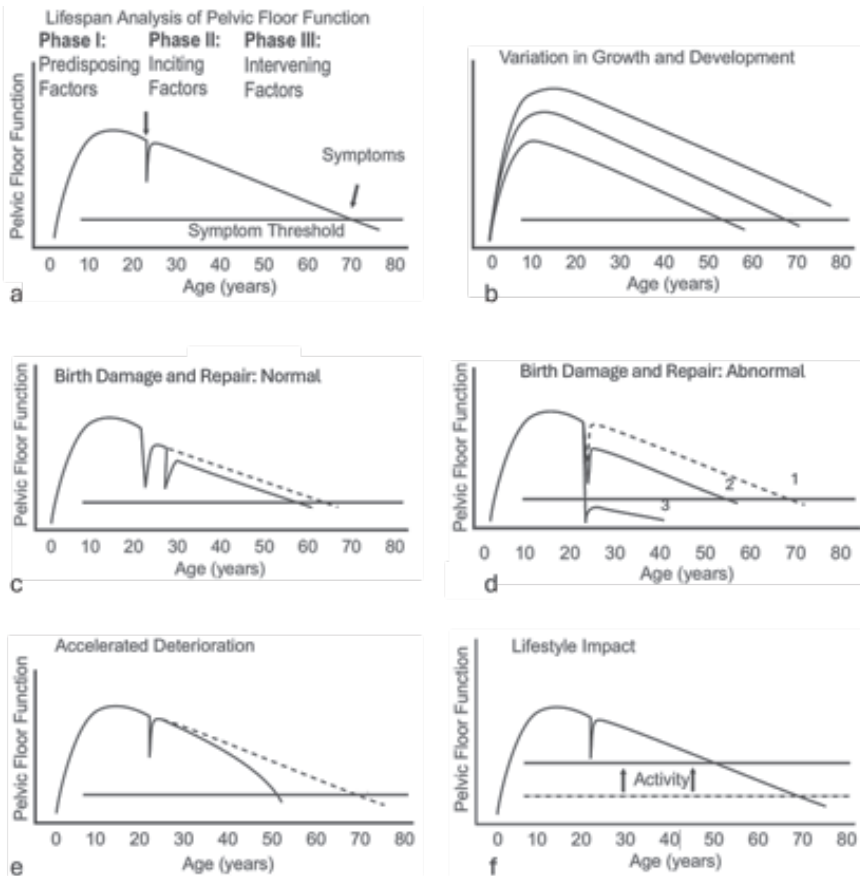


Figure 8. Graphical display of the concept of pelvic floor function considering: (a) Phases of a woman's life span; (b) Different degrees of functional reserve; (c) and (d) Variations in birth damage and repair; (e) Accelerated deterioration; (f) Lifestyle impact. *From DeLancey et al.*[96] *© DeLancey*

1.3.1.1 SURGICAL TREATMENT OF PELVIC ORGAN PROLAPSE

Surgery primarily aims to alleviate prolapse symptoms, with colporraphy as a common approach (103). A vertical incision is made along the length of the vaginal wall, followed by dissection to separate the urinary bladder or rectum from the vaginal mucosa. The fibromuscular tissue from the vaginal sulci is then adapted in the midline with sutures, and excess mucosa is excised before closing the incision with sutures (Figure 9).

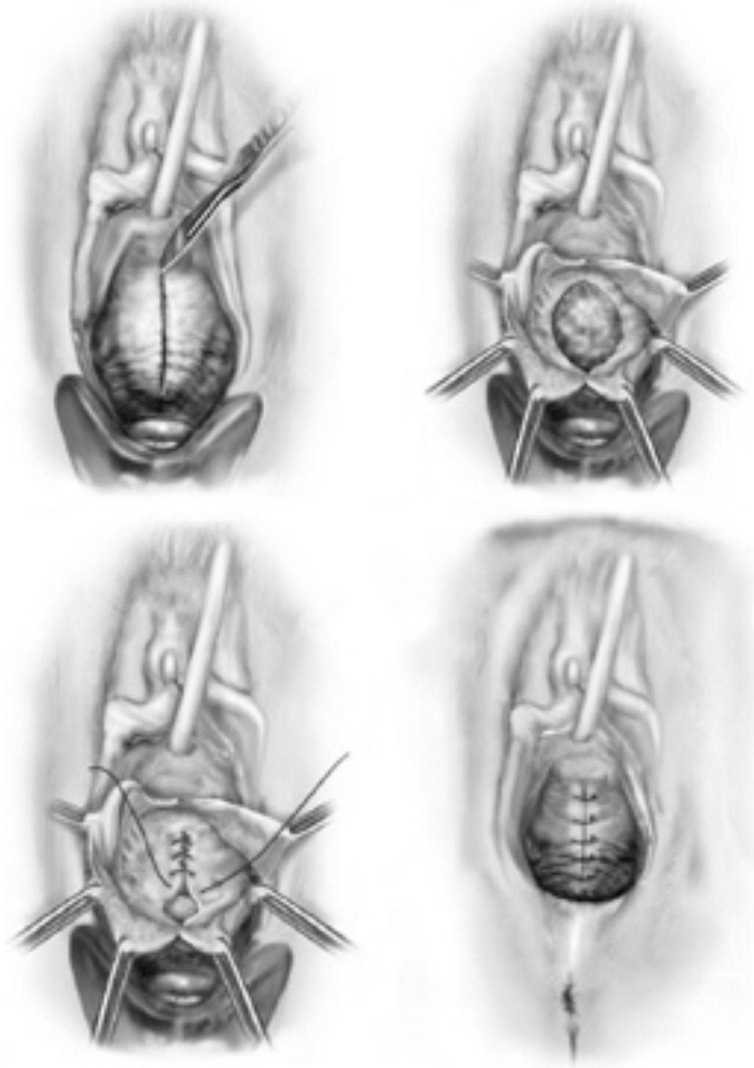


Figure 9. Illustration of steps of anterior repair of cystocele. *Copyright 2010, RD Moore and JR Miklos. Reprinted with permission from © miklosandmoore.com*

1.3.2 STRESS URINARY INCONTINENCE

To maintain urinary continence during increased abdominal pressure, several factors are required: (I) a functional striated sphincter muscle with pudendal nerve control, (II) well-vascularized urethral mucosa, (III) properly functioning intrinsic urethral smooth muscle, and (IV) intact urethra-vaginal support (104,105). Two main theories explain the cause of SUI: The Integral Theory attributes SUI to tissue laxity in the vagina or its supporting ligaments, while the Urethral Hanging Theory suggests that proximal urethral funneling, which shortens the urethra's functional length, is the key factor (106, 107). DeLancey's "hammock hypothesis" posits that the anterior vaginal wall acts as a supportive backboard, compressing the urethra during increased intra-abdominal pressure (108). The pubococcygeus muscles and the stability of the endopelvic fascia are essential for effective urethral closure during stress events like coughing (109,110). As a result, during periods of increased intra-abdominal pressure, the proximal urethra and bladder neck descend and rotate out of the pelvic cavity, causing the urethral lumen to open, which allows urine to leak (111). Additionally, obesity is strongly associated with SUI, likely due to elevated resting intravesical pressure and higher maximal pressure generated during activities such as coughing (112, 113).

In contrast to theories focused on vaginal position and mobility, ISD is proposed as a distinct cause of SUI. ISD, or primary urethral weakness, occurs when the urethral sphincter is unable to generate sufficient pressure to retain urine in the bladder during episodes due to defects in pudendal nerve innervation, reduced striated sphincter mass and function, and abnormalities in the urethral smooth muscle, mucosa, and submucosal cushions (114-117). Unlike patients with hypermobility, individuals with ISD typically exhibit little or no urethral mobility and may experience continuous leakage or leakage with minimal physical effort.

1.3.2.1 SURGICAL TREATMENT OF STRESS URINARY INCONTINENCE

Several surgical options are available for treating SUI, with the mid-urethral sling (MUS) being a highly effective, safe, and less invasive alternative to earlier techniques (21-23). The MUS procedure begins with a 1.5 cm incision in the midline of the anterior vaginal wall, approximately 0.5 cm from the external urethral meatus. Two small skin incisions are then made above the

pubic bone. A blunt paraurethral dissection is performed up to the lower edge of the pubic bone, followed by perforation of the urogenital diaphragm using a tunnelling instrument to position a synthetic mesh sling in a U-shape around the mid-urethra (Figure 10, Tension-free Vaginal Tape (TVT) sling). The vaginal and skin incisions are subsequently closed with sutures. In some cases, cystoscopy is performed at the end of the procedure to verify that the bladder or urethra has not been injured.

In contrast to the retropubic approach described above, the transobturator approach involves passing the ends of the sling laterally through the obturator foramen, exiting at the groin (Figure 10, Trans-Obturator tape (TOT) sling). The sling supports the urethra by providing resistance during increases in intra-abdominal pressure while remaining tension-free at rest, thereby mimicking the function of the pubourethral ligament. Both surgical approaches result in comparable objective and subjective cure rates in the short and medium terms (23).

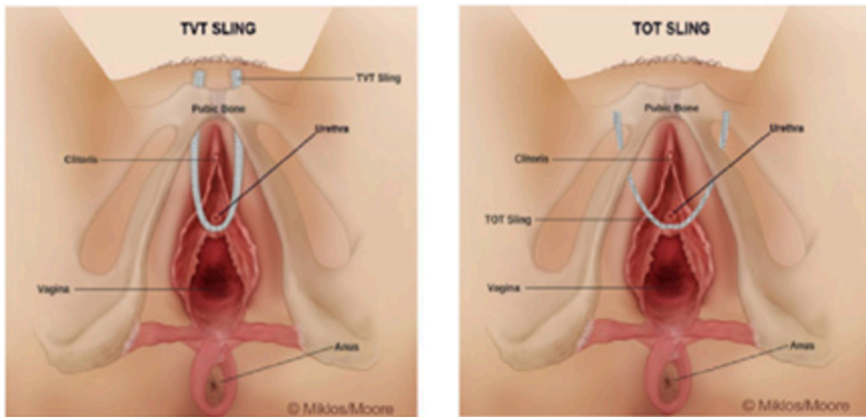


Figure 10. Tension-free vaginal tape and Trans obturator tape. *Reprint with permission from © miklosandmoore.com*

1.3.3 OBSTETRICAL ANAL SPHINCTER INJURY

An OASI is defined as a complete or partial rupture of the EAS and or rupture of the IAS during vaginal delivery (31). Obstetrical trauma is widely recognized as the primary cause of anal incontinence (AI), though symptom

onset may be delayed for several years post-delivery. This latency is thought to be influenced by factors such as aging, declining sex hormone levels, and the progression of neuropathy (105). Incidence of AI within the first year following vaginal delivery has been reported to range from 5-26% (31,118,119). AI incidence was 2-fold higher among those with tears affecting more than half of the EAS thickness and or a rupture of the IAS (120). Longitudinal data suggest a cumulative impact of one or two OASIs on AI severity, with rates of bothersome fecal incontinence reported at 3.3%, 10.4%, and 16.5% in women with no, one, or two OASI, respectively, two decades after vaginal delivery (49,121). Qualitative studies have demonstrated severe consequences, including limitations in daily activities, social debilitation, and isolation (50,51). Secondary sphincter repairs, while initially improving incontinence, often yield disappointing long-term results (122).

1.4 EPIDEMIOLOGY AND RISK FACTORS

1.4.1 PELVIC ORGAN PROLAPSE

Estimates of the prevalence of POP vary depending on how the condition is defined. When based on the symptoms of a sensation of a mass bulging into the vagina, prevalence is consistently reported across studies, ranging between 5-10% (17,90,91,93,123,124). However, when using anatomical findings, the prevalence of POP varies between 30-75% (125-127). Another approach to assess the epidemiology of POP is to study the rate of surgical treatment for POP, which presupposes an objectively confirmed condition and bothersome symptoms affecting quality of life. Estimates of the lifetime risk for undergoing at least one surgical procedure for POP range from 6-19% (9,11,88). Environmental factors that contribute to POP include vaginal delivery, chronic increases in intra-abdominal pressure, obesity, advanced age, and estrogen deficiency (8,90-94). However, studies on nulliparous women under 60 years show clinical POP with symptoms in 2-9.8% (128,129), and evidence suggests a possible genetic influence and familial predisposition of POP (130).

1.4.2 STRESS URINARY INCONTINENCE

Urinary incontinence (UI) is defined as the involuntary loss of urine. The most common subtypes of UI are UUI, characterized by the involuntary loss of urine

associated with urgency; SUI, defined as the involuntary loss of urine during physical exertion or effort; and mixed urinary incontinence (MUI), which is a combination of both UUI and SUI. Prevalence estimates for UI vary considerably between studies due to methodological differences, including the phrasing of survey questions, recall periods, cultural factors, and variations in individuals´ willingness to seek medical attention or report symptoms. Approximately 10% of adult women report experiencing leakage at least weekly, while 25% and 45% report occasional leakage. Isolated SUI accounts for about half of all incontinence cases, with prevalence estimates typically ranging from 10% to 39% in most studies (131). Annual incidence rates for SUI also vary based on recall periods; Liu et al. reported a 15.4% annual incidence for "any SUI" (132), while Nygaard et al. found a lower rate of 4.77% (133). Rates for "monthly SUI" ranged from 5.0–8.3% annually (134,135). Vaginal delivery and parity are strongly linked to the development of SUI. Tähtinen et al.'s systematic review and meta-analysis found that vaginal delivery nearly doubled the long-term risk of SUI compared to cesarean section (136). As previously noted, the protective effect of cesarean delivery on the risk of UI remains controversial; evidence suggests that this advantage diminishes over time and may be lost after multiple deliveries. (16,17).

1.4.3 OBSTETRICAL ANAL SPHINCTER INJURY

The rate of OASI varies between countries and birth centres over time (28,137). It differs even more comparing primi- and multiparas and delivery modes. In a study from 4 countries by Gyhagen et al., with 1,933,930 primiparous women or women with a VBAC, the authors found that the incidence of OASI varied from 4.1 to 15.5% between countries across the study period (30). In Sweden, there has been a downward trend in OASI, from 3.5% in 2014 to a rather stable incidence of ~2.6% since 2018. Among primiparas in Sweden, in 2022, the rate was 3.9% in spontaneous vaginal delivery (SVD) and 10% in instrumentally delivered women (138). Nulliparity, instrumental delivery, infant birth weight >4 kg, shoulder dystocia, occiput-posterior position, previous OASI, advanced maternal age, and prolonged second stage of labor have been identified as major risk factors for OASI (31,35,41,53,139–141). In addition, perineal wound complications in the first birth appear to increase the risk of OASI in the second birth (142). The use of forceps in operative vaginal deliveries varies over time and across different countries. An

increase in forceps use has been linked to higher and increasing rates of OASI compared to vacuum extraction (VE) (43). Although VE also carries a risk of OASI, particularly in primiparous women (36,143,144), episiotomy appears to provide a protective effect in this context (145,146). The OECD (2023) reported that the incidence of OASI following SVD among member countries ranged from 0.3% to 3.5% across all parities, whereas the incidence increased substantially to 1.1% to 15.8% following instrumental vaginal delivery (147). Consistent with these findings, data from the Swedish Medical Birth Register demonstrated an OR of 2.9 for OASI after VE compared with SVD (148). Additionally, previous research indicates an increased risk of OASI in women undergoing VBAC, with an elevated risk ranging from 10% to 60% compared to first-time SVD (27,33,41,119,149,150).

1.5 ON PREDICTION MODELLING

Prediction modelling is a data-driven method that uses machine learning to predict future outcomes based on past data. It involves creating mathematical models that establish connections between input variables (predictors) and the desired outcome. Traditionally, prediction models fall into three main categories: regression, classification, and neural networks. Regression modelling is the most used approach in medicine, relying on prior knowledge from previous studies or expert opinions on the subject.

1.5.1 APPLICATIONS OF PREDICTION MODELS FOR CLINICAL USE

Evidence-based medicine (EBM) seeks to use the best available evidence in a conscientious, explicit, and judicious way to guide patient care decisions (151). However, EBM has been criticised for not adequately considering patient values and preferences, which are essential in Shared Decision-Making (SDM) (152). SDM involves both physicians and patients actively participating in decisions about diagnostic tests and treatment options. A key requirement of SDM is providing patients with tailored information on their options, including the benefits and risks specific to their situation.

In response, personalised medicine has emerged as a new paradigm, focusing on determining which interventions work best for each individual patient (153). Current prediction models, which estimate the likelihood of future events for individual patients, align with this personalised approach by emphasising patient preferences, values, and autonomy in decision-making (154,155). These models and scoring systems have been successfully utilised in various medical fields to identify patients at risk (55,56).

Earlier efforts to assess the risk of OASI in EBM primarily relied on group-level relative risk estimates from meta-analyses (35,156). A review spanning the past 30 years identified 263 prediction models for maternal and fetal outcomes in obstetrics, but none have seen widespread clinical adoption (157). To date, only a limited number of studies have developed and validated OASI-specific prediction models, with varying adherence to current guidelines (36,52,53,158-160).

Accurately identifying women at high risk of birth-related injuries helps clinicians reassure those unlikely to face harm during vaginal delivery and implement protective measures for those at higher risk of medium- to long-term pelvic floor damage (161,162). Additionally, scoring systems are being developed to provide evidence-based antenatal guidance, aiming to reduce unnecessary cases of PFDs that might require future surgical intervention. When validated and consistently used, these scoring systems can empower more women to approach labor confidently, decreasing the risks of long-term pelvic floor complications (96).

2. AIM

The overall objective of this thesis was to examine how childbirth factors, such as delivery mode, number of births, and infant birth weight, affect long-term pelvic floor health in mothers, with a focus on the risks of pelvic floor disorders, surgical interventions, and prevention of anal sphincter injury.

The specific aims were:

In **Paper I,** to use data from three high-quality national registers to analyse the relative contribution of vaginal delivery and cesarean delivery, parity, and factors not related to childbirth on the long-term relative and absolute risk for reconstructive pelvic floor surgery.

In **Paper II,** to evaluate how chronological age and physical status, defined by the American Society of Anesthesiologists (ASA) classification, affect surgical outcomes and adverse events at a one-year follow-up, based on the hypothesis that physical status could significantly influence postoperative success.

In **Paper III,** to analyse the influence of infant birth weight on the mode of delivery. Secondly, to quantify the risk of multiple maternal and neonatal complications in nulliparous women with a planned vaginal delivery compared to those with a planned cesarean delivery. Thirdly, to assess the subjective impact of infant birth weight on mothers' delivery experiences, evaluated at 8 weeks postpartum, for each mode of delivery.

In **Paper IV,** the objective was to create and validate prediction models for OASI across three birth scenarios: first vaginal delivery, second vaginal delivery, and VBAC. These models incorporated antenatal and intrapartal factors to build an interactive, user-friendly, web-based calculator.

3. MATERIALS AND METHODS

3.1 ETHICAL CONSIDERATIONS

All studies in this thesis were ethically approved by the Regional Ethical Review Board in Gothenburg, Sweden, or the Swedish Ethical Review Authority, following the General Data Protection Regulations.

Ethical approval for the studies, obtained from the Regional Ethical Review Board in Gothenburg, Sweden;

Reference no. 345-17; June 15, 2017, **Paper I-IV**

Reference no. 345-17 and T321-18; April 12, 2018, **Paper I-IV**

Reference no. 345-17 and T891-18; October 15, 2018, **Paper I-IV**

Ethical approval obtained from the Swedish Ethical Review Authority;

Reference no. 2020-01359; May 6, 2020, **Paper II**

Reference no. 2022-04466-02; September 3, 2022, **Paper IV**

Reference no. 2024-00127-02; January 25, 2024, **Paper III**

All national registers used in these studies provided their formal approval. Only pseudonymized datasets were used in the statistical analyses, ensuring that no personal data were accessible to the research group. A statistician at Statistics Sweden replaced all Personal Identification Numbers with unique serial numbers, with Statistics Sweden securely retaining the key for three years, with the option to apply for an extension. The key file was sent to the respective register holders. Before transfer to the research team, all data were encrypted, with the password provided separately. Data storage and management were securely handled by Statistiska Konsultgruppen in Gothenburg. Across **Papers I-IV**, common ethical dilemmas emerge that are typical of register-based studies. Although the databases used in this thesis are

large and pseudonymized, it remains hypothetically possible to identify individual women based on unique outcomes or specific demographic characteristics. To address this, data should be presented within carefully defined groupings to protect individual privacy. When handled correctly, the benefits of register-based studies generally outweigh the risks, as the potential harm to individual integrity is minimised and is far outweighed by the population-level benefits of increased knowledge and insights. It should be noted that participants in the register will not derive any direct benefit from the results; however, subsequent patients may benefit from the findings. For **Papers I** and **II**, data from pre- and postoperative questionnaires were used. All women were provided written information about the registry and the possibility to opt out at any time.

3.2 SUMMARY OF STUDY DESIGNS

Study	Study design	Population	Intervention	Comparison	Outcome
I. The influence of pregnancy, parity, and mode of delivery on urinary incontinence and prolapse surgery-a national register study	Register based cohort study	Women ≥ 45 years in Sweden registered in the GynOp	POP and SUI surgery	Nulliparous women, women with CD only, and women with at least one VD	AR and RR for surgery for POP or SUI. Vaginal or cesarean parity and the risk of surgery for POP or SUI
II. The influence of age and health status for outcomes after mid-urethral sling surgery-a nationwide register study	Register based cohort study	Women in the GynOp aged 55-94 years between 2010-2017	Mid-urethral sling surgery	Three age groups, and ASA-classes 1-2 vs. 3-4	1-year post operative rates of cure for SUI, satisfaction, and improvement. Rates of de novo and improvement in LUTS. Complications and adverse events
III. Larsudd-Kåverud J, Åkervall S, Molin M, Milsom I, Kuusela P, Gyhagen M. The influence of infant birthweight on mode of delivery and short-term maternal and neonatal complications in primiparous pregnancies.	Register based cohort study	Nullipara women with a singleton live pregnancy in gestational week ≥37+0, cephalic or breech presentation	Planned vaginal delivery or elective cesarean delivery	Birthweight categories: 3000-3999g (reference), 4000-4499g, 4500-4999g, and ≥5000g and delivery mode.	Adverse maternal and neonatal outcomes within 42 days of delivery.
IV. Predicting obstetric anal sphincter injury in the first and second vaginal delivery and after a cesarean delivery: development and validation of an intrapartal model	Clinical prediction model	First and second deliveries in gestational week ≥37+0 with singleton pregnancies and cephalic presentation	Development and validation of prediction models for OASI	Performance in different birth scenarios (first VD, VABC, second VD) and subset models.	Key predictors of OASI. Performance of prediction models. Web-based risk calculator.

3.3 REPORTING GUIDELINES

This thesis adhered to several reporting guidelines established by The EQUATOR Network (163). Specifically, **Paper III** followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (164), ensuring comprehensive reporting of observational research. In contrast, **Paper IV** was conducted in accordance with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines, which focus on the development and validation of prediction models (165). Additionally, to assess the risk of bias and applicability in **Paper IV**, the PROBAST checklist, developed by Moons et al., was applied (166).

3.4 THE REGISTERS

3.4.1 THE SWEDISH MEDICAL BIRTH REGISTER

The Swedish National Board of Health and Welfare oversees the MBR, established in 1973. The MBR includes data on approximately 98% of all deliveries in Sweden, encompassing over five million births (167). Reporting to the MBR is mandatory for all Swedish birth centres, ensuring comprehensive national coverage. Data collection begins at the first antenatal visit and continues throughout pregnancy, delivery, and the neonatal period. Information is systematically recorded in standardised antenatal, obstetric, and neonatal records, concluding with the mother and infant's discharge. At this point, data are submitted to the MBR, which is updated annually (57). Maternal data in the MBR include biometric measurements, medical and obstetric history, and any concurrent medical conditions. Birth and neonatal data encompass infant birth weight, mode of delivery, head circumference, Apgar scores, and other critical metrics. The MBR is widely regarded as a high-quality registry, benefiting from Sweden's universal access to antenatal care and a semi-automated data extraction process (167).

3.4.2 THE SWEDISH NATIONAL QUALITY REGISTER OF GYNECOLOGICAL SURGERY

The GynOp, established in 1995, serves as a comprehensive tool for audit and research purposes in gynecological healthcare (58). Legally and

administratively managed by the County Council of Västerbotten in Umeå, Sweden, GynOp covers seven key areas of gynecological surgery: hysterectomy, adnexal procedures, gynecological tumour surgery, hysteroscopy, endometrial ablation, third- and fourth-degree perineal tears, as well as surgeries addressing POP and SUI. Data collection for POP and SUI surgeries began in 2006. Since 2011, GynOp has seen a significant increase in clinic participation, with registry coverage expanding from 86% to over 90% by 2017. 96% of eligible patients are represented in GynOp, capturing approximately 3,500 SUI and 6,000 POP procedures annually. These surgeries are day-care or inpatient procedures under local, regional, or general anesthesia. Data for GynOp is collected through several sources: a preoperative questionnaire (completed via mail or web), hospital records from admission to discharge, and postoperative questionnaires administered at 8 weeks and 1 year following surgery. Patient enrolment is coordinated by a surgical coordination nurse or department secretary at the time of scheduling, who provides patients with written information about the registry and an option to opt out. The Swedish Association of Local Authorities and Regions (SALAR) has awarded GynOp its highest quality certification (level 1), attesting to the registry's data integrity and role in advancing gynecological surgery standards in Sweden (168). In a recent study, Geara et al. demonstrated that GynOp has strong internal validity (169).

3.4.3 THE SWEDISH NATIONAL INPATIENT REGISTER

The Swedish National Inpatient Register (NPR), established in 1964, has provided complete national coverage since 1987, supported by mandatory participation from all county councils. In 2001, the register expanded to include data on outpatient specialist care (59). The NPR contains detailed patient information, including sex, age, geographic location (county), hospital, department type, mode of admission and discharge, and primary and secondary diagnoses. Since 2007, the reporting of all performed procedures has also been required. In a 2011 validation study, Ludvigsson et al. assessed the accuracy of the NPR, confirming its value as a resource for register-based research. Their review reported a high positive predictive value of 85–95% for diagnoses recorded in the register, demonstrating the reliability of NPR data for epidemiological studies (170).

3.4.4 THE SWEDISH CAUSE OF DEATH REGISTER

The Swedish Cause of Death Register (SCDR), maintained by the National Board of Health and Welfare, is a nearly comprehensive record of all deaths in Sweden since 1952. The register is updated annually (171). Data is categorised according to the latest version of the International Classification of Diseases (ICD). In 2015, only 0.9% of all recorded deaths were missing an underlying cause (as reported by R99.9, "death certificate not received"). The SCDR is regarded as a high-quality data source for both official statistics and research purposes (172).

3.4.5 REGISTERS BY STATISTICS SWEDEN: THE LONGITUDINAL INTEGRATED DATABASE FOR HEALTH INSURANCE AND LABOUR MARKET STUDIES AND THE TOTAL POPULATION REGISTER

The Total Population Register (TPR) and the Longitudinal Integrated Database for Health Insurance and Labor Market Studies (LISA) are nationwide registers and managed by Statistics Sweden. Since 1990, LISA has been able to collect annual data on individuals' education, income, occupation, and employment by calendar year (173). The register is based on all individuals aged ≥16 and is part of the Total Population Register (TPR). A list of all LISA data sources can be found on the register´s web page (174).

The TPR started in 1968, is updated every four weeks, and has 99.7% coverage. The register contains data on life events such as birth, death, name change, marital status, and migration within Sweden and to and from other countries. At birth, the hospital reports the birth to the Total Population Register, maintained by the Swedish National Tax Agency (PR-Tax), and the child is automatically assigned a personal identification number (PIN). It is estimated that <0.1% of newborns are not reported to the PR-Tax within 30 days. The Tax Agency records the citizenship and the newborn´s family name. The husband is assumed to be the biological father if the couple is married. If not, paternity is confirmed through a notification to the Social Welfare Committee signed by both parents. The PR-Tax reports to the TPR. Within 30 days, 100% of deaths and births, 95% of immigration cases, and 91% of emigration cases are reported, with reporting completeness increasing over

time. For non-Swedes, the country of birth is registered with the country's name at the year of birth of each individual. The TPR may overestimate the number of individuals in Sweden, 0.25-0.5% of the Swedish population, due to the underreporting of emigration. The quality and timeliness of the TPR have been considered high (175).

3.4.6 THE SWEDISH PREGNANCY REGISTER

The Swedish Pregnancy Register (SPR) is a national quality database that collects maternal, delivery, and neonatal data through automated processes directly from medical records (176). Information not systematically captured in medical records is manually recorded by maternal healthcare providers. From 2019 to 2021, the register achieved an annual coverage rate of 97.9% to 98.4%. However, delivery data from two out of Sweden's 21 regions, accounting for 5.5% of births during that period, were missing due to technical issues.

3.4.7 PERSONAL IDENTITY NUMBER

This thesis linked data from various registers using the personal identity number (PIN), a ten-digit, sex-specific identifier assigned at birth or immigration. While the primary purpose of the PIN in Swedish healthcare is to support individual patient care, it also facilitates research and healthcare quality assurance (177). Established in 1947, the Swedish PIN system has occasionally required adaptations due to immigration, resulting in a small number of reused PINs, which can pose challenges for researchers. To address this, Statistics Sweden maintains a list of reused PINs. Individuals with more than one PIN (due to sex change or protected identity status) are rare, representing only 0.33% of those born in Sweden, and these changes are documented in a dedicated register.

3.5 PAPER I

3.5.1 STUDY COHORTS

In this study, all women in GynOp aged 45 years or older who underwent surgery for SUI or POP between 2010 and 2017 were eligible for inclusion (n=59,415). The study comprised three cohorts to assess the risk of surgery associated with different scenarios: (1) nulliparous women, (2) women whose first and all subsequent deliveries were by CD, and (3) women with at least one VD, regardless of any subsequent CDs. The number of births (0,1,2,3, ≥4) was recorded for all women. Parity data in the GynOp was verified against the TPR, with discrepancies resolved using the highest parity count (observed in 5% of cases). Delivery mode data was cross-checked with the MBR.

The reference cohort comprised all women born in Sweden in 1960 who were 57 years old in 2017. Since the 1930s, approximately 13% of women in Sweden have remained nulliparous throughout their lives; in this study, the 2017 rate for nulliparous women in the reference cohort (aged ≥45 years) was set at 13.8% (TPR). Among parous women (86.2%), the delivery mode was categorised using MBR data: 7.7% had at least one CD, and 92.3% had at least one VD. These distributions resulted in the following reference group classifications: 13.8% nulliparous, 79.6% with at least one VD, and 6.6% with only CD. Using these proportions from the cohort of 2,309,765 women (all women in Sweden aged 45 years or older, calendar year 2017), the number of women at risk for surgery was calculated for each reference category (Figure 11).

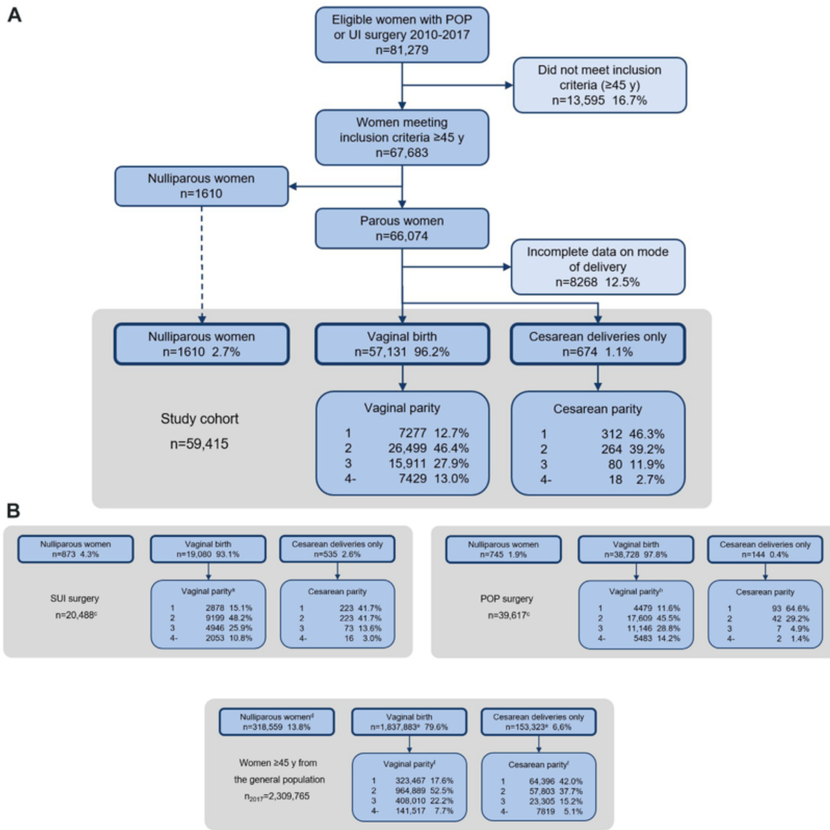


Figure 11. Flowchart of the study population. *A, The study population of women ≥ 45 years. B, Women having prolapse and incontinence surgery according to parity and mode of delivery. Superscript letter a denotes 4 women with uncertain parity; thus, the total number of women with known parity was 19,076. The superscript letter b denotes 11 women with uncertain parity; thus, the total number of women with known parity was 38,717. The superscript letter c denotes women with both incontinence and prolapse procedures, which were included in each treatment category. The superscript letter d denotes set according to the rate of nulliparous women aged ≥ 45 years in 2017 in the TPR. The superscript letter e denotes based on women born in 1960 recorded in the MBR. The rate of surgery for women with ≥1 CD and those with ≥1 VD was 7.7% vs. 92.3%, and given the rate for nulliparous women, the final distribution was 13.8%, 79.6%, and 6.6%, respectively. From these percentages, the number of women in all cohorts according to the mode of delivery and parity (0, 1, 2, 3,4) was calculated from the total number of women of 45-57 years of age in 2017 (n=2,309,765) down to the singular. Reproduced from Larsudd-Kåverud J, Gyhagen J, Åkervall S, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of pregnancy, parity, and mode of delivery on urinary incontinence and prolapse surgery – a national register study. Am J Obstet Gynecol. 2023 Jan;228(1):61.e1-61.e13.*

3.5.2 DEFINITIONS OF OUTCOME

The study's primary outcome is the long-term risk of undergoing reconstructive urogenital surgery for POP and SUI, based on factors such as mode of delivery and parity. The secondary outcomes include examining the absolute and relative risks of surgery considering the cumulative effect of parity and the potential protective effect of cesarean delivery against POP and SUI surgery. This analysis also covers additional variables like the comparative risks among nulliparous women and those who delivered exclusively by cesarean, relative to women with one or more vaginal births.

3.6 PAPER II

3.6.1 STUDY COHORTS

The study included all women in GynOp aged 55 years and older who underwent MUS surgery for SUI, with or without UUI, between 2010 and 2017 (n=5,200). Eligible surgeries included both transvaginal retropubic and transobturator procedures, performed as either day or inpatient cases under local, regional, or general anesthesia. Women with previous continence surgeries were included, while those who underwent concurrent prolapse surgeries were excluded.

Participants were grouped into three age cohorts: 55–64, 65–74, and 75–94 years (Figure 12). They were further categorized according to three criteria: (1) the American Society of Anesthesiologists (ASA) physical status class, with ASA 1–2 indicating no or mild systemic disease and ASA 3–4 indicating severe, potentially life-threatening systemic disease; (2) whether they had a history of previous UI surgery; and (3) the presence or absence of diabetes.

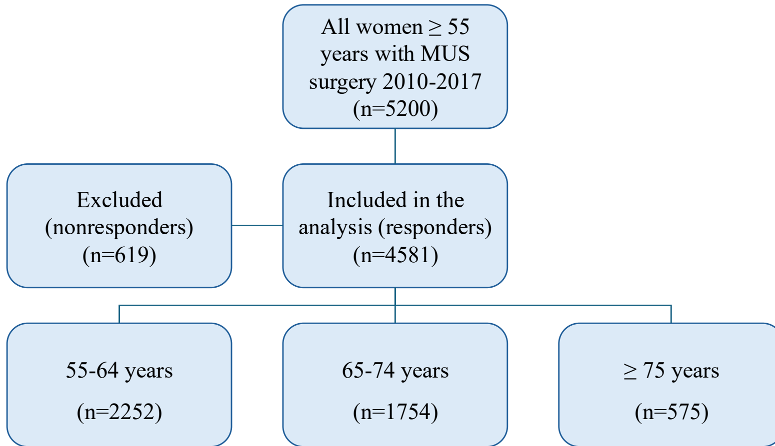


Figure 12. Flowchart of study participants in **Paper II.**

3.6.2 THE QUESTIONNAIRES

The preoperative questionnaire gathers a variety of important demographic and medical information, including height, weight, parity, and previous abdominal and gynecological surgeries, as well as any coexisting medical conditions and assessments of physical performance. It also includes validated questions about lower urinary tract symptoms (LUTS), as outlined in the work of Kulseng-Hanssen and Borstad (178). Using self-reported follow-up data on surgical outcomes for MUS is effective and correlates well with objective findings, as demonstrated in the national study by Kulseng-Hanssen et al. (179).

The assessment of SUI relied on the question, "How often do you experience leakage of urine associated with physical activity, or when you laugh, cough, or sneeze?" with response options of "Never" and "1-4 times per month" indicating no SUI, while options of "1-6 times per week," "once a day," and "more than once a day" indicated the presence of SUI. Urge urinary incontinence was assessed through the question, "How often do you experience a sudden onset of a strong need to urinate and leak urine before you reach the toilet?" Responses of "1-6 times per week," "once a day," or "more than once

a day" indicated UUI, while lower frequencies were classified as no UUI. For urinary urgency, the question "Have you had problems with a sudden onset of a strong need to urinate?" was used, with positive cases identified when respondents answered "1-3 times/week" or more often. Additionally, women were asked about difficulties in emptying the bladder, with a positive response indicated by experiencing such difficulties 1-3 times a week or more frequently.

Postoperatively, cure was defined as SUI reporting of "Never" or "1-4 times per month." Patient satisfaction was categorised as either satisfied ("very satisfied" or "satisfied") or dissatisfied ("neither satisfied nor dissatisfied," "dissatisfied," and "very dissatisfied"). Improvement in SUI was noted with responses of "greatly improved" or "improved," while failure was identified as a similar or increased frequency of leakage post-surgery.

De novo symptoms, such as urgency and difficulty emptying the bladder, were confirmed if patients reported a frequency of less than three times per month preoperatively but more than once or three times per week postoperatively. Additionally, de novo nocturia was defined as a change from fewer than two micturitions per night to two or more micturitions per night. Remission was defined as having symptoms at least once a week preoperatively, with a reduction to less than once a week one year postoperatively. The questionnaires are available online at https://www.gynop.se/home/gynops-questionnaire/.

3.6.3 DEFINITIONS OF OUTCOMES

UI and subtypes were defined according to the International Urogynecological Association (IUGA) and the International Continence Society (ICS) as a complaint of involuntary loss of urine. SUI was further specified as UI occurring on effort, physical straining, sneezing, or coughing, UUI was UI associated with urgency, and mixed UI was a combination of SUI and UUI (180). Having had prior POP or UI surgery was defined as reported by the woman in the pre-operative questionnaire. According to the definition of IUGA/ICS, the definition of clinically significant nocturia (≥2 times/night) was used. MUI was defined as having SUI and UUI in combination, according to IUGA/ICS joint terminology (180). Complications of surgery (bladder

injury, ureteric injury, and fistulas) were reported by the woman in the post-operative questionnaire.

3.7 PAPER III

3.7.1 STUDY COHORTS

Nulliparous women in the MBR aged 15–50 and their offspring were enrolled between January 1, 2008, and December 31, 2021. The inclusion criteria included a singleton live birth at term (≥37+0 weeks), an IBW ≥3000 g, and presentation in cephalic or breech position. The study population comprised 519,491 women who were allocated into planned VD, n=495,628 (spontaneous VD, vacuum extraction, and an acute CD), or a planned CD, n=23,863. 1073 forceps deliveries (1.4% of instrumental deliveries) were excluded. Women from non-OECD countries comprised 15.8% of the study population (https://www.oecd.org/en/about/members-partners). A flowchart of the study population is shown in Figure 13.

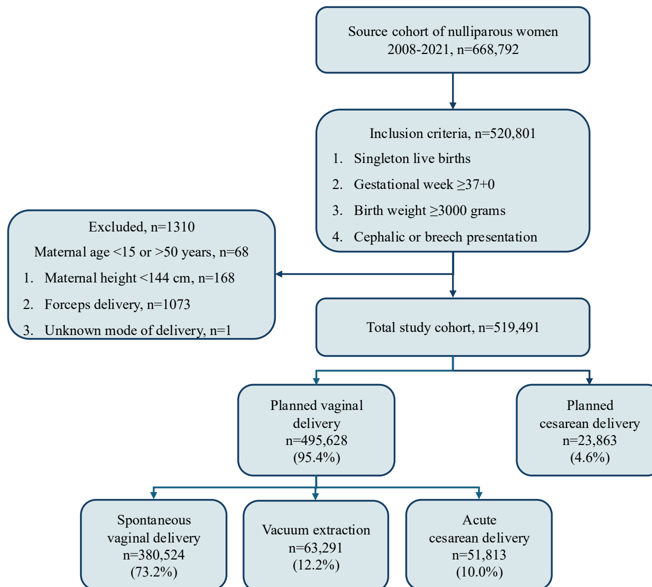


Figure 13. Flowchart of study population in **Paper III.**

3.7.2 DEFINITIONS OF EXPOSURES AND OUTCOMES

Gestational age, as verified by ultrasound, was assessed between 11 and 22 weeks of gestation or estimated based on the last menstrual period. Infant birth weight was split into 3000–3999g, 4000–4499g, 4500–4999g, and ≥5000g. We analysed 15 maternal and 9 neonatal, single and concurrent complications and used the Swedish Perinatal Core Outcome Set (SPeCOS) agreement for neonatal outcomes (181). Since few core outcome set studies have focused on labor and maternal postpartum complications, comparison with previous research was difficult (182,183). In this study, the selection of maternal complications was based on clinical experience, severity, and accessibility in the registers. A self-reported questionnaire linked to the Swedish Pregnancy Register, assessing women's birth experiences at 8 weeks postpartum, was started on October 1, 2020 (19,694 respondents). The questionnaire rated the experience on a 10-point scale, where 1 represented the "worst possible," and 10 the "best possible".

3.8 PAPER IV

3.8.1 STUDY COHORTS

This clinical prediction study analysed data from all 45 maternity units reporting to the MBR, including first and second singleton births at ≥37 weeks of gestation in cephalic presentation, between January 1, 2009, and December 31, 2017. Data were contributed by 159,627 women, each providing records for both deliveries, with each birth recorded as an independent episode.

3.8.2 DEFINITIONS OF OUTCOMES

According to the classification by Sultan et al., third-degree lacerations, known as OASI, involve damage to the EAS and/or the IAS. Fourth-degree OASI includes laceration of the rectal mucosa (31). In this study, OASI was categorized as a single group, regardless of the specific degree, and cases were identified in the MBR using ICD-10 codes O70.2 and O70.3, alongside the surgical Diagnosis Related Groups code MBC33.

3.8.3 STUDY DESIGN

All births were allocated into one of three scenarios: Scenario 1, the first vaginal delivery in nulliparous women, Scenario 2, VBAC; and Scenario 3, the second vaginal delivery in two-para women. Relevant predictors were selected prior to analysis based on registry data, subject matter expertise, prior research, and systematic reviews. Predictors were categorised into five domains: A. Maternal biometrics and characteristics; B. Obstetric information and infant biometrics from the previous delivery; C. Maternal morbidity; D. Labor events and interventions in the current delivery; E. Infant biometrics in the current delivery. Out of an initial 54 potential predictors, seven were excluded due to inadequate registration or collinearity, resulting in a final set of 47 candidate predictors for analysis.

3.9 MISSING DATA

The overall rate of missing data for outcomes across the studies was low. In **Paper I,** 11 women had missing information about vaginal parity in the POP surgery group, and 4 in the SUI surgery group. In **Paper II**, the proportion of missing values for the main outcomes ranged from 2.9% to 9.2%, with the highest non-response rate observed in the youngest age group. No analysis of non-responders was conducted. In **Paper III**, we excluded births with missing data for each analysis (n=1310). Regarding the analysis of birth experiences, no analysis was conducted for non-responders. In **Paper IV**, in the first vaginal delivery cohort, 301,680 out of 332,457 cases were complete (90.9%). In the VBAC cohort, 19,525 of 22,829 were complete cases (85.6%), and in the second vaginal delivery cohort, 242,532 of 254,630 were complete cases (95.2%). A complete-case analysis was performed, as the missing values were relatively low. Thirty-one predictors had no missing data, while maternal BMI (body mass index, kg/m2), pre-pregnancy smoking, smoking during pregnancy, maternal height, and BMI gain between births had slightly higher rates (4-11%). Overall, no imputation methods were used for missing data.

3.10 STATISTICS

The statistical analyses of this thesis were performed with SAS 9.4, SAS Inc., Cary, NC, USA. Descriptive data for continuous variables were presented as mean and standard deviation (SD), median, and interquartile range (IQR).

Categorical variables were presented as numbers, percentages, and a 95% CI. Results were presented as the mean difference for continuous variables and the difference in percentages for categorical variables with 95% CI and P value. For **Papers I** and **II**, trends across three independent categorical groups were evaluated using Mantel-Haenszel statistics. Pairwise comparisons of categorical variables were performed using Fisher's exact test, while the Mann-Whitney U test was applied to assess continuous variables. All statistical tests were two-sided, and the significance level was set at $P < 0.05$. No adjustment was made for multiple testing. **Paper III** and **Paper IV** used logistic regression to estimate OR and 95% CI. In **Paper III**, birthweight was analysed both categorically and per 500 g increase, with penalized B-spline curves applied to explore non-linear associations. In **Paper IV**, model development involved backward elimination using the Bayesian Information Criterion, assessment of performance with Nagelkerke's R^2 (R^2N), Brier scores, and c-statistics, and internal validation through bootstrap resampling.

3.10.1 PAPER I

Results for continuous variables were expressed as mean differences, and categorical variables were reported as percentage differences, each accompanied by a 95% CI and P value. The incidence rate (per 1,000 women) for surgery was determined by dividing the number of SUI or POP surgeries recorded in GynOp by the number of at-risk women in the reference population aged 45, with results presented along with a 95% CI. An observed-to-expected ratio was calculated, and Ulm's method was employed to determine the CI of the RR when comparing the proportions of cases in GynOp to those in the general female population aged 45 (184).

3.10.2 PAPER II

The 95% CI for differences in proportions between categorical variables was calculated using the exact method. Logistic regression models were used to estimate the age-related probabilities of cure, improvement, and satisfaction with SUI per 10-year intervals, adjusted for BMI and UUI**.**

3.10.3 PAPER III

The association between background characteristics and IBW was analysed using linear regression, with results reported as beta estimates, 95% CI, and P

values. Maternal and neonatal outcomes (binary) were analysed using logistic regression across IBW categories (3000g-3999g, 4000g-4499g, 4500g-4999g, and ≥5000g), stratified by delivery mode (spontaneous VD, vacuum extraction, acute CD, and planned CD), with 3000g-3999g in spontaneous VD as reference. Results were presented with OR and 95% CI. OR and 95% CI were calculated for the increase in IBW per 500g (continuous) and analysed for each mode of delivery.

Birth experience, assessed on a 10-point Likert scale, and the rate of complication-free deliveries (yes/no) were visualised against IBW using penalised B-spline curves, with smoothing parameters determined automatically. Differences in the overall prevalence of complication-free deliveries between delivery modes (planned CD and spontaneous VD vs. acute CD and vacuum extraction) were explored using Fisher's exact test. Birth experience comparisons across these groups were evaluated using Student's t-test. Lastly, Spearman's rank correlation was employed to examine the relationship between IBW and the number of maternal and neonatal complications, reported with correlation coefficients (r) and P values.

3.10.4 PAPER IV

Multiple logistic regression was employed to model OASI as a binary outcome, incorporating various continuous and categorical predictors for each birth scenario. Predictor selection was conducted through backwards elimination, using the minimisation of Bayesian Information Criteria (BIC) as the stopping criterion (185). To enhance predictor identification, BIC was supplemented with a bootstrap procedure (200 replications) (186). Non-linear effects of continuous predictors were evaluated using natural cubic splines with knots at the 10th, 50th, and 90th percentiles. Both linear and spline effects, and interaction terms were examined to achieve optimal BIC reduction. Final model formulas for each scenario were documented.

Model performance was assessed using R^2_N and the scaled Brier score, both presented as percentages with bootstrapped 95% CI based on 1000 replicates. Discrimination was measured with c-statistics and the discrimination slope, while calibration was evaluated through Observed/Expected statistics, calibration slope, and calibration intercept. To correct for potential optimism, model performance was adjusted using bootstrap validation (1000 replicates)

(187,188). The relative contribution of each predictor was quantified using R^2_N across the full, final, and subset models (189).

Additionally, a propensity score approach was applied to examine the impact of antepartum predictors on intrapartum interventions. After estimating the likelihood of each intervention, propensity scores were incorporated into the models, allowing a comparison between adjusted and original model effects.

4. RESULTS

4.1 PAPER I

Baseline characteristics were generally comparable across the parous groups, although nulliparous women were, on average, older than their parous counterparts. Among women who underwent SUI surgery, nulliparous individuals more frequently reported a history of hysterectomy, current estrogen therapy, and preoperative UUI. In total, 39,617 women underwent POP surgery and 20,488 underwent SUI surgery, of whom 690 (1.2%) had concomitant procedures. Within the study population, 57,131 women had ≥1 VD, 674 had CD only, and 1,610 were nulliparous. Among those who underwent SUI surgery, 93.1% had ≥1 VD, 2.6% had CD only, and 4.3% were nulliparous. For POP surgery, the corresponding proportions were 97.8%, 0.4%, and 1.9%, respectively (Figure 14).

The relative and absolute risk for surgery

Compared with vaginally delivered women aged ≥45 years in the general population (n=1,837,883), those in the VD group were significantly overrepresented in GynOp, both for SUI surgery (RR 1.17; 95% CI 1.15–1.19) and for POP surgery (RR 1.23; 95% CI 1.22–1.24; both $P < .0001$). Within the VD group, the expected number of POP procedures based on population data was 31,535; however, 38,728 were recorded in GynOp, corresponding to an 18% excess. In contrast, nulliparous women and those with CD only were markedly underrepresented. For SUI surgery, the RR was 0.31 (95% CI 0.29–0.33) in nulliparous women and 0.40 (95% CI 0.36–0.43) in the CD group (both $P < .0001$). A similar pattern was observed for POP surgery, with RR values of 0.14 (95% CI 0.13–0.15) for nulliparous women and 0.055 (95% CI 0.046–0.065) for the CD group (both $P < .0001$). Relative to the expected numbers, the incidence of POP procedures was reduced by 94% in the CD group and by 88% in the nulliparous group, while for SUI surgery, the corresponding reductions were 60% and 69%, respectively.

Figure 14. The distribution of study cohorts in GynOp and the general population. *Reproduced from Larsudd-Kåverud J, Gyhagen J, Åkervall S, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of pregnancy, parity, and mode of delivery on urinary incontinence and prolapse surgery-a national register study. Am J Obstet Gynecol. 2023 Jan;228(1):61.e1-61.e13. doi: 10.1016/j.ajog.2022.07.035. Epub 2022 Aug 3. PMID: 35932880.*

The absolute risk (AR) of POP surgery, defined as the number of procedures in GynOp relative to the number of women at risk in the reference population aged 45 years, was lowest among women delivered exclusively by CD (≥1 CD) (AR 0.09 per 1,000 women; 95% CI 0.08–0.11). In contrast, the AR in the VD group was 21.07 per 1,000 women (95% CI 20.9–21.3), representing a 23-fold elevation in risk.

The effect of parity on the AR of surgery differed markedly between the VD and CD groups. Using nulliparous women as the reference, the cumulative AR of surgery increased progressively with the number of VDs for both POP and SUI. For POP surgery, the AR was 2.3 per 1,000 women (95% CI 2.2–2.5) in nulliparous women, rising to 38.7 per 1,000 women (95% CI 37.8–39.8) among those with ≥4 VDs, representing a 17-fold higher risk. For SUI surgery, the increase was more modest but still consistent, from 2.7 per 1,000 women (95% CI 2.6–2.9) in nulliparous women to 14.5 per 1,000 women (95% CI 13.9–15.1) after ≥4 VDs, corresponding to a 5-fold higher risk.

Furthermore, significant trends in the AR for surgery according to parity were observed within the CD group, revealing a positive trend for SUI and a negative trend for POP surgery (both P < 0.0001). However, the magnitude of this effect was relatively small and comparable to that observed in nulliparous women (Figure 15).

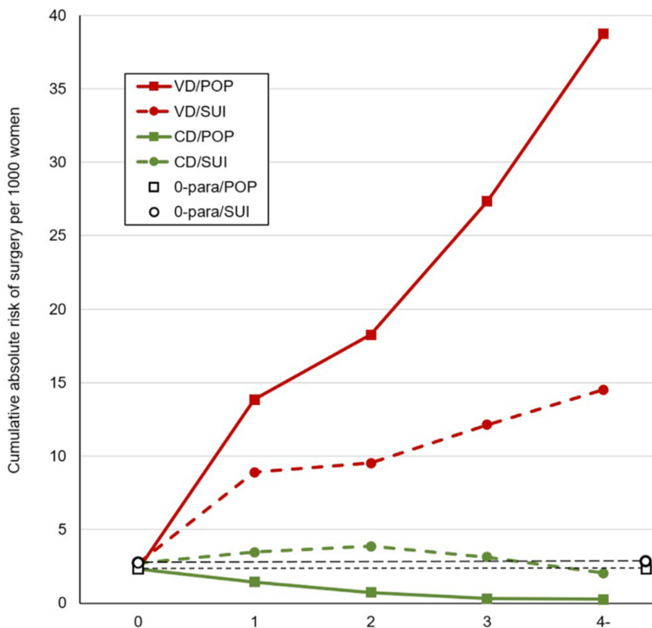


Figure 15. The cumulative absolute risk of surgery. *Reproduced from Larsudd-Kåverud J, Gyhagen J, Åkervall S, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of pregnancy, parity, and mode of delivery on urinary incontinence and prolapse surgery-a national register study. Am J Obstet Gynecol. 2023 Jan;228(1):61.e1-61.e13. doi: 10.1016/j.ajog.2022.07.035.*

The first VD was identified as contributing the most significant risk increase for both POP (AR difference, 11.5 per 1,000 women; 95% CI 11.1–11.9; P < 0.0001) and SUI surgeries (AR difference, 6.2 per 1,000 women; 95% CI 5.8–6.5; P < 0.0001), surpassing the risk associated with subsequent births. The second VD added the least additional risk, with an AR difference of 4.4 per 1,000 women (95% CI, 3.9–4.9; P < 0.0001) for POP and 0.6 per 1,000 women (95% CI, 0.3–1.0; P = 0.0011) for SUI surgeries. This trend was particularly pronounced for SUI surgery, where the second birth accounted for 10% of the risk increase observed with the first birth. In contrast, for POP surgery, the second birth contributed only 38% of the risk associated with the first birth (Figure 16).

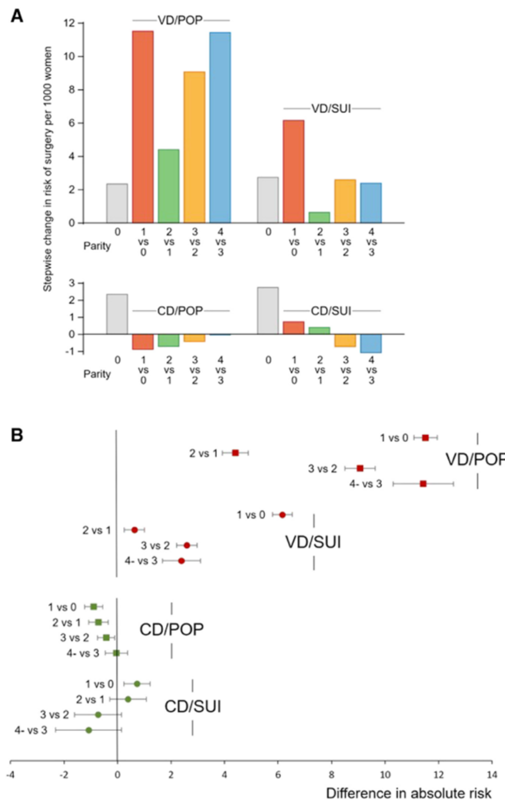


Figure 16. Stepwise change in risk of surgery according to parity. *Reproduced from Larsudd-Kåverud J, Gyhagen J, Åkervall S, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of pregnancy, parity, and mode of delivery on urinary incontinence and prolapse surgery-a national register study. Am J Obstet Gynecol. 2023 Jan;228(1):61.e1-61.e13. doi: 10.1016/j.ajog.2022.07.035.*

4.2 PAPER II

It should be noted that in Tables 1 and 2 of the published article, there is a comma error in the presentation of the results. This, however, does not affect the statistical analyses or the conclusions.

Demographics

Preoperative rates of LUTS, ASA class 3–4, BMI ≥30, and prior surgery for SUI or POP increased progressively with age (all trend tests, $P < 0.0001$). The use of obturator slings was comparable across the three age groups (~30%; $P = 0.23$).

Study population and 1-year outcomes

The cure rate for SUI was found to be 88.5% (95% CI 87.1–89.8) among women aged 55–64 years, but this rate decreased to 64.2% (95% CI 60.0–68.4) in women aged 75 years or older, with a significant trend across age groups ($P < 0.0001$). This decline in cure rate corresponded to an adjusted odds ratio per 10 years (aOR_{10yr}) of 0.51 (95% CI 0.45–0.57; $P < 0.0001$), as shown in Figure 17. Similarly, patient satisfaction and perceived improvement rates decreased with age. Satisfaction declined with an OR_{10yr} of 0.59 (95% CI 0.53–0.66; $P < 0.0001$), while improvement showed an OR_{10yr} of 0.53 (95% CI 0.47–0.60; $P < 0.0001$), both of which were statistically significant trends ($P < 0.0001$), as illustrated in Figure 17. The age-related probabilities of cure, improvement, and satisfaction outcomes for SUI followed similar trends across the age groups (Figure 17).

Women classified as ASA 3–4 had a significantly lower cure rate for SUI than those in ASA class 1–2, with cure rates of 65.5% versus 83.7%, respectively ($P < 0.0001$). Similarly, the satisfaction rate was lower among women in ASA class 3–4 compared to those in ASA class 1–2, at 65.7% versus 80.6% (both $P< 0.0001$). Across all age groups, the estimated probability of cure was consistently 10–15 percentage points lower for women in ASA class 3–4 as well as for those with a history of prior UI surgery (Figure 18).

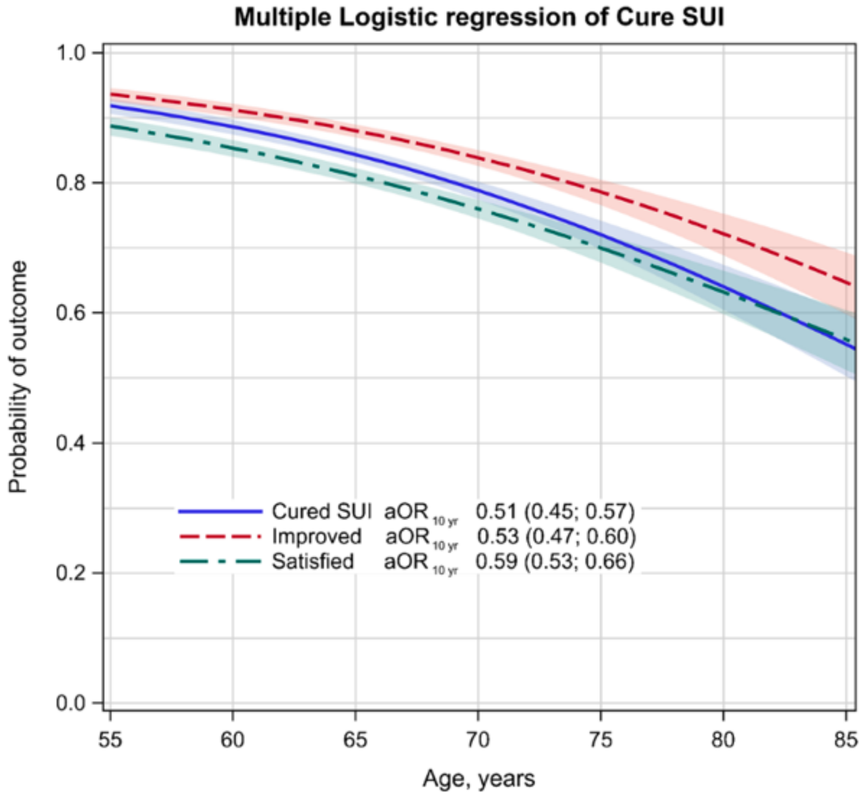


Figure 17. The probability of main outcomes according to age. SUI, stress urinary incontinence; aOR, adjusted odds ratio. aOR was calculated from a logistic regression model with adjustment for BMI and urgency urinary incontinence. *Reproduced from Gyhagen J, Åkervall S, Larsudd-Kåverud J, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of age and health status for outcomes after mid-urethral sling surgery-a nationwide register study. Int Urogynecol J. 2023 Apr;34(4):939-947.*

A strong association was observed between satisfaction and cure rates for SUI, regardless of ASA class or history of prior surgery. Both cure and satisfaction rates were significantly lower in women with diabetes ($P < 0.0001$). Additionally, women with a history of prior surgery showed reduced cure rates (84.3% versus 73.5%, $P < 0.0001$) as well as lower satisfaction levels (81.5% versus 71.2%, $P < 0.0001$).

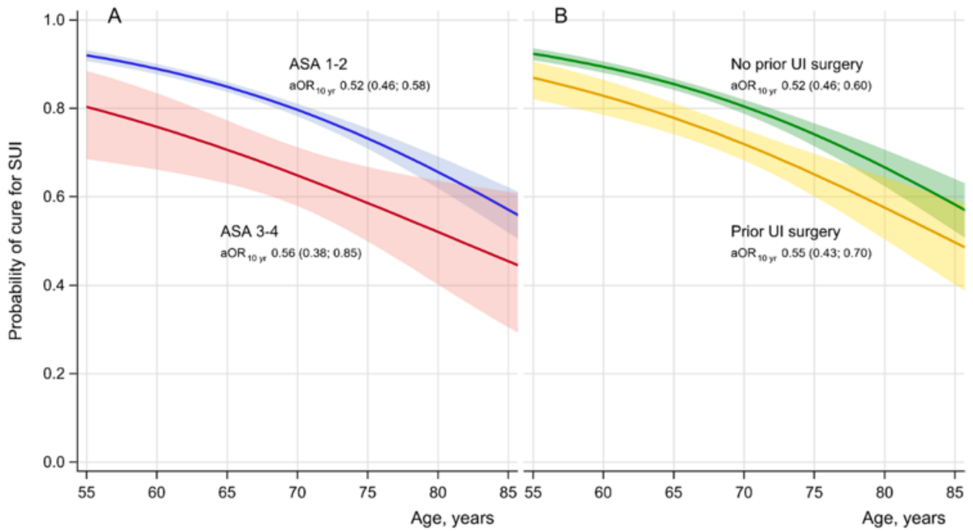


Figure 18. The probability of cure for stress urinary incontinence. *A. According to age and ASA class. B. According to age and prior surgery. ASA is the classification system adopted by the American Society of Anesthesiologists; SUI, stress urinary incontinence; aOR, adjusted odds ratio. aOR was calculated from a logistic regression model with adjustment for BMI and urgency urinary incontinence. The estimated age-related probability (0–1) for the cure of SUI was calculated from logistic regression models. The shaded areas show the 95% two-tailed confidence intervals for the estimated probability of the mean. Prior surgery as reported in the questionnaire. Reproduced from Gyhagen J, Åkervall S, Larsudd-Kåverud J, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of age and health status for outcomes after mid-urethral sling surgery-a nationwide register study. Int Urogynecol J. 2023 Apr;34(4):939-947.*

Remission, de novo symptoms

The incidence of de novo urgency was lower in women aged 55–64 years compared with those aged ≥75 years (12.0% vs. 17.2%; trend P = 0.0022). Rates of de novo bladder emptying difficulty were similar across age groups (trend P = 0.23). De novo urgency was more frequent among women in ASA class 3–4 (P = 0.0018). A BMI ≥30 was associated with both de novo urgency (P < 0.0002) and de novo nocturia (≥2 episodes per night) (P < 0.014) compared with women with a BMI <30. Remission of urgency and nocturia (defined as ≥2 episodes per night) was common, with the highest prevalence

observed in the youngest age group (trend P < 0.0001, Figure 19). Remission rates for nocturia, bladder emptying difficulty, and urgency were unaffected by ASA class (Figure 19).

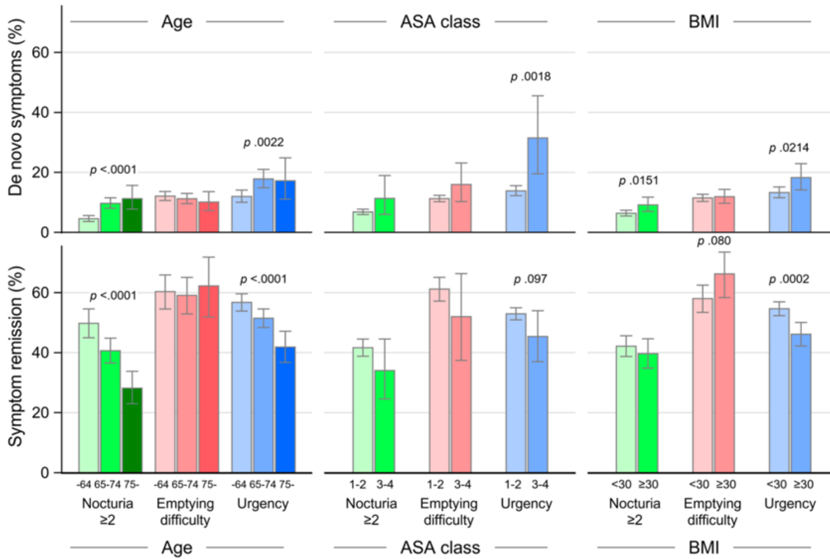


Figure 19. Remission and de novo lower urinary tract symptoms. *ASA, the classification system adopted by the American Society of Anesthesiologists; BMI body mass index; p values ≥ 0.10 are not shown. Reproduced from Gyhagen J, Åkervall S, Larsudd-Kåverud J, Molin M, Milsom I, Wagg A, Gyhagen M. The influence of age and health status for outcomes after mid-urethral sling surgery-a nationwide register study. Int Urogynecol J. 2023 Apr;34(4):939-947.*

4.3 PAPER III

Higher infant birthweights (IBWs) were positively associated with maternal biometric factors, gestational diabetes, pre-existing diabetes mellitus, prolonged pregnancies (≥42 weeks), labor induction, use of epidural anesthesia, male fetal sex, and occiput posterior fetal position.

Infant birthweight and mode of delivery

Among women with a planned vaginal delivery, the probability of spontaneous VD declined markedly as IBW increased, from 80.4% at 3000 g to 44.9% at ≥5000 g (Figure 20). In contrast, the rate of acute cesarean delivery rose from 8.3% to 41.6% across the same weight spectrum. The frequency of vacuum extraction remained stable at 10–15% across IBW categories. No distinct threshold effects were identified. Maternal and neonatal complications were also analysed independently of IBW to assess their distribution across different modes of delivery.

Maternal complications

Maternal complications were significantly more frequent than neonatal complications across all delivery modes and birthweight groups, with an overall incidence seven times higher (29.2% vs. 4.0%). The highest rates of maternal complications occurred following vacuum extraction (42.3%) and acute cesarean delivery (52.7%). Among infants with IBW ≥4500 g, maternal complication rates increased further to 68.1% and 66.0%, respectively. The lowest complication rates were observed following spontaneous VD (23.9%) and planned CD (29.1%), although these increased to 42.8% and 40.0% for IBWs ≥4500 g. Having three or more maternal complications was more common following vacuum extraction (15.8%) and acute cesarean delivery (13.4%) than after planned cesarean delivery (7.0%) or spontaneous vaginal delivery (9.1%) (Figure 21).

The maternal complication rate per 100 births was lowest for spontaneous vaginal delivery when IBW was below 4200 g. For infants with higher IBW, planned CD was associated with the lowest complication rates. At approximately 4200 g, vacuum extraction surpassed acute CD as the mode of delivery associated with the highest maternal risk. Women's reported delivery

experience declined with increasing IBW, paralleling the rise in complications across all delivery modes. Shoulder dystocia in spontaneous VD increased sharply from 0.1% in infants weighing less than 4000 g to 6.4% at ≥5000 g. In vacuum deliveries, shoulder dystocia rose from 2.9% in the 4000–4999 g range to 9.4% at ≥5000 g.

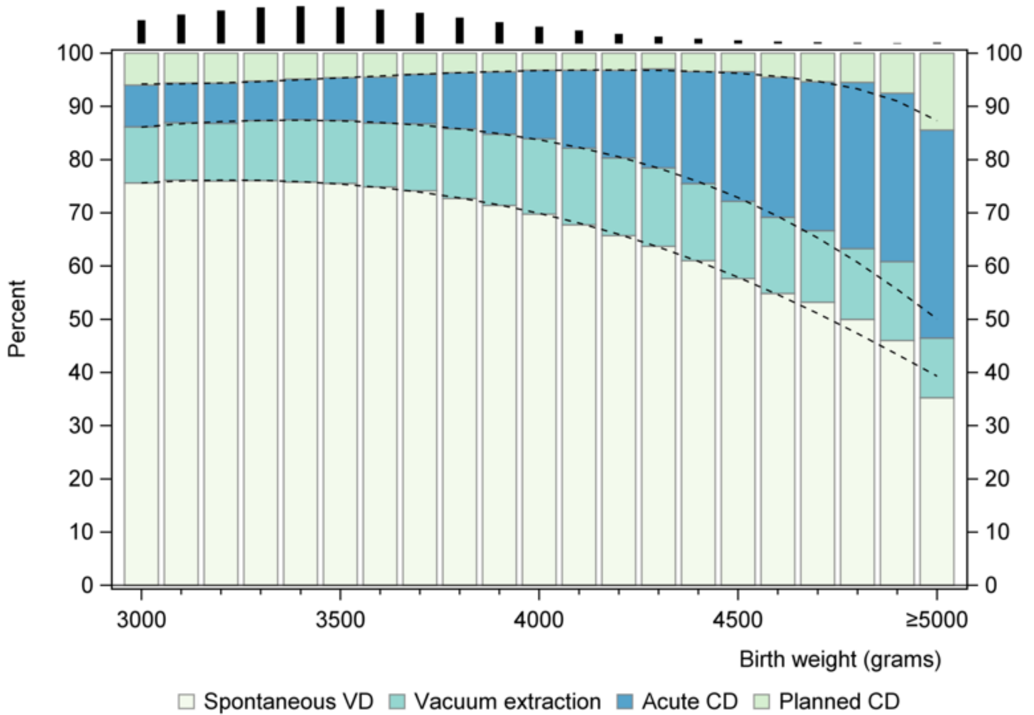


Figure 20. Infant birth weight and the distribution of all modes of delivery. *Black bars at the top indicate the distribution of individuals across 100-g birth weight categories. The dotted lines illustrate the estimated percentages from logistic regression, with third-grade polynomials across 100g infant birth weight categories.*

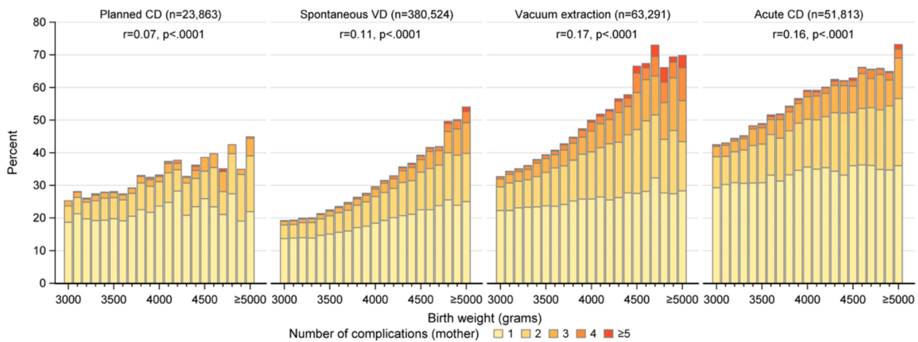


Figure 21. Infant birthweight and the total number of maternal complications in each mode of delivery. *Spearman´s rank correlation coefficient and P value were calculated for the number of complications and infant birth weight per mode of delivery.*

Postpartum hemorrhage of ≥1000 ml occurred in all delivery modes but was most common in vacuum extraction and acute CD, reaching 34.0% and 38.4%, respectively, in the highest birthweight categories. Sepsis and endometritis were also more prevalent in vacuum-assisted and acute CDs compared with other delivery types. The proportion of mothers requiring hospital stays longer than three days, as well as those readmitted within 30 days, increased consistently with IBW, regardless of delivery mode.

Neonatal complication

Neonatal mortality within 28 days was 15 times higher than maternal mortality (3.72 vs. 0.25 deaths per 10,000 births). The proportion of infants without complications was highest after planned cesarean delivery (98.5%), followed by spontaneous VD (97.1%), acute CD (93.2%), and vacuum extraction (90.5%). Among infants born via vacuum extraction, the complication rate ranged from 8.6% to 24.5% across birthweight categories. For IBWs ≥4500 g, the highest rates of neonatal complications were observed following vacuum extraction (17.6%), with lower rates after acute CD (8.5%), spontaneous VD (7.8%), and planned CD (3.7%). The occurrence of three or more neonatal complications was most common following vacuum extraction (4.9%) and acute CD (5.9%), compared with planned CD (2.2%) and spontaneous VD (1.9%) (Figure 22). Apgar scores below 6 at 10 minutes occurred in fewer than 1% of cases across delivery modes, except in infants ≥4500 g delivered via vacuum extraction, where rates rose to 1.5% and 3.2% (≥5000g). Neonatal

fractures and peripheral nerve injuries were significantly more common in infants ≥5000 g delivered by vacuum extraction (14.5%) compared with spontaneous VD (5.4%). Such injuries were rare during CD, with only 74 cases reported (<0.1%). Of all infants ≥5000 g, 14.4% were born with planned cesarean section.

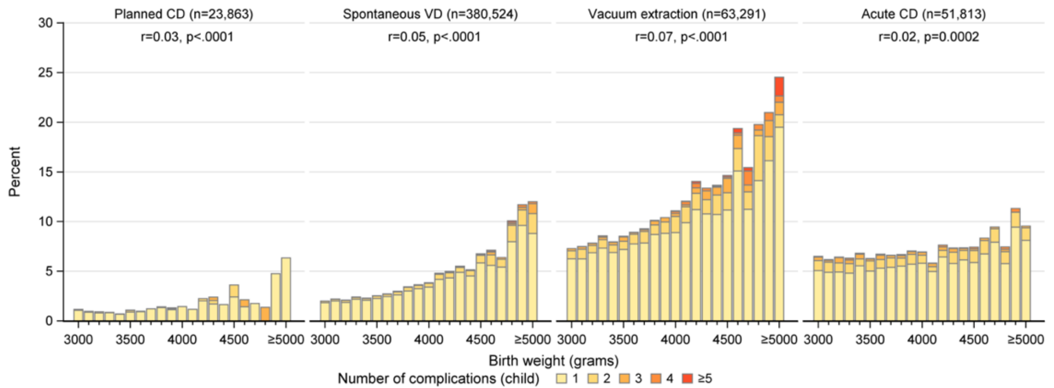


Figure 22. Infant birthweight and the total number of maternal complications in each mode of delivery. *Spearman´s rank correlation coefficient and P value were calculated for the number of complications and infant birth weight per mode of delivery.*

Intracerebral hemorrhage and hypoxic-ischemic encephalopathy were rare but occurred almost exclusively in VDs, with ORs nearly doubling for every 500 g increase in IBW. Only three cases of HIE were reported among infants born by planned CD. Higher IBW was also significantly associated with an increased likelihood of neonatal intensive care unit admission for two or more days. Although rare, neonatal mortality showed a statistically significant association with increasing IBW in vacuum-assisted deliveries, with an OR of 1.46 for every 500 g increase in birthweight.

4.4 PAPER IV

A flowchart of the study population is presented in Figure 23. Across the three scenarios, only minor differences were observed in the mean incidence of OASI over time.

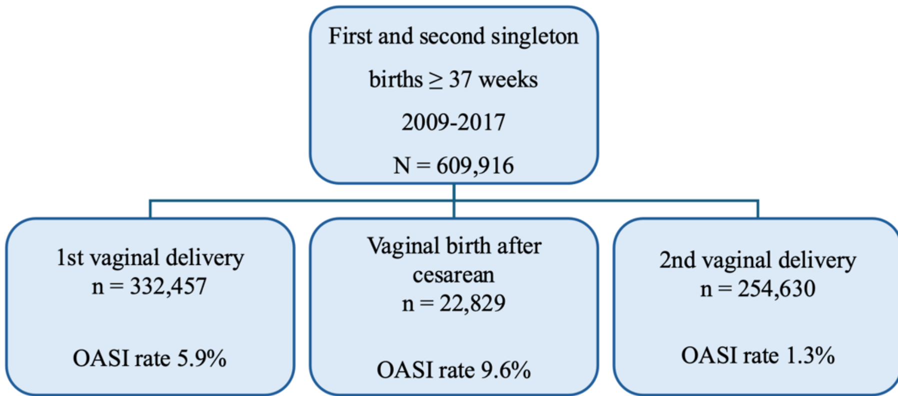


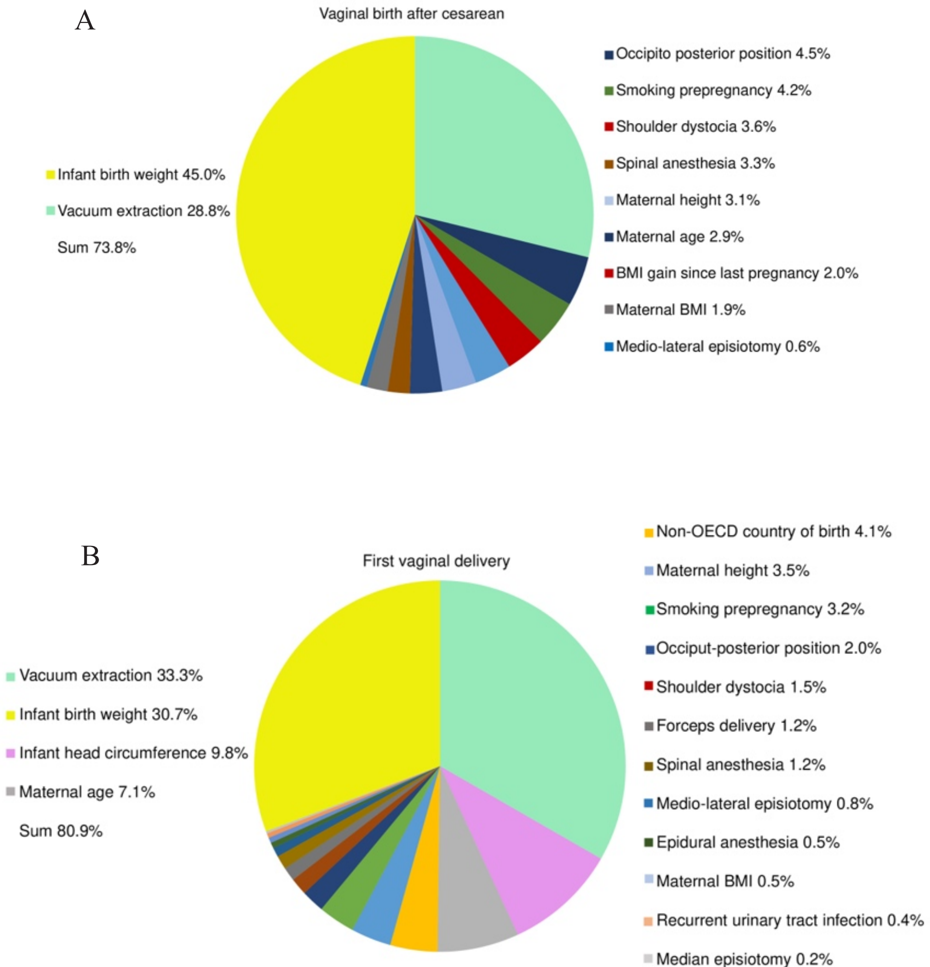
Figure 23. Flowchart of the study population, **Paper IV**.

In all scenarios, births complicated by OASI were associated with higher infant birth weight and larger head circumference. Additional risk factors included smoking, non-OECD (Organisation for Economic Co-operation and Development) country of birth, vacuum delivery, shoulder dystocia, occiput-posterior position, and median (midline) episiotomy. Among the participants, 14% of the women were born outside of OECD countries. Obstetric information from the first vaginal delivery was pivotal for assessing the risk of OASI in the second. Notably, a prior OASI increased the risk of recurrence sevenfold in the subsequent delivery (7.2% vs. 1.0%). All predictors of maternal morbidity were uncommon and distributed evenly across the sample.

Bootstrap-based optimism correction had only a minimal impact on overall performance, calibration, and discrimination metrics. For instance, R^2_N decreased slightly from 12.9% (95% CI 12.2-13.7) to 12.72% (95% CI 12.01-13.54) in the 2nd vaginal delivery scenario, while c-statistics changed from 0.67 (95% CI 0.66-0.69) to 0.66 (95% CI 0.65-0.68) in the VBAC scenario.

The relative contribution of individual predictors of maternal morbidities was <1%. In contrast, information from the previous delivery was important in the

2nd vaginal delivery, contributing >50% to the R^2_N values. IBW in the current delivery was the strongest predictor, accounting for 31–45% of R^2_N in scenarios 1-3 of the final models. An OASI in the first vaginal delivery was a strong predictor of recurrence in the second, explaining 40% of the R^2_N. Additionally, vacuum delivery occurring in the current birth contributed 33% and 29% in Scenarios 1 and 2 (Figure 24A-C). An interactive, freely accessible online calculator has been developed to facilitate clinical application (http://www.sphinctercalc.com).



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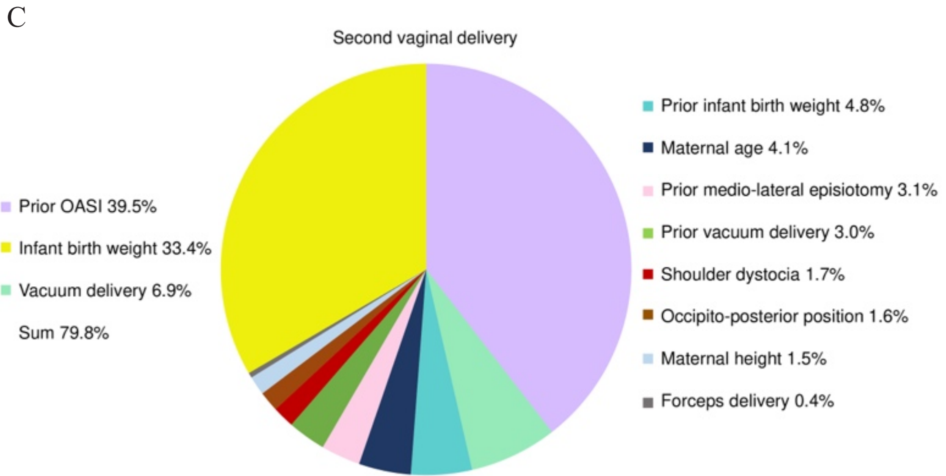

Figure 24A-C. The relative contribution of predictors in the final models. (A) The first vaginal delivery. (B) Vaginal birth after a cesarean. (C) The second vaginal delivery. OASI, obstetric anal sphincter injury; BMI, body mass index; OECD, The Organisation for Economic Co-operation and Development. *Reproduced from: Larsudd-Kåverud J, Åkervall S, Molin M, Nilsson IE, Steyerberg EW, Milsom I, Gyhagen M. Predicting obstetric anal sphincter injury in the first and second vaginal delivery and after a cesarean delivery: development and validation of an intrapartal model. J Clin Epidemiol. 2025 Jul;183:111782. doi: 10.1016/j.jclinepi.2025.111782.*

5. DISCUSSION

5.1 STUDY DESIGN

In many areas of obstetric and gynecologic research, randomisation of pregnant women is often impossible or unethical (190). Register-based studies provide a valuable alternative for examining long-term health outcomes using large national datasets. This study design is crucial in epidemiological research, as it supports disease prevention by enabling the exploration of associations and outcomes through longitudinal, population-wide analysis. Historical cohort studies, with a prospective assessment of exposure and covariates, are more cost-effective than prospective (concurrent) cohort studies (191). However, they are limited by the quantity and quality of the data available. Although registers support longitudinal follow-up, they remain observational, which restricts their capacity for establishing causation. For example, associations such as those between parity and pelvic floor disorders indicate correlation but must be interpreted cautiously, as causal inference is limited. Unlike observational studies, prediction models offer personalised approaches to medical treatments based on specific patient risk factors and aid in clinical decision-making and resource allocation.

5.2 METHODOLOGICAL CONSIDERATIONS

5.2.1 INTERNAL VALIDITY-SYSTEMATIC ERROR

In essence, internal validity assesses whether the study design, methods, and control of potential confounders were sufficient to minimise biases and establish a reliable cause-and-effect relationship. Three main categories influence internal validity: confounding, selection bias, and information bias.

Restricting the inclusion criteria is a key strategy to prevent *confounding* from known risk factors (191). A confounder may lead to both over- and underestimation of results. In this thesis, variables such as regional differences, multiparity, infant birth weight, and mode of delivery were controlled to reduce confounding. Nevertheless, some potentially relevant obstetric factors, such as the duration of the second stage of labor, the use of manual perineal protection, the experience of the obstetrician or midwife, and postnatal pelvic floor

exercises, were not available in the registers and may have acted as confounders in the association between pelvic floor disorders and both surgical risk (**Paper I**) and prediction of OASI (**Paper IV)**.

In **Paper II**, the lack of data on intrinsic sphincter deficiency could have introduced a possible confounding bias when assessing the subjective cure rates of SUI. Adjusting for BMI and urgency urinary incontinence was found to be relevant in the logistic regression with SUI cure as the outcome.

In **Paper III**, we adjusted for maternal age and height, BMI, smoking, and diabetes when calculating ORs using multivariate logistic regression.

Selection bias occurs when the sample in a study is not representative of the target population, resulting in systematic differences between those included in the study and those excluded. Since data in registers is collected routinely and independently of specific research aims, it reduces the risk of selection bias often present in survey-based studies. All study participants in this thesis are selected from nationwide population-based registers, which minimizes bias that may occur due to how patients enter the studies. The eligibility criteria can introduce bias if the sample does not represent the broader population. For instance, **Paper III** examines the risks for both the mother and neonate in women giving birth for the first time. Therefore, the study´s result would not apply to women giving birth a second time vaginally.

However, although questionnaire surveys are considered among the most valid measures for assessing the presence, severity, and impact of sensitive conditions such as pelvic floor disorders (192), participation rates may be higher among symptomatic women, potentially overestimating symptom prevalence (193,194). Low response rates, typically under 60%, correlate with a high risk of response bias; however, the ~90% response rate in **Paper II** is generally considered advantageous (195). Missing values (described elsewhere) of possible confounding variables can also introduce selection bias (196).

Information bias occurs when inaccuracies in data collection, measurement, or classification introduce systematic errors in study findings. Common forms include recall bias, in which participants' memory inaccuracies affect data accuracy. Misunderstandings of questions or reporting errors can lead to

misinterpreted outcomes, potentially weakening internal validity (191). However, when measurement errors are random, they generally bias results toward the null (191). In **Papers I** and **II**, some outcomes were recorded based on real-time clinical assessments rather than patient recall, thereby reducing the potential inaccuracies associated with retrospective reporting. Additionally, birth register data in **Papers I** and **II** were combined with self-administered, validated questionnaires on current PFD symptoms, further controlling for recall bias.

Paper IV demonstrated high internal validity, as evidenced by strong data quality and a substantial number of events across the three scenarios. The Events per Predictor Variable (EPV) ratios were 704 (19,723/28), 55 (2,188/40), and 72 (3,334/46) for Scenarios 1-3, respectively, which are well above the standard recommendation of at least 10 EPV for reliable model validity (197). Additionally, the apparent performance of the final models was adjusted for optimism using bootstrapping (1,000 replicates), resulting in minimal changes to overall performance, calibration, and discrimination measures (Figure 24). This adjustment confirmed the reliability of the prediction models across each scenario.

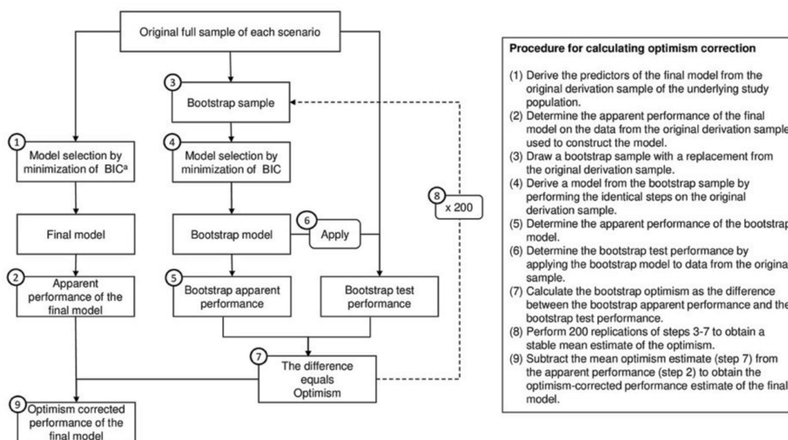

Figure 24. Procedure for calculating optimism correction. *Reproduced from: Larsudd-Kåverud J, Åkervall S, Molin M, Nilsson IE, Steyerberg EW, Milsom I, Gyhagen M. Predicting obstetric anal sphincter injury in the first and second vaginal delivery and after a cesarean delivery: development and validation of an intrapartal model. J Clin Epidemiol. 2025 Jul;183:111782. doi: 10.1016/j.jclinepi.2025.111782.*

5.2.2 EXTERNAL VALIDITY

External validity refers to the extent to which study findings can be generalised to other populations, settings, times, and situations beyond the specific conditions of the research. In other words, it assesses whether the results apply to groups or contexts outside the study sample. National register-based studies, which often encompass large and diverse populations, provide a representative view of patient outcomes that can be generalised to broader groups.

The applicability of findings across health systems may be influenced by differences in healthcare quality and access, such as those between universal tax-funded systems and private insurance systems.

In **Paper II**, most participants were healthy and had no co-existing morbidities, which may have limited the external validity of the results. Additionally, no analyses were conducted to examine differences between responders and non-responders, which could potentially mask systematic differences and thus limit the generalisability of the findings.

An important but often overlooked factor in studies assessing surgical outcomes is the experience and skill level of the surgeon (198). A meta-analysis found a positive correlation between surgical volume and outcomes across procedures, including hysterectomy, gynecological oncology, surgical mesh complications, and incontinence procedures (199). Register data, especially when assessing outcomes of surgical interventions, can thus offer a realistic description of intervention impacts across a range of practice settings, rather than reflecting outcomes only from highly skilled surgeons.

In this thesis, participants were sampled from nationwide registers, which generally have high external validity due to their extensive coverage. The clinics involved in this study ranged from large teaching hospitals to smaller private practices, further enhancing the applicability of the findings across different healthcare contexts. In **Paper IV**, 14% of the study population were born in a non-OECD country. Using geographical cross-validation did not reveal any differences in performance between the different subsets, indicating high external validity. Further, an external validation of a population from a European country and continuous model updates are planned.

5.2.3 RANDOM ERROR

Systematic errors, or biases, consistently skew results in a particular direction, whereas random errors occur by chance and affect the precision of study measurements or estimates. Unlike systematic errors, which introduce consistent distortions, random errors cause fluctuations around the true value, leading to unpredictable and unsystematic variations. To mitigate the impact of random error, large sample sizes are employed across all studies in this thesis. In **Papers I, II**, and **III**, confidence intervals are used to indicate the range within which the true effect is likely to fall, accounting for the presence of random error. In **Paper III**, stratification of the population resulted in smaller sample sizes within subgroups, which is reflected in wider confidence intervals. Random error affects smaller study samples more, which can skew the results. In **Paper IV,** the bootstrap optimism correction resamples the data to assess how the model might perform with different samples, thereby reducing the risk of overestimating predictive accuracy due to random chance. The optimism correction had minimal effect on the results. Random error may occur due to variability in clinical practice across the 45 participating maternity units, as well as measurement error in variables like infant birth weight and maternal biometric data.

5.3 STRENGTHS AND LIMITATIONS

The strengths of all studies in this thesis include the large cohorts based on prospective data from national registers, considered to be of high quality, which minimizes regional biases. Additionally, large cohorts reduce the influence of random error, providing a more reliable basis for subgroup analyses, such as age, delivery mode, and ASA classifications. Moreover, the Swedish public healthcare system is state funded, ensuring that medical assessment and surgery are accessible to all citizens at a low cost, thereby minimising potential bias related to socio-economic status. The use of existing national registers represents a resource-efficient approach, enabling large-scale research without the expenses associated with primary data collection.

In **Paper I**, including a reference group of nulliparous women to specifically evaluate the long-term effect of pregnancy in the CD group, isolated from the influence of VD, is a major strength. Pelvic floor disorders are a stigmatising condition in many populations (19), which creates a high risk for respondent

bias in UI epidemiology. However, self-administered questionnaires are considered the most suitable tool for gathering information about sensitive issues (200). In **Paper II**, symptoms were self-reported. Several studies have shown that self-reported symptoms are consistent and valid when they exist at the time of report (201,202). Since randomising according to the mode of delivery would be considered unethical, applying the intention-to-treat principle in **Paper III**, by separately analysing planned and acute cesarean deliveries, enhances the clinical applicability of the results. As for **Paper IV,** the large number of patients and the quality and extensiveness of data contributed to model reliability.

Limitations

In **Paper I**, the nulliparous group was used as the reference population, as they may best represent women unaffected by childbirth. However, this group likely carries a negative health bias compared with parous women. For instance, hysterectomy was more common among nulliparous women (28%) than among parous women (20%). Such health-related differences may have led to an overestimation of the AR of surgery for POP and UI in the nulliparous cohort. Furthermore, **Paper I** estimated the proportion of women delivering solely by CD based on women born in 1960 within the reference group. This estimation approach could be considered a limitation, as it does not fully account for the increasing CD rates and evolving trends in mean parity, resulting in higher CD rates among younger women by 2017.

Additionally, as registers are primarily designed for administrative purposes rather than research, certain relevant variables may be missing, or critical details may be inadequately recorded. In **Paper II**, for instance, lifestyle factors such as smoking, which could serve as potential confounders, were not consistently recorded. Variability in data completeness, depending on patient follow-up and reporting practices, may introduce bias, particularly in patient-reported outcomes. The underrepresentation of specific subgroups, such as older populations, in follow-up data can further impact the estimation of long-term outcomes. In **Paper II**, while 86% of the participants completed the 1-year follow-up questionnaire, this rate rose to 90% among women aged 65–74, illustrating potential discrepancies in response rates by age.

In **Paper IV**, the limited rate of explained variation, reflected by an R^2_N of 7–13% and a scaled Brier score of approximately 4% in the final models, indicates notable uncertainty (203,204). Additionally, both traditional covariate adjustments and propensity score adjustments, while useful, may fail to address critical confounding factors that were either unrecorded or inadequately modelled. This shortfall underscores the need for caution in interpreting findings where certain confounders remain unaccounted for.

For **Paper IV**, it is important to recognise that the risk of OASI may be underestimated in high-risk deliveries if clinical decisions have already been influenced by known risk factors. This phenomenon, known as the treatment paradox, may be further amplified when using our prediction model to guide care. The treatment paradox occurs when effective interventions lower the observed risk of an outcome, thereby making key predictors appear less influential than they would be without treatment. To account for this, we examined the differential effects of predictors across models and incorporated selected interaction terms into the final models. As a result, the model is intended to support, rather than replace, clinical judgment.

A key strength of our model is the use of actual birthweight, which improves predictive accuracy and reduces bias. However, because clinical decisions are typically based on estimated fetal weight, our model does not capture the uncertainty inherent in antenatal weight estimation.

5.4 CONSIDERATIONS OF DEFINITIONS AND CLASSIFICATIONS

5.4.1 THE QUESTIONNAIRES

While questionnaires are a powerful tool in academic research, their effectiveness hinges on careful design, appropriate use, and awareness of their limitations. For example, easy-to-use electronic Patient-Reported Outcome Measures (ePROMs) have been shown to improve compliance and patient satisfaction (205). These were used in 41% of the cases, and the response rate, as reported by the register holders, was 83%. **Papers I** and **II** are population-

based cohort studies based on data retrieved from the GynOp, which prospectively collects information on routine gynecological surgical care in Sweden. The Swedish Urogynecology Association (UR-Arg) is responsible for part of the content of these forms.

Although the GynOp questionnaires have not been validated in their entirety, they incorporate items from established and validated instruments, including the IIQ-7, UDI-6, and ICIQ-UI (99,206). The potential influence of the number and sequence of questions on responses is acknowledged, but any such bias would likely be evenly distributed across cohorts, minimising its impact on comparative analyses. Several studies have previously utilised these questionnaires to generate robust findings (207-209).

5.4.2 PELVIC ORGAN PROLAPSE AND STRESS URINARY INCONTINENCE

The symptom of 'feeling a vaginal bulge' is the most strongly correlated threshold symptom for prolapse when the bulge protrusion reaches near the hymen (210). In 2005, Tegerstedt et al. validated a short-form questionnaire for sPOP, the question "Do you have a sense of tissue protrusion (vaginal bulge) from your vagina" had almost all the predictive capacity of the test (99), which has been verified by others (211,212). In GynOps questionnaires the question "Do you have a feeling that something is bulging out from the vagina?" is used, with the answers "Never", "Almost never", "1-3 times per month", "1-3 times per week", and "Daily". In **Paper I**, the subjective experience of POP reported in the questionnaire is objectively verified by a surgeon, as surgical intervention requires the presence of an anatomical defect.

UI is a common symptom in epidemiological surveys, with a reported prevalence of 25–45%. However, the clinical relevance lies more in the severity and impact of UI rather than its mere prevalence. To enhance the understanding of UI, determining its subtypes through questionnaires has been recommended for inclusion in epidemiological studies (19,213), as subtypes are associated with varying degrees of severity and bother (214,215). Furthermore, Sandvik et al. demonstrated that clinical and urodynamic evaluations often reveal a misdiagnosis of stress UI as mixed UI in epidemiological surveys (216).

The short-form International Consultation on Incontinence Questionnaire (ICIQ-SF) has been shown to correlate well with objective measures of SUI severity, such as the 1-hour and 24-hour pad tests (217,218). Despite these advances, most previous epidemiological studies on POP and UI have relied on patient-reported data, which depends on women's subjective perception of symptoms and their willingness to report them.

An alternative approach to assessing the impact of pregnancy and childbirth on PFDs is to analyse the epidemiology of reconstructive surgical treatments, as in **Papers I** and **II**. Unlike self-reported symptoms, surgery requires objectively confirmed anatomical defects and symptoms significant enough to affect quality of life. Subjective perception, whether the condition is bothersome and to what degree, is critical in determining whether a pelvic floor disorder warrants prevention or treatment (19). Thus, the perceived impact and relevance of the condition remain central to its clinical management.

5.4.3 ASA CLASSIFICATION

The American Society of Anesthesiologists (ASA) Physical Status Classification System is a widely used tool to assess a patient's preoperative health status. The intended use of the ASA Physical Status system is to allow the preoperative health status of surgical patients to be summarised and compared. However, studies have identified significant interrater variability in its application, raising concerns about its reliability and consistency (219).

One of the most comprehensive studies on this topic was conducted by Cuvillon et al., who analysed ASA Physical Status scores assigned by attending anesthesiologists in 1,554 cases. These cases, along with the original ASA Physical Status assignments, were reviewed by other experienced anesthesiologists to evaluate the agreement. The lowest discordance rate was observed for ASA Physical Status I (24.5%), while the highest was found for ASA Physical Status IV (83.3%). The study reported a Cohen's kappa coefficient of 0.53, indicating weak to moderate agreement (220). This variability underscores the challenges in applying the ASA system consistently across different clinicians.

The ASA system intentionally excludes chronological age, except for the very young, as age is generally considered a poor correlate of functional status.

Instead, the system focuses on the severity of systemic diseases and their impact on the patient's health. However, in recent years, "frailty" has emerged as a critical factor influencing surgical outcomes, particularly in older adults (221,222). Frailty is characterised by decreased physiological reserves and increased vulnerability to stressors, which can significantly affect postoperative recovery and complication rates. Despite its growing recognition, frailty is not explicitly included in the ASA system. Some researchers suggest that frailty, due to its impact on functional status, could justify classification as at least ASA Physical Status III (serious systemic disease) or even ASA Physical Status IV (a systemic disease that is a constant threat to life) (219). Incorporating frailty into future iterations of the ASA system has been proposed to improve its utility in risk assessment. The omission of frailty as a variable in the ASA classification poses a limitation in **Paper II**. Since the registers used in this study lack specific data on frailty, the analyses may not fully account for its influence on surgical outcomes. If frailty had been included, either alone or in conjunction with ASA class, the findings could have been altered by providing a more nuanced understanding of the patients' preoperative health.

5.4.4 OBSTETRIC ANAL SPHINCTER INJURY

In **Papers III** and **IV**, OASI were analysed as a single entity without distinguishing between third- and fourth-degree injuries. This decision was driven by the low rate of fourth-degree injuries, which would have significantly limited the statistical power of the studies if analysed separately. Both grades represent severe trauma with substantial short- and long-term morbidity, including fecal incontinence and pelvic floor dysfunction. Combining these grades mitigates the potential for misclassification inherent in the subjective clinical assessment of sphincter injuries, reducing its impact on study findings. From a patient-centred perspective, this approach is justified as both grades severely disrupt the anal sphincter complex, resulting in comparable implications for quality of life.

Additionally, women with diagnoses of OASI separate from the time of delivery were not included in **Papers III** and **IV**. This exclusion, coupled with the known underreporting of anal sphincter injuries, may further limit the generalizability and accuracy of the findings. Sultan et al. demonstrated that many sphincter injuries classified as "occult" could be identified by trained

clinicians using anal endosonography, suggesting that underreporting is partly due to inadequate detection techniques (223). A study by Groom and Paterson-Brown concluded that less than 1% of "occult" injuries are truly undetectable, emphasizing the need for improved clinical training and standardized diagnostic protocols (224). Given the nationwide scope, any misclassification of OASI between third- and fourth-degree injuries is likely to be evenly distributed across the dataset. This reduces the risk of systematic bias related to regional differences or specific clinical settings, lending credibility to the combined analysis of these injury grades.

5.5 MAIN FINDINGS AND COMMENTS

5.5.1 PAPER I

VD emerged as the predominant risk factor for subsequent urogenital surgery. In the study population, women with VD were overrepresented, whereas nulliparous women and those delivered exclusively by CD were underrepresented. After one or more pregnancies and delivery via CD, the AR for POP and SUI surgery was negligible, similar to the AR observed in nulliparous women. An increasing number of vaginal births was associated with a cumulative rise in the AR for surgery related to POP and SUI. The first vaginal birth contributed the largest additive increase in AR for POP and SUI surgery, while the second vaginal birth had the smallest.

A key contribution of this study was the inclusion of a substantial group of nulliparous women who had undergone urogenital surgeries, alongside an at-risk reference group from the general population of women aged 45 years. Access to known parity and delivery mode enabled precise calculations of the RR and AR for surgery across all cohorts. Additionally, the inclusion of a nulliparous cohort allowed for the assessment of factors unrelated to childbirth, facilitating a clearer evaluation of the long-term impact of pregnancy independent of VD and enabling measurement of the additive AR associated with each birth.

In this study, 1,610 nulliparous women aged ≥45 underwent urogenital surgeries, with a corresponding at-risk cohort of 318,559 in the general

population. Previous research on the epidemiology of PFDs has struggled to access sufficiently large groups of nulliparous women. For example, in a Norwegian cross-sectional survey, only one of 252 nulliparous women reported POP surgery among 1,123 total surgical procedures (225). Similarly, a register-based study by Mant et al. identified only five nulliparous women who underwent POP surgeries, while Carley et al.'s case-control study included 13 nulliparous women among 480 with urogenital surgeries and 27 among 150 controls (91,226). These small sample sizes introduce a high risk of selection bias and imprecision in outcomes. Our finding that nulliparous women aged 45 underwent POP or SUI surgery only slightly more often than women who delivered exclusively by CD suggests additional health mechanisms may underlie PFD development and potentially impact fertility in these women (227).

The present findings align with earlier research by Mant et al., which indicated that women with one, two, and four VDs had four, eight-, and eleven-times higher likelihoods, respectively, of undergoing POP surgery than nulliparous women (91). Similarly, studies by Leijonhufvud et al. and Larsson et al. showed an increasing risk for POP diagnosis and POP or UI surgery with each additional VD, in contrast to those who only delivered by CD (87,228). Recent reviews have debated whether elective CD offers long-term protection against PFD surgeries compared to VD (228). In this study, we found that a single CD was indeed protective relative to one VD regarding the cumulative risk for POP and SUI surgeries, with each additional VD amplifying this risk.

However, a remaining unresolved question remains the risk for surgery for POP and SUI according to the order of vaginal births. Several studies report a linear increase in risk for SUI and POP surgery with each additional VD (87,229,230). Previous studies that introduced nulliparous women as a baseline reference for these comparisons demonstrated a strong effect of the first birth on the prevalence of UI, SUI, and POP surgeries, as well as an overall biphasic pattern with increasing vaginal parity, in harmony with this study (99,231,232).

5.5.2 PAPER II

The cure rate was 64.2% in women aged ≥75 years compared with 88.5% in those aged 55–64 years. Advanced age, ASA class 3–4, and a history of prior

surgery were all associated with lower cure rates and less favourable outcomes. However, physical status and comorbid conditions were generally more predictive of outcomes than chronological age alone. Women reported satisfaction with the procedure when they experienced reduced leakage episodes, regardless of age. Overall outcome measures following MUS surgery, cure of SUI, improvement, and patient satisfaction appeared largely interchangeable. Women with lower preoperative leakage frequency were less likely to fulfil the study's criteria for "cure". The incidence of de novo urgency increased with age, yet remission of symptoms was common among those with preoperative urgency and nocturia of two or more episodes per night, with the most notable improvements seen in the 55–64-year age cohort. Across all age groups, adverse events, readmissions, and 30-day postoperative mortality were infrequent. From 2007 to 2017, the rate of MUS surgeries among women aged 75 years and older declined by over 50% in Sweden.

As a measure of cure of SUI, chosen due to its clinical relevance, this study classified women as cured if they had no leakage or leakage 1-4 times per month postoperatively. This definition varied between studies. In a Norwegian national register study conducted in 2018 (n = 21,832), Engen et al. reported a cure rate, defined as the absence of objective stress leakage, of 78.9% in women aged ≥70 years at 6–12 months of follow-up (233). Similarly, Hellberg et al. observed a cure rate of 62% following TVT surgery in 113 women aged ≥75 years, which is comparable to the cure rate reported in the present study (64%) (234). By contrast, Stav et al. found no significant difference in subjective cure rates between 96 women aged ≥80 years and 1,016 women <80 years (81% vs. 85%; P = 0.32) after a mean follow-up of approximately four years (235).

Differences in the definition of cure for SUI are paralleled by variations in age stratification across studies. Our study, along with that of Hellberg et al. (2007), used an age threshold of 75 years, whereas Engen et al. categorised participants into 70–79 and 80–99-year groups and Stav et al. set the cutoff at 80 years or older (233-235). These differing age groupings likely contribute to the variability in outcomes across studies.

The satisfaction rate among older women in this study was lower than that reported by Engen et al. (70% vs. 63%) (233). The higher rate observed in their study may be attributable to the use of only the response category "Very

satisfied" in a slightly younger cohort, whereas the present study combined "Satisfied" and "Very satisfied". Among younger women, satisfaction rates were nearly identical between the two studies (84% vs. 82%), with comparable criteria applied.

De novo urgency occurred in 12% of women aged 55–64 years and 17% of those aged 75 and older (P = 0.0022), aligning with findings by Hellberg et al. (14% vs. 21%, OR 1.63; 95% CI 0.77–3.19) and Stav et al. (16% vs. 18%, P = 0.41) (234,235). In contrast, Malek et al. reported lower rates of de novo urgency (7.5% vs. 4.3%, P = 0.22), likely due to their younger age threshold for older women (≥ 70 years) (236). We observed a remission rate of approximately 55% for urgency in the younger age group, consistent with findings by Abdel-Fattah et al., who reported a 56.1% remission rate at one year among women with a mean age of 55 years (237) However, this improvement does not appear to persist over time (238).

In this analysis, cure, satisfaction, and subjective improvement rates were approximately 10% lower in women with a history of prior surgery (all P < 0.0001). A recent systematic review on prior surgery for SUI found a pooled success rate of 69% across 24 studies, though these studies varied in age of participants, follow-up duration, and definitions of "cure" (239). Prior surgery has also been associated with rates of de novo urgency ranging from 8% to 30%, as reported by Stav et al., Liapis et al., and Verbrugghe et al., in comparison to our observed rate of 24% (240-242).

Significant complications were rare and showed little variation across age groups and ASA classes, in harmony with Anger et al., who reported no statistical difference in major surgical complications after MUS surgery between women aged 65–74 years (21.4%) versus women aged ≥ 75 years (21.3%) (243). However, a 2017 study of 7,113 women reported higher 30-day readmission rates among those with ASA class 3–4 compared to ASA class 1–2 (2.3% vs. 0.9%, P < 0.0001) (244).

5.5.3 PAPER III

Among women with a planned VD, the proportion of spontaneous VD declined significantly with increasing infant birth weight, while the incidence of acute CD rose correspondingly. Maternal and neonatal complications were strongly

associated with higher IBW across all modes of delivery, with complications occurring seven times more frequently in mothers than in infants. The highest maternal complication rates were observed in cases involving vacuum extraction and acute CD, at 39% and 53%, respectively. Notably, for infants with an IBW ≥4500 g, the rate of maternal complications increased markedly, affecting approximately two-thirds of mothers. Furthermore, maternal satisfaction with the delivery experience declined with increasing IBW, mirroring the trend observed for complications.

Although substantial evidence links macrosomia to labor difficulties and birth-related complications, direct comparisons with previous studies are challenging (245-248). Many reports group acute and planned CDs together and contrast them with VDs, often without accounting for clinical context. To address this limitation, our analysis differentiated among four distinct delivery modes: spontaneous VD, instrumental VD, acute CD, and planned CD.

Additionally, most prior studies included multiparous women and evaluated a limited number of complications. To our knowledge, no previous study has exclusively focused on primiparous women. Restricting the study to primiparas enhances internal validity by eliminating confounding from prior births and is particularly relevant, as this group faces the highest risk of adverse delivery outcomes. Our analysis identified 25 maternal and neonatal complications, both individually and as a composite outcome, whereas most earlier studies assessed fewer than five complications, except for two notable reports (249,250).

For example, a Norwegian registry study from 2010 reported an acute CD prevalence of approximately 10% among infants with a birth weight of 4000–4499 g (249). In contrast, our study found a prevalence of 15.6%, likely reflecting differences in study populations: the Norwegian cohort included 60% multiparous women, whereas our sample consisted exclusively of primiparous women.

Gregory et al. reported minimal maternal and neonatal risks associated with planned CD, consistent with our findings (251). However, their study lacked information on instrumental delivery—an important gap, as our results indicate that instrumental VD is associated with the highest risk for infants weighing ≥4000 g. Similarly, Åberg et al. found that vacuum extraction was associated

with a higher rate of severe neonatal complications across all macrosomic categories compared to acute CD, supporting our observations (252).

Finally, our findings related to maternal birth experience align with those of Vercellini et al., who studied 559 nulliparous women delivering infants >4000 g and reported significantly greater "birth satisfaction" among those undergoing planned CD compared to those attempting VD (253).

5.5.4 PAPER IV

In this large population-based cohort study, infant birth weight emerged as the most influential predictor across all birth scenarios. Only five predictors individually contributed more than 5% to the total predictive information. Notably, obstetric data from the first delivery accounted for over half of the predictive information for a second vaginal delivery. The minimal bootstrap optimism-correction indicated that the predictive models demonstrated stable and reliable performance across scenarios. However, model performance was markedly reduced in the absence of current antenatal data on antenatal infant birthweight, head circumference, and obstetric events and interventions.

We did not define cut-offs for high- or low-risk of OASI. Within the field of individual prediction and patients´ consent, we think it is inappropriate to decide on a decision threshold or to designate a certain risk ratio as "high" or "low" (254,255). In harmony with this reasoning, achieving self-identified patient goals after gynecologic surgery is closely associated with patient satisfaction (154,255). Eliciting patients' values and goals regarding the mode of delivery may similarly improve satisfaction and reduce regret in obstetric patients.

One crucial aspect is that the prediction model provides information about alternatives that we can act upon, e.g. meaningfully alter clinical management. A model incorporating factors available during delivery can be effectively used for real-time clinical decision-making to optimize outcomes for both the mother and the baby. We recognize that this interpretation and application of the during labor model implies a causal interpretation of covariate effects. Further analysis may be necessary to elucidate the plausibility of a causal relationship between interventions, such as vacuum extraction and OASI, and events, such as shoulder dystocia and OASI. When the calculator is used

antenatally, the default setting assumes negative responses to questions regarding labor events and interventions. In a subsequent step, conditional scenarios can be explored, for example: 'If vacuum delivery with mediolateral episiotomy were required, how would this affect my predicted risk of OASI?' The impact of such hypothetical events can then be assessed by comparing the individual predicted probabilities generated with and without the specified intervention.

Subject matter knowledge in obstetrics, an essential element for introducing predictor candidates in developing prediction models (155), has conclusively established that fetal macrosomia is a major risk factor for OASI (256). All relevant parameters of fetal biometry are now either routinely available or easily obtainable (257). If the result of the ultrasound is deemed unreliable, MRI might provide a more precise fetal weight and head circumference in less than 10 minutes (258,259) In summary, the exclusion of fetal biometrics in an antenatal prediction model of OASI is not defensible.

6. CONCLUSIONS

6.1 PAPER I

Based on the results of this study, no evidence was found that pregnancy alone, that is, when all deliveries were by CD, increased the risk of surgery for POP or SUI beyond that observed in nulliparous women. Additionally, giving birth solely via CD appeared to preserve pelvic floor support in the long term, similar to that of nulliparous women. Therefore, healthcare resources allocated for urogenital surgery may primarily reflect the negative consequences of vaginal delivery. However, this is only one part of women's total reproductive burden.

6.2 PAPER II

Although cure rates declined with advancing age and higher ASA class, most women reported satisfaction when experiencing a reduction in incontinence episodes. Women with severe incontinence were more likely to demonstrate improvement and to report satisfaction with outcomes. The findings underscore several key preoperative factors associated with risk of failure, including age, physical status, prior UI surgery, and diabetes. While this study confirms a continued decline in the number and proportion of MUS procedures performed in older women, they do not provide an explanation for this trend.

6.3 PAPER III

This study underscores the substantial impact of IBW on the mode of delivery, as well as on associated maternal and neonatal morbidities. It also incorporates an evaluation of the maternal birth experience. The findings provide strong support for the clinical value of estimating IBW prior to delivery, as doing so enables women and healthcare providers to collaboratively identify the safest mode of delivery, thereby minimizing risks and improving outcomes for both mother and infant. Furthermore, antenatal estimation of IBW facilitates informed, individualized decision-making that considers each woman's clinical circumstances, personal concerns, preferences, and future reproductive plans.

6.4 PAPER IV

Accurate information on infant biometrics is essential for the development of reliable and clinically meaningful prediction models for OASI. The findings of this study support ongoing efforts to improve antenatal access to fetal biometric data. A predictive model that incorporates variables available at the time of delivery may serve as a valuable tool for clinical decision-making, potentially enhancing outcomes for both mother and infant when applied via an online calculator. Further research is warranted to evaluate the clinical integration of this tool as an evidence-based aid that supports women's informed and autonomous decision-making during childbirth.

7. FUTURE PERSPECTIVES

The goal of epidemiologic research is to prevent disease while simultaneously improving clinical outcomes, reducing morbidity, and enhancing the quality of life for women throughout their lifespan. The integration of personalised medicine into obstetrics and gynaecology holds significant promise for optimising outcomes and improving the overall quality of care (260). Nationwide studies leveraging linked registries have been instrumental in quantifying the cumulative risk of conditions like PFDs, providing essential data to inform future clinical and policy decisions.

The economic and clinical burden of PFDs highlights the need for a life span approach to care. The Life Span Study framework has proven invaluable in understanding the epidemiology and long-term economic burden of PFDs (95,261). For instance, in the United States, the costs of a first CD at maternal request versus a first planned vaginal birth are estimated at $14,259 and $13,283, respectively (18). However, over the long term, the economic toll increases due to reconstructive surgeries for POP and SUI, conditions primarily attributed to VD. Additional costs emerge from managing other birth-related conditions, such as fecal incontinence resulting from OASIs, contributing to years of suffering, financial burden, and reduced quality of life. Broadly incorporating this lifespan perspective into antenatal counselling is crucial to shaping clinical practice, aligning patient expectations, and guiding informed decision-making.

At the same time, while demographic shifts suggest an increasing demand for surgical interventions like MUS procedures for older women, procedural rates have remained stagnant. This may reflect inequities in resource allocation or the de-prioritisation of older women, a trend similarly observed in the United Kingdom, where the proportion of MUS surgeries declined from 7% to 5% between 2000 and 2011 (262). Understanding the underlying factors influencing access and prioritisation of these procedures is crucial to addressing potential inequities and ensuring clinical resources align with population needs.

Another critical focus for future research is the development of predictive tools for maternal and neonatal outcomes. Despite significant advancements in

identifying risk factors for adverse maternal and neonatal outcomes, the challenge lies in pinpointing individuals at the highest risk. Existing models for maternal and neonatal risk scoring are often built on extensive national datasets, but few have been successfully implemented in clinical practice (257). Future research must prioritise the development of predictive tools that integrate maternal and fetal characteristics, with a focus on accurately estimating fetal weight, such as advanced MRI applications (263) and optimising delivery methods.

The low incidence of OASI highlights the need for large, high-quality datasets to ensure robust and reliable predictive modelling, particularly for subsequent vaginal deliveries beyond the first. To maintain clinical relevance, prediction models must undergo continuous refinement and validation across diverse populations and settings. This includes accounting for temporal heterogeneity (variations over time) and geographic heterogeneity (differences in population demographics, obstetric practices, OASI rates, and healthcare contexts) to reflect evolving clinical landscapes (264-266). Regular updates and recalibrations are essential to ensure the equitable and effective application of these models in contemporary obstetric practice.

Finally, taking a comprehensive lifespan approach to obstetric outcomes is essential, covering both immediate and long-term effects of delivery decisions. Such an approach enhances patient counselling, supports evidence-based risk management, and informs policy development. By integrating predictive tools, innovative technologies, and longitudinal data, personalized medicine in obstetrics and gynecology can enhance care and ensure better outcomes for both mothers and infants.

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