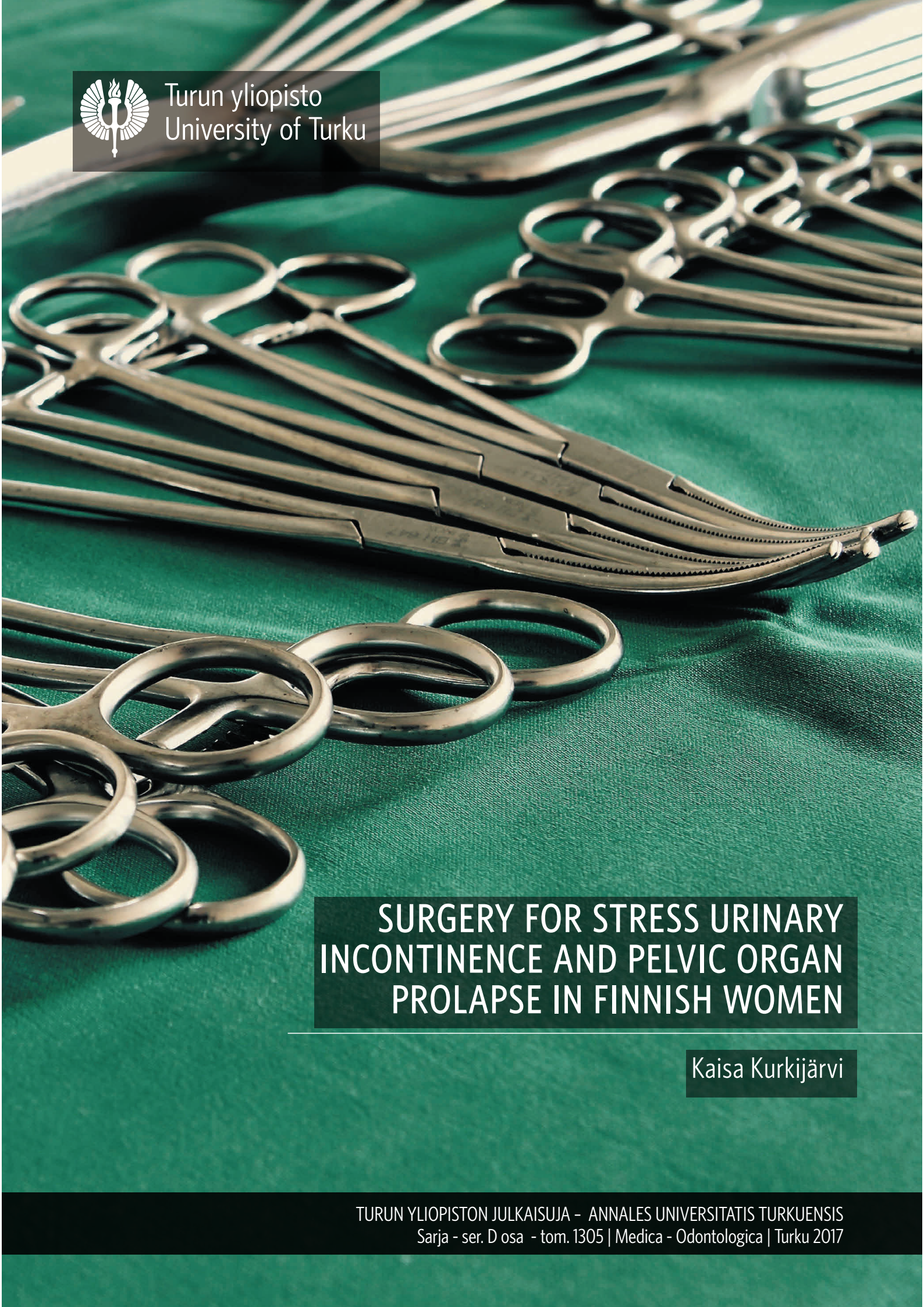

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To my family

"If we knew what it was we were doing,
it would not be called research, would it?"
Albert Einstein

ABSTRACT

Kaisa Kurkijärvi

Surgery for stress urinary incontinence and pelvic organ prolapse in Finnish women

University of Turku, Faculty of Medicine, Department of Obstetrics and Gynecology, Doctoral Program of Clinical Invesigation, Turku, Finland

Annales Universitatis Turkuensis 2017

Pelvic floor disorders are highly prevalent among women. Surgical treatment is common, and it has been estimated, that approximately every fifth woman will undergo surgery for stress urinary incontinence (SUI) or pelvic organ prolapse (POP) during her lifetime.

The aim of this study was to establish the time trends of the surgical procedures for SUI and POP in Finland and to calculate the incidence of surgery as well as defining the lifetime risk for pelvic floor surgery in Finnish women. The risks for reoperation after primary SUI and further operations after POP surgery were evaluated.

The Care Register for Health Care (HILMO), maintained by the Institute for Health and Welfare, was used to collate all surgeries for SUI and POP from 1987 to 2009. A total of 38,500 women had undergone surgery for SUI and 77,960 women for POP during this time. The incidence of SUI surgery increased notably in 1997, after the introduction of the midurethral (MUS) procedure, declining thereafter. The incidence for POP surgery has remained stable. The lifetime risk of surgery for SUI was 6% and for POP 13%.

At the beginning of the study period, open and subsequently laparoscopic colposuspension was the most prevalent method for treatment of SUI; this is no longer performed as in practice, MUS has become the only operative method in use. With respect to POP, native tissue repairs of anterior and posterior vaginal wall were the most commonly applied techniques. Reoperations after SUI surgery were not common i.e. 7.8 operations per 1000 women-years; the 5-year reoperation rate is higher after Burch colposuspension compared to MUS. Incidence of reoperation after retropubic MUS was lowest, but the difference between retropubic and transobturator MUS was not statistically significant. Risk for further operation after POP surgery is 10.8% in 10-year follow-up.

Keywords: Stress urinary incontinence, Pelvic organ prolapse, Surgery, Incidence, Lifetime risk

TIIVISTELMÄ

Kaisa Kurkijärvi

Ponnistusvirtsankarkailu- ja lantionpohjan laskeumaleikkaukset suomalaisilla naisilla

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Lantionpohjan toimintahäiriöt ovat yleisiä aikuisilla naisilla. Kirurginen hoito on tavallista ja arvioidaan, että noin 20 % naisista joutuu elämänsä aikana leikkaukseen ponnistusvirtsankarkailun tai synnytinelinlaskeuman vuoksi. Tämän väitöstutkimuksen tavoitteena oli selvittää virtsankarkailun ja laskeuman leikkaustapojen ja leikkauksien ilmaantuvuuden muutosta Suomessa sekä määrittää suomalaisen naisen elinikäinen riski joutua virtsankarkailu- tai laskeumaleikkaukseen. Lisäksi selvitettiin uusintaleikkauksen riskiä.

Terveyden ja hyvinvoinnin laitoksen (THL) ylläpitämästä hoitoilmoitusrekisteristä (HILMO) etsittiin kaikki ne hoitojaksot vuosilta 1987-2009, joihin liittyi leikkaus virtsankarkailun tai laskeuman takia. Tällä aikavälillä 38 500 naista leikattiin virtsankarkailun ja 77 906 laskeuman takia. Virtsankarkailuleikkauksen ilmaantuvuus nousi merkittävästi vuoden 1997 jälkeen, jolloin keskiuretran nauhaleikkaukset otettiin käyttöön. Myöhemmin ilmaantuvuus jälleen laski. Laskeumaleikkausten ilmaantuvuus pysyi varsin tasaisena tutkimusjakson ajan. Elinikäinen riski joutua virtsankarkailuleikkaukseen oli 6 % ja laskeumaleikkaukseen 13 %.

Tutkimusjakson alussa avoin ja myöhemmin tähystämällä tehtävä kolposuspensio oli yleisimmin käytetty leikkausmenetelmä virtsankarkailun hoitoon. Nauhaleikkauksen käyttöönoton jälkeen sitä ei juurikaan enää tehdä. Laskeuman hoidossa yleisimpiä ovat omin kudoksin tehtävät emättimen etu- ja takaseinän kiristykset. Uusintaleikkaus virtsankarkailuleikkauksen jälkeen on harvinaista, 7,8 leikkausta tuhatta naisvuotta kohden; viiden vuoden seurannassa kolposuspension jälkeen uusintaleikkauksia oli eniten, häpyluun takaa asetettavan nauhan jälkeen uusintaleikkauksia oli vähiten; tilastollista eroa obturatoraukon kautta laitettavaan nauhaan ei kuitenkaan ollut. Kymmenen vuoden aikana riski uusintaleikkaukselle laskeumaleikkauksen jälkeen oli 10,8 %.

Avainsanat: ponnistusvirtsankarkailu, synnytinelinlaskeuma, ilmaantuvuus, elinikäinen riski

TABLE OF CONTENTS

ABBREVIATIONS

ATFP	Arcus tendinous fascia pelvis
AUGS	American Urogynecologic Society
BMI	Body mass index
CL	Cardinal ligament
CS	Cesarean section
FDA	US Food and Drug Administration
HILMO	The Care Register for Health and Welfare (Hoitoilmoitusrekisteri)
ICS	International Continence Society
ISD	Intrinsic sphincter deficiency
IUGA	An International Urogynecological Association
KTL	National Public Health Institute (Kansanterveyslaitos)
LUTS	Lower urinary tract symptom
MMK	Marshall-Marchetti-Krantz
MUCP	Maximal urethral closure pressure
MUI	Mixed urinary incontinence
MUS	Mid-urethral sling
OECD	Organization for Economic Cooperation and Development
OR	Odds Ratio
PFDR	The Pelvic Floor Disordes Registry
PFMT	Pelvic floor muscle training
PIC	Personal Identity Code
POP	Pelvic organ prolapse
POP-Q	Pelvic Organ Prolapse Quantification System
PUL	Pubourethral ligament
PVR	Paravaginal repair
PVS	Pubovaginal sling
QoL	Quality of life
RCT	Randomized controlled trial
RP-MUS	Retropubic midurethral sling
SCP	Sacrocolpopexy
SSLF	Sacrospinosus ligament fixation
SUI	Stress urinary incontinence

THL	National Institute for Health and Welfare (Terveyden ja hyvinvoinnin laitos)
TO-MUS	Transobturator midurethral sling
TOT	Transobturator tape (outside-in)
TVT	Tension-free vaginal tape
TVT-O	Tension-free vaginal tape obturator (inside-out)
UI	Urinary incontinence
UUI	Urge urinary incontinence
USL	Uterosacral ligament
USLS	Uterosacral ligament suspension
VD	Vaginal delivery
WHI	The Women's Health Initiative

LIST OF ORIGINAL PUBLICATIONS

I Kurkijärvi K, Aaltonen R, Gissler M, Mäkinen J. Surgery for stress urinary incontinence in Finland 1987-2009. Int Urogyn J. 2016;27:1021-7.

II Kurkijärvi K, Aaltonen R, Gissler M, Mäkinen J. Pelvic organ prolapse surgery in Finland from 1987 to 2009: A national register based study. Eur J Obstet Gynecol Reprod Biol. 2017;214:71-7.

III Kurkijärvi K, Aaltonen R, Gissler M, Mäkinen J. Reoperations for female stress urinary incontinence – A Finnish national register study. Eur Urol Focus, *In press,* DOI: 10.1016/j.euf.2017.05.005

IV Kurkijärvi K, Aaltonen R, Gissler M, Mäkinen J. Reoperations for pelvic organ prolapse in Finland. *Submitted*

1 INTRODUCTION

Disorders of pelvic floor function are common; up to 25% of women report having at least one of the following symptoms: urinary incontinence, pelvic organ prolapse or anal incontinence (Wu et al. 2014b). The most evident risk factors for pelvic floor dysfunction are increasing age and vaginal delivery (Hallock & Handa 2016). With the ageing of populations in the developed countries, it has been predicted that we will face an epidemic of pelvic floor disorders as more and more women, will seek evaluation and care for their problem, partially as a result of improved awareness and greater availability of treatments (DeLancey 2005, Dieter et al. 2015). In Finland, it has been projected, that the number of persons aged 65 or over will be 1 478 426 (26%) in 2030 and 1 723 944 (29%) in 2060, as compared to 1 091 837 (19.9%) in 2015 (Source: Population and Justice Statistics, Statistics Finland). It must be acknowledged, however, that fewer Finnish women will have children: in 1990 13.4% of women aged 45 years did not have children, whereas in 2013, 19.1% women of the same age did not have children (Source: Population Structure, Annual Review 2013, Statistics Finland). On the other hand, parturients are older: in 1987 13.3% of women giving birth in Finland were older than 35 years of age but by 2016, that value had risen to 22.0% (Source: Perinatal statistics – parturients, deliveries and newborns 2016, National Institute for Health and Welfare).

Stress urinary incontinence (SUI) and pelvic organ prolapse (POP) can be treated surgically if conservative methods fail, such as lifestyle management and physiotherapy, including pelvic floor muscle training for SUI and mechanical support devices (prolapse rings and cubes and the Gellhorn pessary) for POP. The operative treatment of SUI has gone through a major change in the last two decades with the introduction of midurethral slings (MUS) (Rapp & Kobashi 2008) which display both good efficacy and safety. Native tissue repairs of POP have not changed extensively in the past one hundred years; the enthusiasm of vaginal procedures augmented with artificial mesh kits has attenuated due to unforeseen complications (van Geelen & Dwyer 2013), and the results of traditional methods need to be reassessed. One way to address the issue of success of surgical treatment is examine the reoperation rate, which has been fairly good with respect to SUI procedures (Foss Hansen et al. 2016a). The reported reoperation rate after POP surgery varies widely and is more ambiguous due to difficulties with its definition (Ismail et al. 2010).

There is a notable variation in the rates of SUI and POP surgery internationally, even between countries with equivalent standards of living (Haya et al. 2015). Estimates of the lifetime risk for a woman to have a surgery for either SUI or POP vary from 11% to 20%; although a risk of 19% to 21.5% for POP surgery alone have been proposed (Smith et al. 2010, Wu et al. 2014a, Løwenstein et al. 2015). These calculations are always based on the local incidence at a certain time and therefore are not universally generalizable.

A report from OECD-countries revealed the extensive variation in trends and rates of pelvic floor surgery in different countries. The national rates of SUI and POP surgery in Finland have not been studied before. As the international literature seems to reveal an increase in the number of operation and as stated, it is clear that the Finnish population is ageing, it is important to establish the surgery rates if we wish to make reliable predictions about the future need for pelvic floor surgery. This thesis evaluates the time trends of the surgical procedures for SUI and POP from 1987 to 2009 in Finland are evaluated as well as estimating the rates of SUI and POP surgery. A need for reoperation after recurrence of the condition is a common problem in urogynecological surgery, most notably for POP surgery. There are no national reports on reoperation rates after SUI and POP surgery and therefore this was assessed in this study. The lifetime risk for a woman to require SUI and POP surgery has been reported in several studies, but the actual risk for a Finnish woman has yet to be established; this issue is addressed in this study. These topics are important when counselling patients, if possible surgery for pelvic floor dysfunction is being considered.

2 REVIEW OF LITERATURE

2.1 Normal function of the female pelvic floor

As a result of evolution and the change from quadruped to bipedal locomotion, the function of pelvic floor, and more specifically the levator ani muscles, has changed from a vertical tail-wagging apparatus to providing more horizontal support for the abdominal and pelvic organs (Abitbol 1988, Schimpf & Tulikangas 2005). The pelvic floor has to permit urination and defecation while maintaining continence; the female pelvic floor must also allow parturition of a neonate, which because of another biproduct of evolution, has a relatively large head (Rosenberg & Trevathan 2002). In the standing position, the pelvic inlet of bony pelvis is tilted anteriorly and as such, most of the abdominal pressure can be distributed to the bony structures instead of soft tissues, see figure 1.

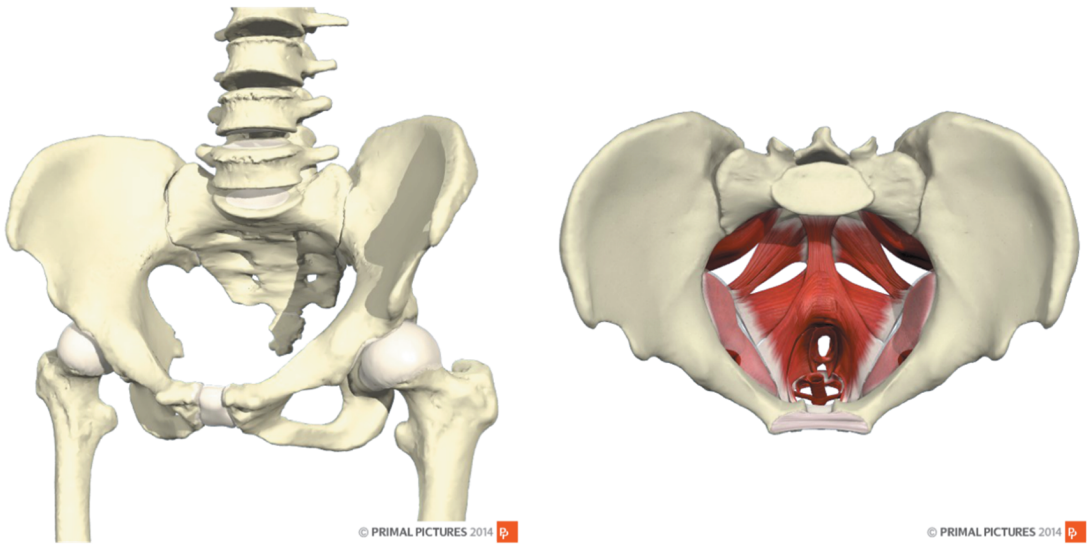


Figure 1 On the left, female bony pelvis. On the right, levator ani muscles (reprinted with permission from Primal Pictures)

The levator ani muscle complex consists of pubovisceral, puborectal and ilicoccygeal muscles, figure 1. Arcus tendineus of fascia pelvis (ATFP) is a dense fibrous structure, which attaches anteriorly to the pubic bone and posteriorly to the ischial spine and thus forms a cable-like structure bilaterally, into which iliococcygeal muscles attach laterally. In the midline, there is a keyhole shaped opening, through which the urethra, vagina and rectum pass. The pubovisceral muscle attaches to the organs in the midline and puborectalis loops from pubic bone behind the rectum (Barber 2004, Ashton-Miller & DeLancey 2007). The levator ani muscles are innervated by the levator ani nerve, that

originates from sacral roots S3-S5. The pudendal nerve originates from S2-S4 and innervates external anal and urethral sphincters and perineal muscles (Barber et al. 2002). In the resting state, there is a constant tone in the levator muscles, particularly in the puboviceral part, which is directed anteriorly toward pubic bone, thus closing the vaginal and urethral opening (Barber 2004).

2.1.1 Pelvic floor support theories

While muscles provide lifting and closing of the pelvic structures, connective tissues offers support. A three level support system, figure 2, was described in 1992 by DeLancey. The highest level I supports the cervix and upper vagina by suspending them to the pelvic side walls by mesenteric condensations called the uterosacral (USL) and cardinal (CL) ligaments. The middle level II attaches the vagina into the ATFP and also posteriorly. At the most distal level III the vagina is fused with levator ani muscles and perineal body in the midline (DeLancey 2016).

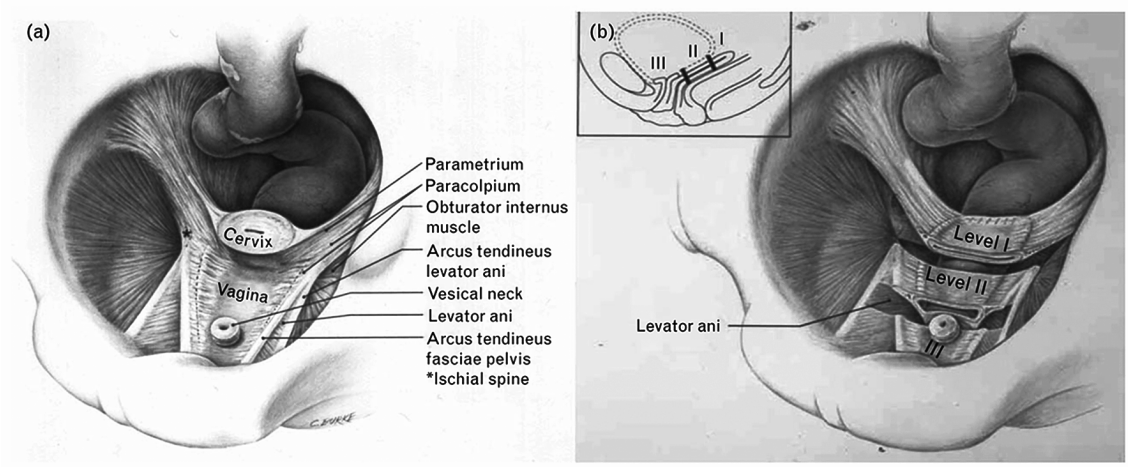


Figure 2 Three levels of pelvic support (reprinted with permission from DeLancey 2016)

The integral theory offered a cohesive explanation to all defects in the pelvic floor function (Petros & Ulmsten 1990). Accordingly, pelvic floor structures are suspended by pubourethral ligaments (PUL), CL, USL and ATFP, against which muscle tone compresses the urethra and vagina. Any laxity of these ligament structures will result in dysfunction; when PULs are damaged, the urethra fails to close in response to a rise in the abdominal pressure and leakage of urine occurs (Boustead 2002, Petros & Woodman 2007). The upper vagina and bladder base are supported by the pericervical ring, composed of the aforementioned ligaments and pubocervical and rectovaginal fascias. Distension of this ring leads to apical prolapse, contributing also to SUI and UUI.

2.1.2 Physiological changes

2.1.2.1 Childbirth

Pregnancy and vaginal delivery impose a great challenge to the pelvic floor. This raises a dilemma - how can a woman bear the weight of the growing uterus and eventually pass the baby through her pelvic floor, and still maintain its structure and function? During the last fifteen years, *ex vivo* studies and computed finite element models (Easley et al. 2017) as well as advances in imaging, have shed light on events occurring in the pelvic floor during parturition.

Figure 3 illustrates schematically the end of the second stage of labor, when the fetal head is crowning. Table 1 summarizes parameters related to the distension. Postpartum MRI imaging revealed that 20% of vaginally delivered primiparas sustained a levator avulsion, 90% of which were in the pubovisceral muscle, either uni- or bilaterally (DeLancey et al. 2003), whereas 36% of primiparas, examined with 3D translabial ultrasound, were found to display signs of levator avulsion. The mobility of pelvic organs, urethra, bladder neck, vaginal walls and cervix, becomes increased after delivery, most notably in women, who had less mobility before delivery (Dietz 2003, 2006). Levator avulsions are seen more often in women who are older at their first delivery and who have a longer duration of active second stage of labor. Instrumental delivery is a risk factor for levator avulsion, especially forceps delivery, with an odds ratio (OR) of 14.7 for avulsion; the effect of vacuum extraction is not as clear (Dietz & Lanzarone 2005, Kearney et al. 2006, 2010). When measuring the dimensions of the urogenital hiatus at five months postpartum, a greater enlargement (28%) was seen in women with avulsion, compared to those with no avulsion (6%) (Shek & Dietz 2009).

Denervation of pelvic floor muscles was encountered in 30% of primiparas, who had electromyography before and after delivery, of which 35% were cured within six months postpartum (South et al. 2009). A regenerative effect may be seen in pelvic floor muscle strength; after the initial weakening, the contractility recovers within one year (Elenskaia et al. 2011). Women who delivered vaginally, experienced a decrease in the strength of pelvic floor muscle of 20.1 kPa, whereas those who delivered by cesarean section (CS), had a much less severe decline in its strength, only 5.2 kPa. Instrumental vaginal delivery had the most severe effect with a decrease of 31.4 kPa. Other factors influencing the strength of the pelvic floor muscles are older maternal age and large fetal head circumference (Diez-Itza et al. 2011, Sigurdardottir et al. 2011).

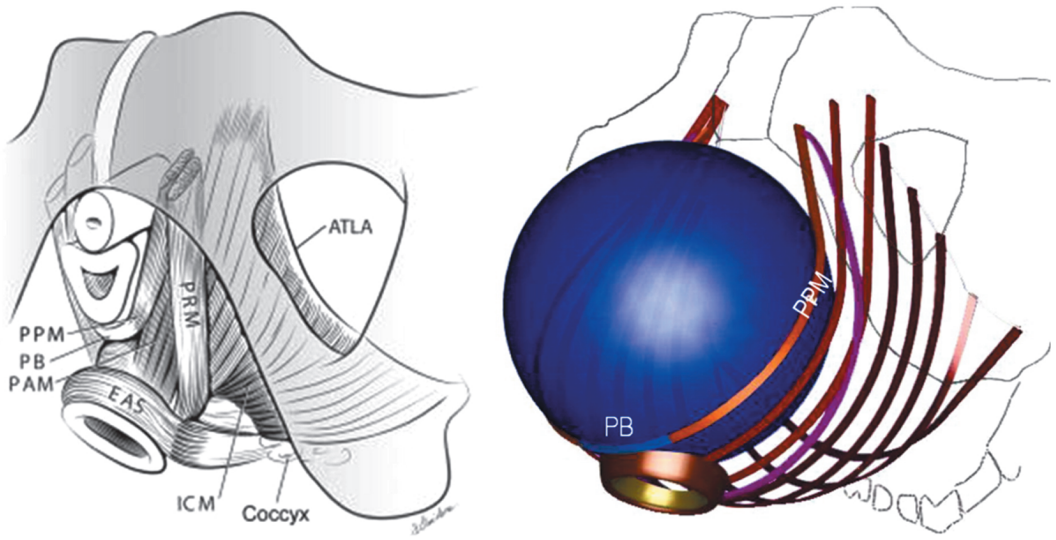


Figure 3 On the left are the levator ani muscles. EAS external anal sphincter, PPM puboperineal muscle, PAM puboanalis muscle, which are parts of pubovisceral muscle. On the right, the figure shows a stretch of pelvic floor structures during crowning of the fetal head (blue ball) at the end of the second stage of labor. PB perineal body, PRM puborectalis muscle, ATLA arcus tendineus levator ani, to which ICM iliococcygeal muscle attaches (reprinted with permission from Chen et al. 2015)

Table 1 Delivery induced alterations in the pelvic floor structures. Muscle stretch is displayed as the stretch ratio from the original length, hiatal stretch is for hiatal area

Levator ani muscle stretch		Pudendal nerve stretch	
Iliococcygeus	2.7	Inferior rectal branch	35%
Pubovisceralis	2.5-3.3	Branch to anal spincter	33%
Puborectalis	2.3-3.5	Branch to posterior labia	15%
		Branch to urethral sphincter	13%
Lien et al. 2004, Hoyte et al. 2008		Lien et al. 2005	
Levator hiatal stretch		**Pressure to the pelvic floor**	
Stretch during II stage of labor:		Volitional pushing during labor	120N
25-245% up from maximal Valsalva		Vacuum extraction	113N
62-276% up from rest		Forceps	200N
		(Quiet standing)	37N
Svabík et al. 2009		Ashton-Miller & Delancey 2009	

2.1.2.2 Ageing

Ageing seems to be a risk factor for all modalities of pelvic floor dysfunction. This raises the question - is it simply the aftermath of propagation or an independent factor? Cadaver studies comparing young and elderly women, adjusted for parity, have revealed that the sizes of pelvic floor muscles, coccygeus, iliococcygeus, pubovisceralis and obturator internus are significantly smaller in elderly women; the decrease was notably greater than the expected age-related decline in muscle mass (Alperin et al. 2015). Older women also had more fat tissue and connective tissue between the pelvic organs compared to young (Wu et al. 2017, Cook et al. 2017). Tissue composition becomes altered with age (Tinelli et al. 2010): the collagen content of muscles is markedly increased in older women and this is independent of parity (Alperin et al. 2015). These changes result in decreased muscle strength: older women have inferior squeezing power in the external anal sphincter compared to their younger counterparts (Lewicky-Gaupp et al. 2009). An ageing effect was also identified in pelvic floor muscle strength and hiatal dimensions, when adjusted for parity and levator avulsion, with a more pronounced effect on nulliparas (Weemhoff et al. 2010).

Pelvic tissues express estrogen and progestin receptors, which are found in bladder and urethra, vaginal mucosa, uterosacral ligaments and levator ani muscles (Robinson & Cardozo 2003, Trutnovsky et al. 2013). As the ovarian hormonal production comes to an end after menopause, it would be tempting to speculate that hormonal therapy would be helpful for pelvic floor dysfunction. However, a Cochrane review found no improvement of POP with estrogen use (Ismail et al. 2010). In contrast, systemic estrogen administration resulted in worsening of UI symptoms and previously continent women reported de novo incontinence after starting estrogen medication. Locally delivered estrogen, on the other hand, may be helpful in UI (Cody et al. 2012).

2.2 Urinary incontinence

2.2.1 Definition and etiology

Continence is the ability to voluntarily control the function of bladder and bowel. The International Urogynecological Association (IUGA) and International Continence Society (ICS) define the symptom of urinary incontinence (UI) as a complaint of involuntary loss of urine. Stress urinary incontinence (SUI) is a complaint of involuntary loss of urine on effort or physical exertion, on sneezing or coughing. Urgency urinary incontinence (UUI) is the complaint of involuntary loss of urine associated with urgency, which in turn is a complaint of a sudden, compelling desire to pass urine. The objective sign of SUI is the

observation of involuntary leakage from urethra while coughing or sneezing. Mixed urinary incontinence (MUI) has features of both conditions (Haylen et al. 2010).

While sharing the majority of the same risk factors (table 2), the etiologies of SUI and UUI are different. UUI is part of the entity of overactive bladder (OAB), also named as OAB wet, in contrast to OAB dry, where leakage of urine does not occur The pathophysiology of OAB is not completely understood, but it involves disturbances in the complex interplay of the central nervous system, peripheral nerves and bladder (Banakhar et al. 2012). Theories attempting to account fot the changes in the bladder include altered receptor function in the urothelium and aberrant contractions of the smooth muscle fibers of the detrusor muscle (Koelbl et al. 2013).

Table 2 Risk factors for UI (modified from Wood & Anger 2014)

Level I evidence	Level II evidence	Level III evidence
Pregnancy	Physical function	Smoking
Labor	Diabetes mellitus	Caffeine intake
Vaginal delivery	Hysterectomy	Constipation
Obesity, waist circumference	Dementia, impaired cognition	Urinary tract infection
Genetics		Depression
Per oral estrogen		Exercise

The pathophysiology of female stress urinary incontinence has undergone through a major evolution during the last century. The initial observations by Kelly and Bonney were based on the open vesical neck on cystoscopy and the distorted anatomy of anterior vaginal wall, leading to hypermobility of bladder neck of incontinent parous women. The development of technical interventions, such as manometry and cystography led to the theories that there were alterations of pressure transmission behind SUI (Cundiff 2004). Subsequently, a dualistic view explained SUI as either resulting from urethral support failure or incompetence of the intrinsic sphincter of urethra (intrinsic sphincter deficiency, ISD) (Hosker 2009). In 1990 Peter Petros and Ulf Ulmsten introduced the integral theory of female incontinence (Petros & Ulmsten 1990), in which they stated that stress urinary incontinence would be caused by a failure of active closure mechanism of pubourethral ligaments and muscles by lax tissues.

The work of John DeLancey further clarified the nature of SUI as a multifactorial condition caused by damage to the muscles, fascial structures and nerves (Delancey 1994, DeLancey 1996). The support unit of the continence mechanism (Figure 4) has been described as a hammock: anterior vaginal wall and the surrounding muscles and fascial tissue act as a backboard, against which the urethra becomes compressed, when abdominal pressure is elevated. The sphincteric unit consists of the multilayered urethra and alpha-adrenergically innervated bladder neck (DeLancey 2010). The control of the

sphincteric system is mediated by the lower motor neurons from the Onuf's nucleus to the striated urinary sphincter and intrinsic smooth muscle via the pudendal nerve (Kalejaiye et al. 2015).

It is uncertain the extent to which these different factors contribute to the formation of stress urinary incontinence. In a study of continent and incontinent 48-year old women, the greatest differences between groups were detected in maximal urethral closure pressure (MUCP); there were less differences with respect to the resting urethral axis, urethrovaginal support and size of urogenital hiatus differed less. No difference was found in levator strength and levator defects (DeLancey et al. 2008b). On the contrary, in a group of younger women aged 30 years with one vaginal birth, incontinent women were twice as likely to have levator defects (DeLancey et al. 2003); they also had lower MUCP compared to continent women, whose MUCP on the other hand did not differ from nulliparas of the same age (DeLancey et al. 2007). Indeed, age is a strong contributing factor: MUCP was found to decrease by 15 H_2O cm with every decade in a study examining nulliparous women (Trowbridge et al. 2007).

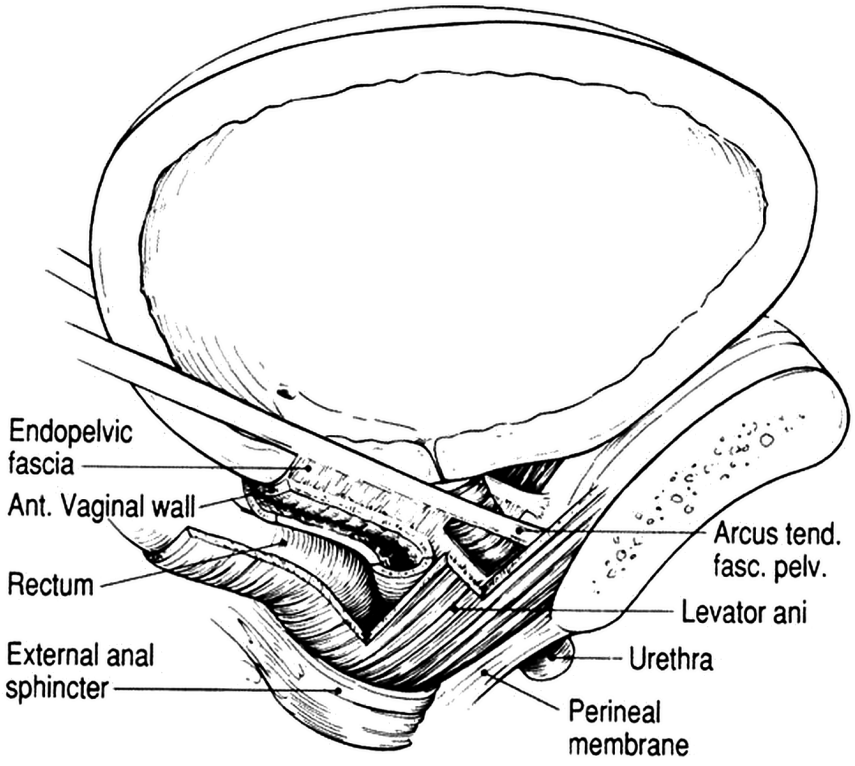


Figure 4 The support system of continence mechanism (reprinted with permission from DeLancey 1996)

Pregnancy and delivery are acknowledged risk factors for SUI. The effect is clearest for the first vaginal delivery, as seen in Figure 5, supported by findings of Altman et al. in

2006. The prevalence of SUI increases after the first and second CS compared to women with no deliveries, highlighting the impact of pregnancy itself (Rortveit et al. 2003). Over the long term, the adjusted OR for SUI is 1.85 after one vaginal delivery compared to CS. Vaginal delivery increases all types of UI: ORs for SUI, UUI and MUI were 1.42, 1.66 and 1.46, respectively, when one vaginal delivery was compared to one CS twenty years later (Gyhagen et al. 2013c). It has been estimated that eight to nine CSs should be performed in order to prevent one case of UI (Gyhagen et al. 2013b). The effect of vaginal delivery diminishes over time; in a recent meta-analysis, the odds ratio for SUI after vaginal birth was 2.51 (1.96-3.21) when compared to CS at the age of 30 years but had declined to 1.29 (0.97-1.72) at the age of 60 years (Tähtinen et al. 2016).

With proper management of the second stage of labor, it is possible to reduce the occurrence of pelvic floor dysfunction in both the post partum period and over the long term. Guidelines both in the US (Caughey et al. 2014) and in the UK (Source: NICE guidelines) limit the active pushing time during the second stage to three hours for primiparas and to two hours for multiparas. When exceeding these limits, the risk for urinary incontinence at three months' post-partum was elevated, OR 2.2 (1.1-3.4); also an instrumental vaginal delivery increased the risk for post-partum UI, OR 1.9 (1.0-2.8) (Brown et al. 2011). In the same cohort of women, prolonged second stage of labor ending with instrumental delivery, increased the odds of UI at 4 to 18 months' post-partum to 2.46 (1.32-4.60) (Gartland et al. 2012).

The maneuver of manually supporting the perineum while slowing down the crowning of fetal head with the other hand has been traditionally implemented by midwives in Finland; a mother is also asked not to push with full force during the final moments of the second stage. This practice may account for the notably lower number of obstetric anal sphincter ruptures occurring during labor in Finland (0.6%) when compared to the other Nordic countries (3.6-4.2%) (Laine et al. 2009). After introducing this technique to labor ward staff, the incidence of anal sphincter ruptures decreased from 4.03% to 1.17% in Norway (Laine et al. 2008) and from 4.4% to 1.7% in Denmark (Leenskjold et al. 2015). By reducing anal sphincter damage , the risk of other pelvic floor problems may also be reduced, as 44% of parous women who had suffered an anal sphincter rupture, reported also urinary incontinence post-partum (Linneberg et al. 2016). A difference is also seen in the episiotomy rate, which has been higher in Finland than in other Nordic countries. This may, in part, explain the lower rate of anal sphincter ruptures (Laine et al. 2009). Routine episiotomy is not recommended; selective episiotomy results in a better perineal outcome (Jiang et al. 2017).

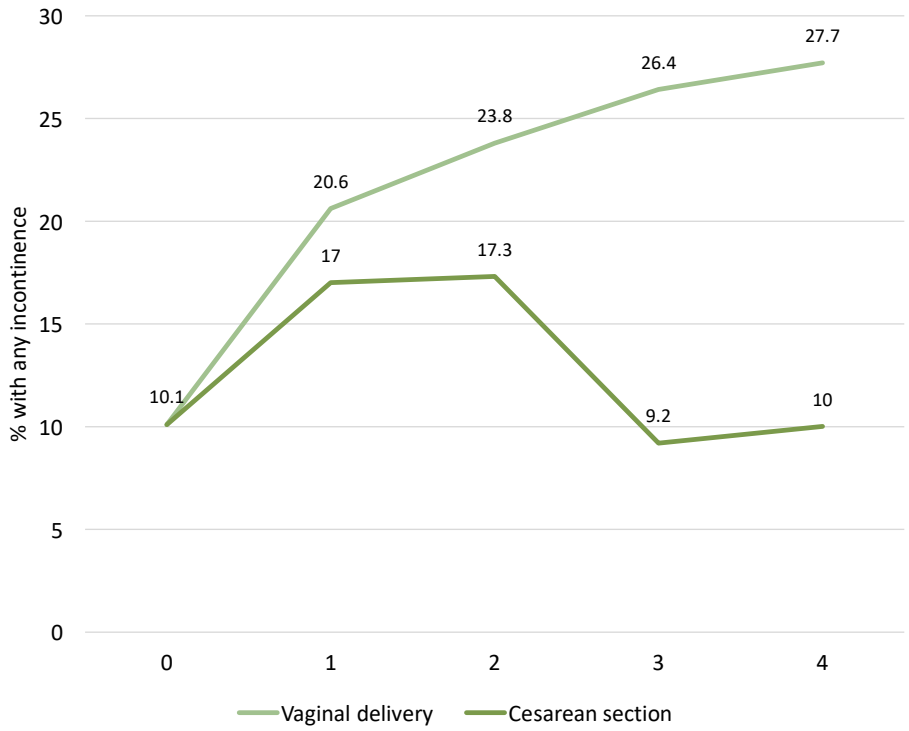


Figure 5 Prevalence of UI after vaginal deliveries and cesarean sections (modified from Rortveit et al. 2003)

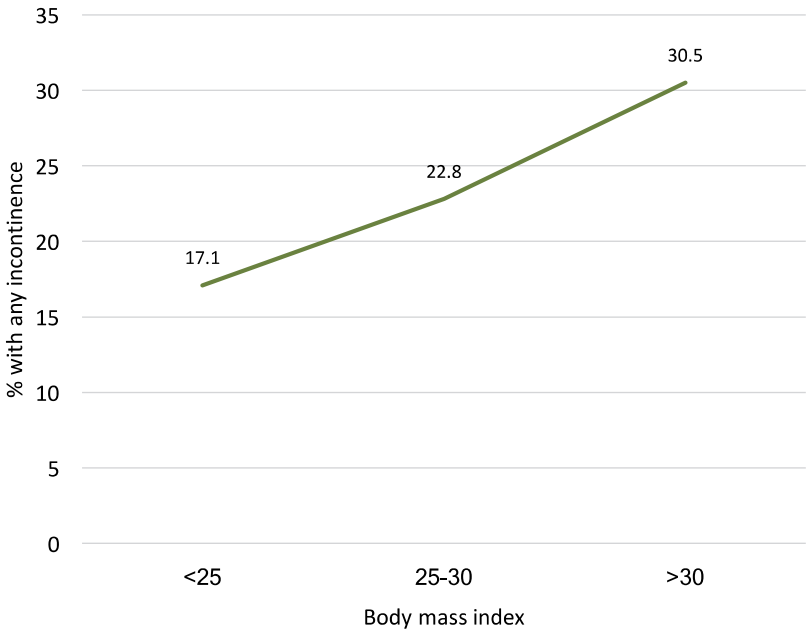


Figure 6 Prevalence of UI and BMI (modified from Rortveit et al. 2003)

Obese women are more likely to have UI; when comparing women with different BMIs, those women with body mass index (BMI) ≥35 had the highest prevalence of UI (67.3%), whereas among women with BMI <25, the prevalence of UI was 40.6% (Schreiber Pedersen et al. 2017). Women, who were overweight before their first pregnancy were

at risk of having UI twelve years after the pregnancy; this effect of BMI is more pronounced in those women who did not have SUI during postpartum period (Viktrup et al. 2006, Viktrup et al. 2008). The effect of obesity on the prevalence of UI can be seen in figure 6 and in table 3.

Table 3 Relative risk factors for UI and POP. Modified from (Hannestad et al. 2003, Rortveit et al. 2003, Lukacz et al. 2006, Miedel et al. 2009a, Gyhagen et al. 2013a, b, Lonnée-Hoffmann et al. 2015, Volløyhaug et al. 2015, Linde et al. 2017, Schreiber Pedersen et al. 2017)

			UI		POP	
Risk factor		Compared to	OR	95% CI	OR	95% CI
BMI	25-29	<25	1.4	1.3-1.5	1.6	1.3-2.0
	30-34	<25	1.9	1.7-2.1	1.6	1.3-2.1
	35-39	<25	2.4	2.1-2.8	1.6	1.2-2.3
	>40	<25	2.7	2.1-3.5	-	-
Parity	1	0	1.3	1.1-1.6	3.5	1.5-7.9
	2	0	1.7	1.4-2.0	4.7	2.2-10.0
	3	0	1.4	1.1-1.8	4.4	1.9-10.5
	>4	0	1.5	1.1-2.1	6.3	1.8-22.7
Obstetric	VD	CS	1.6	1.5-1.9	2.6	2.0-3.3
	CS	Nullipara	1.5	1.2-1.9	1.6	0.8-3.2
	VD	Elective CS	3.9*	1.4-10.8	5.8	0.8-42.0
	VD	Labored CS	1.6*	1.0-2.6	1.2	0.6-2.2
	Operative VD	VD	1.0	0.77-1.2	1.7	1.2-2.5
	Constipation	No	1.5	1.1-2.2	1.8	1.3-2.5
	Pulmonary disease	No	1.5	1.2-1.9	1.3	1.0-1.6

*SUI, VD=vaginal delivery, CS=cesarean section

Hysterectomy has been found to increase the risk of SUI, especially when performed for POP vaginally, indicating the underlying structural defect (Forsgren et al. 2012). On the contrary, when hysterectomy had been performed abdominally for women with no SUI or POP, it seemed to be related to a smaller risk of SUI with an OR 0.55. In a large cohort study (WHI) of postmenopausal women, hysterectomy increased the risk for UUI (OR 1.61) and SUI (OR 1.39) (Kudish et al. 2014). Genetic factors also affect the risk of UI; in a twin study, the genetic effect for all UI was 51% whereas for SUI, it was 34% (Wennberg et al. 2011). The relative risks for both UI and POP for obstetrics and non-obstetrics risk factors are presented in table 3.

2.2.2 Incidence and prevalence

A wide range of population-based studies has estimated the prevalence of pelvic floor disorders and urinary incontinence as one of them, but comparisons are difficult due to

the different questionnaires and the varying definitions being used (Milsom et al. 2013). In addition, studies with short follow-up times tend to overestimate the incidence (Irwin et al. 2010). In Norway, in a cohort of women aged 20 years or older (n=27936), the prevalence of any UI was 25%, with the prevalence of significant UI being 7% in the population. Every second UI was SUI, 11% UUI and 36% MUI (Hannestad et al. 2000). The same women were interviewed by mail 16 years later. The incidence of UI was 1.7% per year for those who did not have UI at the beginning. The majority still had UI (66%), but remission was also notable, 3.1% per year (Ebbesen et al. 2013). In a Swedish longitudinal population based survey, the incidence of UI during 16 years was 1.3% per year (Wennberg et al. 2009); in another Norwegian cohort of women aged 41-55 years, the incidence was claimed to be 4.9% per year during a follow-up of ten years (Jahanlu & Hunskaar 2010).

In a series of population based surveys in the US, the overall prevalence of moderate to severe UI was 15.8% in 2005-2007 and 17.8% in 2009-2010 with no statistical difference (Nygaard 2008, Wu et al. 2014b). In a postal survey in four European countries, notable differences were observed between countries: women in France, Germany and the UK reported 41-44% prevalence of UI, whereas in Spain the prevalence was much less, 23%. SUI constituted 37% of UI (Hunskaar et al. 2004). In another study with four European countries and Canada, the prevalence of any lower urinary tract symptoms (LUTS) was on average 66.6%, including all storage and voiding symptoms. With respect to the UI, SUI constituted 43% (Irwin et al. 2006). There may be cultural differences in reporting pelvic floor symptoms, which explains part of the variation in values. The heterogeneity in the prevalence of UI in different studies can be seen in table 4.

Table 4 Prevalence of any UI among community dwelling women according to four large (n=7 924-27 936) interview studies

	Any UI (%)			
	≤39 years	40-59 years	≥60 years	
Canada, Germany, Italy, Sweden, UK	7.3	13.7	19.3	Irwin et al. 2006
France, Germany, Spain, UK	28.0	40.5	31.2	Hunskaar et al. 2004
US	6.4	18.7	30.9	Wu et al. 2014c
Norway	15.8	27.5	32.4	Hannestad et al. 2000

2.2.3 Quality of life and socio-economic impact

Urinary incontinence can severely impair the quality of life (QoL) (Bartoli et al. 2010). In a study comparing the effect of 20 chronic conditions, women with UI had the third lowest scores for QoL only surpassed by two conditions (Alzheimer's disease and stroke).

For example, the QoL scores were better for patients with, for example, cancer, diabetes and back problems (Mittmann et al. 1999). In another study, many aspects of the health related quality of life was impaired for women with UI: they had more pain and discomfort, problems with mobility and moving as well as trouble with daily activities and self-care, compared to other chronic conditions (Villoro et al. 2016). MUI and UUI have been shown to double the negative effect on QoL compared to pure SUI (Lasserre et al. 2009, Coyne et al. 2012). QoL deteriorates with a worsening of SUI symptoms (Tennstedt et al. 2007, Riss & Kargl 2011). UI has been linked to psychiatric disorders; women with mild to severe UI are 80% more likely to become depressed, with an OR of 1.82 (Nygaard et al. 2003, Stach-Lempinen et al. 2003) and depression and anxiety have been linked to SUI as well as with other incontinence or MUI in women (Coyne et al. 2012). Since anxiety and depression are independent risk factors for UI and furthermore UI worsens these conditions, a vicious circle is formed (Felde et al. 2017).

The economic burden of incontinence is heavy, both for society and for the individual patient. In a study from the US, 76% of the total costs of incontinence were caused by the care of women with the remaining 24% being attributable to men. Community-dwelling women accounted for 69% of the costs, compared to institutionalized women (31%). In all 70% of the total amount is estimated to be spent on basic care, such as pads, supplies, and laundry, compared to 9% which is allocated to specific treatment of UI (Wilson et al. 2001). In a Finnish study, women used on average EUR 231 per year on pads, EUR 95 on medication and EUR 40 on other conservative treatment (Aukee et al. 2007). In the US, women suffering from SUI, spent USD 750 per year on incontinence management and would be willing to pay USD 1400 per year for a cure (Subak et al. 2008). When considering only SUI, the cost of conservative management is still 70% of the expenditures (Chong et al. 2011).

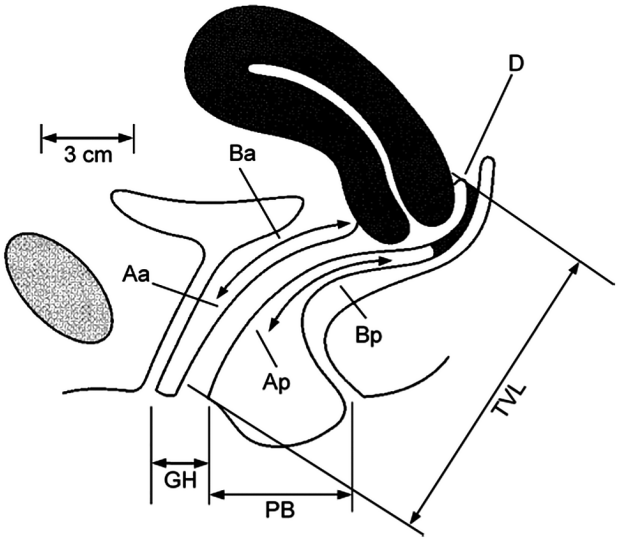
2.3 Pelvic organ prolapse

2.3.1 Definition and etiology

According to the IUGA/ICS Standardization and Terminology Committee, pelvic organ prolapse is defined as the descent of the vaginal walls, uterus, cervix or the vaginal vault, together or separately. This objective finding should be correlated with symptoms of POP, which are defined as vaginal bulge, pelvic pressure, bleeding or discharge, splinting or digitation and low backache (Haylen et al. 2016). Describing a prolapse verbally is not exact enough for clinical and scientific purposes. With the Baden-Walker halfway-system, the prolapsed structure can be graded as I when halfway between the hymen, II at the hymen, III halfway below the hymen and IV when completely prolapsed (Baden et al.

1968). In an attempt to determine the actual measurements of the prolapse, a more accurate system was proposed by the ICS standardization committee in 1996 (Bump et al. 1996). With this POP-Q system, the locations of nine anatomical points are measured with a ruler with respect to the hymen, see Figure 7. Stage I is defined as the most distal part of the prolapse higher than one cm above the hymen, stage II as one cm above to one cm below the hymen, III as further than one cm below the hymen and IV as complete eversion of the total length of the vagina. The use of the POP-Q system is recommended for clinical studies as it has proven to display good interobserver and intraobserver reliability (Hall et al. 1996). Although POP-Q is utilized in over 80% of scientific work on POP, it has failed to be adopted into clinical practice; it has been considered too time consuming, too complicated and too hard to learn as well as not exhibiting clinical relevance. A simplified version of POP-Q has been developed (Karp et al. 2010, Parekh et al. 2011).

Vaginal delivery and parity are known risk factors for POP (Tegerstedt et al. 2006, Lukacz et al. 2006, Vergeldt et al. 2015), see figure 8. Serial 3D-ultrasound examinations during delivery show, that avulsion of levator ani muscles, namely the pubovisceral part, occurs at the end of the second stage of labor (Blasi et al. 2011). Of women with POP, 55% have levator avulsion, compared to 16% of those, who do not have this disorder (Delancey et al. 2007); correspondingly 83% of women who have sustained avulsion, have also POP (Dietz & Shek 2008). The damaged levator ani muscle is unable to create enough tone to close the urogenital hiatus and abdominal pressure pushes vaginal structures downwards (DeLancey 2016). Connective tissue at the support level I (USL and CL) and II is stretched by this downward pull, which further increases the POP. Anterior descent is more pronounced, if both apical (levelI) and lateral (level II) support fail (Dietz & Steensma 2006, Chen et al. 2006, 2009).



Aa	Anterior wall, 3cm proximal to urethral meatus
Ba	Anterior wall, most distal point
Ap	Posterior wall, 3 cm proximal to hymen
Bp	Posterior wall, most distal point
C	Cervix or vaginal cuff
D	Posterior fornix
TVL	Total vaginal length
GH	Genital hiatus
PB	Perineal body

Figure 7 POP-Q system (reprinted with permission from Digesu et al. 2005)

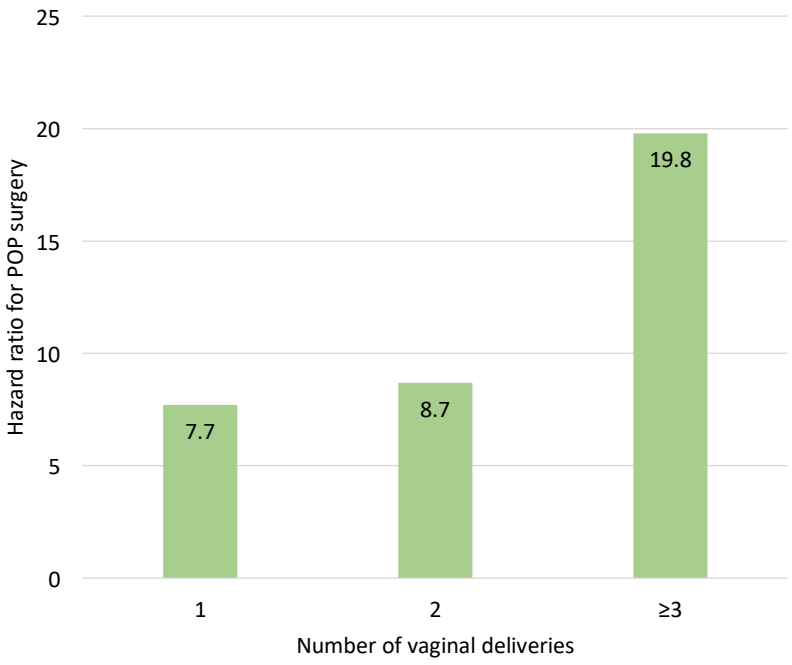


Figure 8 Hazard ratio for POP surgery with advancing number of vaginal deliveries (modified from Leijonhufvud et al. 2011)

Forceps delivery is known to increase the odds for levator avulsion (OR 2.9, 1.3-6.7) when compared to uncomplicated vaginal delivery (Caudwell-Hall et al. 2017), whereas vacuum assisted delivery does not have the same effect; when compared to vacuum, after forceps delivery the OR for levator avulsion was 4.40 (1.42-13.6) (Memon et al. 2015) The occurrence of obstetric anal sphincter rupture increases the probability of simultaneous levator avulsion (OR 3.2-4.4) as well as protracting the second stage of labor (OR 1.03 for every five minutes) as does increased maternal age at the first delivery (Van Delft et al. 2014, Rahmanou et al. 2016, Caudwell-Hall et al. 2017). Therefore, it could be proposed that optimal management of the second state of labor in order to avoid anal sphincter rupture could also prevent levator avulsion and further POP. Non-randomized studies have revealed a reduction in anal sphincter damage with manual perineal support, but this has not been confirmed in RCTs (Bulchandani et al. 2015). A Delphi-survey was conducted among authorities in the UK: there was a consensus that active perineal support should be applied despite the lack of evidence from RCTs (Ismail et al. 2015).

Women with POP have been shown to have a wider transverse inlet of the bony pelvis, as well as a narrow conjugata vera; diminished lumbar lordosis results to a less vertical position of the pelvic inlet directing more of the abdominal pressure towards the pelvic floor (Sze et al. 1999, Mattox et al. 2000, Nguyen et al. 2000, Handa 2003). Genetic predispositions have been studied as a risk factor: in register studies, mothers and sisters of POP patients have been found to have had more surgical procedures for POP (Lince et al. 2012, Andrada Hamer & Persson 2013); women of African descent seem to have less POP compared to Caucasian women (Whitcomb et al. 2009). The properties and types of

collagen in connective tissues may be one explanation for the heredity of POP; collagen type III is over expressed in POP tissue with AA-genotype (Kerkhof et al. 2009, Ward et al. 2014, Vetuschi et al. 2016). Several other mechanisms involving connective tissue metabolism and function have also been studied (Chen et al. 2004, Twiss et al. 2007, Word et al. 2009).

Large register studies show that hysterectomized women have more POP surgeries later in life compared to women with intact uteruses, with a hazard ratio of 1.7. The risk is more pronounced after vaginal hysterectomy (hazard ratio 3.8), which may be due to predisposing factors (Forsgren et al. 2008, Altman et al. 2008, Lykke et al. 2015). Lifestyle factors and some chronic medical conditions are also linked to POP: the OR for POP was 2.04 and 2.11 in women whose BMI values were 25-30 and over 30, respectively (Miedel et al. 2009b). Obesity was found also to be a risk factor for progression of POP (Kudish et al. 2009). Constipation, chronic pulmonary disease and occupational heavy lifting have been linked to POP (Blandon et al. 2009, Miedel et al. 2009b). With regard to lifetime physical activity, no difference was found between women seeking care for POP and controls, with the possible exception of strenuous activity during teenage years (Nygaard et al. 2014).

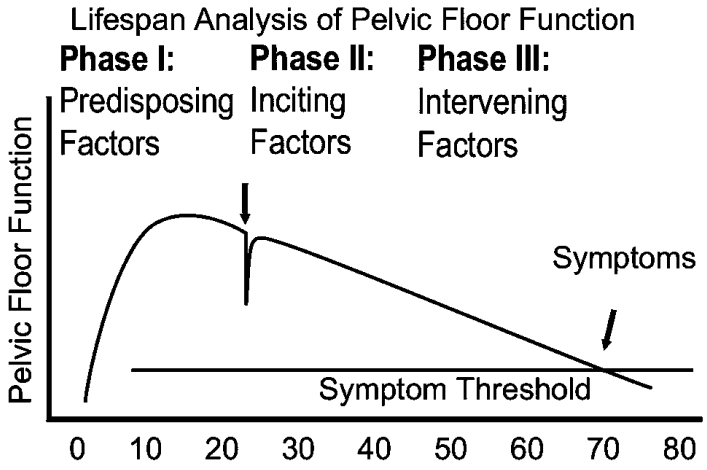


Figure 9 Lifespan model of pelvic floor function (reprinted with permission from DeLancey et al. 2008a)

A lifespan model of pelvic floor function shown in figure 9, integrates the risk factors for POP into a continuum of predisposing, inciting and intervening factors (DeLancey et al. 2008a), table 5. Predisposing factors determine the capacity of pelvic floor, which is tested by pregnancy and delivery. Intervening factors may impair the function until the symptom threshold is crossed. Odds ratios for POP are also presented in table 3 in comparison with incontinence.

Table 5 Etiologic factors for POP according to the lifespan model of pelvic floor function (modified from DeLancey et al. 2008a, Barber 2016)

Predisposing	Inciting	Intervening
Family history	Vaginal delivery	Ageing
Genetic conditions	Parity	Obesity
Shape of bony pelvis	Forceps delivery	Hysterectomy
Teenage activity	Fetal weight	Constipation
		Occupational heavy lifting

2.3.2 Incidence and prevalence

The natural evolution of POP is not fully understood even though it has been investigated with different study designs: in a study of 259 women with mean age of 68 years, the incidence of objectively measured POP was 26% during a follow-up of one year, increasing to 40% in the three years' follow-u; the corresponding resolution rates were 21% and 19% (Bradley et al. 2007), whereas in another study of 412 postmenopausal women, the incidence rates for anterior, posterior and apical descent were 9.3, 5.7 and 1.5 per 100 women-years, respectively. In the same study, progression rates for (non-POP-Q staged) grade I POP were 9.5, 13.5 and 1.9 per 100 women years, whereas regression was 23.5, 22 and 48 (Handa et al. 2004). When followed for five years, POP-Q stage for 160 women with a mean age of 56 years, remained the same in 47%, progressed in 13% and regressed in 40 % (Miedel et al. 2011). These findings suggest, that POP is not inevitably a progressing condition.

Objective prevalence of POP depends on the target population, mainly age and parity. The overall POP objective prevalence for postmenopausal women in the large WHI (Women's Health Initiative) study was 41.1% for those with a uterus (uterine prolapse 14.2%, cystocele 34.3% and rectocele 18.6%) and 38% for hysterectomized women (cystocele 32.9% and rectocele 18.3%) (Hendrix et al. 2002). Vaginal vault prolapse was found in 11.6% of women after hysterectomy for POP and in 1.8% when there had been no POP prior to hysterectomy (Marchioanni et al. 1999). POP-Q was not used in these studies. The three studies that have utilized POP-Q to estimate the prevalence of POP for community dwelling women are summarized in table 6.

Table 6 Distribution of pelvic organ support staged with POP-Q in different age cohorts

Author	Nygaard et al. 2004[1]	Swift et al. 2005[2]	Trowbridge et al. 2008[3]
Age (years)	57-84	18-83	35-64
N	270	1,004	394
Stage 0 (%)	2	24	9
Stage 1 (%)	33	38	21
Stage 2 (%)	63	35	68
Stage 3 (%)	2	2	2
Stage 4 (%)	0	0	0

[1]Subset of WHI study (161 808 US women, aged 50-79 in 1993)
[2]Women coming for PAP smear or routine check in 6 outpatient clinics in the US
[3]Community-dwelling women from south

The prevalence of subjective symptoms of POP has been investigated in several studies. Comparison of the results is complicated by the different questionnaires used. Studies are summarized in table 7. In summary, the prevalence of subjectively reported symptoms of POP is considerably lower than that objectively observed in a pelvic examination.

Table 7 Prevalence of subjective symptoms of POP

Author	N	Age (years)	Prevalence (%)
Tegerstedt et al. 2005	5489	30-79	8.3
Lawrence et al. 2008	4103	25-84	6
Nygaard et al. 2008	1961	≥20	2.9
Wu et al. 2014b	7924	≥20	2.6
Cooper et al. 2015	1832	≥18	8.4
Rortveit et al. 2007	2001	40-69	6
Slieker-ten Hove et al. 2009	1869	45-85	11.4
Fritel et al. 2009a	2640	50-61	3.6
Zeleke et al. 2016	1548	65-79	6.8

2.3.3 Quality of life and socio-economic impact

The overall and more specifically, prolapse related quality of life has been assessed in community-dwelling women as well as in women waiting for POP surgery with several different questionnaires. Self-reported POP symptoms significantly correlated with lower QoL, when compared to symptom-free women, even when adjusted for other conditions significantly impairing QoL, such as back pain and neurological disease (Digesu et al. 2005, Fritel et al. 2009). Leong et al. (2017) compared the QoL of women awaiting POP surgery

and those awaiting hip or knee replacement: although POP had less impact on pain and physical components of QoL, emotional distress and mental problems were similar compared to women with severe arthrosis. Body image is altered by POP, and women with POP-Q stage II-IV feel more self-conscious, less physically and sexually attractive, less feminine, more isolated and different (Jelovsek & Barber 2006, Lowder et al. 2011). Women may feel unenlightened and ashamed about their condition (Dunivan et al. 2014). Sexual function is also impaired; only 17% of women waiting for surgery, were content with their sex life, which improved after surgery, although *de novo* dyspareunia can occur (Novi et al. 2005, Roos et al. 2014, Lukacz et al. 2016). The odds for improvement of dyspareunia after POP surgery is 2.5 when compared to a deterioration of the condition (Jha & Gray 2015). After surgery in the anterior compartment, no difference was detected in the occurrence of dyspareunia between native tissue repair and vaginal mesh (Schimpf et al. 2016). After surgery for apical prolapse, less dyspareunia was seen after colposacropexy compared to vaginal operations (Maher et al. 2016b) and for posterior compartment, it has been claimed that levatorplasty increases the occurrence of dyspareunia (Karram & Maher 2013).

Most analyses on costs of pelvic floor dysfunction have concentrated on urinary incontinence. One study examined the costs of ambulatory care for POP in the US, which covers mainly visits to outpatient clinics. Costs were USD 262 million in 1995-1996 but they had nearly doubled in 2005-2006 to USD 412 million (Sung et al. 2010). One study reported the costs of inpatient POP care in three European countries: the total cost was EUR 144 million in Germany, EUR 83 million in France and EUR 81 million in the UK. The cost per single hospital admission was EUR 3900, EUR 2300 and EUR 2800, respectively (Subramanian et al. 2009). A cost-effective analysis compared different strategies for post-hysterectomy POP management and initial pessary use, regardless of whether some patients later opted for surgery, and vaginal surgery were found to be cost-effective. Vaginal surgery obtained 11.4 quality adjusted months, for pessary use, the corresponding value was 10.4, at the cost of USD 15000 and USD 10000 per patient, respectively (Hullfish et al. 2011). Pessary use was found to be cost-effective also when compared to pelvic floor muscle training (PFMT) (Panman et al. 2016). Native vaginal surgery is the most cost-effective compared to other surgery types (Cheon & Maher 2013). Several trials found that vaginal mesh (Prolift®, total) was either more costly (Maher & Connelly 2012) or conferred no significant excess expence (Prolift®, anterior, posterior or total) compared to laparoscopic sacrocolpopexy (SCP) (Carracedo et al. 2017). Robotic SCP was more expensive when compared to laparoscopic SCP (Anger et al. 2014) and vaginal a meshkit (Elevate®, anterior, posterior or both) (Ehlert et al. 2016). An additional concern is that a functional limitation, such as in muscle strength and body mobility, are highly prevalent in elderly women with POP, which may increase costs and impair treatment outcomes (Sanses et al. 2016).

2.4 Surgical treatment

2.4.1 Urinary incontinence

2.4.1.1 Evolution of surgical techniques

Before the publication of the works of Petros, Ulmsten and DeLancey (Petros & Ulmsten 1990, Delancey 1994), the fundamental concept behind the surgical approaches used to treat stress urinary incontinence was to restore the anatomy of the anterior vaginal wall or to lift the urethrovesical junction. Anterior colporraphy (AC) and paravaginal repair (PVR), not regarded as continence surgery *per se* nowadays, have been utilized for correcting the disturbed anatomy. In 1923, Viktor Bonney observed urinary leakage related to the hypermobility of urethrovesical junction behind the pubic symphysis. The first clinical application that utilized this observation was published by Viktor Marshall, Andrew Marchetti and Kermit Krantz in 1949. In their MMK colposuspension the retropubic space was approached abdominally, placing one to three sutures on both sides of the urethra, attaching the paraurethral tissue to the periosteum of the pubic bone (Marshall et al. 1949). The continence rates after five and ten years were 86% and 75% respectively, but the overall complication rate was high, 21% (Hinoul et al. 2009).

In 1961, John Burch described his modification of the MMK, where he placed three bilateral sutures onto the pectineal ligament of Cooper instead of the periosteum of pubic bone (Burch 1961). He subsequently published details of a nine year series with a 93% success rate. A laparoscopic modification of Burch colposuspension was introduced in 1991 with promising short term results, however long term results were found to be inferior to the open procedure (Robinson & Cardozo 2010). In a recent Cochrane review of randomized studies assessing the open Burch colposuspension, the overall objective and subjective cure rates were 68.9% and 88.0% respectively. When compared to any sling, including traditional and midurethral slings, no significant difference was found at any time periods (Lapitan & Cody 2016).

The first needle suspension was described by Armand Pereyra in 1959. The fixation points for the suspensory materials were the fascial structures of the abdominal wall. Suspension was achieved with some non-absorbable material; such as steel wire (Pereyra 2002). The needle suspension became more popular only later, when Tom Stamey and Schlomo Raz described their modifications of needle suspension in 1973 and 1981, respectively. The longterm results of needle suspensions have proved disappointing, although extensive variation is reported, ranging from a 20% objective cure to a 90% subjective cure at widely differing time points (Lucas 2010).

The idea of a sling looping under the urethra in order to provide support is not new; it had been tried at the beginning of 20th century, but it was not until Alridge described his technique in 1942 using bilateral autologous strips from rectus fascia (Lucas 2010). Traditional sling procedures, also referred to also as pubovaginal slings (PVS), differ from midurethral slings in that they were placed at the bladder neck and in that sense, do not follow the principles of the integral theory (Gomelsky 2010). Several different materials have been used, ranging from autologous slings derived from rectus fascia and fascia lata, allogenic material from cadavers as well as porcine dermis, to different artificial materials, such as Gore Tex. The reported objective cure rates range between 61-100% with subjective cure rates between 73-93% (Bidmead & Cardozo 2000).

Since they are the least invasive surgical approaches for SUI, injectable bulking agents have been used to coaptate the urethra during the filling phase of the bladder. Objective cure rates are poor, 25.4%-73.3% but subjective cure rates are better, 66%-89.7% (Siddiqui et al. 2017) although as many as 24.3% of patients may require repeated injection to maintain continence (Kasi et al. 2016). There is little data on long term results; a recent Cochrane review summarized that urethral bulking might not be cost-effective if the follow-up lasts longer than 15 months (Kirchin et al. 2017).

Surgical treatment of SUI in Finland before the introduction of midurethral slings relied heavily on Burch colposuspension. Mäkinen et al. (1991) reported a series of 186 women, operated between 1984-1988 for SUI; the surgical technique was only slightly modified from the method published by Burch in 1961. In this study, 81% of women who had primary operation for SUI were continent 2 years later. With respect to women who underwent a secondary operation, 60% were continent. The primary operation had usually been the Kelly plication. The national guideline for treatment of female urinary incontinence recommended the Burch colposuspension as the first line surgical treatment for SUI; a traditional sling was recommended for secondary treatment and for complicated cases (Kujansuu 1993). In 1998, 4937 women aged 25-60 attending PAP screening in the county of Päijät-Häme, were interviewed about urinary incontinence. Every fifth (21%) of those, who suffered from UI, had had surgery; only 28% of those were satisfied with the outcome. The surgical methods in use were Burch colposuspension and traditional slings (Hulkko et al. 1999).

2.4.1.2 Mid-urethral slings

In 1996, Ulmsten et al. published a two-year follow-up of a novel, ambulatory method for the treatment of SUI, performed under local anesthesia. They reported that 84% of patients enjoyed a complete cured and only 8% were not cured (Ulmsten et al. 1996). This method, which was based on the integral theory, that emphasizes the importance of the mid-urethra in the maintenance of continence (Petros & Ulmsten 1990), was further

developed into a commercially available kit: the tension-free vaginal tape (TVT). This involves a narrow, 11 mm wide polypropylene mesh placed retropubically through a small 15 mm vaginal opening with sharp trocars, to support the middle part of urethra. According to the original method, the patient is asked to cough with a bladder volume of 300 ml, in order to adjust the tape (Nilsson 2010), figure 10. In Finland, TVT was primarily used in Helsinki University Hospital as a part of multicenter trail from January 1995 to October 1996 (Ulmsten et al. 1998, Nilsson et al. 2001) and soon thereafter Finnish gynecologists were trained to use the technique, which was introduced into general use in 1997 (Nilsson 2000).

The TVT soon became widely used with good results, however, evidence on typical complications started to accumulate. The most common perioperative complication related to TVT is bladder perforation, with an incidence of 6.9% within the first 160000 procedures, followed by urinary tract infection (5.5%), de novo urgency (5.9%) and urinary retention (4.0%) (Boustead 2002). Some severe complications, such as vascular and bowel injuries were also reported (Boustead 2002, Klinger & Marberger 2003), table 8. To avoid these complications, caused by the blind entry to the retropubic space, a novel application of the midurethral sling was introduced using the transobturator passage of the tape (Rapp & Kobashi 2008). Emmanuel Delorme published outside-in (TOT) and Jean de Leval inside-out (TVT-O) techniques (Delorme 2001, De Leval 2003), figure 11.

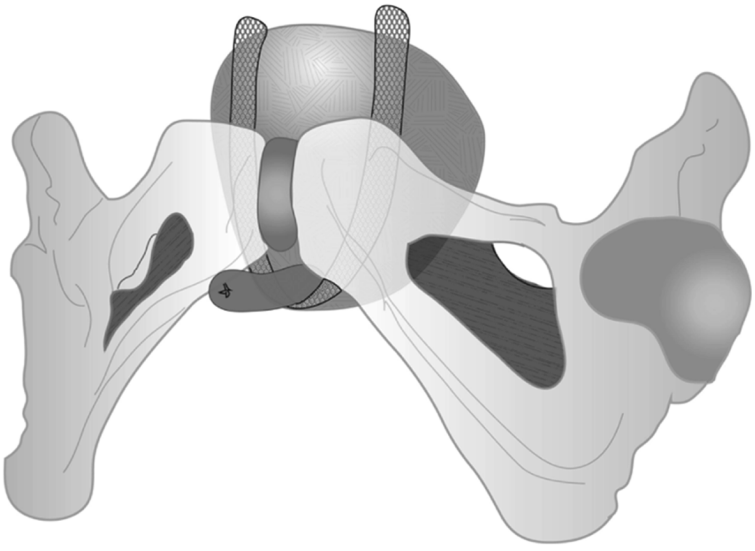


Figure 10 Passage of a retropubic MUS (reprinted with permission from Kirby et al. 2015)

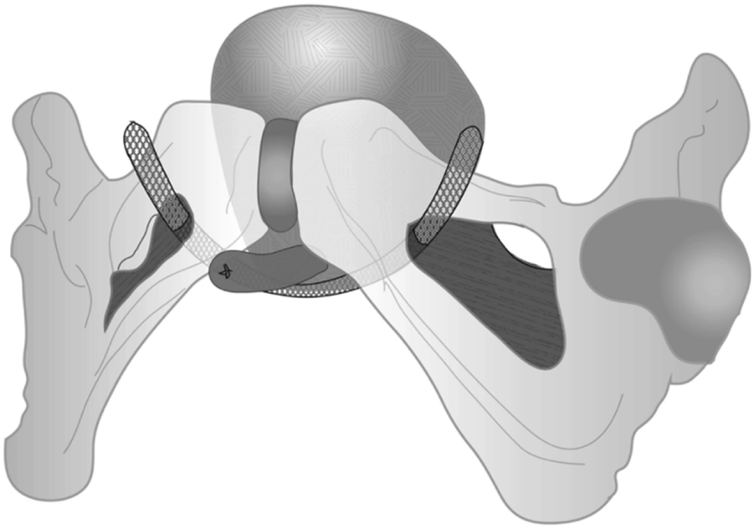


Figure 11 Passage of the a transobturator MUS (reprinted with permission from Kirby et al. 2015)

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Although avoiding the perils of passing behind the retropubic space, transobturator techniques proved to introduce another typical complication related to the positioning through the obturator foramen and piercing the obturator membrane and obturator internus and externus muscle (Kirby et al. 2015). Groin pain has been shown to be more frequent after transobturator MUS compared to retropubic MUS (Ford et al. 2015). Minislings were developed to overcome the complications of both retropubic and transobturator MUS, by shortening the passage of the tape within the tissue and omitting the puncture of skin. Either the urogenital diaphragm or obturator internus muscle could be used as the anchoring point (Walsh 2011). Short term results comparable to transobturator slings were found in a meta-analysis (Zhang et al. 2015), but an another meta-analysis found inferior results in comparison with MUS (Schimpf et al. 2014). Since they are a quite heterogenous group of procedures, the results of which are not interchangeable and the long term results are sparse, their routine use is not recommended (Frydman & Cornu 2015, Medina et al. 2017).

The efficacy and safety of midurethral slings have been rigorously studied. In one report. The results of a 17 years' follow-up was published for retropubic MUS, with 87.2% of patients remaining cured or at least enjoying an improvement in symptoms; 91.3% had a negative cough test (Nilsson et al. 2013). Studies on retropubic MUS with ten-year follow-up are presented in table 9. A comprehensive meta-analysis has been published, comparing different mid-urethral slings with each other as well as with traditional methods. A comparison of transobturator MUS (both inside-out and outside-in) and retropubic MUS, based on a Cochrane-review (Ford et al. 2015) is presented in table 8.

Table 8 Comparison of transobturator (both outside-in and inside –out) to retropubic midurethral slings, 81 studies, 12,113 women (modified from Ford et al. 2015). Statistically differing outcomes are marked with *.

Outcome	RR	95% CI	
Short term cure, subjective (<1 year)	0.98	0.96-1.00	
Short term cure, objective (<1 year)	0.98	0.96-1.00	
Medium term cure, subjective (1-5 years)	0.97	0.92-1.03	
Long term cure, subjective (>5 years)	0.95	0.87-1.04	
Bladder perforation	0.13	0.08-0.20	*
Voiding dysfunction	0.53	0.43-0.65	*
De novo urgency	0.98	0.82-1.17	
Groin pain	4.62	3.09-6.92	*
Suprapubic pain	0.29	0.11-0.78	*
Vaginal tape erosion	1.13	0.78-1.65	
Reoperation, short term (<1 year)	1.64	0.85-3.16	
Reoperation, long term (>5 years)	8.79	3.36-23.00	*
Comparison for all outcomes is Transobturator MUS vs Retropubic MUS			

Table 9 Studies of TVT with 10-year follow up

Author	n	Subjective cure rate	Objective cure rate	Erosion	De novo urgency	Reoperation
Nilsson et al. 2008 (11 years)	69	77% (20% improved)	90.2%	0	NA	0
Aigmueller et al. 2011	141	57% (23% improved)	84%	n=3	20%	n=2
Serati et al. 2012	58	89.7%	93.1%	0	18.9%	NA
Svenningsen et al. 2013	483	76.1% (18% improved)	89.9%	0.3%	14.9%	2.3%
Schauer et al. 2016	139	62.6% (20.9% improved)	82.7%	n=1	14.4%	n=1

Subjective and objective cure rates from a recent meta-analyses of randomized studies with follow-up-times longer than five years are presented in table 10. A systematic review compared midurethral and pubovaginal sling and Burch colposuspension; if three randomized studies with the same outcome were found, a pooled odds ratio could be calculated. Results are presented in table 11.

Table 10 Long term (>5 years) cumulative objective and subjective cure rates of midurethral slings in RCTs (modified from Leone et al. 2017)

	Objective %	Subjective %
TVT	61.6	76.5
TOT	57.2	81.6
TVT-O	68.8	81.3

Table 11 Meta-analysis of RCT's comparing midurethral and pubovaginal slings and Burch colposuspension (modified from Schimpf et al. 2014).

Treatment	Compared to	OR	95% CI
SUBJECTIVE CURE			
RP-MUS	Burch	0.95	0.63-1.42
TO-MUS	Burch	1.99	0.94-4.19
Any MUS	Burch	1.12	0.79-1.60
PVS	Burch	1.65	1.13-2.43
PVS	RP-MUS	0.54	0.27-1.09
RP-MUS	TO-MUS	1.17	0.91-1.51
Any MUS	minisling	2.65	1.36-5.17
OBJECTIVE CURE			
RP-MUS	TO-MUS	1.18	0.95-1.47
TO-MUS	minisling	4.16	2.15-8.05
SATISFACTION			
RP-MUS	TO-MUS	0.77	0.52-1.13

Based on a vast amount of evidence, it has been concluded, that MUS should be in the first line surgical treatment of SUI; national guidelines in Finland (source: kaypahoito.fi) and in the UK (source: nice.org.uk); furthermore, statements from urological associations in the US (source: auanet.org) and in Europe (source: uroweb.org) recommend MUS as either the primary treatment or as an alternative to open Burch colposuspension and autologous sling. Transobturator and retropubic approaches are equally effective but differ in the spectrum of adverse effects, although both have low rates of adverse effects.

2.4.1.3 Rate of surgery for stress urinary incontinence

The rate of surgical treatment for SUI, as well as the mode of treatment has undergone through a notable change during the last decades. In 1979 the overall rate of SUI surgery in the USA was 0.32/1000 women (Boyles et al. 2003b). Several reports from the US (Oliphant et al. 2009, Wu et al. 2011, Jonsson Funk et al. 2012a) and Europe (Cammu et al. 2010) have been published referring to different periods; they clearly reveal that the rate of SUI surgery has risen. The highest rate was found in Australia; 4.2/1000 women over 55 years in 2009 (Lee & Dwyer 2010). The type of care has changed towards outpatient procedures, probably due to the less invasive procedures (Boyles et al. 2004, Erekson et al. 2010, Rogo-Gupta et al. 2013). The notable increase in the rate of SUI surgery coincided with the introduction of the retropubic MUS (Lee & Dwyer 2010, Cammu et al. 2010, Wu et al. 2011), and MUS slings have become the mostly used method in many developed countries, as seen in table 12. A declining trend in the use of MUS has been seen after the FDA notification concerning vaginal meshes in 2011 (Rac et al. 2017).

Table 12 Operations for SUI in OECD countries in 2012 (modified from Haya et al. 2015)

Country	Procedures per 1000 women	Percentage of MUS (%)
Australia	1.0	83
Canada	1.2	91
Denmark	0.5	82
England	0.6	80
France	1.5	64
Germany	0.5	82
Holland	0.7	86
New Zealand	0.6	87
Sweden	0.8	98
Switzerland	0.5	70
USA	1.7	67
median	0.8	82

In 1997 Olsen et al. estimated the lifetime risk for pelvic floor surgery, including both surgery for SUI and POP to be 11.1% by (Olsen et al. in 1997). This value has been reinforced by other studies (Fialkow et al. 2008a, Abdel-fattah et al. 2011), but a combined lifetime risk of 20% has also been proposed (Wu et al. 2014a). Wu et al. demonstrated the lifetime risk for SUI-surgery alone to be 13.6%, with the highest rate for women aged 70-79 years. A shift towards a higher rate in the older age groups (65-74, 75-84 and older) was also reported by Lee & Dwyer (2010).

2.4.1.4 Reoperation for stress urinary incontinence

In the classic study of Olsen et al. (1997), reviewed the records of a group of 384 women who had been operated in 1995. At that point, 29.2% of the women being operated on, were found to have undergone a previous surgery for POP, SUI or both. In all,13% of this same cohort of women had undergone reoperation for POP or SUI during the following five years (Clark et al. 2003) and 17% during ten years (Denman et al. 2008). In the US, women operated on between 1987 and 2005 with sling (PVS or MUS) or Burch colposuspension, had a cumulative risk for reoperation of 8.6% during the nine year period with the rate of 5.5/1000 women-years. The rate was higher for slings (6.7/1000 women years) than for Burch (4.2/1000 women years) (Fialkow et al. 2008b). Reoperation rates of the same magnitude were found in a study from Taiwan: the reoperation rate in a follow-up of 7 (±2.2) years was 5.4 for all operations, 4.4 for Burch, 4.0 for PVS and 5.7 for MUS per 1000 women years (Wu et al. 2015). The cumulative risk for reoperation in a follow-up of five years was 6% for Burch, PVS and retropubic MUS and 9% for transobturator MUS in Denmark (Foss Hansen et al. 2016a), whereas in a follow-up of nine years the cumulative risk was 10.8% for Burch, 13.0% for slings (PVS and MUS) and 22.2% for needle operations (Jonsson Funk et al. 2012b). The mean time interval from the primary to the reoperation as been found to be 5.2 years for Burch and 4.4 years for slings (PVS and MUS) (Fialkow et al. 2008b). In another study the median time interval between the primary and reoperation was 4.2 years for Burch and 0.93 years for retropubic MUS (Abdel-fattah et al. 2011).

2.4.2 Pelvic organ prolapse

2.4.2.1 Surgery types for pelvic organ prolapse

Although the first description of vaginal hysterectomy for prolapse dates from 1705 by Berengaria da Capri (Lensen et al. 2013), it was during the late 19th century that urogynecological surgery took its first steps. In 1866, Sim described the first version of anterior repair, which included denuding the anterior vaginal wall and suturing it. White described the importance of lateral support already in 1909, but his ideas may have been ahead of his time and it was the anterior colporraphy described by Kelly in 1913 and refined by Kennedy in 1937, which predominated in the decades to come and is still used today (Barbalat & Tunuguntla 2012). The technique, which is based on the idea of distension of vagina, involves plication of muscularis and adventitia layers of anterior vaginal wall (Walters 2010). The lateral defect was re-invented by Richards in 1976, when he described an abdominal paravaginal repair; addressed vaginally by Shull and Baden in

1989 (Barbalat & Tunuguntla 2012). The aim is to reattach the lateral vaginal wall to the ATFP (Walters 2010).

Posterior vaginal wall was initially addressed in 1870, when Hegar repaired a prolapse by creating a tight introital ring (Barbalat & Tunuguntla 2012). The interest was then turned to Denonvillier's fascia; Nichols among others described the traditional posterior repair and Richardson introduced a site-specific repair, where the exact defect site is sought and repaired. The transanal repair of posterior prolapse was described by Sarles, although a vaginal method has been proven to be more efficient (Nieminen et al. 2004). Posterior repair may be added to sacrocolpopexy; abdominal preparation is extended to the levator ani muscles, where the graft is sutured and the most distal part is addressed vaginally (Amir & Bent 2009, Pancholy et al. 2010).

After the medieval efforts, the first vaginal hysterectomy for prolapse was performed by Choppin in 1861 and the method was later refined in 1912 by Mayo (Downing 2012). The so-called Manchester operation for descended uterus was described by Donald in 1888 and it included amputation of the cervix. The method was later modified by Fothergill; anterior and posterior repairs were added and USL and CL ligaments were sutured in front of the cervical stump in the midline to support the uterus (Lensen et al. 2013). Efforts to enhance apical support were made already in the 1920's, when the cul-de-sac was obliterated vaginally and the vaginal vault was suspended bilaterally to USLs (Klauschie & Cornella 2012). In 1951, Amreich described vaginal sacrotuberal fixation, which was modified by Richter; sacrospinous ligament was easier to reach for fixation of the vaginal apex. The SSLF method was made popular by Randall and Nichols in 1971 (Downing 2012). Iliococcygeal fixation was invented for those situations, when sacrospinous ligament was unattainable (Alarab & Drutz 2010).

An abdominal procedure to attach the uterus to the sacrum was described in 1957 and it was almost identical to modern sacrocolpopexy, except for the absence of a graft (Downing 2012). The usage of artificial graft was introduced in 1962 by Lane. Although some light modifications to the method have been made; the basic idea is to attach the vagina to the anterior ligament of sacrum via an artificial mesh. Vesicovaginal and rectovaginal spaces are dissected and a Y-shaped mesh is sutured to vaginal wall and fixed to the sacrum, preferably at the level of S2 (McDermott & Hale 2009, Hill & Barber 2015). Laparoscopic and robotic methods were introduced in 1992 and 2004, respectively (Nguyen et al. 2010).

Another method for prolapse repair is partial or total colpocleisis, performed initially by Le Fort already in 1877 (Lensen et al. 2013). The Le Fort technique leaves the uterus behind; the epithelium of anterior and posterior vagina is stripped off and the walls are sutured together. The procedure is finished with high perineorraphy. Colpocleisis closes the vagina and therefore may not be performed on women wishing to maintain the possibility of intercourse (Abbasy & Kenton 2010). Sometimes, especially for younger

women, apical support is needed, but the uterus is not to be removed and obliterative surgery is not an option, abdominal or sacral hysteropexy may be performed. There is little evidence that the anatomical result is better if laparoscopic hysterectomy or supravaginal amputation of the uterus is performed with SCP (Goldberg 2010, Gutman 2016).

The idea of enhancing surgery with some kind of graft dates back to the early days of pelvic floor surgery, when autologous grafts were used. An artificial mesh was introduced in 1955, when tantalum was used in anterior repair; Marlex was introduced in 1964. Macroporous, monofilament mesh has been found to be safest; polypropylene is the most used material nowadays (Amir & Bent 2009, Murphy 2009, Lensen et al. 2013). The purpose of meshes is to reinforce tissue and restore the supporting structures. Modern vaginal mesh kits were approved in the US in 2001 and since 2005, their popularity started to increase despite the fact that very little was known about their long term safety (Iyer & Botros 2017). From 2000 to 2006 the proportion of POP surgery using mesh rose from 3.3% up 13.5%, respectively, and then stabilized i.e. the proportion was 12.8% in 2010. In 2010, 75% of all POP meshes used in the US were vaginal (Rogo-Gupta et al. 2012, Jonsson Funk et al. 2013). With the appearance of complications (erosion of the mesh,pelvic pain dyspareunia, vaginal discharge, bleeding) FDA issued a public health notification concerning meshes. A safety communication was released in 2011, further defining the risks (US Food and Drug Administration 2011, Iyer & Botros 2017).

2.4.2.2 Efficacy and safety of POP surgery

Patient characteristics influence the safety and outcome of surgical treatments; several algorithms have been proposed to assess the risk of perioperative complications (source: kaypahoito.fi). The preoperative functional status has been shown to predict the postoperative outcome and complications in women over 60 years of age (Greer et al. 2013, 2015). Increasing age adds to the risk of mortality and morbidity: compared to women under 60 years of age, the odds ratio for postoperative complications for women 70-79 years is 4.9 but for women older than 80 years, the ORs rise substantially to 13.6 (Sung et al. 2006). Obesity (BMI over 30 kg/m^2) increases complication rate 40% (OR 1.40) (Pratt et al. 2017).

To assess the efficacy of a treatment, one should know the goal of the treatment. The results of POP surgery are often judged in anatomical terms, but these do not correlate well with the patient's symptoms (Aponte & Rosenblum 2014). The absence of a vaginal bulge is found best to relate to the patient's subjective cure (Barber et al. 2009). In order to facilitate the comparison and unify the criteria, the IUGA/ICS standardization committee has proposed, that when reporting POP surgery outcome, a subjective cure is

defined as the absence of bulge and this should be further examined, along with patient satisfaction and QoL, with standardized questionnaires (Toozs-Hobson et al. 2012).

Success rates for native tissue repair vary widely. Some ranges for objective and subjective cure rates are presented in table 13. With respect to the more rarely used native tissue repairs, the subjective or objective cure rates for cervical amputation (Manchester operation) and colpocleisis are reported to be good, 80-94% (Song et al. 2016, Katsara et al. 2016, Tolstrup et al. 2017, Bergman et al. 2017).

Table 13 Success rates for native tissue repairs for POP (modified from Hill & Barber 2015, Ismail et al. 2016, Richter & Sokol 2016, Siff & Barber 2016)

Procedure	Objective cure %	Subjective cure %
Iliococcygeus fixation	54-84	89-91
Sacrospinous ligament fixation	35-67	80-94
Uterosacral ligament suspension	48-96	83
Anterior repair	30-89	62-94
Posterior repair	89-93	84-93

Vaginal artificial meshes were introduced in order to enhance the anatomical cure, and according to the study of Altman et al. (2011), this goal has been achieved; the composite cure was acquired with anterior mesh-kit in 60.8%; almost twice better than that attained with native tissue anterior repair (cure in 34.5% of cases). A previous Cochrane review outlined the problem: an objective cure is better and there is less feeling of bulge but at the cost of increased complications, most notably erosion of the mesh (Maher et al. 2013). One RCT had to be terminated prematurely when the erosion rate in the mesh group reached 15.6% (Gutman et al. 2013a). Erosion rates reported from different studies vary from 0 to 25% (Iyer & Botros 2017).

Abdominal sacrocolpopexy (SCP), regardless of route (open, laparoscopic or robotic) is considered the gold standard treatment for apical POP. Results using polypropylene mesh are good, with success rates of 91-99% (Richter & Sokol 2016). Reoperations for mesh-related complications neede to be performed for 1.2% of cases after open SCP and 1.7% after laparoscopic SCP (Dandolu et al. 2017). Anatomic success is superior compared to native tissue vaginal repair and vaginal meshes. Laparoscopy is the preferred route; costs are lower compared to robotic and patient recuperation is faster than with open surgery (Siddiqui et al. 2015, Costantini et al. 2016). It must be acknowledged, that the vaginal mesh kits used in most RCT, also included in Cochrane review (Maher et al. 2016b) are Prolifts®, either total (Maher et al. 2011, Halaska et al. 2012, Svabik et al. 2014) or total and anterior (Gutman et al. 2013b, Dos Reis Brandão da Silveira et al. 2015) meshes, which have now been withdrawn from the market. To et al. (2017) compared laparoscopic SCP with Elevate® anterior and apical mesh kit, which also is no longer available.

Comparative studies of POP treatment have recently been reviewed in three Cochrane reports, which are summarized in table 14. The outline from these reports is that based on the complications related to vaginal meshes, for anterior or apical repair, the evidence does not support their usage in primary surgery. SCP is superior to vaginal repairs in apical POP, as it results in a lower risk of subjective prolapse symptoms as well as prolapse on examination and repeated surgery for prolapse (Maher et al. 2016b). In general, comparing results of POP surgery is extremely hard and results vary widely, as seen table 13; take SSLF for example. Benson et al. (1996) report outcome labelled as "optimal" was present in only 29% of patients, whereas Lo & Wang (1998) report an "optimal" result for 80.3% of patients. Some authors report objective (91%) and subjective (69%) success (Maher et al. 2004) separately, some use composite outcomes, such as "surgical success" 63.1% (Barber et al. 2014).

2.4.2.3 Rate of surgery for POP

While approximately every second woman will develop POP, based on objective clinical examination, only a minority i.e. 10-20%, of those will seek help for the problem (Barber & Maher 2013). The rate of POP surgery varies depending on the time point of observation and country. Several studies have monitored the rate in the US since 1979; the trend has declined from 2.9/1000 women to 1.0-1.5/1000 women in 2006-2007. POP operations have decreased most notably in younger women although a slight increase was observed for older women (Brown et al. 2002, Boyles et al. 2003a, Shah et al. 2008, Jones et al. 2010, Bradley et al. 2011). A decline in the rates from the 70's and 80's was observed also in Australia and Denmark (Hunt et al. 2013, Løwenstein et al. 2015). In more recent years, an increase has been reported; from 2000 to 2012 hospital admissions for POP doubled (Mascarenhas et al. 2015). A comprehensive report on surgical treatment of POP and SUI in OECD countries reveal notable differences in the rate of POP surgery, Figure 12. The rate is highest in the US (2.6/1000 women) and seems to have risen when compared to previous reports. The same phenomenon seems to be occurring in European countries; when compared to the rate in 2005, increases have been reported from Germany (from 0.9 to 2.1 per 1000 women), France (from 1.1 to 1.5 per 1000 women) and the UK (from 1.1 to 1.4 per 1000 women) (Subramanian et al. 2009, Haya et al. 2015).

Lifetime risk for POP and SUI surgery was estimated to be 11% in 1997 in the US, a value confirmed in 2008 (Olsen et al. 1997, Fialkow et al. 2008a). A significantly higher lifetime risk for only POP surgery, 19%, was published in Australia (Smith et al. 2010); a lifetime risk of the same magnitude, 18.7%, was reported from Denmark (Løwenstein et al. 2015).Based on the rate in the US in 2007-2011, the lifetime risk for POP surgery was estimated to be 12.6% (Wu et al. 2014a).

Table 14 Summary of Cochrane reviews on different surgical techniques for POP surgery. 1. comparison is for vaginal surgery on any compartment. 2. comparison is for anterior prolapse. 3. comparison is for any vaginal surgery versus sacrocolpopexy via any route. 4. comparison is for vaginal mesh versus vaginal colopexy (sacrospinous and uterosacral). Significant findings are marked with *.

Outcome	RR	95% CI	
1. **Transvaginal permanent mesh** vs **native tissue repair**; follow-up 1-3 years (Maher et al. 2016c)			
Awareness of prolapse	0.66	0.54-0.81	*
Reop for POP	0.53	0.31-0.88	*
Reop for SUI	1.07	0.62-1.83	
Reop total (incl. complications)	2.40	1.51-3.81	*
Recurrent POP	0.40	0.30-0.53	*
Bladder injury	3.92	1.62-9.50	*
De novo SUI	1.39	1.06-1.82	*
De novo dyspareunia	0.92	0.58-1.47	
2. **Anterior prolapse**: native tissue vs transvaginal polypropylene mesh; follow-up 1-3 years (Maher et al. 2016a)			
Awareness of prolapse	1.77	1.37-2.28	*
Reop for POP	2.03	1.15-3.58	*
Reop for SUI	1.19	0.60-2.36	
Reop total (incl. complications)	0.59	0.41-0.83	*
Recurrent anterior POP	3.01	2.52-3.60	*
De novo SUI	0.67	0.44-1.01	
De novo dyspareunia	0.54	0.27-1.06	
3. **Apical prolapse**: vaginal surgery vs sacrocolpopexy, follow-up 1-4 years (Maher et al. 2016b)			
Awareness of prolapse	2.11	1.06-4.21	*
Reop for POP	2.28	1.20-4.32	*
Reop for SUI	1.87	0.72-4.86	
Recurrent POP	1.89	1.33-2.70	*
Bladder injury	0.57	0.14-2.36	
De novo SUI	1.86	1.17-2.94	*
De novo dyspareunia	2.53	1.17-5.50	*
4. **Apical prolapse**: vaginal mesh vs native tissue repair, follow-up 1-3 years (Maher et al. 2016b)			
Awareness of prolapse	1.08	0.35-3.30	
Reop for POP	0.69	0.30-1.60	
Reop for SUI	4.19	0.86-27.94	
Recurrent POP	0.36	0.09-1.40	
Bladder injury	3.00	0.91-1.40	
De novo SUI	1.37	0.94-1.99	
De novo dyspareunia	1.21	0.55-2.66	

Surgical practices differ extensively from one country to the next, see figure 12. In France, more than 50% of operations include a method for apical prolapse while in Denmark apical repairs are much rarer, only conducted in 13% of procedures.

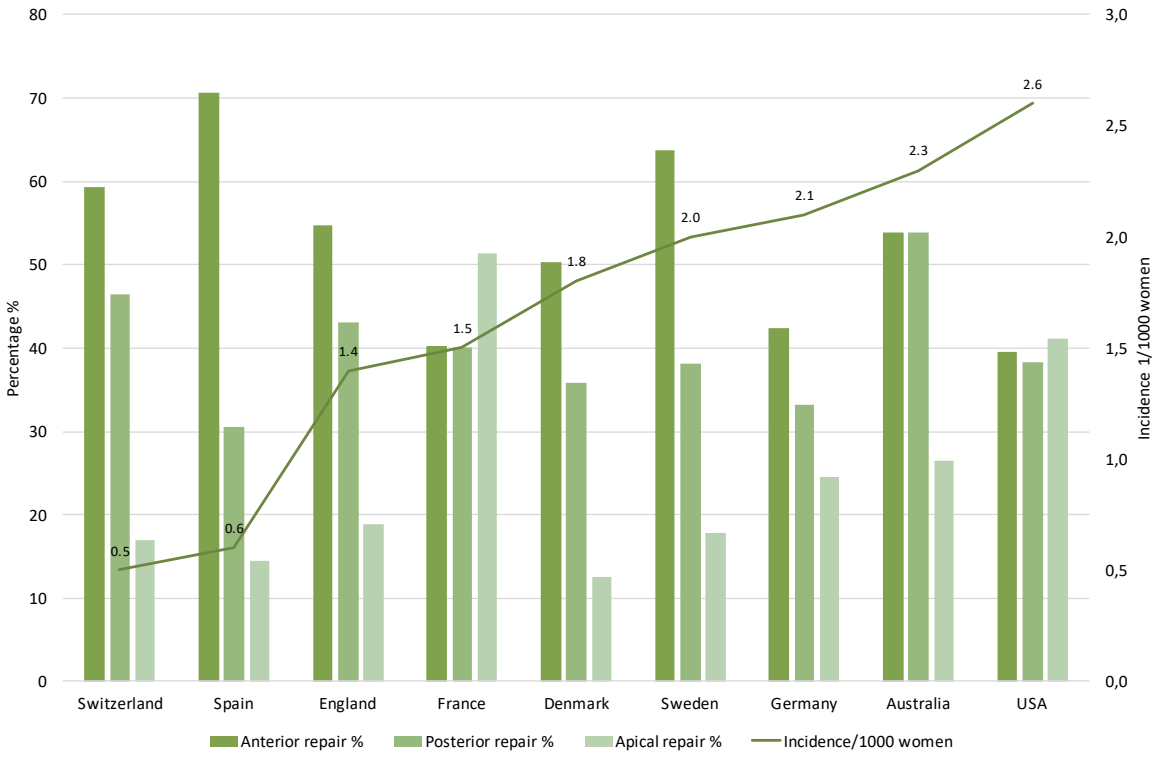

Figure 12 Anterior, posterior and apical repairs in OECD countries in 2012. Rate of POP surgery per 1000 women is depicted with line (modified from Haya et al. 2015)

2.4.2.4 Reoperations for POP

Reoperations have been used as a proxy for treatment failure in the absence of uniform criteria to determin effectiveness.It is questionable whether surgery to a different compartment should be considered as a reoperation (Ismail et al. 2016). IUGA/ICS Standardization Committee recommends using the terms “primary surgery” and “further surgery”, which is subdivided into primary surgery/different site, repeat surgery (to the same site), surgery for complications and surgery for non-POP reasons such as SUI (Toozs-Hobson et al. 2012). For this reason, it is extremely difficult to compare the results of different trials. Lavelle et al. (2016) reported reoperation rate after native tissue anterior repair to be 3.3%, but when including primary surgeries/different site, the rate was much higher, 33%.

Although some authors report reoperation rates of native tissue repairs between 10% and 20% (Clark et al. 2003, Denman et al. 2008, Abdel-fattah et al. 2011, Eilber et al. 2013), there is abundant evidence for reoperation rates of less than 10% (Price et al. 2008, Dällenbach et al. 2008, Miedel et al. 2008, Diwadkar et al. 2009, Gotthart et al. 2012, Jonsson Funk et al. 2013, Oversand et al. 2014, Rappa & Saccone 2016). In the aftermath of problems with artificial meshes, it has been concluded, that the results of native tissue surgery are better than their reputation (van Geelen & Dwyer 2013, Rogo-Gupta 2013). Combining an apical procedure to native tissue repair has been claimed to reduce the reoperation rate (Cvach & Dwyer 2012, Eilber et al. 2013)

2.5 Registers in medical research

Keeping records has been of interest to mankind since the dawn of early civilizations in Mesopotamia, where the earliest archival records developed, hand in hand with the arts of writing and accounting (Brosius 2003, Hudson 2004). Although the first impetus for record-keeping was economical, the health, birth and death related registers are not modern innovations. The Nordic countries have a longstanding tradition of collecting reliable and exhaustive data collecting (Rosén 2002). In Finland, a national data collection system was established already in 1749 (Pitkänen & Laakso 1999), and data on forensic autopsies can be found dating back to 1841, representing the earliest health-related records, followed by registers recording infectious diseases in 1888 and sterilizations in 1935 (Gissler 1999). The first register to include personal-level computerized data was the Cancer Register which was initiated in 1952: before this time the data was mainly aggregated (Gissler & Haukka 2004). The precursors for the Health Care Register for Health Care, formerly known as the Hospital Discharge Register, which was used in this study, were the discharge records from tuberculosis sanatoriums and mental institutions, dating back to 1956 and 1957, respectively (Sund 2012).

Health registers can be classified into four main categories: disease, reimbursement, quality and administrative registers (Sund et al. 2014). The disease registers collect information on a specified condition, or on a group of closely related conditions. A good example is the Finnish Cancer Register, which is one of the oldest health registers in Finland (Teppo et al. 1994). The reimbursement registers collect data on the costs related to healthcare, such as insurance claims, and to social benefits. Quality registers, as well as the disease registers, concentrate on a certain condition, but the main motivation for maintaining quality registers is to assess and improve the delivery of health care and the quality of the treatment of the disease in question. These quality registers may be national, as in Sweden (Emilsson et al. 2015) or local, institution based-registers. The need for a comprehensive, national quality register in the field urogynecology emerged also in the US in the aftermath of the safety communication issued by FDA (US Food and

Drug Administration) concerning artificial transvaginal meshes, requiring manufacturers to perform postmarketing studies (US Food and Drug Administration 2011). As a consequence, the Pelvic Floor Disordes Registry (PFDR) was established by the American Urogynecologic Society (AUGS), in order to evaluate the effectiveness and quality of both conservative and surgical treatment of pelvic floor disorders and to provide framework for clinical studies (Weber LeBrun 2016).

Administrative data is, by definition, used to administer individual objects (Wallgren & Wallgren 2014), but this does not apply to the Finnish administrative heath registers. The OECD Glossary of Statistical terms define administrative data as statistical data derived from an administrative source (Organisation for Economic Co-operation and Development 2007). In addition, according to the Act on national personal records kept under the health care system (556/1989), data in the health registers may not be used for decision making concerning an individual or handed over to be used for that purpose.

The usage of the data in the health related registers for scientific research purposes is strictly regulated by law (Gissler & Haukka 2004). Nonetheless, it represents research without the consent of the individual from whom the data has originated. When considering the justification to perform such research, some ethical aspects need to be assessed. First, we should treat all citizens equally, when it comes to the distribution of resources of health care. It is therefore reasonable, that the resources invested into health care, should benefit the whole population in the form of evidence-based improvements to treatments. One can also argue that, as a probable user of mostly publicly funded health care, it is a citizen's duty to participate by allowing the use of the data. In addition, when the resources are limited, they should be used in such a way that the greatest benefit can be derived from them (Launis 2005). In this sense, a register-based study is well justified, in fact if we were to try to gather informed consent, it would considerably diminish the power of register studies; with very large samples, it would be totally impossible to conduct these studies (Ludvigsson et al. 2015). The Nordic countries share somewhat uniform legislation with respect data protection. At the European Union (EU) level, the Data Protection Directive dates back to 1995. The planned reform of the directive to harmonize the applications within the member countries of the EU raised a concerns; it would benefit some countries, but for Finland, Sweden and Denmark, where the legislation is permissive when it comes to well conducted research, the harmonization would hamper the possibilities of utilizing the health registers in research (Carinci et al. 2011, Hakulinen et al. 2011). On the 27th April 2016, however, the new Data Protection Regulation (2016/679) replaced the former directive. In the fifth article of the regulation, it is stated that, for scientific and historical research purposes, access to the data without consent is allowed (Chassang 2017). This Regulation shall apply in all member states of EU from 25th May 2018 (European Commission 2012).

Register-based research is observational, in contrast to involving some intervention, such as in randomized controlled trials (RCT), studies(Webb & Bain 2011). In addition, registered data from administrative registers is always secondary i.e. it is collected for purposes other than scientific research. This raises questions about the validity of register-based data. The possibilities of register studies lie within the large populations and the cross-linkage between different registers (Räisänen 2013). The advantages and disadvantages of register-based research are summarized in table 15. A well-designed, population-based register study has the power of conferring the maximal benefit to national health care.

In order to produce reliable and good quality research, the register data should be accurate and exhaustive. The reliability of the Health Care Register and Finnish Birth Register has been addressed in several studies (Gissler & Shelley 2002, Sund 2012), and the quality is very good or at least satisfactory. Recently Finnish Registers on Induced Abortions and Sterilisations were compared to Health Care Register: the validity of the data in these two forementioned registers ranged from good to very good (Heino et al. 2017). Although cross-linking different registers has produced valuable data on outcome of care, for exampleas for stroke (Meretoja et al. 2011), the information included in the Care Register has been found to be insufficient, e.g. to study efficacy of treatments, such as cardiologic interventions, which is why there has been a call for the establishment of specific quality registers (Laine 2013).

2.5.1 Registers in gynecologic research

Finnish registers have been used for research on several topics within gynecology and obstetrics. Hysterectomy, for example, has been thoroughly studied in Finland; the hysterectomy rate (from Hospital Discharge Register) in 1988 was cross-linked to the population census which revealed that higher household income and higher socioeconomic status and education increased the odds for hysterectomy, particularly for uterine fibroids. This was thought to be due to operations in private hospitals and other forms of private medicine (Luoto et al. 1997). Between 1987-1995, the hysterectomy rate increased in Finland by 22% (Vuorma et al. 1998), subsequently declining by half (Mäkinen et al. 2013), which can be, in part, explained by the widespread use of levonorgestrel-releasing intrauterine system (Mirena®) in Finland (Heikinheimo & Gemzell-Danielsson 2012). A cross-linkage study between Medical Reimbursement Register and Finnish Cancer Register revealed a lower than expected incidence of endometrial and ovarian cancer in Mirena®-users (Soini et al. 2014), but has raised concern of increased risk for breast cancer in these women(Soini et al. 2016). Registers have also been used to study the learning curve for laparoscopic hysterectomy and related complications in Finland (Brummer et al. 2008).

Cross-linkage of Hospital Discharge Register with the Finnish Birth Register has been used in many studies within obstetrics and gynecology. For example, cesarean section has been shown to increase severe maternal morbidity compared to vaginal delivery (Pallasmaa et al. 2008, 2015); also cross-linkage was used to prove that there was an increased risk of preterm birth after loop conization of cervical dysplasia (Heinonen et al. 2013). Most recently, there has been concerns of increased side effects and complications related to the hysteroscopic implants used for female sterilization (Essure®) (Klimczak et al. 2016). A cross-linkage study combining information from Hospital Discharge Register, Finnish Birth Register, Registers for Sterilisations and Termination of Pregnancy showed, that Essure® was a reliable method for sterilization but resulted in greater numbers of further surgeries compared to laparoscopic sterilization (Jokinen et al. 2017).

Table 15 Advantages and disadvantages of surveys based on registers (modified from Räisänen 2013, Wallgren & Wallgren 2014).

	Advantage	Disadvantage
Study subject	No need for contact	Cannot ask questions
Costs	Markedly lower than with clinical studies	Some registers are costly
Collecting data	Fast	Administrative data are completed with delay; acquiring research authorization is time-consuming
Population	Wide; regional-national-international. Good coverage.	Identification method may contain errors
Reliability of data	Administrative data carefully collected and stored	May contain errors; changes in coding systems
Variables	Cross-linkage of registers gives wide range of option	Limited availability of variables within register
Study design	e.g. cohort, case-control; incidence, prevalence, risk factors, relationship, prognosis, efficacy	Data collected for administrative use; may impair the study
Time	Good coverage; longitudinal, cross-section, retrospective and prospective studies	Proving causality may be difficult

3 AIMS OF THE STUDY

The objective of this national register study was to evaluate the trends in the surgical treatment for female pelvic floor dysfunction in Finland during a 23-year period from 1987 to 2009.

The specific aims were:

1. To evaluate the change in the surgical treatment methods for stress urinary incontinence and pelvic organ prolapse.
2. To determine whether the incidence of pelvic floor surgery has varied over time.
3. To establish the lifetime risk of a Finnish woman to undergo a surgery for either stress urinary incontinence or pelvic organ prolapse.
4. To examine the risk of a recurrent operation after the surgical treatment of stress urinary incontinence and pelvic organ prolapse.

4 MATERIALS AND METHODS

As the objective of this study was to obtain information trends of pelvic floor surgery in Finland, the Care Register for Health Care was selected as the source of data, since it has good coverage of national care, and it can be linked with census data from Statistics Finland. The study was conducted in Turku University Hospital, Department of Obstetrics and Gynecology in 2011-2017 as a retrospective register based study.

4.1 Registers

4.1.1 THL and Statistics Finland

The register data used in this study was obtained from THL (Terveyden ja hyvinvoinnin laitos, National Institute for Health and Welfare), which is a national organization, formed in January 2009, when the National Research and Development Center (STAKES) and the National Public Health Institute (KTL) were fused into a new research unit in the field of health and welfare in Finland. THL operates under the Ministry of Social Affairs and Health (STM) and its tasks are defined in the Act on the National Institute for Health and Welfare (688/2008). One of THL's duties is to function as a statistical authority as further defined in the Statistics Act (280/2004) and to maintain registers in the field of health and welfare as well as to collect and organize the data in these registers. All the data from THL were such that it could be identified and therefore it could be linked to Cause of death –data from Statistics Finland.

The data concerning population used in this study were obtained from Statistics Finland, which is a public authority established to produce statistics and information services, mainly concerning data on society, also defined in the Statistic act (280/2004). The number of female inhabitants in Finland according to age grouped by year used in studies I and II, was obtained from the publicly accessible Statfin database (http://www.stat.fi/tup/tilastotietokannat/index_en.html) maintained by Statistics Finland. In studies III and IV the data from THL were linked to the Cause of death – database from Statistics Finland to obtain the date of possible death of the study subjects.

4.1.2 The Care Register for Health Care (HILMO)

Data on specialized health care are collected to the Care Register for Health Care (Hoitoilmoitusrekisteri, HILMO), this was known as the Hospital Discharge Register until

the year 1994. All public as well as private hospitals and institutions offering specialized inpatient and outpatient care are obliged to supply the information to the Care Register, as defined in the legislation. The nationwide data collection started in 1967 (Sund 2012) and the range of collected information has gradually expanded: data on day surgeries were included in 1994 and data on specialized outpatient care in 1998. Surgery for SUI and POP has not been performed in outpatient settings in Finland until recent years. The core information has nevertheless remained unchanged, including data on admission and discharge dates, diagnosis according to the current code (ICD-9 since 1987 and ICD-10 since 1996) and surgical procedure codes. The number of recorded procedure codes per single hospital stay has changed over time: 1987-1993 up to two codes were recorded, 1994-1996 up to three and from 1997 up to five codes. The patients are coded with the personal identity code (PIC), which is used universally in all health registers in Finland, allowing linkage between different registers (Sund et al. 2014). The linkage was used to combine data from the Health Care Register and the Cause of Death –database.

4.1.3 Code system for surgical procedures

During our study period, two different classifications were used in Finland to code surgical procedures. The classification of Finnish Hospital League was first published in 1983 and used in the Hospital Discharge Register from 1986 until 1996. The Finnish version of Nomesco (Nordic Medico-Statistical Committee) procedure classification was introduced in 1997 (Sund 2012), with annual revisions, and a major revision in 2004. Additional codes were entered to the classification as novel surgical methods were introduced: tension free vaginal tape (TVT) in 1997, the outside-in obturator technique (TOT) in 2003 and the inside-out transobturator technique (TVT-O) in 2004.

4.1.4 Ethics and research authorization

According to the Statistics Act (280/2004), the Personal Data Act (523/1999) and the Act on national personal records kept under the health care system (556/1989), identifiable data may be accessed for scientific purposes without the informed consent from the individual whom the data concerns. A right of use for the data is granted for a certain period of time, after which the data is destroyed or filed by permission. When using the national registers as the data source, the number of study subjects is often massive and some of the study subjects may be deceased; thus soliciting consent would be very difficult or impossible and therefore the waiver of consent is well-founded.

The research authorization to the Health Register as the data source for this study was sought from THL, where the validity of the study was evaluated. The Data Protection

Ombudsman was consulted during the process. A permission for the linkage of the Cause of Death –database was applied from Statistics Finland. As this study is purely register-based and there was no interaction or contact with any registered people, the study was exempted from an evaluation by a local ethical board. The medical director granted the permission to conduct this study in the premises of Hospital District of Southwest Finland (VSSHP).

The data were delivered from THL and Statistics Finland in a CD secured with a password or via a secured telecommunications link. The data were de-identified by giving a study number to each individual and therefore the PICs were not in the possession of the study group.

4.2 Data collection

4.2.1 Studies on stress urinary incontinence (I and III)

All Finnish women aged 18 years or older, who had surgery for stress urinary incontinence from 1987 to 2009 were identified from the Health Care Register. Additional sources, such as operations in private hospitals reimbursed by Kela (social insurance institution) were not searched, as those operations should be included in Care Register. Those inpatient and outpatient visits which included a surgical code for SUI were collated from the register. The hospitalization was included even if the primary code for that visit was for something other than for SUI (for example for prolapse, hysterectomy or not gynecological). The Classification of Finnish Hospital League included nine procedures and the Nomesco classification included 17 procedures for SUI as listed in table 16. The Nomesco classification was introduced into operation at the beginning of 1997, during 1996 both old and new classification may have been used. The procedures were grouped into four categories: abdominal Burch colposuspension, tension-free transvaginal tape (TVT), Transobturator tape (including both outside-in TOT and inside-out TVT-O methods) and Other. The group Other consists of procedures used in relatively small numbers and therefore they were not analyzed separately.

The grouping is presented in table 17. After the introduction of the TVT and TOT, there was overlapping usage of different procedure codes for the same procedure until the uniform practice was established nationally. The different codes used for the same procedure were taken into account and are presented in table 17.

The raw data included possible repeated operations for SUI for the same patient. By comparing the study numbers given to each study subject, those patients occurring several times within the data could be identified. The data were arranged in such a way

Table 16 Classification of surgical procedures for SUI

Classification of Finnish Hospital League 1987-1996	
7431	Tubularization of bladder neck
7432	Vaginal urethrocystorraphy
7433	Vaginal urethropexy
7434	Burch colposuspension (abdominal urethropexy)
7435	Vaginal hysterectomy with urethrocystopexy
7436	Combined abdomino-vaginal operation
7437	Other vaginal operation
7438	Implantation of prosthesis
7449	Other operation for urinary incontinence
Finnish version of Nomesco Classification 1997-2009 (revised in 2004)	
KDG00	Retropubic urethropexy (Marshall-Marchetti-Kranz)
KDG01	Needle suspension (Pereyra, Raz,Stamey)
KDG10	Combined abdomino-vaginal operation
KDG20	Burch colposuspension
KDG21	Laparoscopic Burch colposuspension
KDG30	Sling operation
KDG31	Laproscopic sling operation
KDG40	Urethropexy using adhesive material or sutures
KDG50	Abdominal prolapse operation for stress urinary incontinence
KDG96	Other abdominal operation for stress urinary incontinence
KDG97	Other laparoscopic operation for stress urinary incontinence
LEG00	Kelly plication
LEG10	Tension-free vaginal tape (TVT)
LEG12	Outside-in transobturator tape (TOT)
LEG13	Inside-out transobturator tape (TVT-O)
LEG20	Levatorplasty
LEG96	Other vaginal operation

Table 17 Grouping of surgical procedures for SUI

	Classification of Finnish Hospital League 1987-1996	Finnish version of Nomesco Classifiation 1997-2009 (revised in 2004)
Burch	7434	KDG20
TVT		KDG30
(retropubic MUS)		KDG96
		LEG10
Transobturator		LEG12
MUS		LEG13
		LEG96 (grouped as TOT 2003-2009)
Other	7431	KDG00
	7432	KDG01
	7433	KDG10
	7435	KDG21
	7436	KDG31
	7437	KDG40
	7438	KDG50
	7449	KDG97
		LEG00
		LEG20
		LEG96 (grouped as Other 1997-2002)

that the recurring operations for the woman were in a chronological order. This allowed the distinction between the primary and the secondary operations. The data concerning pelvic organ prolapse were arranged in a similar manner.

4.2.2 Studies on pelvic organ prolapse (II and IV)

In a comparable manner as conducted with the patients operated on for SUI, we identified from the Health Care Register all hospitalizations including a procedure code to correct pelvic organ prolapse (POP) for Finnish women older than 18 years of age. The earlier classification used up to the year 1996 included eight procedures and the latter Nomesco classification included 14 procedures for POP. The procedures are listed in table 18.

The procedures were grouped into seven categories as presented in table 19. Anterior and posterior colporraphies were grouped into a single group as they were not separated in the earlier classification of the codes. In the Nomesco classification, the code LCD10, defined as vaginal hysterectomy is omitted since it does not qualify as a prolapse procedure, although some vaginal hysterectomies for descending uteri are most likely coded as LCD10. Mesh kits and tailored meshes were introduced in Finland around the year 2005, but mesh-enhanced procedures did not have specific codes until 1.1.2012. Additional codes for gynecologic implants (ZLX20 for biologic implant and ZLX21 for synthetic implant) were not available until 1.1.2009. Some codes for tissue transplants (ZZ-group) were used, but these are sporadic in the data and were not differentiated in the data. Between 2005 and 2009 meshes were not widely used in gynecologic surgery in Finland.

Table 18 Classification of surgical procedures for POP

Classification of Finnish Hospital League 1987-1996	
8431	Colpopexy
8432	Anterior and/or posterior colporraphy
8433	Anterior and/or posterior colporraphy and amputation of uterine cervix
8434	Colpocleisis
8435	Repair of enterocele
8436	Vaginal hysterectomy with/without colporraphies
8437	Combined vaginal-abdominal procedure
8449	Other prolapse surgery
Finnish version of Nomesco Classification 1997-2009 (revised in 2004)	
LEF00	Anterior colporraphy
LEF03	Posterior colporraphy
LEF10	Colporraphies with amputation of uterine cervix
LEF13	Vaginal hysterectomy with/without colporraphies
LEF20	Partial colpocleisis
LEF23	Total colpocleisis
LEF30	Cystovaginal interposition of uterus
LEF40	Vaginal repair of enterocele
LEF41	Laparoscopic repair of enterocele
LEF50	Abdominal repair of vaginal vault prolapse
LEF51	Laparoscopic repair of vaginal vault prolapse
LEF53	Vaginal repair of vaginal vault prolapse
LEF96	Other abdominal prolapse surgery
LEF97	Other laparoscopic prolapse surgery

Table 19 Grouping of surgical procedures for POP

	Classification of Finnish Hospital League 1987-1996	Finnish version of Nomesco Classification 1997-2009 (revised in 2004)
Anterior and/or posterior colporraphy	8432	LEF00
		LEF03
Anterior and/or posterior colporraphy with amputation of cervix	8433	LEF10
Vaginal hysterectomy with/without colporraphies	8436	LEF13
Operations for enterocele	8435	LEF40
		LEF41
Operations for vaginal vault prolapse	8431	LEF50
		LEF51
		LEF53
Colpocleisis	8434	LEF20
		LEF23
Other procedures	8437	LEF30
	8449	LEF96
		LEF97

4.3 Study design and statistics

4.3.1 Studies I and II

The number of procedures per each study year was calculated and summed according to the aforementioned groups. If more than one procedure code for SUI for the same date was detected, patients were excluded (n=160) as it is probable that only one procedure for SUI would be performed at a time and therefore the double coding was an error. For prolapse no such exclusion was made since several prolapse operations are often performed simultaneously. As repeated operations after the primary occurrence of a SUI or POP surgery for the same patient could be identified, these further operations were excluded from studies I and II for both SUI and POP. Annual rates for each procedure groups were calculated.

The age-specific incidence of SUI and POP surgery was calculated with the demographic data from the population data of Statistics Finland for the following age groups: 18-39, 40-49, 50-59, 60-69, 70-79, and 80 years or older. Age-standardization (analogous to age adjustment) is defined as the process of correcting an estimate, in this case a rate, to reduce the confounding effect of varying age distributions of different populations (Webb & Bain 2011). Direct standardization was performed and this was achieved using the Nordic Standard Population (Såby et al. 2006) and the age-standardized incidence was calculated for both SUI and POP surgeries.

Cumulative incidence or risk is defined as the probability that an event (surgery in this case) occurs during a specified period of time (Kirkwood & Sterne 2003). To estimate the risk of having undergone at least one operation for SUI, POP or both, a cumulative incidence was calculated by adding age-specific incidences divided by the number of years at risk for the age-points of 49, 59, 69, 79 years. These were selected according to Olsen et al. (1997) to facilitate comparison with these widely adopted ages in urogynecology. Exclusion of women once counted from the population at risk was not performed; as the impact was considered to be small. The lifelong risk for surgery has been reported as the cumulative incidence until a certain age; age points 79 and 85 years have often been used (Olsen et al. 1997, Smith et al. 2010, Løwenstein et al. 2015). The lifelong risk was calculated to the age of 96 years as this was the age of the oldest patient in our study. Since the incidence varies every year, the cumulative incidence could be calculated with the incidence of any year and the result would be different. Several time points were chosen to depict the variation of the cumulative incidence attributable to the changes in the incidence rate. Cumulative incidence at different time points has also been reported by other investigators (Smith et al. 2010, Løwenstein et al. 2015).

In study II, the temporal trend of age-adjusted incidence of POP surgery was tested by fitting a linear regression model (in which incidence was explained by the year) and checking whether the slope parameter differed from zero in a statistically significant manner which was considered achieved when $p<0.05$.

4.3.2 Study III

In study III, reoperations for SUI were identified from the data. Only the first reoperations were included in the analysis, although some patients had also further operations for SUI. Procedures were searched from the Care Register from the beginning of the year 1987; it is most likely that several patients had surgery for POP and SUI before that year. A washout period of 13 years was used for POP surgeries in study IV; procedures performed during this period were not regarded as true primary procedures. A washout period was not applied for SUI surgery as the reoperation rate for SUI in the early years of the study period was considered to be low. In order to compare the rate of recurring operation after different types of SUI surgery, the procedures were grouped into four types as described before. The data from the Cause of Death –database were added in order to determine the total follow-up time of each patient. Emigration during the study period was not accounted for, as it was not considered to have exerted a significant effect.

The Burch colposuspension was the most widely used surgical method at the beginning of the study period. The retropubic MUS was introduced in 1997 and transobturator MUS in 2003. Therefore two sub-cohorts were extracted from the data. The first sub-cohort utilized a follow-up time of ten years to enable a comparison between the Burch colposuspension and retropubic MUS; Burch colposuspensions were performed between 1987 and 1999 and retropubic MUS between 1997 and 1999. The second sub-cohort had a follow-up time of five years to allow a comparison between Burch, retropubic and transobturator MUS, which were performed in 1987-2004, 1997-2004 and 2003-2004.

The mean age, the mean time until reoperation, the mean follow-up time and the total follow-up time were calculated for the whole cohort as well as the reoperation percentage and reoperation rate per 1000 women years. The normality of the distribution of descriptive variables was tested with the Kolmogorov-Smirnov test. When the normality was not met, the non-parametric Kruskal-Wallis test was used to test continuous variables (age, mean time until reoperation, mean follow-up time) in the whole cohort. Pair-wise comparisons for variables, which were not normally distributed, were done with the Wilcoxon method (comparison of age at the primary operation for reoperated and non-reoperated women in 10-year and 5-year follow-up groups). Fisher's exact test was used for categorical variables (reoperation versus no reoperation in different surgery types in the whole cohort). To calculate odd ratios for reoperation between different surgery type groups for both the 10-year and 5-year follow-ups,

logistic regression was used; χ^2 test was used to test for statistical significance. For the two sub-cohorts (five and ten years), a Kaplan-Meier survival curve was drawn to show the survival time without reoperation since the primary operation; reoperation for SUI was the event in the analysis. The difference between the curves of each surgical method was tested with the Log Rank test. In these tests statistical significance was considered met, when $p<0.05$.

4.3.3 Study IV

The purpose of IV study was to assess the incidence of further operations after the first surgery for POP. As recommended by IUGA/ICS, repeat operations for POP are termed further surgery, as the sites of surgery were not classified according to the primary surgery. It is, however, impossible to know whether the operations in the early years of the study period are primary operations or further operations. Therefore a washout period of 13 years was used. Previous studies have reported the mean time between the first and the second operation to be 3-5.5 years (Price et al. 2008, Abdel-fattah et al. 2011, Dällenbach et al. 2012, Gotthart et al. 2012). A longer time of 12.5 years has also been reported (Olsen et al. 1997), but in this report procedures for SUI were also included. Based on former reports, 13 years was presumed sufficient to exclude those patients who had had a true primary operation before 1.1.1987.

The ten-year period of 2000-2009 was looked at in several different ways. In order to find out the proportion of further operations of all operations for POP, all primary and recurring operations between 2000-2009 were identified. Women who had the primary operation before 2000, but a further operation between 2000-2009, were also included, see figure 13. The distributions of POP procedures at the primary surgery and at the first following surgery were calculated.

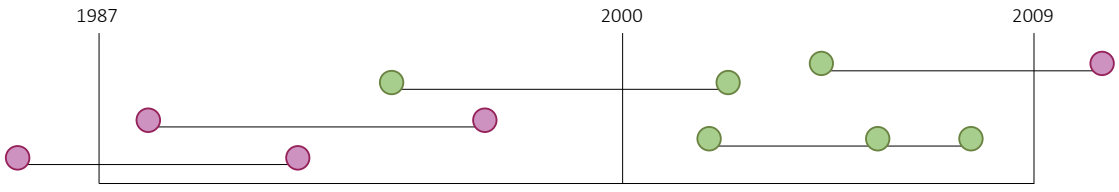

Figure 13 Schematic drawing of the POP data. The dots represent the surgeries. Green dots are included in the analysis, whereas red dots are not. Primary operations before 2000 were identified as primary but were not included in the analysis.

The proportions of primary and further operations for POP during 2000-2009 were calculated. The ten-year period was divided into two: 2000-2004 and 2005-2009 and these five-year periods were compared to estimate whether the proportion of repeated operations for POP had changed. The trend of change was analyzed further with the Cochran Armitage Trend Test.

The time interval between the primary and the secondary operation was calculated for all secondary operations conducted between 2000-2009 regardless of the date of the primary procedure. The deceased were not accounted for as the calculation was done only for those who had further surgery. A cumulative risk for the first further operation by year was calculated for those women who had the primary operation after 1.1.2000. A cohort life table method was used in a similar manner as devised by Price et al. (2008) The life table was constructed by calculating the incremental risk of further operation for each passing year. Those who were deceased were removed from the calculation. The incremental risks were added up in order to obtain the cumulative risk.

All statistical analyses were performed JMP Pro 12.0.1 for Mac (SAS Institute Inc. North Carolina, USA).

5 RESULTS

5.1 The change in the number of operations for SUI and POP

The data included all surgical procedures made for stress urinary incontinence and pelvic organ prolapse for women in Finland in the time period 1987-2009 and therefore the part of the population at risk included all Finnish women aged 18 years or more. The number of women of that age in Finland in 1987 was 1,990,470, slightly increasing thereafter being 2,193,636 in 2009. In all, 38,500 women underwent surgery for SUI and 77,906 for POP according to the Care Register, when searched by the procedure codes, during the study period. In addition, 2,776 women had a further operation for SUI and 7,652 women for POP.

5.1.1 Operation for SUI

As only one procedure for SUI is performed at a time, the number of procedures, 38,340 represents the number patients. Of these, midurethral sling (MUS) procedures accounted for 23,635 operations (61.6%), Burch colposuspension for 9,437 (24.6%) with other procedures amounting to 5,268 (13.7%). After the introduction of the tension free vaginal tape (TVT) in 1997, the number of Burch colposuspension rapidly declined such that after time, it was seldom performed. Transobturator tapes were introduced in Finland in 2003 and surpassed the numbers of TVTs in number in 2007. The total number of SUI surgeries rose sharply after 1997, peaking in 2002, then subsequently decreasing, see figure 14. In 1997, there was a peak in the number of Other procedures. This is mainly explicable with problems of coding after the introduction of the new classification and the as yet unestablished coding of the newly introduced TVT, as a small portion of TVT is likely to have been classified in the group Other.

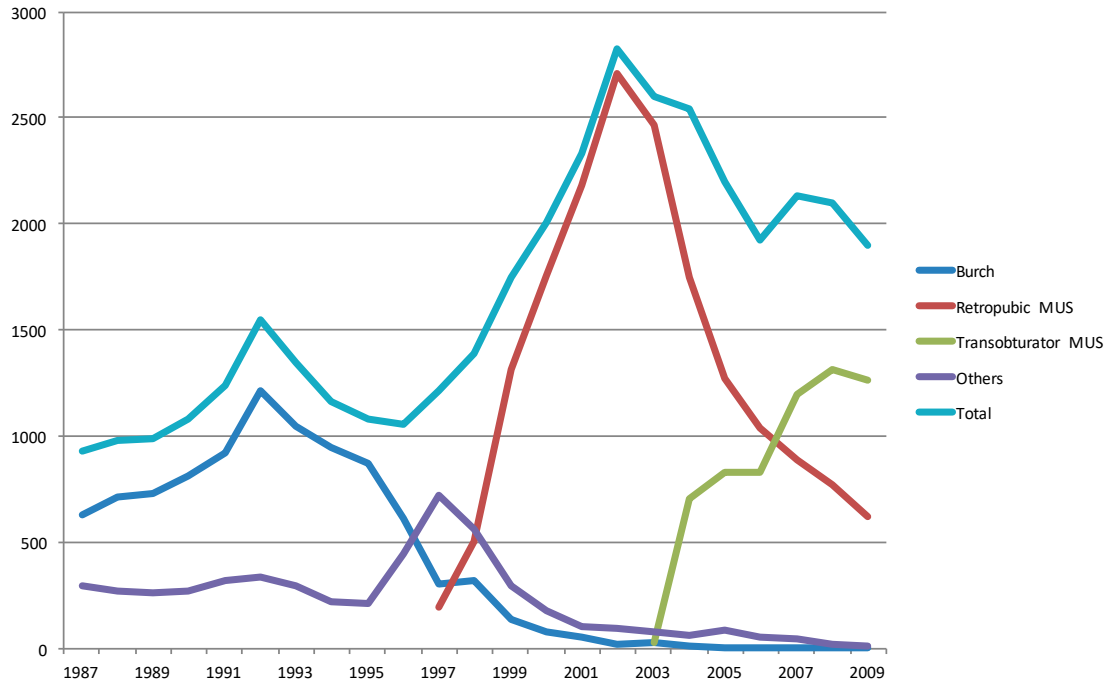

Figure 14 The numbers of operations for SUI (modified from Kurkijärvi et al. 2016)

5.1.2 Operations for POP

It is not uncommon that several operations are performed to correct POP at the same time. Therefore, the number of individual procedures for POP was 93,226, with a total of 77,906 women being operated. The number of procedures registered in the Care Register increased in two steps during the study period, which results in a notable increase in the number of procedures; in other words more procedure codes per individual patient at the same. In the early years of the study period, the Manchester operation, i.e. amputation of cervix with colporraphies was the most commonly adopted operation, this being surpassed in the early nineties by colporraphies, with or without vaginal hysterectomy. Operations for vaginal vault prolapse and for enterocele and colpocleisis were performed in markedly smaller numbers. The change in the number of POP operations are presented in figure 15.

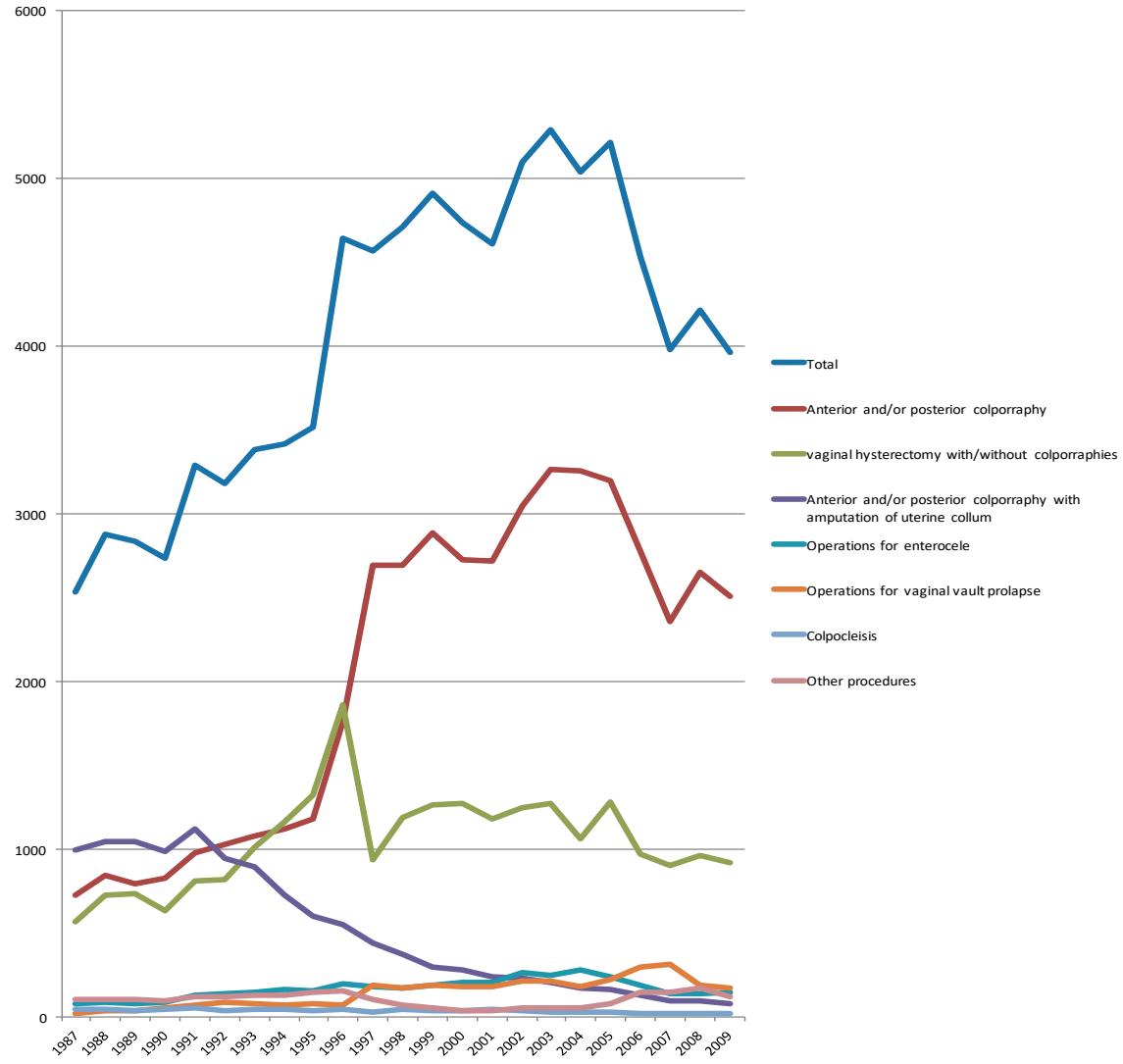

Figure 15 The numbers of primary operations for POP (modified from Kurkijärvi et al. 2017)

5.2 Incidence and lifetime risk

5.2.1 Incidence of SUI and POP surgery

The age-specific incidence of SUI surgery increased markedly after 1997, at the point when the Burch colposuspension was replaced by the midurethral sling. Women in the age-groups 40-49 and 50-59 had the highest incidence of SUI surgery. Women in the age-group 60-69 had an incidence half of that of the younger age-groups in 1987 (0.5/1000 women) but in 2002, it had risen by almost six-folded (2.9/1000 women) compared to the same age group. The same phenomenon was observed for women aged 70-79 as the

incidence increased by ten-folded (from 0.2/1000 in 1987 to 1.9/1000 women in 2000). In addition, the incidence in the oldest age-group of 80 years or older began to rise in halfway through the study period. SUI surgery for youngest women before the age of 40 years remained uncommon and did not change, figure 16.

When the age-specific incidences of POP surgery were examined it was noted that there were no such intersections between age-groups; the highest incidence was always in the age-group 70-79, followed by those aged 60-69 and then in the group 50-59 years. This order remained the same throughout the whole study period. The incidence of POP surgery for young women under the age of 40 remained low. No distinctive changes in the trend on incidence were seen, apart from the peak for the age group of 40-49 in 1996, figure 16.

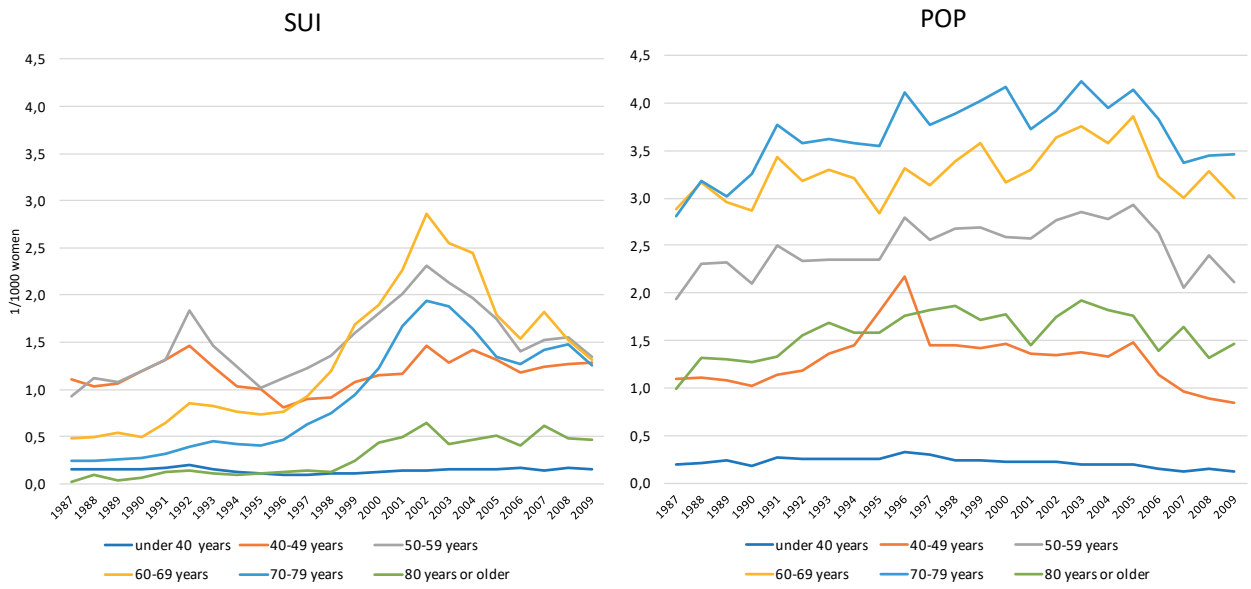

Figure 16 The age-specific incidence of primary SUI and POP surgery by age-groups (modified from Kurkijärvi et al. 2016, Kurkijärvi et al. 2017)

5.2.2 Age-adjusted incidence of SUI and POP surgery

The age-adjusted incidences of both SUI and POP surgery are presented in figure 17. POP surgery has remained more common throughout the study period, although nearly intersecting with the peak of SUI surgery incidence in 2002. When the incidence of POP was examined, it was found that there was a statistically significant linear increase of 0.023/1000 women per year between 1987 and 2005 ($p<0.001$). Since 2002 for SUI and since 2005 for POP, a clear decline in incidence has occured.

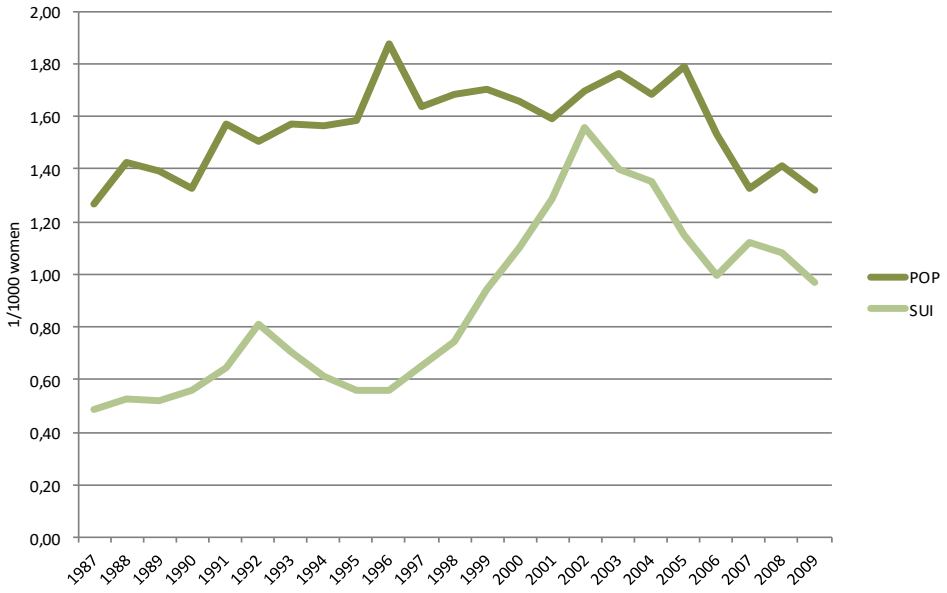

Figure 17 The age-adjusted incidence of primary SUI and POP surgery. Adjusted to Nordic Standard Population (modified from Kurkijärvi et al. 2016, Kurkijärvi et al. 2017)

5.2.3 Lifetime risk of SUI and POP surgery

The cumulative incidence was calculated to estimate the risk of a woman having to undergo at least one surgical operation for SUI or POP by a given age or during her lifetime. This estimate changes based on which year's incidences were used. In figure 18, the cumulative incidence is presented for years 1987, 1995, 2002 and 2009. The mean cumulative incidence is calculated using the mean incidences of the whole study 1987-2009. The lifetime risk of a SUI surgery was 3.1% at the beginning of the study, whereas in 2002 it was 9.9%, meaning that every tenth woman would undergo a surgery for SUI, if the incidence was to stay at the same level as in 2002. The lifetime risk for POP has not changed as dramatically but still is high when examined with respect to the incidence in 2002.

The risk to have undergone surgery either for SUI or for POP was calculated. This is presented in figure 19. With the rates in 2002, every fourth woman would expect to need surgery for pelvic organ dysfunction whereas with the rates in 2009, fewer than every fifth women would require surgery.

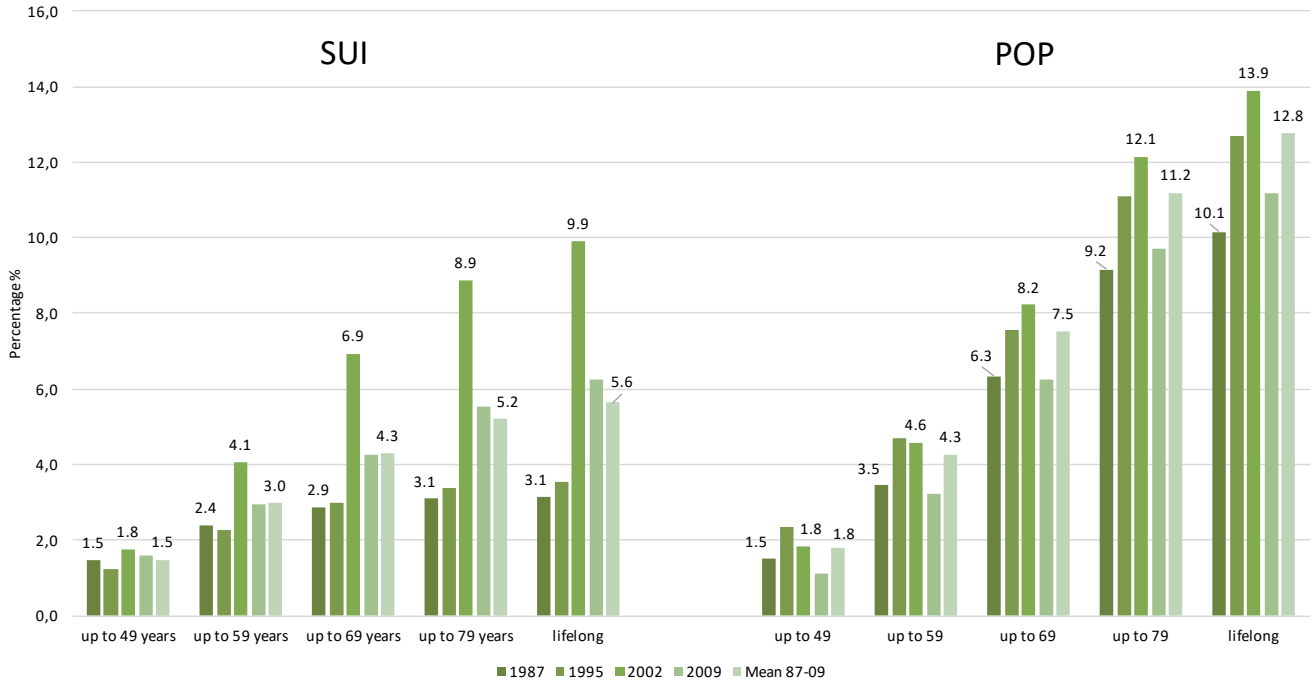

Figure 18 Cumulative incidences of primary SUI and POP operations (modified from Kurkijärvi et al. 2016, Kurkijärvi et al. 2017)

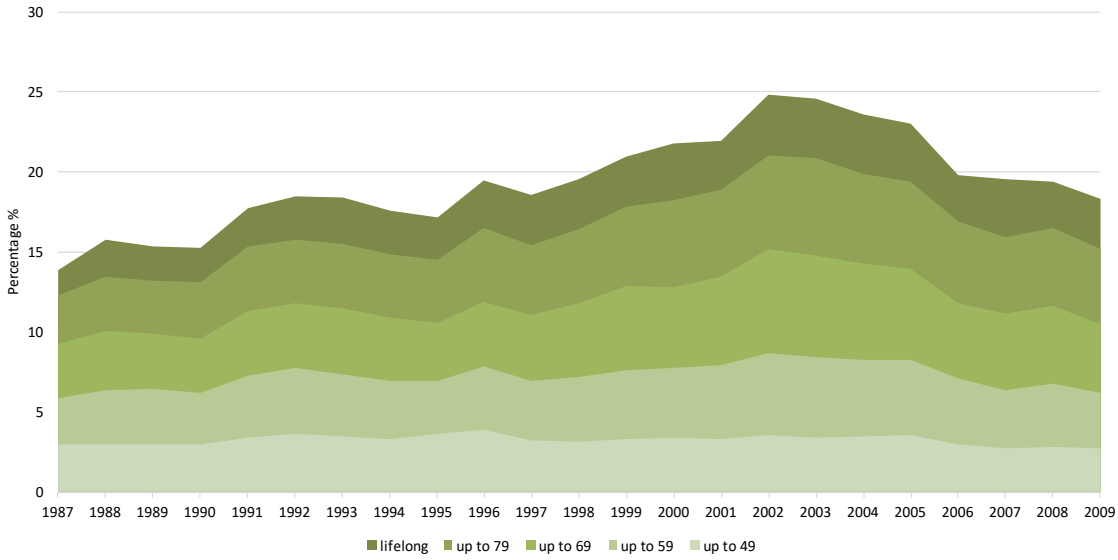

Figure 19 Combined cumulative incidence for either primary SUI or POP surgery

5.3 Reoperations for SUI

The whole cohort of 38,500 women was analysed to determine the incidence of reoperations for SUI. The mean age at the primary operation was 55.9 (SD 11.6) years. Of the 38,500 women, 2,776 (7.2%) were operated on for a recurrent SUI, during the study

period which represents a re-operation rate of 7.8/1,000 women-years. The reoperation rate during the whole study period was highest for the surgery group Other (11.2/1,000 women-years) and lowest in the retropubic MUS group (4.8/1,000 women years). The data summarizing the whole cohort are presented in table 20.

Table 20 Characteristics of the whole cohort of women with surgery for SUI (modified from study III)

	Complete cohort	Burch	Retropubic MUS	Transobturator MUS	Other	p-value
N (%)	38,500 (100)	9,458 (24.6)	17,494 (45.4)	6,261 (16.3)	5,287 (13.7)	
Mean age years (SD)	55.9 (11.6)	50.8 (9.8)	57.9 (11.6)	58.0 (11.8)	55.6 (11.8)	<0.0001*
Reoperation N (%)	2.776 (7.8)	1.294 (14.0)	547 (3.0)	142 (2.0)	793 (15.0)	<0.0001**
Mean time until reop years (SD)	6.1 (5.1)	8.3 (5.2)	2.8 (2.6)	1.3 (1.1)	5.8 (4.7)	<0.0001*
Mean follow-up years (SD)	9.3 (6.1)	16.4 (4.0)	6.5 (2.8)	2.6 (1.7)	13.4 (5.1)	<0,0001*
Total follow-up years	356,585	155,454	113,821	16,538	70,772	
Reoperation rate/1,000 women-years (95% CI lower; upper)	7.8 (7.5; 8.1)	8.3 (7.9; 8.8)	4.8 (4.4; 5.2)	8.6 (7.3; 10.1)	11.2 (10.4; 12.0)	

*Kruskal-Wallis, **Fisher's Exact Test

5.3.1 10-years follow-up cohort

To compare the reoperation rate between the Burch colposuspension and retropubic MUS, a sub-cohort of 10,689 women who had either Burch or retropubic MUS as the primary operation and who could be followed for ten years after the primary operation, was extracted from the data. In all, 8,868 women had Burch as their primary operation, 775 (8.7%) of whom required a reoperation. Of the 1,821 women who had retropubic MUS, 111 (6.1%) were reoperated. Primary Burch colposuspensions were conducted between 1987-1999 and retropubic MUS in the time frame 1997-1999. Women who had a reoperation after retropubic MUS were older at the primary operation ($p<0.0016$) compared to those who did not require a reoperation. This kind of difference was not seen among women with Burch as the primary operation, see table 21. A Kaplan-Meier

curve was created to show the survival without a reoperation, in favor of retropubic MUS (p<0.0001), figure 20. Odds ratio for a reoperation after Burch was 1.6 (95% CI 1.3-1.9) when compared to retropubic MUS.

Table 21 10-year follow-up to compare Burch and retropubic MUS (modified from study III)

	Burch			p*	Retropubic MUS			p*
	Total	No reop	Reop		Total	No reop	Reop	
Number (%)	8,868	8,093 (91.3)	775 (8.7)		1,821	1,710 (93.9)	111 (6.1)	
Mean age (SD)	50.3 (9.4)	50.2 (9.4)	50.5 (9.2)	0.39	56.8 (10.7)	56.6 (10.6)	60.0 (12.1)	0.0016

*Wilcoxon

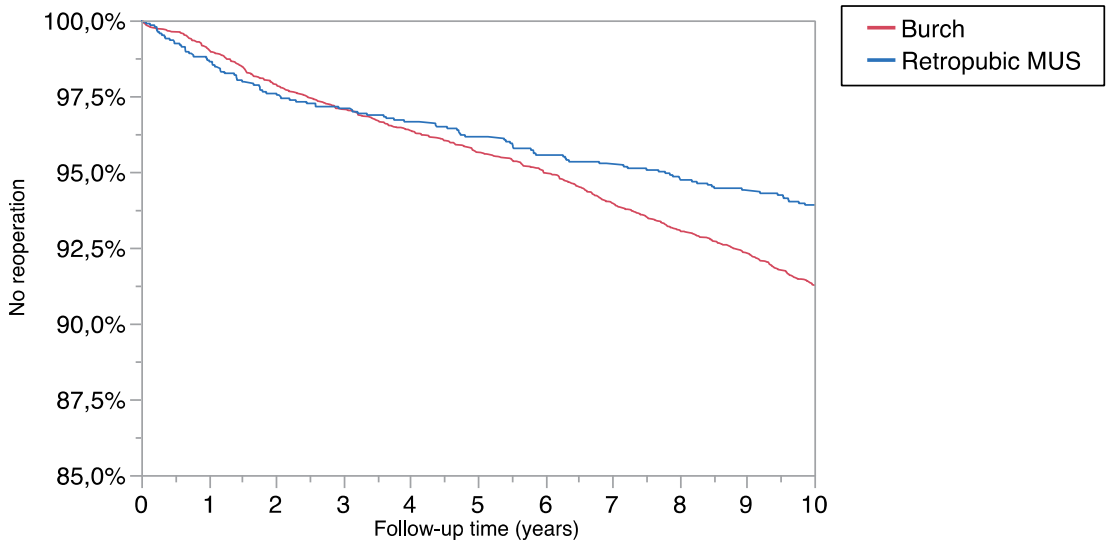

Figure 20 Kaplan-Meier curve showing survival without reoperation with a follow-up of ten years in favor of retropubic MUS (Log Rank Test, p<0.0001) (modified from study III)

5.3.2 5-year follow-up to compare Burch, retropubic and transobturator MUS

In order to include transobturator techniques (TOT and TVT-O), which were introduced in 2003, into the comparison with Burch and retropubic MUS, another sub-cohort of a five-year follow-up was extracted from the data. This yielded 22,549 women, of whom 9,292 had Burch, 12,540 had retropubic MUS and 171 had transobturator MUS as the primary operation; data on reoperations and age at the primary operation are presented

in table 22. The survival without reoperation was highest after retropubic MUS, followed by transobturator MUS and Burch colposuspension, as depicted in figure 21. Survival analysis for ten- and five-year's follow-up was also done by age-group, as summarized in table 23. Survival without a reoperation differed for women aged 40-59 years in the ten-years' follow-up and for women aged 40-69 years in the five-years' follow-up. There was no statistically significant difference in survival between the younger and older groups.

Table 22 5-year follow up to compare Burch, retropubic MUS and transobturator MUS (modified from study III)

		Number (%)	Mean age (SD)
Burch	Total	9,292	50.6 (9.6)
	No reop	8,892 (95.7)	50.6 (9.6)
	Reop	400 (4.3)	51.2 (9.7)
		p*	0.20
Retropubic MUS	Total	12,540	57.7 (11.1)
	No reop	12,217 (97.4)	57.7 (11.1)
	Reop	323 (2.6)	59.3 (12.5)
		p*	0.021
Transobturator MUS	Total	717	58.3 (11.2)
	No reop	693 (96.7)	58.2 (11.2)
	Reop	24 (3.3)	60.6 (11.1)
*Wilcoxon		p*	0.28

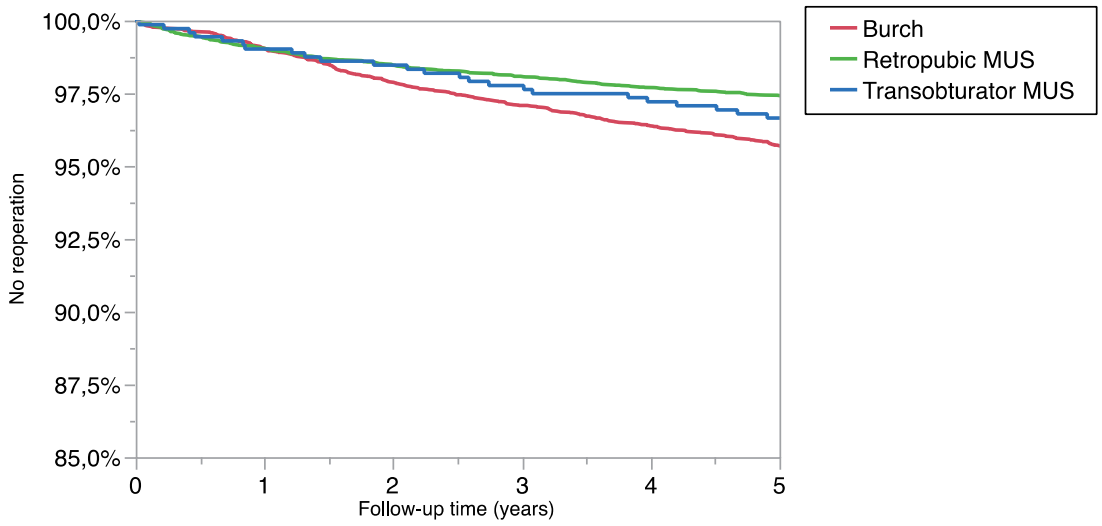

Figure 21 Kaplan-Meier curve of survival without reoperation with a follow-up of five years, showing statistical significance between the curves (p<0.0001, Log Rank Test) (modified from study III)

Table 23 Survival without reoperation in 10- and 5-year follow-up between operation types by age-groups

	10-year follow-up			5-year follow-up			
Age	Burch n	Rp MUS n	Log rank p	Burch n	Rp MUS n	To MUS n	Log rank p
18-39	951	100	0.48	967	548	29	0.34
40-49	3666	378	0.028	3768	2530	140	0.007
50-59	2799	597	<0.0001	2929	4075	228	<0.0001
60-69	1129	506	0.17	1226	3326	195	0.007
70-79	313	225	0.18	378	1813	108	0.19
≥80	10	15	0.24	24	248	20	0.47

The odds ratios for reoperation within the 5-year follow-up were compared, see table 24. A statistically significant difference was found in the odds ratios between Burch and retropubic MUS and Burch and any MUS.

Table 24 Comparison of odds ratios for reoperation (modified from study III)

	OR	CI lower 95%	CI upper 95%	p*
Burch vs Retropubic MUS	1.70	1.47	1.98	<0.0001
Burch vs Transbturator MUS	1.30	0.87	2.03	0.20
Retropubic vs Transobturator MUS	0.76	0.51	1.19	0.23
Burch vs any MUS	1.67	1.45	1.94	<0.0001
*χ^2				

5.4 Further operations for POP

A total of 77,907 women had surgery for POP during the whole study period of 1987-2009. During the last ten years of the study (2000-2009) a total of 39,676 women had surgery for prolapse; either as a primary or a recurring operation. Total numbers of primary and further surgery are presented in figure 22. Distribution of POP procedures at primary and the first further surgery are presented in table 25.

Table 25 Distribution of POP procedures at the primary operation and the first repeat operation. Includes operations after 1.1.2000, both primary and further surgeries.

Operation code	Primary	Further
LEF13 and LCD10*	46.4%	6.5%
LEF00	39.4%	46.4%
LEF03	37.6%	28.6%
LEF40 and LEF41	5.6%	10.8%
LEF50, LEF51 and LEF53	5.8%	25.9%

*In addition to another POP procedure

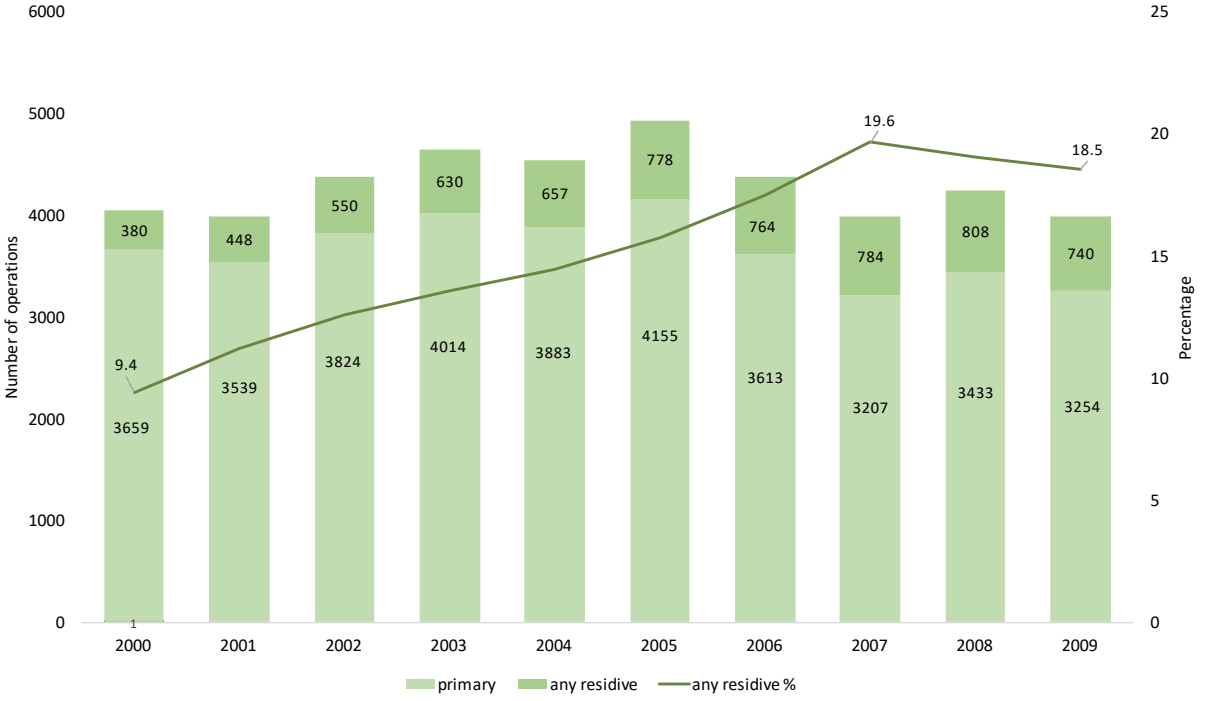

Figure 22 Number of primary and further surgeries are presented inside the bars, the curve shows the percentage of further operations of the total number of operations (modified from study IV)

In order to define the time interval between the primary and the following operation we determined the time from all further operations performed in 2000-2009 to the preceding operation. The time interval ranged from 0 to 23 years, the median time was 4.8 (Q1 1.8, Q3 9.6) years. Figure 23 presents the distribution of the intervals. The time between operations shortened with the advancing number of further operation, being 2.1 (Q1 1.0, Q3 4.7) years between the first and the second operation after the primary surgery but only 1.6 (Q1 0.7, Q3 4.7) years between the second and the third operation after the primary.

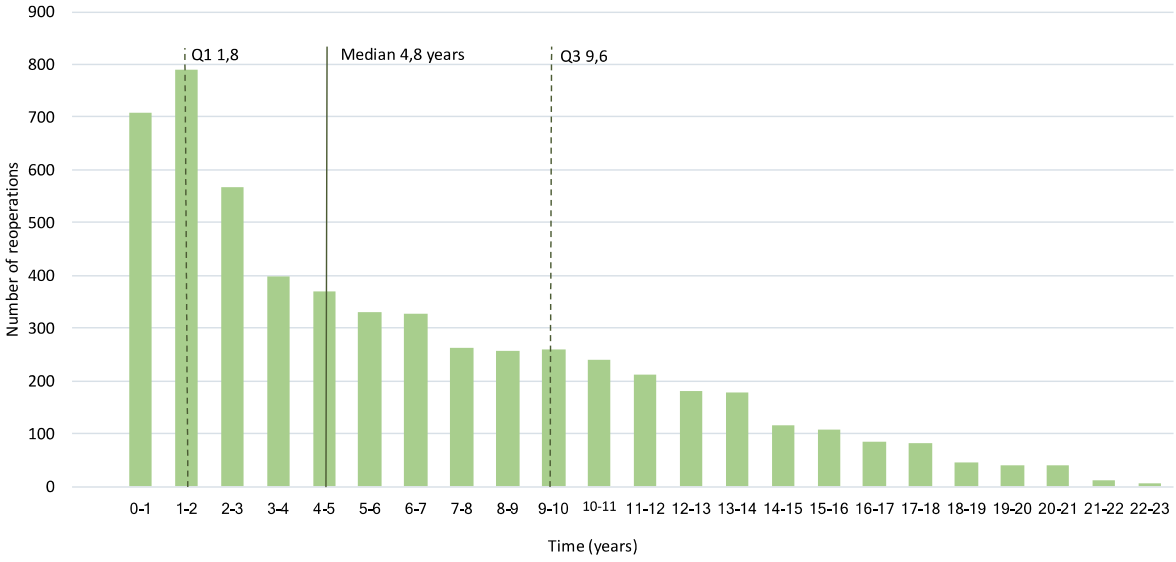

Figure 23 Time intervals between the primary and the first further operation (modified from study IV)

As seen in figure 23, there seems to be a steady rise in the proportion of further operations, as although it accounted for 9.4% of all operations for POP in 2000, this value had more than doubled to 19.6% in 2007. This was further analyzed by comparing the first (2000-2004) and the second (2005-2009) halves of the 10-year period. Statistical significance was observed ($p<0.0001$) between the time periods in the proportion of primary and further operations. The Cochran Armitage Trend Test, which tests for a change in the proportions across a time period, showed the same outcome ($p<0.0001$).

5.4.1 Cumulative risk of further operation for POP

The annual risk rate for a first repeated surgery for POP was calculated by constructing a cohort life table for the ten-year period 2000-2009 for those women who had the primary operation during this time. The annual increases in the risk rates are presented in figure 24. The ten-year cumulative risk was seen to be 10.8%. Any type of prolapse operation is included in this analysis as it is not site specific.

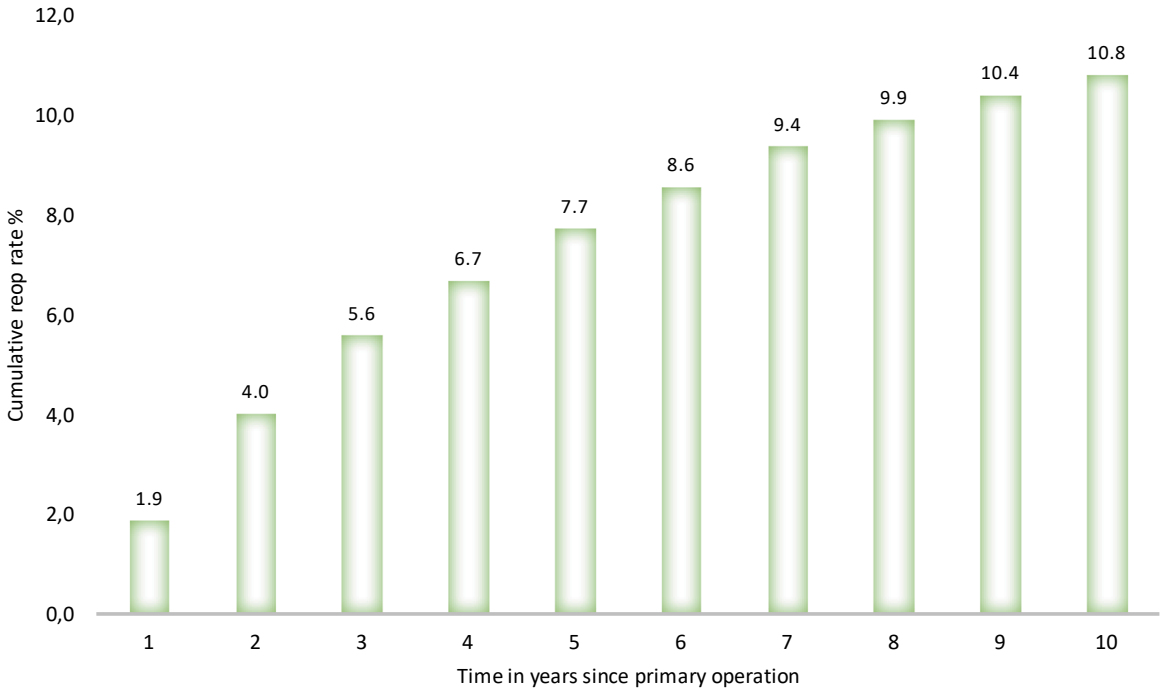

Figure 24 The annual cumulative risk for the first further operation after the primary for POP (modified from study IV)

6 DISCUSSION

There is no denying that gravity and gravidity take their toll on the pelvic floor of an ageing woman. Stress urinary incontinence and pelvic organ prolapse, though not life-threatening, markedly impair a women's quality of life and perceptions of herself as a women. Surgical procedures to alleviate these conditions date back almost 150 years; the last two decades have included both success stories of operative innovations as well as novel methods with less positive impacts. Midurethral slings based on the integral theory rapidly surpassed older methods and have proven to be efficacious in long-term follow-ups. Transvaginal meshes were introduced in an attempt at improving POP surgery results with the unforeseen development of numerous complications, leading to a situation where many of our treatment options are similar to the situation over a hundred years ago.

It has been stated, that 11-20% of women will have to undergo surgery for either POP or SUI during their lifetime (Olsen et al. 1997, Wu et al. 2014d). As rates of pelvic floor surgery differ greatly even between European countries, it has been uncertain, what is the risk for Finnish women and how successful have been our choices of treatment with regard to the need of further operations.

6.1 Methodological aspects

6.1.1 Strengths of large datasets

This was a national population based register study, covering all Finnish women, who had SUI or POP surgery from 1987 to 2009. The data was obtained from THL's Care Register for Health Care. The quality of this register is recognized to be good in terms of completeness and accuracy (Sund 2012). When analyzing national data, the results are easily applied to the general population. In comparison, if register studies are based on data derived from employer-based insurance claim registers (Jonsson Funk et al. 2012a, Wu et al. 2014a), the results may not be applicable to people of low socio-economic status, or the results may apply to only individuals in a certain age-frame.

National register data also reflects a phenomenon as it is in the country. Several studies of excellent quality have been carried out in Finland investigating MUS for the treatment of SUI. The exclusion criteria in such studies, RCTs and observational trials, are in many cases are very strict, for example with respect to BMI, medication and concomitant conditions, (Laurikainen et al. 2007, Nilsson et al. 2008), and as such, they do not represent all of the women who need to undergo SUI surgery. National register data also

represents the quality of treatment in general, whereas in other types of studies, the operative treatment may be in the hands of a few highly skilled individuals.

6.1.2 Pitfalls of register-based study

The problem with the usage of administrative data in health research is that it is not collected for the purpose of any particular study (Sund et al. 2014). It may be lacking information that would benefit the study, for example details about BMI, parity, concomitant diseases, postoperative complications, smoking habits and prescription drug usage. This may be overcome in some instances by cross-linking with different registers; the Finnish Birth Register, which is widely used in research, could have been linked to obtain information on parity. Information on purchase of prescription drugs (such as anticholinergic drugs for UI patients and hormone replacement therapy) could have also been added by cross-linking (Räisänen 2013), nevertheless some essential information is not accessible in the current registers. BMI is a good example: obesity is a known risk factor for failure after both SUI and POP surgery (Diez-Itza et al. 2007, Stav et al. 2010). It is impossible to know the BMI of a patient at the time of primary surgery and whether she has gained weight between operations by only accessing her register data.

Coding errors are likely to be present to some extent in register data, although studies on the quality of Finnish registers have indicated that this is not a significant problem (Gissler & Shelley 2002, Sund 2012). Figure 25 schematically represents those points, where possible errors could occur. First, in this data, the phenomenon is a surgical operation and, as a clinician, I am painfully aware of possible errors happening already in the operating room. The possible sources of error may be communicational, if codes are not entered by the surgeon. There are also different conceptions about which is the correct procedure code to be applied. Coding of vaginal hysterectomy is one potential source of error. In the Nomesco classification of surgical procedures, vaginal hysterectomy is included in the POP codes as LEF13, which is performed with or without colporraphies. It is not rare, however, that even though the uterus has descended, the code used is LCD10 for hysterectomy and colporraphies are added separately. This decreases the number of vaginal hysterectomies in this data, as LCD10 is not taken into account since it is not the code representing POP surgery. There are also situations, when the surgery cannot be carried out as a standard procedure and is difficult to fit into any procedural code. Second, the transfer of data from hospitals to register may also introduce errors, but this is less likely, as the data is computerized nowadays, when it leaves the operating room, although this was not the case in the earlier years of the study. Third, when the study is conducted, retrieval of data from the register may be defective because of misconceptions between clinicians and the personnel operating the register. Last, handling large datasets is not without problems and possible mishaps.

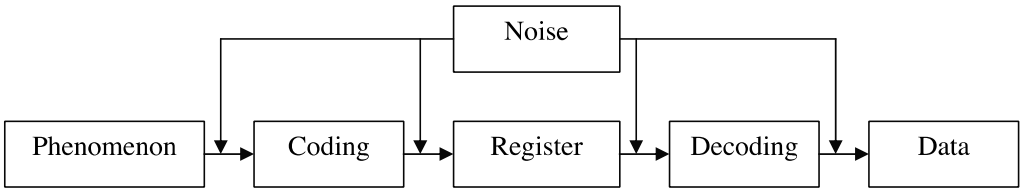

Figure 25 Schematic diagram representing the transfer of information to and from administrative database (reprinted with permission from Sund 2003)

A change from the classification of Finnish Hospital League to the Finnish version of Nomesco classification system took place between 1996 and 1997. This was a major change, as the number of codes was notably smaller in the old system. Thus joining the data from these different systems is not without problems. Since there was not specific code in the older system, some compromises had to be made, for example, anterior and posterior repairs were not separated in the old system; therefore, before 1997 it is not known if a women underwent anterior repair, posterior repair or both. The number of codes per single hospitalization also changed; until 1993 two codes were recorded, until 1996 three codes and from then on, five codes. This affects primarily POP surgery, as several POP procedures may be performed at the same time. The introduction of novel techniques during the study period is a likely source of coding errors concerning SUI surgery codes. When TVT was introduced, the was no specific code for this technique and during the initial years of its use, several different codes were used. The practice varied between hospitals. The same holds true for transobturator MUS.

6.1.3 Time lines and wash-out periods

The onset year, 1987, for the study was chosen because of technical reasons. We are not aware of any interventions which took place before 1987 for the women in the data. This poses a problem, which is greater for the POP surgery data, as further POP procedures are more commonly performed, and the incidence of SUI surgery in the early years of the study period was quite low. Thus, it is likely that there is little possibility that number of those SUI surgeries, which have been presumed to be primary surgery, but were, in fact, reoperations. This assumption could not be made for POP surgery. Therefore, in study IV, we used a washout period of 13 years, during which no operation was assumed to be primary. Thirteen years was chosen based on the literature i.e. most further operations for POP occur within less than ten years (Price et al. 2008, Abdel-fattah et al. 2011, Dällenbach et al. 2012, Gotthart et al. 2012). In study II, we excluded the real further operations from the data; this is likely to overestimate the incidence of POP surgery in the early years, since the number contains both primary and further operations but from the latter part of the study, further operations are excluded. This is likely to affect to some

extent the incidence calculations in the early years as well as the lifetime risk calculations. Our method is different from that applied in a Danish study (Løwenstein et al. 2015), where they included all POP surgeries, and therefore their results are not fully comparable with the present values.

6.2 National trends in pelvic floor surgery

6.2.1 Declining incontinence surgery – are we dry already?

A dramatic increase in incidence of SUI surgery occurred after the introduction of retropubic MUS; at the same time Burch colposuspension stopped being used. The same phenomenon has also been seen elsewhere as well (Lee & Dwyer 2010, Cammu et al. 2010). Before MUS, Burch was the most commonly used method. At the beginning of the study period, for some unknown reason, there was a peak in the number of Burch operations. The rise in "Other methods" in 1997 is due to the introduction of novel MUS slings and the change in the coding system. The rapid decrease in incidence after 2002 is interesting. In study I, we excluded reoperations from the study. Based on the findings in study III on the time interval between primary Burch and the possible reoperation, it seems reasonable to assume, that a group of women had Burch before 1987, then after the introduction of retropubic MUS, they were soon reoperated; afterwards the rate of these reoperations slowed down.

One might speculate that since it is a mini-invasive procedure MUS was attractive to women, who did not wish to be subjected to Burch and may have suffered from incontinence for a long time; the rapid increase of incidence in older age-group is suggestive that this is the explanation. The decline from the most enthusiastic years has probably ceased and settled at a level of 1/1000 women years. This is close to the median of OECD countries, which is 0.8/1000 women (Haya et al. 2015).

6.2.2 Steady state in prolapse surgery?

As suggested before, there could have been some increase in the incidence in POP surgery if further operations had not been excluded from the study II. Otherwise, there are no major changes to the incidence; after a subtle increase, the incidence falls back to the same level as in 1987. The major increase in the total number of procedures in 1997 is due to the change in the coding system. This most likely contributes also to the peak in vaginal hysterectomies. There was also an increase in 2005, which may be caused by the Ward Guarantee announced that year; this stated that a treatment had to be provided

within six months after the need had been ascertained. Before this decree, there may have been patients waiting for over a year to undergo POP surgery.

The amputation of cervix with colporraphies, the Manchester procedure, was a popular procedure in the 80's, but it is seldom performed nowadays. It has however enjoyed a renaissance during the last few years (Tolstrup et al. 2017, Bergman et al. 2017), probably as an alternative to mesh augmented surgery. In our data, true apical repairs were rather few in number, 5.8% during primary surgery. Internationally, there are wide variations in the percentage of apical repairs, from 51.3% in France to 12.5% in Denmark, in the percentage of apical repairs (Haya et al. 2015). It is possible, that in some countries, vaginal hysterectomies as well as repairs of enterocele are coded as apical repairs. Uterus-sparing POP surgery, different hysteropexies and the Manchester operation may also have been considered as apical procedures.

6.3 Burden of recurring pelvic floor surgery

In a classic study (Olsen et al. 1997), it was stated, that 29.2% of women, who have SUI or POP surgery will need a further operation; this has been cited in almost every urogynecologic paper, even very recent publications (Barber 2016). The study was a retrospective analysis of 395 women, of which 29.2% had undergone a previous operation for POP or SUI. Prospective analysis of the same cohort showed 13% risk of requiring a further operation in five years (Clark et al. 2003) and a 17% risk within ten years (Denman et al. 2008).

What is the true reoperation rate? In this study, the reoperation rate after any SUI surgery was 7.8/1000 women years. Retropubic MUS was the procedure with the lowest reoperation rate i.e. 4.8/1000 women years, however, the mean time until reoperation was significantly longer after Burch colposuspension. This may reflect a methodological problem or more meticulous patient selection with Burch. Patients may be inclined to seek a reoperation after MUS more easily, as the procedure is less invasive. Our findings are in good concordance with internationally published data; reoperation rates after MUS procedures are low and the overall reoperation rate remains well below 10% (Aigmueller et al. 2011, Svenningsen et al. 2013, Foss Hansen et al. 2016a, b).

The variation in reported reoperation surgery rates after a POP operation is markedly wider from, ranging just few a percents to up to 36%. Comparison of studies is complicated by the lack of a unanimous view as to what should be considered as reoperation. The IUGA/ICS Standardization Committee recommends the term "further surgery", subdivided into primary surgery/different site and repeat surgery/same site (Toozs-Hobson et al. 2012). The problem of suboptimal results of POP surgery has been known for long: already in 1909 Ahlfelt stated that the only unresolved issue in

urogynecology was finding a permanent cure for cystocele (Lensen et al. 2013). In this study, we found that the cumulative risk for further surgery during 10 years since the primary POP operation was 10.8% including all compartments, which matches with the current view that the further surgery rate after native tissue repair does not greatly exceeding 10% (Siff & Barber 2016).

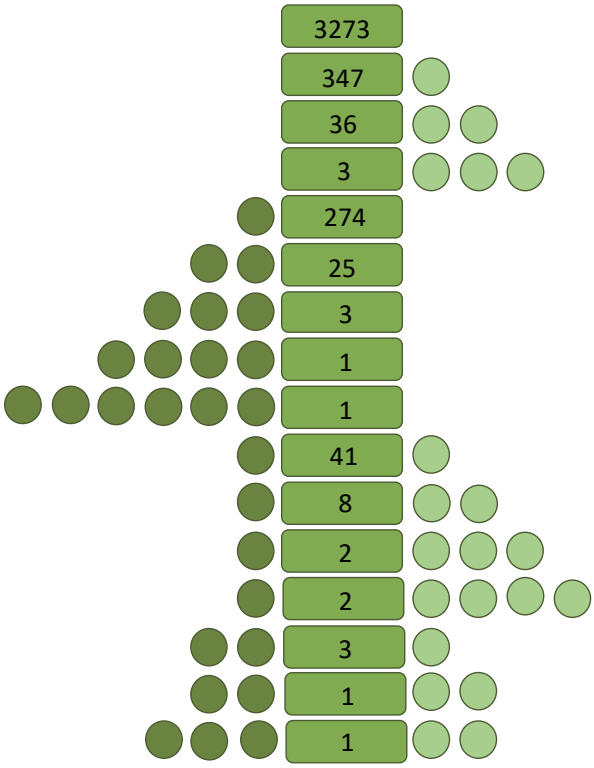

Figure 26 Operations for prolapse in 2000 with preceding and succeeding operations. Boxes represent the first operation occurring in 2000; dark green balls represent those done before that and light green balls afterwards.

Nonetheless, there are women who will undergo a series of POP operations. It also seems, that a greater number of further operations are being performed towards the end of the latter decade in the study; there was a statistically significant upward trend in the proportion of further operations for POP from 2000 to 2009. Figure 26 represents all POP surgeries from 2000, in the middle of our study period. It would be important to have some way of identifying those women, who are prone to frequent recurrences or further prolapse at some different sites. Different prediction models have been developed in an attempt to find women at risk for pelvic floor disorders after delivery (Wilson et al. 2014), for urinary incontinence after hysterectomy (Lakeman et al. 2011) and for recurrence after anterior repair (Vergeldt et al. 2016). Although vaginal parity is the most evident risk factor, it has been estimated that relative to CS, 8.9 additional vaginal deliveries and 6.8

instrumental deliveries would lead to one additional case of prolapse (Handa & Blomquist 2012). Evidence of a putative inherent predisposition for POP relates also to the short interval between operations; in this study, the median time interval was 4.8 years. This time interval shortens with advancing number of further operations indicating that repeated operations are likely to have poor outcomes.

In this study, a distinction between primary surgery/different site and repeat surgery/same site could not be made in many cases and therefore was not attempted. The main problem lies within the procedure and diagnosis codes: for example, a patient may be diagnosed with uterovaginal descent (N81.2) and undergo a procedure coded as LEF13. It is impossible to know whether colporraphies were performed and to which compartment, and the diagnosis code is not helpful in this respect, as the patient probably has descent of both anterior and posterior compartment as well as apical prolapse.

The distribution of different procedures at the time of primary surgery and further surgery is difficult to interpret and includes several uncertainties and was therefore omitted from study IV. It was noted, however, that for operations performed at the beginning of this current century (1.1.2000-31.12.2009), 46.6% of primary procedures for POP included vaginal hysterectomy (LEF13 and LCD10); anterior and posterior repairs were performed in 39.4% and 37.6% of surgeries, respectively, which are underestimations, as LEF13 also may include those repairs. Anterior repair was performed in 46.4% of further surgeries, whereas posterior repair in 28.6%. Operations for enterocele and apical prolapse are represented in 5.6% and 5.8% of primary procedures, respectively. The proportion is doubled (10.8%) for enterocele and is even five times higher (25.9%) for apical prolapse at the time of second surgery.

Is the number of apical suspensions sufficient? It has been suggested, that recurring operations for POP were reduced, when an apical suspension was performed concomitant with some other POP procedure (Eilber et al. 2013). In the US the apical suspension rates at the time of hysterectomy for POP have increased during the past two decades (Hudson et al. 2015, Kantartzis et al. 2015), but it has been concluded, that 60% of hysterectomies for POP are not accompanied with apical suspension, i.e. more should be conducted (Madsen et al. 2017). There is also wide variation in what is regarded as an apical suspension: in a Danish study, gynecologists reported to a national hysterectomy register that they conducted apical suspension in 90% of benign hysterectomy patients but the number was only 60% when checked from patient records (Bonde et al. 2017), whereas in the US, only 3.1% of non-POP hysterectomies included an apical suspension (Ross et al. 2017); it is unlikely, that these reports are discussing identical methods. For example, when performing vaginal hysterectomy, USLs are attached to the vaginal cuff, as described by Bonde et al. (2017), but the procedure is seldom performed at the level of ischial spine, which is the proper way to suspend the vaginal vault (Alas & Anger 2014).

In Finland, procedure codes for apex (LEF50, LEF51, LEF53 and LEF54) are named colpopexies after a previous hysterectomy and thus there are no proper codes to be used at the time of hysterectomy.

6.3.1 Future is in the history? – After the rise and fall of vaginal meshes

The transvaginal mesh was introduced in order to improve the results of POP surgery; although the anatomical result and reoperation rate for prolapse did improve, the increase in distressing complications resulted in endless numbers of law suits in the US after FDA issued a warning concerning mesh surgery (Maher et al. 2016c, Iyer & Botros 2017). In Scotland, the authorities reacted to increased reports of complications by ordering hospitals to suspend the use of MUS kits as well; a later report did state that MUS operations could continue (Wilkie et al. 2015, Hawkes 2015). Since the FDA warning, several mesh kits have been removed from the market and the popularity of vaginal mesh surgery has plummeted to close to zero in the US (Skoczylas et al. 2014). This does not hold true to every country; in 2012, a mesh was used in every fourth anterior repair in Germany (Haya et al. 2015). As mesh products keep disappearing from the market, it seems that old methods will need to be reinvented and mesh surgeons will have to learn how to support vaginal cuff with traditional methods. A recent consensus statement issued by European Urology Association and European Urogynecology Association however, stated that vaginal meshes may be used to repair recurrent POP at the same site in complex cases, although they should be in the hands of an experienced surgeon (Chapple et al. 2017).

In this study, vaginal mesh augmented procedures were not separated. At the time, they did not have specific procedure codes, which were introduced into the Nomesco classification in 2012. An additional code may have been used, but these were not identified, as the usage of vaginal mesh procedures was minor during the study period. Thus, it can be stated, that these results on POP procedures represent mainly native tissue repairs. Abdominal (LEF50) and laparoscopic (LEF51) SCPs meshes were used also during the study period.

6.4 Pelvic floor surgery – a hallmark of old age

6.4.1 Lifelong risk for surgery

Olsen et al. (1997) stated, that a woman has an 11.1% risk of requiring a surgery for SUI or POP until the age of 79. This number was based on a retrospective cohort of 395

women operated on for SUI or POP in 1995 in the US, thus reflecting the incidence rates in that particular year with its unique demographic structure. More recent calculations were based on over 10 million US women, whose records were evaluated between 2007 and 2010. The combined lifetime risk for SUI and POP was 20%; separately, 13.6% for SUI and 12.6% for POP by the age of 80 years (Wu et al. 2014a). In Denmark, the risk of a 80 year old woman to have undergone an operation for POP, with the incidence calculated in 2008, was 18.7%; the number has been as high as 26.9% in 1978 (Løwenstein et al. 2015). In Australia, the lifetime risk for POP surgery was 19%, when calculated with incidence rates from 2001-2005 (Smith et al. 2010). Due to the dramatic change in the incidence of SUI surgery in Finland, it is important to appreciate which incidence rates have been used to calculate the lifetime risk. The lifetime risk, up to 100 years, would be 9.9% for SUI and 13.9% for POP, if the 2002 incidence was used, but significantly less i.e. 6.3% for SUI and 11.2% for POP when using the incidence of 2009. When the estimate was based on the whole study period, the lifetime risk for SUI surgery was 6% and for POP surgery 13%.

6.4.2 Effect of aging population

The Finnish population is aging. This change could be seen already during the years of this study. The numbers of women in the age-groups used in this study are presented in figure 27, showing a slight decrease in the younger age groups and an increase in the older members of the female population, which, in part, resulted in an increased number of operations being conducted towards the end of the study.

In 2009, it was proposed, that the numbers of women suffering from urinary incontinence in the US would increase by 55% and those suffering from POP by 46% by the year 2050 (Wu et al. 2010). This is due to the increase in the population and the increase in the proportion of elderly women in the population. Furthermore, the proportion of women seeking help for pelvic floor dysfunction from those with symptoms, will increase (Kirby et al. 2013). Thus, the increase in the need for treatments exceeds the value estimated if one considers only the increase in the number of women with symptoms (Dieter et al. 2015).

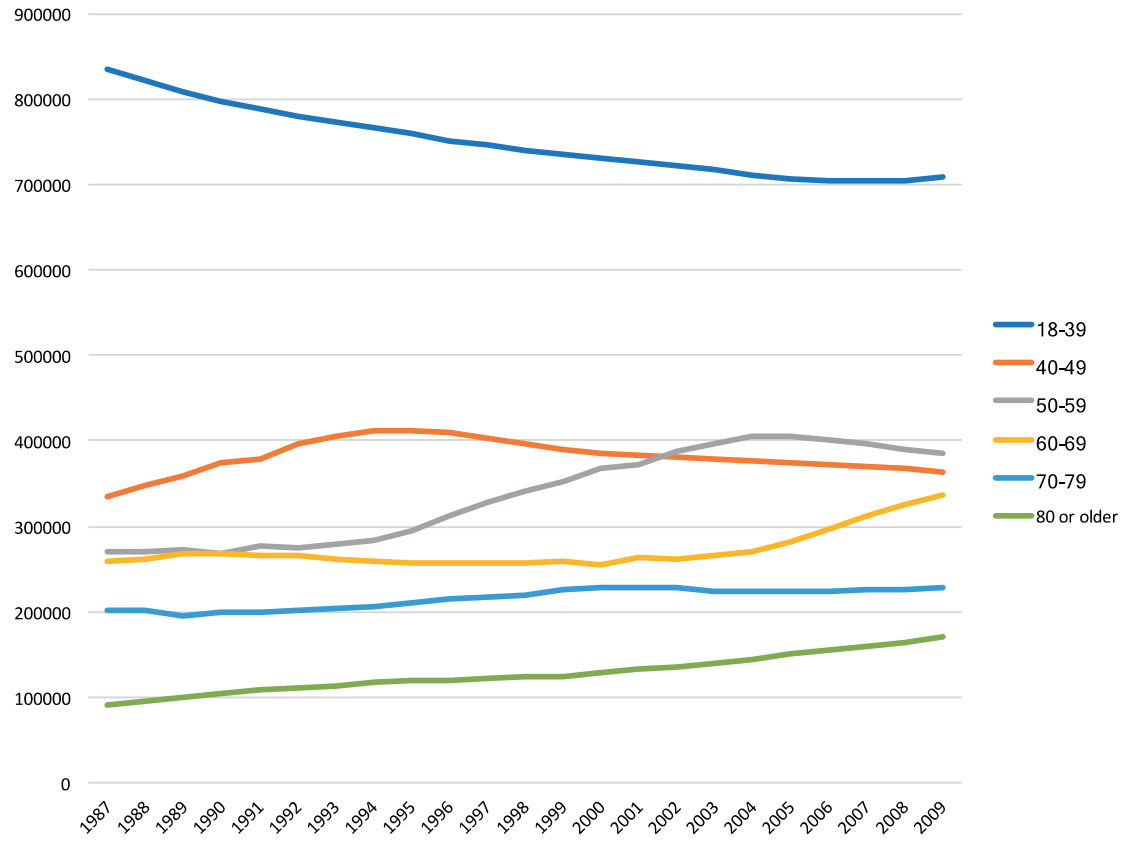

Figure 27 Changes in the population 1987-2009 (Source: Population Statistics, Statistics Finland)

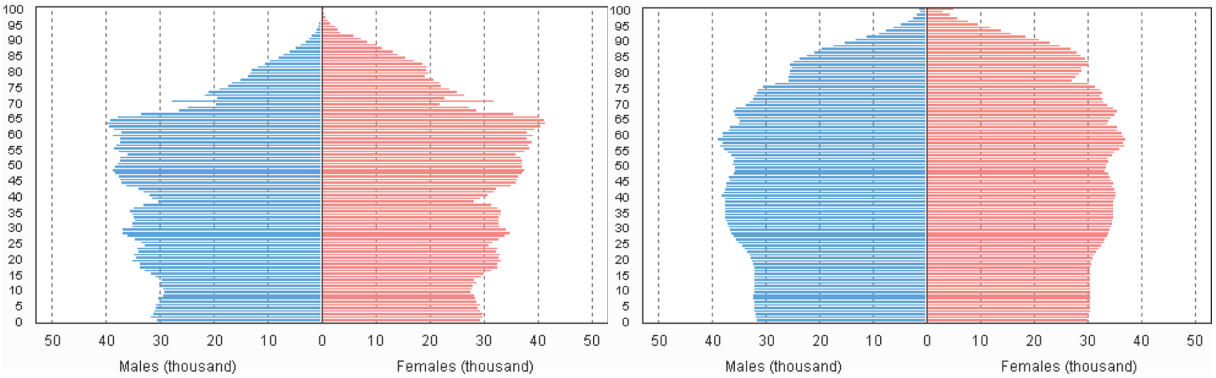

Figure 28 Population by age and gender. Left 2011, right 2050 as projected in 2012 (source: Population Statistics 2012, Statistics Finland)

Figure 28 shows the Finnish population distribution by age and gender in 2011 and as projected for 2050. It can be clearly seen that especially the female population will be older. There was a notable increase in the proportion of elderly women, aged 70 years or older, of those who were operated, especially for SUI during the study period. Thus, we

will have more elderly women and we will have to be prepared to offer more surgical treatment. It has been discussed whether elderly women need a different type of care from their younger counterparts, due to the natural effects of aging (Miller & Baraldi 2012, Betschart & Rizk 2014). In this study, it was noted, that women requiring a reoperation after a retropubic MUS, were significantly older. This difference was not seen in patients operated with transobturator MUS, but the number of reoperations was lower, which may have contributed to this finding. The mini-invasive nature of the MUS procedures makes it tempting to offer this procedure to elderly patients, but it must be acknowledged, that older patients are more prone to complications, not necessarily related to the intervention (Sung et al. 2006).

There are also factors which may counteract the increase of pelvic floor problems. The percentage of primiparas was 32.3% of all parturients in 2016 compared to 30.3% in 1987, although the percentage of women with three or more previous deliveries was also greater in 2016 (10.3%) compared to the corresponding values from 1987 (8.0%). The number of women not giving birth at all is increasing. Cesarean section rate in Finland has increased only slightly, i.e. it was performed in 14.5% of births in 1987 and 16.4% in 2016. Vacuum delivery rate has increased, but it does not exert the same effect on the pelvic floor as forceps, which are no longer used in Finland (Source: Perinatal statistics – parturients, deliveries and newborns 2016, National Institute for Health and Welfare).

6.5 Future aspects

In the near future, quality registers in the field of urogynecology will be adopted in several university hospitals in Finland. This is of the utmost importance in order to unify treatments and to track complications. These registers should be national, as in Sweden (Emilsson et al. 2015). As data accumulates, these registers can be effectively used in research, as has been done in the other Nordic countries. Compared to national, administrative registers, data in quality registers will be more exhaustive and focused on to the subject.

When compared to the literature, there were too few primary apical prolapse procedures in the data. This needs to be acknowledged since the apical defect plays a major role in most prolapses. Laparoscopy is now the preferred method for sacrocolpopexy; This technique has increased its popularity, compared to abdominal procedure, since it is less invasive, allowing a markedly shorter recuperation time. More attention should be focused on the apical repair during vaginal surgery, as well as on the suspension of the vaginal cuff during hysterectomy for causes other than POP.

More detailed procedure codes are needed to record procedures accurately: specifically the codes catecorizing apical support should be more precise and usable at the time of

hysterectomy. At the institutional level, this may be overcome with the help of quality registers, but as long as these registers are not national, the information, which is coded to the Care Register data should be more specific, which would demand more additions to the coding system. In the optimal situation, a quality register would be nationally based and the information from it could be integrated into the Care Register and thus could be linked with other national registers.

As the population ages, attention must be paid to the specific needs of elderly patients. Mini-invasive procedures are beneficial for these frail subjects. At the other end of the patient spectrum are those young women who develop troublesome POP soon after delivery. Research should focus on how to identify these women and how to prevent prolapses, by possibly "training" the pelvic floor to endure childbirth without suffering major trauma, how to manage the delivery in a safe way and should trauma occur, how to repair it in a durable manner. More attention should also be paid to preventive methods as well as to the development of conservative treatment and pelvic floor training.

Since 2009 vaginal mesh augmented surgery has been more widely used. The outcomes of these procedures should be evaluated at the national level, as well as the results of laparoscopic sacrocolpopexies. More detailed information should be obtained on the site of POP recurrences. To study the impact of different aspects of childbirth (e.g. duration of second stage, age and BMI at the delivery) on the incidence of POP and SUI in the Finnish female population, the Birth Register and the Care Register could be cross-linked. A register-based study to compare the rate of POP surgery after different types of hysterectomy (abdominal, laparoscopic and vaginal) has been planned. The effect of vaginal cuff suspension on the incidence of prolapse should also be investigated in a standardized setting to help draw up recommendations for the optimal preventive method at the time of hysterectomy. Another interesting research prospect would be to compare the popular method LEF13 (vaginal hysterectomy and possible colporraphies) with apical suspension to laparoscopic sacrocolpopexy with amputation of uterine corpus for patients with uterovaginal descent. An appreciation of the long term efficacy and consequences of these procedures would be of great value when counselling women with POP in their fifties, with potentially another fifty years ahead of them.

7 CONCLUSIONS

1. Burch colposuspension was the most prevalent method for SUI from 1987 to 1997, when retropubic MUS was introduced. The popularity of Burch soon declined and retropubic MUS became the treatment of choice for SUI. Transobturator MUS was introduced in 2003 and surpassed retropubic MUS in 2007 in terms of the number of procedures performed. Burch colposuspension and procedures other than MUS are no longer performed in Finland. Vaginal hysterectomy and colporraphies have remained the most commonly used surgical method for POP. Amputations of the uterine cervix are no longer performed concomitant with colporraphies. Apical repairs were not commonly performed
2. The incidence of SUI surgery increased after the introduction of MUS. The effect was clearest for women aged 60-69 and 70-79 years; for these women, the age-specific incidence was increased by six- and ten-fold, being 2.9/1000 and 1.9/1000 women, respectively. Incidence rates increased after MUS in all age-groups but declined after 2002 for women aged 50-79 years. No such change was observed for POP surgery, which is most common in the age-group 70-79 years, followed by women in the next younger age groups i.e. 60-69 and 50-59 years.
3. Any estimate of the lifetime risk for SUI and POP surgery is dependent on the incidence rates and thus varies year by year. The lifetime risk for SUI surgery was 9.9% if one applies the incidence rates for 2002 but only 6.3% if one uses the 2009 value. In Finland, the lifetime risk for POP surgery was estimated to be 13.9% with the incidence rates from 2002 and 11.2% with the corresponding value from 2009.
4. The reoperation rate after SUI surgery was low, 7.8/1000 women years. When followed-up for ten years after the primary operation, the odds ratio for repeated surgery was 1.6 for Burch colposuspension when compared to retropubic MUS. When followed-up for five years, a reoperation was more likely after Burch colposuspension when compared to MUS (OR 1.7). There was no statistically significant difference in reoperations between retropubic and transobturator MUS, although the number was lowest after retropubic MUS. With respect to POP surgery, the cumulative risk was 10.8% for the patient to require a further operation in any compartment within ten years of the primary surgery.

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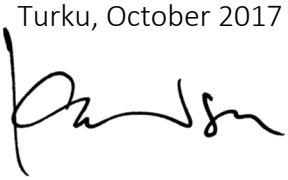
Turku, October 2017



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