PUBLICATIONS OF
THE UNIVERSITY OF EASTERN FINLAND

Dissertations in
Health Sciences

PÄIVI KRISTIINA KARJALAINEN

PELVIC FLOOR SYMPTOMS IN WOMEN UNDERGOING PELVIC ORGAN PROLAPSE SURGERY

PELVIC FLOOR SYMPTOMS IN WOMEN UNDERGOING PELVIC ORGAN PROLAPSE SURGERY

Päivi Kristiina Karjalainen

PELVIC FLOOR SYMPTOMS IN WOMEN UNDERGOING PELVIC ORGAN PROLAPSE SURGERY

To be presented by permission of the Faculty of Health Sciences,

University of Eastern Finland for public examination

in Hospital Nova of Central Finland, Main Auditorium, Jyväskylä,

on February 23rd, 2024, at 12 o'clock noon

Publications of the University of Eastern Finland

Dissertations in Health Sciences

No 804

Department of Obstetrics and Gynecology, Institute of Clinical Medicine,
Faculty of Health Sciences,

University of Eastern Finland, Kuopio

2024

Series Editors

Research Director Jari Halonen, M.D., Ph.D., M.A. (education)
Institute of Clinical Medicine, Surgery
Faculty of Health Sciences

Professor Ville Leinonen, M.D., Ph.D.
Institute of Clinical Medicine, Neurosurgery
Faculty of Health Sciences

Professor Tarja Malm, Ph.D.
A.I. Virtanen Institute for Molecular Sciences
Faculty of Health Sciences

Lecturer Veli-Pekka Ranta, Ph.D.
School of Pharmacy
Faculty of Health Sciences

Lecturer Tarja Välimäki, Ph.D.
Department of Nursing Science
Faculty of Health Sciences

PunaMusta
Kuopio, 2024
Distributor: University of Eastern Finland
Kuopio Campus Library

ISBN: 978-952-61-5105-2 (print)
ISBN: 978-952-61-5106-9 (PDF)
ISSNL: 1798-5706
ISSN: 1798-5706
ISSN: 1798-5714 (PDF)

Author's address: Department of Obstetrics and Gynaecology
Wellbeing Services County of Central Finland /
Hospital Nova of Central Finland
JYVÄSKYLÄ
FINLAND

Doctoral programme: Doctoral Programme in Clinical Research

Supervisors: Professor Anna-Maija Tolppanen
School of Pharmacy
University of Eastern Finland
KUOPIO, FINLAND

Adjunct Professor Kari Nieminen
Department of Obstetrics and Gynaecology
Tampere University Hospital
Faculty of Medicine and Health Technology
Tampere University
TAMPERE, FINLAND

Adjunct Professor Jyrki Jalkanen
Wellbeing Services County of Central Finland
JYVÄSKYLÄ, FINLAND
Faculty of Medicine and Health Technology
Tampere University
TAMPERE, FINLAND

Reviewers: Adjunct Professor Seija Ala-Nissilä
Department of Obstetrics and Gynaecology
Turku University Hospital
University of Turku
TURKU, FINLAND

Professor Martin Rudnicki
Department of Obstetrics and Gynaecology
Odense University Hospital
ODENSE, DENMARK

Opponent: Professor Tomi Mikkola
Department of Obstetrics and Gynaecology
Helsinki University Hospital
University of Helsinki
HELSINKI, FINLAND

Karjalainen, Päivi
Pelvic floor symptoms in women undergoing pelvic organ prolapse surgery
Kuopio: University of Eastern Finland
Publications of the University of Eastern Finland
Dissertations in Health Sciences 804. 2024, 129 p.
ISBN: 978-952-61-5105-2 (print)
ISSNL: 1798-5706
ISSN: 1798-5706
ISBN: 978-952-61-5106-9 (PDF)
ISSN: 1798-5714 (PDF)

ABSTRACT

One in eight Finnish women undergoes pelvic organ prolapse surgery in her lifetime, primarily due to vaginal bulging. Bladder and bowel symptoms are also common, but the extent to which they result from the anatomical defect of prolapse remains unclear, leading to diverse management approaches.

This doctoral thesis investigates the association between prolapse and overactive bladder, stress urinary incontinence, and anorectal symptoms and it provides tools for gauging the impact of prolapse surgery. Nearly 3,000 prolapse patients were observed for two years postoperatively. The Pelvic Floor Distress Inventory-20 (PFDI-20) was used as the outcome measure.

Overactive bladder symptoms and their postoperative improvement were more pronounced in anterior and apical prolapse than in the posterior compartment. The preoperative degree or compartment of prolapse minimally influenced the stress urinary incontinence status or its postoperative changes. For half of the women, pre-existing stress incontinence improved or resolved postoperatively; bothersome *de novo* symptoms were rare. Severe preoperative symptoms predicted persistent stress incontinence, and older age was a risk factor for *de novo* symptoms. Obstructed defecation correlated with the posterior vaginal wall stage, and

a greater improvement was noted after posterior compartment surgery than after corrections in other compartments.

Minimal important difference and patient acceptable symptom state estimates were established to interpret changes in the PFDI-20 and its subscale, the Pelvic Organ Prolapse Distress Inventory (POPDI-6). Mean differences of 24 points in the PFDI-20 score and 11 points in the POPDI-6 score denote clinically meaningful improvements. Postoperative PFDI-20 scores ≤ 60 and POPDI-6 scores ≤ 17 indicate acceptable symptom states after surgery.

These findings advance our understanding of pelvic organ prolapse and guide realistic treatment expectations. Overactive bladder symptoms frequently improve after prolapse surgery, particularly following anterior or apical compartment procedures. For many patients, prolapse surgery is the only procedure needed to address stress incontinence. Women with obstructed defecation can anticipate improvements after posterior vaginal wall prolapse correction. However, residual bladder and bowel symptoms remain prevalent, likely due to these symptoms' multifaceted nature.

Keywords: pelvic organ prolapse, pelvic organ prolapse surgery, pelvic floor, overactive bladder, stress urinary incontinence, obstructed defecation, anal incontinence, minimal important difference, patient acceptable symptom state

Karjalainen, Päivi
Lantionpohjan toimintaan liittyvät oireet laskeuman vuoksi leikattavilla naisilla
Kuopio: Itä-Suomen yliopisto
Publications of the University of Eastern Finland
Dissertations in Health Sciences 804. 2024, 129 s.
ISBN: 978-952-61-5105-2 (nid.)
ISSNL: 1798-5706
ISSN: 1798-5706
ISBN: 978-952-61-5106-9 (PDF)
ISSN: 1798-5714 (PDF)

TIIVISTELMÄ

Joka kahdeksas suomalainen nainen päätyy elämänsä aikana laskeumaleikkaukseen, tavallisimmin häiritsevän emätinpullistumaoireen vuoksi. Suurin osa potilaista raportoi lisäksi rakko- ja suolioireita, mutta näiden syy-seuraussuhteet ovat edelleen epäselviä, mikä näkyy vaihtelevina hoitokäytäntöinä.

Tämän väitöskirjatutkimuksen tavoitteena oli tutkia laskeuman ja yliaktiivisen rakon, ponnistusvirtsankarkailun sekä suolioireiden välisiä suhteita. Lisäksi tarkoituksena oli tuoda käyttöön työkaluja laskeumakirurgian vaikutusten arviointiin. Tutkimuskohortti koostui lähes 3 000 laskeumaleikkauksesta, joita seurattiin kahden vuoden ajan leikkauksen jälkeen. Oireet mitattiin Pelvic Floor Distress Inventoryn lyhyttä versiota (PFDI-20) käyttäen.

Yliaktiivisen virtsarakon oireet olivat yleisempiä ja niiden paraneminen leikkauksen jälkeen oli selvempää emättimen etuseinämän ja apeksin laskeumassa kuin takaseinämän laskeumassa. Laskeuman sijainti ja aste selittivät vain vähän ponnistuskarkailun esiintyvyydestä ennen leikkausta ja muutoksesta leikkauksen jälkeen. Ennen leikkausta esiintyvä ponnistuskarkailu parantui osittain tai kokonaan puolella naisista, ja hankala-asteiset *de novo* -oireet olivat harvinaisia. Karkailun vaikea-asteisuus ennusti oireen jatkumista leikkauksen jälkeen ja korkea ikä *de*

novo -oiretta. Ulostamisvaikeus oli riippuvainen takaseinämän laskeuman asteesta, ja oireiden lievittyminen oli merkittävämpää takaseinämän korjaamisen jälkeen verrattuna leikkauksiin, joissa sitä ei korjattu.

Neljännessä osatyössä määritettiin kynnysarvoja PFDI-20-kyselylle ja sen Pelvic Organ Prolapse Distress Inventory (POPDI-6) -osiolle. 24 pisteen eroa PFDI-20-pistemäärissä ja 11 pisteen eroa POPDI-6-pistemäärissä voidaan pitää kliinisesti merkittävänä. PFDI-20-pistemäärää ≤ 60 ja POPDI-6-pistemäärää ≤ 17 voidaan käyttää määrittämään hyväksyttävää oiretilaa leikkauksen jälkeen.

Tulokset syventävät ymmärrystämme laskeumasta ja sen vaikutuksista oireisiin sekä auttavat asettamaan realistisia hoitotavoitteita. Yliaktiivisen rakon oireet paranevat usein, etenkin etuseinämän ja apikaalisen laskeuman korjauksen jälkeen. Useissa tapauksissa ponnistusvirtsankarkailuleikkauksen yhdistäminen laskeumaleikkaukseen ei ole tarpeen. Useimmiten ulostamisvaikeus lievenee takaseinämän laskeuman korjaamisen jälkeen. Osa hankalista rakko- ja suolioireista kuitenkin jatkuu leikkauksen jälkeen, mikä liittynee oireiden monisyiseen etiologiaan.

Avainsanat: laskeuma, laskeumakirurgia, lantionpohja, yliaktiivinen rakko, ponnistusvirtsankarkailu, ulostamisvaikeus, ulosteenkarkailu, pienin kliinisesti merkittävä ero, potilaan hyväksymä oiretilanne

To my family

ACKNOWLEDGEMENTS

I would like to express my gratitude to all those who supported and encouraged me in making this dissertation a reality.

The FINPOP study was organised and funded by the Finnish Society for Gynecological Surgery. Their contribution has been indispensable, and I deeply acknowledge its invaluable significance. I extend my sincere appreciation to the more than 3,500 women who volunteered for the FINPOP study, the contact persons across 41 hospitals, and the numerous gynaecologists involved in recruitment and surgeries.

The successful execution of this work, carried out alongside clinical commitments, was made possible through research leave grants from the Finnish Cultural Foundation, the Finnish Medical Foundation, and the State Research Funding/Hospital District of Northern Savo.

This doctoral study was undertaken within the University of Eastern Finland Doctoral Programme in Clinical Research. I am privileged to have pursued this research under the guidance of Anna-Maija Tolppanen, the professor of effectiveness in healthcare. I am grateful to you for so many things: your academic mentorship, expertise, encouragement, kindness, unwavering readiness to provide help, and concrete step-by-step instructions on statistics. I extend my deepest gratitude to my two other supervisors, Adjunct Professors Jyrki Jalkanen and Kari Nieminen, not only for their mentorship in research but also for their roles as teachers of clinical and surgical skills. I appreciate the time you've dedicated, the advice you've provided, and the support you've offered across various aspects of life. Your relentless belief in me, coupled with gentle encouragement, has helped me get to where I am today.

My co-authors, the formidable FINPOP sisters Nina Mattsson, MD, PhD, and Olga Wihersaari, MD, deserve heartfelt thanks for their irreplaceable peer support. It is essential to recognise Nina's vital role in initiating the entire process; without her efforts, attaining this point would not have been possible. With Olga, I am confident that the FINPOP story is bound to have beautiful sequels.

I am sincerely thankful to Professor Martin Rudnicki and Adjunct Professor Seija Ala-Nissilä, the preliminary examiners of this thesis, for generously dedicating their precious personal time to provide constructive reviews. Their insightful suggestions undeniably enhanced the quality of this thesis.

I want to express my appreciation to the esteemed Professor Tomi Mikkola for accepting the role of opponent at the public examination of my doctoral thesis.

As a proud member of the gynaecology collegium in the Department of Obstetrics and Gynaecology at Hospital Nova of Central Finland, I want to express my special gratitude to Adjunct Professor Pauliina Aukee, the current head, for her unfailing support in all my endeavours, be it in research or clinical work – it means a lot to me. Many thanks to Jaana Seikkula and Kirsi Väyrynen for their exceptional flexibility and understanding regarding my comings and goings when constructing challenging rosters. I am fortunate to work alongside the best colleagues in the world. I cherish the collegiality and friendship we share. Thank you all for your continuous help, standing in when I have been engaged in research work, and for appreciating me just the way I am. I also want to express a separate note of gratitude to my idol, Marja-Liisa Eloranta, for imparting invaluable surgical skills – I am forever indebted to her.

I highly value the experience gained during my years of specialist and subspecialist training at Kainuu Central Hospital, Oulu University Hospital, Monash Health Melbourne, and Tampere University Hospital. The journey has been enriched by the guidance of numerous brilliant mentors and the camaraderie of talented fellow doctors, making it impossible to list them all here. I am grateful for the skills and knowledge acquired and for the lasting friendships forged along the way; collectively, they have played a major role in both professional and personal growth. The fellowship period in Melbourne, in Professor Anna Rosamilia's pelvic floor unit, was truly unique, providing our entire family with an adventure on the opposite side of the globe. Additionally, I've had the opportunity to participate in research outside of FINPOP, collaborating with Professors Anna Rosamilia, Caroline Gargett, and Kari Tikkinen; these experiences have greatly contributed to my development as a researcher.

Friends have been an invaluable source of emotional strength amidst the demands and busyness of recent years. Moments together have helped me recharge, offered perspective, and reminded me of life's true priorities. Just a few examples of cherished memories include the annual girls' weekends with the Ylivieska gang, ad hoc fiestas with the Saarenlahdentie 18 commune, Pummin Suunta training camps, Villa's Christmas parties, and orienteering weeks at home and abroad. The bonds formed during medical school remain exceptionally dear to me, and I trust that there will be more opportunities for us to spend time together in the future.

I cannot express enough gratitude to my parents, Sinikka and Pentti Näpänkangas, for their lifelong support, love, care, and assistance in every request I've made. Your endless trust in me means the world. My dear

brothers, Juha and Antti, and your families, I am extremely thankful for having you in my life. The extended family from my better half's side also holds a special place in my heart; thank you for your support and for bringing joy into my life. The marvellous au pairs we have been fortunate to have with us have undeniably been a huge practical help, but even more importantly, they have immensely enriched the life of our family.

The most profound thank you belongs to my beloved family for standing by me throughout these challenging years. Juggling research, clinical work, and motherhood has not always been easy. Linnea, Anttijussi, and Ohto, I love you more than words can express, and I apologise for you having to share your mother's time with all of her ambitions. At the same time, I recognise that you have grown into independent individuals who are unafraid to pursue their dreams. You are all remarkably talented and, most importantly, possess beautiful hearts. I couldn't be prouder of you. Our kitchen table research hub now has a third strong member – I also thank Linnea for her technical assistance.

Teemu, completing this project wouldn't have been possible without you. Thank you for your mental and financial support, as well as your assistance with methodology and revision. I appreciate your courageous help, even when confronted with my occasional suspicions. Thanks for taking the lead at home when I was unavailable. I admire your exceptional energy, intelligence, and determination. Simultaneously, I value your ability to treat all people equally and your selfless willingness to help others. I love you very much, and I am immensely grateful to share my life with someone as remarkable as you.

Muurame, January 2024

Päivi Karjalainen

LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications:

I Karjalainen PK, Tolppanen AM, Mattsson NK, Wihersaari OAE, Jalkanen JT, Nieminen K. Pelvic organ prolapse surgery and overactive bladder symptoms – a population-based cohort (FINPOP). Int Urogynecol J. 2022;33(1):95-105.

II Karjalainen PK, Tolppanen A-M, Wihersaari O, Nieminen K, Mattsson NK, Jalkanen JT. Changes in stress urinary incontinence symptoms after pelvic organ prolapse surgery: A nationwide cohort study (FINPOP). Manuscript.

III Karjalainen PK, Mattsson NK, Nieminen K, Tolppanen AM, Jalkanen JT. The relationship of defecation symptoms and posterior vaginal wall prolapse in women undergoing pelvic organ prolapse surgery. Am J Obstet Gynecol. 2019;221(5):480.e1-480.e10.

IV Karjalainen PK, Mattsson NK, Jalkanen JT, Nieminen K, Tolppanen AM. Minimal important difference and patient acceptable symptom state for PFDI-20 and POPDI-6 in POP surgery. Int Urogynecol J. 2021;32(12):3169-3176.

The publications were adapted with the permission of the copyright owners.

In addition, some previously unpublished, complementary data are presented.

CONTENTS

ABSTRACT **7**

TIIVISTELMÄ **9**

ACKNOWLEDGEMENTS **13**

1 INTRODUCTION **23**

2 REVIEW OF THE LITERATURE **25**

2.1 Pelvic organ prolapse 25

2.1.1 Definition 25

2.1.2 Epidemiology 25

2.1.3 Functional anatomy of pelvic floor support 27

2.1.4 Pathophysiology and risk factors 30

2.2 Pelvic organ prolapse and associated symptoms 31

2.2.1 Tissue protrusion symptoms 32

2.2.2 Voiding dysfunction 33

2.2.3 Overactive bladder symptoms 33

2.2.4 Stress urinary incontinence 35

2.2.5 Anorectal symptoms 39

2.2.6 Sexual dysfunction and pain 43

2.3 Evaluation of pelvic organ prolapse 44

2.3.1 Quantification 44

2.3.2 Ancillary testing 45

2.4 Non-surgical management of pelvic organ prolapse 46

2.5 Surgical treatment of pelvic organ prolapse 48

2.5.1 Outcome assessment 49

2.5.2 Anterior compartment reconstructive surgery 50

2.5.3 Apical compartment reconstructive surgery 51

2.5.4 Posterior compartment reconstructive surgery 52

2.5.5 Obliterative surgery 53

2.6 Patient-reported outcome measures 54

2.6.1 Pelvic Floor Distress Inventory -20 (PFDI-20) 54

2.6.2 Minimal important difference (MID) 55

2.6.3 Patient acceptable symptom state (PASS) 56

2.7 Rationale for this thesis 57

3 AIMS OF THE STUDY 59

4 PARTICIPANTS AND METHODS 61
4.1 Design, setting, and participants 61
4.2 Study flow 61
4.3 Data sources and collection 63
4.4 Outcome measures and statistical analyses 64
4.4.1 Study I 65
4.4.2 Study II 65
4.4.3 Study III 66
4.4.4 Study IV 67
4.5 Ethical considerations 68

5 RESULTS 69
5.1 Characteristics of the study populations 69
5.2 Baseline symptom prevalence 70
5.3 Overactive bladder symptoms (Study I) 72
5.4 Stress urinary incontinence symptoms (Study II) 76
5.5 Anorectal symptoms (Study III) 79
5.6 MID and PASS for PFDI-20 (Study IV) 82

6 DISCUSSION 85
6.1 The role of prolapse in overactive bladder symptoms 85
6.2 Changes in stress urinary incontinence symptoms after prolapse surgery 86
6.3 The role of prolapse in obstructed defecation and other anorectal symptoms 89
6.4 Interpreting PFDI-20 scores using MID and PASS 90
6.5 Methodological considerations 92
6.6 Clinical implications 95
6.7 Future considerations 96

7 CONCLUSIONS 99

REFERENCES 101

APPENDICES 131

ABBREVIATIONS

BMI	Body Mass Index
CI	Confidence interval
EAS	External anal sphincter
FI	Faecal incontinence
IAS	Internal anal sphincter
ICS	International Continence Society
IUGA	International Urogynecological Association
LUTS	Lower urinary tract symptoms
MID	Minimal important difference
MRI	Magnetic resonance imaging
NNT	Number needed to treat
OAB	Overactive bladder
OECD	Organization for Economic Cooperation and Development
OR	Odds ratio
PASS	Patient acceptable symptom state
PFDI-20	The short from of Pelvic Floor Distress Inventory
PGI-I	Patient Global Impression of Improvement
POP	Pelvic organ prolapse
POPDI-6	Pelvic Organ Prolapse Distress Inventory -6
POP-Q	Pelvic Organ Prolapse Quantification
PROM	Patient reported outcome measure
RCT	Randomised controlled trial
ROC	Receiver operating characteristic

RR	Relative risk
SD	Standard deviation
SUI	Stress urinary incontinence
TVL	Total vaginal length
UUI	Urgency urinary incontinence

1 INTRODUCTION

Pelvic organ prolapse (POP) is a common condition in which pelvic organs herniate into or out of the vaginal canal.[1] It primarily results from vaginal birth injury, ageing, and genetic predisposition.[2,3] POP can markedly diminish an individual's quality of life by adversely affecting her physical and emotional well-being.[4] In Finland, approximately 13% of women undergo surgical treatment for POP.[5]

Pelvic floor symptoms vary widely in women with POP from complete absence to multiple concurrent complaints related to tissue protrusion, bladder, bowel, and sexual function. Vaginal bulging is the most prevalent and specific indicator of POP.[6] Symptoms originating from the lower urinary tract and anorectum are frequently reported, but directly linking these symptoms to POP is not straightforward since they are also prevalent in the general population.[6,7] POP can co-occur with a specific pelvic floor symptom for various reasons, including causation, a shared aetiology, and mere coincidence.[6]

Previous research has identified weak to non-existent correlations between overactive bladder (OAB) and obstructed defecation symptoms' prevalence and prolapse extent, raising doubts about a causal connection.[7–9] POP surgery seems to relieve these symptoms in certain cases, but residual symptoms and even symptom deterioration can occur. This uncertainty is reflected in the debated role of POP surgery in addressing these symptoms.[8–10]

Many women who undergo POP surgery report pre-existing stress urinary incontinence (SUI), and the potential for new-onset SUI after the procedure generates significant concern.[11] Predictors of postoperative SUI are poorly recognised, and management strategies range from combining SUI surgery with POP surgery for all patients to selectively combining it in individual cases or not at all.[11]

POP surgery's primary goal is to alleviate prolapse-related symptoms and improve patients' quality of life.[12] Limited evidence is available on the comparative effectiveness of different treatment approaches.[13] Due to the

weak correlation between anatomy and symptoms, anatomical outcomes are insufficient for assessing treatment success.[12] Patient-reported outcome measures (PROMs), such as the short form of Pelvic Floor Distress Inventory (PFDI-20), are vital to identify patients' perspectives.[13,14] However, interpreting PROM score differences is challenging; their significance for patients is not readily apparent.[15]

This thesis focuses on advancing the understanding of POP's connection with pelvic floor symptoms, specifically OAB, SUI, and anorectal symptoms. Identifying symptoms that depend on anatomy and improve after surgery delineates the clinical picture, facilitates effective patient counselling, and generates new hypotheses to refine surgical POP management. Furthermore, the thesis establishes meaningful thresholds for interpreting PFDI-20 score differences that can be applied in research assessing the effectiveness of POP surgery.

2 REVIEW OF THE LITERATURE

2.1 PELVIC ORGAN PROLAPSE

2.1.1 Definition

POP is a condition characterised by weakened pelvic support, resulting in the descent of at least one vaginal compartment along with neighbouring organs. The International Continence Society (ICS) and International Urogynecological Association (IUGA) define POP primarily as an anatomical change, but a definite diagnosis ideally involves symptom correlation.[1] However, no particular symptom or degree of descent is specified, reflecting the challenge in establishing clear criteria.

Anterior compartment prolapse is the herniation of the anterior vaginal wall. It is typically associated with the bladder's descent (a cystocele). In apical compartment prolapse, the uterus - or, post-hysterectomy, the vaginal vault – descends. The result is uterine or vault prolapse, respectively. Posterior vaginal wall prolapse commonly involves a rectocele, the rectum's protrusion into the vagina. It can also involve an enterocele, a herniation of the peritoneal sac containing omental fat (a peritoneocele), the small bowel (an enterocele), or the sigmoid colon (a sigmoidocele).[1,16] More broadly, posterior compartment disorders also include conditions such as rectal prolapse and internal rectal prolapse, which is also known as intussusception.[16] (Figure 1)

2.1.2 Epidemiology

The reported prevalence of POP varies significantly, depending on its definitions, diagnostic measures, and populations.[17] Clinical examinations reveal pelvic support loss at least 1 cm above the hymen (POP-Q Stage 2 or higher) in 37–70% of the general female population.[18–24] Prolapse extending to or beyond the hymenal level affects 7% of women aged 18–83 years[20] and 18% of those aged 59–78 years.[18] Prevalences based solely on a

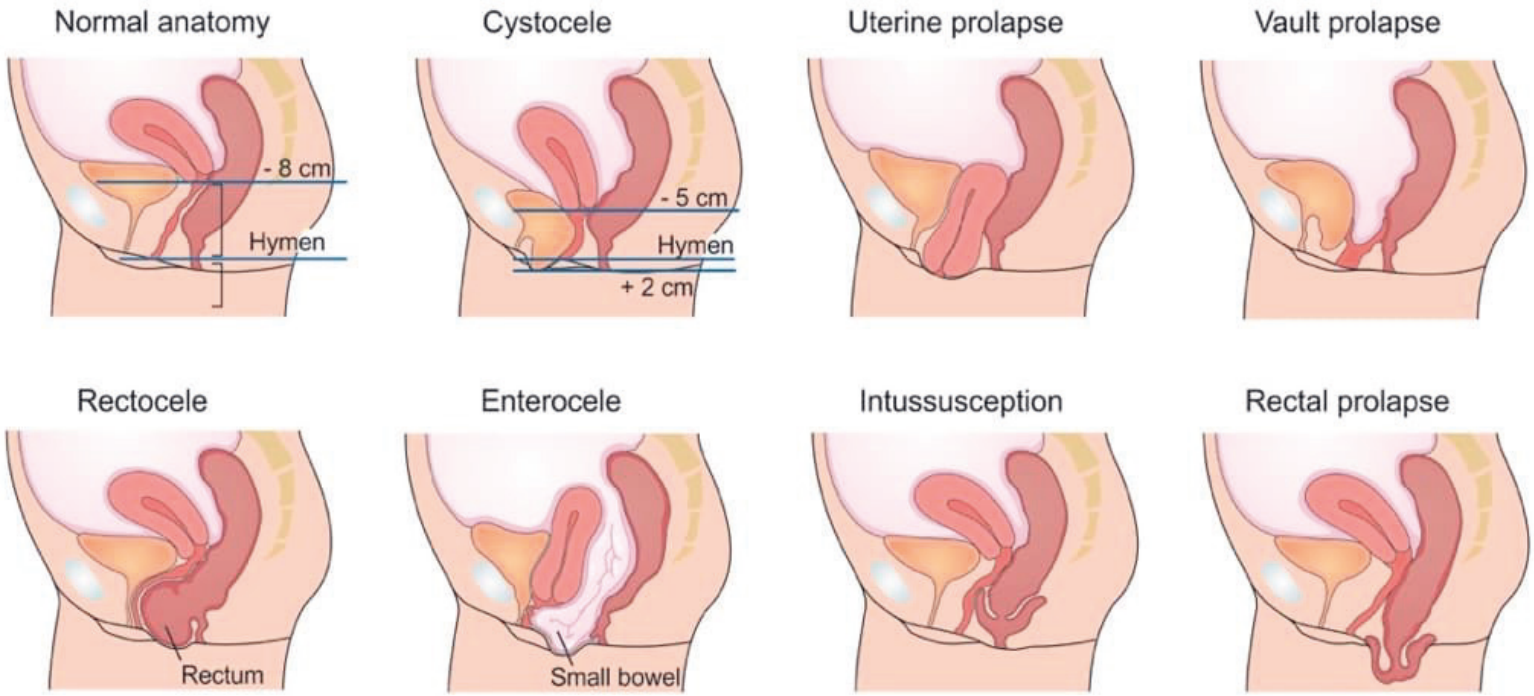


Figure 1. Different types of pelvic organ prolapse. Republished with permission from the Finnish Medical Journal.[25] Copyright Sole Lätti.

vaginal bulge symptom range between 3% and 11%, with a lower prevalence observed in studies including young women.[17,26–29]

The most frequent prolapse site is the anterior compartment, while posterior compartment prolapse is more common than apical prolapse.[26,30,31] In approximately two-thirds of cases, prolapse affects more than one compartment.[27]

Limited data on POP's incidence and natural course are available.[17] Contrary to prior beliefs, its progression does not appear inevitable.[30,32–34] In a five-year study of 160 symptomatic POP patients, 47% had a stable stage, 40% regressed, and 13% progressed.[33] Another study of 64 women with symptomatic POP, half of whom with at least Stage 3 prolapse, noted that 81% did not show progression, and one-third opted for intervention over a median follow-up period of 16 months.[34]

POP is one of the most common reasons for gynaecological surgery, but its rates vary significantly between countries.[35,36] In 2012, data from 15 Organization for Economic Cooperation and Development (OECD) countries showed a fivefold difference, with rates ranging from 0.5 to 2.6 procedures per 1,000 women.[36] In Finland, the rate was 1.3 per 1,000 women in 2009.[5] Women's estimated lifetime risk of undergoing POP surgery is as high as 19% in some countries;[37,38] in Finland, it stands at 13%.[39]

2.1.3 Functional anatomy of pelvic floor support

The female pelvic floor is a complex anatomical structure that provides critical support for the pelvic organs and facilitates the essential functions of urination, defecation, sexual activity, and childbirth. Pelvic floor support relies on both the organs' connective tissue suspension and contributions from the levator ani muscle, regulated via both involuntary and voluntary neural mechanisms.[40]

The supportive connective tissues form a continuous sheet from the perineal body to the vaginal apex. At the apex, the cervix and upper vagina attach to the bony pelvis through denser collagen aggregations, the

uterosacral and cardinal ligaments. The mid-vagina connects laterally to the tendinous arches. The distal vagina merges with surrounding structures, including the urethra, levator ani muscle, and perineal body, which further attach to the ischiopubic rami via the perineal membrane.[41,42] (Figure 2)

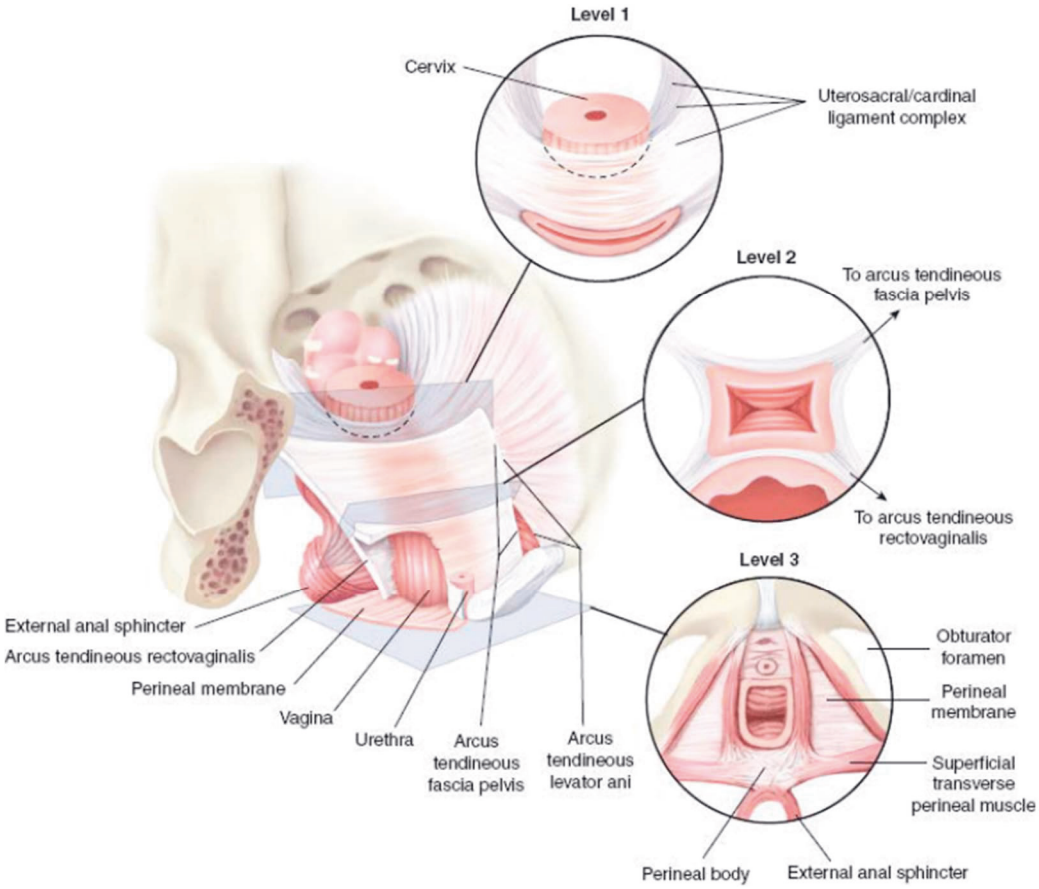


Figure 2. Levels of pelvic floor connective tissue support suggested by DeLancey. Republished with permission from the Cleveland Clinic Journal of Medicine.[43]

The levator ani muscle comprises three main components: the pubococcygeus, puborectalis, and iliococcygeus muscles. These muscle fibres form a U-shape around the levator hiatus, which serves as the opening for the urethra, vagina, and rectum and represents the largest

potential hernial portal in the human body.[40,44,45] (Figure 3) The levator ani muscle maintains a continuous state of contraction, briefly relaxing only during voiding, defecation, and parturition. This lifting force creates a horizontal shelf for the organs, keeps the hiatus closed, and contributes to urinary and faecal continence. Additionally, the muscle reflexively responds to sudden increases in abdominal pressure, and it can also be intentionally contracted.[40,46] Its innervation originates from the sacral nerve roots (S3–S5) and travels along the pelvic floor's cranial surface.[47,48]

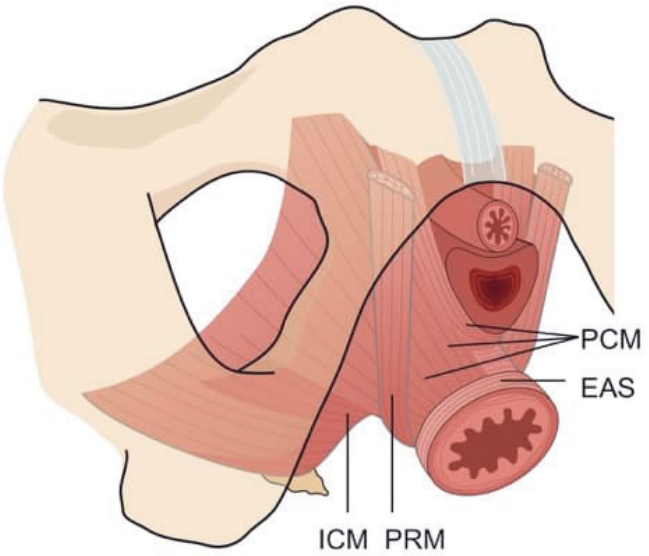


Figure 3. Schematic view of the levator ani muscle from below. EAS, external anal sphincter; ICM, iliococcygeus muscle; PCM, pubococcygeus muscle; PRM, puborectalis muscle. Copyright Sole Lätti

The pelvic floor function has a dual nature. On one hand, interdependent connective tissue features and the broad levator ani muscle operate as a unified cohesive unit. On the other hand, it comprises distinct structures such as the urethral and anal sphincters, each with unique roles and neural control levels.[49] For example, while the pudendal nerve innervates the urethral and anal sphincters, it does not innervate the levator ani muscle.[47]

2.1.4 Pathophysiology and risk factors

The pathophysiology of POP is complex and likely involves combined pelvic floor muscle and connective tissue failure.[42,50] When the levator ani muscle maintains a normal tone, the connective tissues undergo minimal tension. Muscle weakness, whether from trauma or denervation, can widen the levator hiatus, allowing the pelvic organs to descend and exert pressure on connective tissues.[3,42] Lax connective tissues can lead to a similar imbalance.[42] Mid-level connective tissue defects result in cystoceles and rectoceles, and the loss of upper suspensory fibres leads to apical prolapse, often in varying combinations that contribute to diverse clinical problems.[3,41]

Most genital prolapse cases are thought to result from birth injury and subsequent ageing in genetically predisposed women.[2] According to a lifespan model, these factors – along with lifestyles and coexisting medical conditions – interact and accumulate during different stages of women's lives.[49]

Primiparous women have three to five times higher odds of developing POP symptoms and clinically-diagnosed POP compared to nulliparous women.[51] Nulliparous women constitute only 0.4–1.9 % of large prolapse surgery cohorts.[52–54] Caesarean delivery does not seem to increase the prolapse risk compared to nulliparity.[51] Multiparity further elevates the risk, and forceps delivery raises it compared to spontaneous labour.[51,55] Vaginal delivery can contribute to POP through mechanisms such as levator ani muscle deterioration due to avulsion injury, overdistension trauma, or nerve injury, as well as connective tissue failure.[2,3,42,55–58]

The likelihood of having POP increases by 10% in each successive year of life.[55,59] In Finland, the highest prolapse surgery rate occurs among women aged 70–79.[5] Several mechanisms linking ageing and POP are under investigation.[59]

A positive family history elevates the prolapse risk by two to three times.[60,61] The potential genetic variations associated with POP are linked to either connective tissue or sex hormone activity.[62]

POP can also affect young and nulliparous women, indicating other factors' involvement.[63] Causes may differ for the anterior and apical compartments compared to the posterior compartment, which seems less influenced by childbirth.[2] In young women, underlying medical conditions such as connective tissue diseases or pelvic floor nerve damage might be likelier.[64] POP's higher prevalence alongside joint hypermobility, Marfan syndrome, and Ehlers–Danlos syndrome further evidences connective tissue disorders' role in POP's pathogenesis.[65,66] Hispanic and European women are more susceptible to POP than their African and Asian counterparts.[3]

POP's associations with conditions that elevate intra-abdominal pressure – such as obesity, chronic cough, constipation, and occupations involving heavy lifting – have been established.[67] Obesity may specifically elevate the posterior compartment prolapse risk.[30,68]

Hysterectomy probably increases the risk of POP.[3,69] Nonetheless, for women undergoing hysterectomies for indications unrelated to prolapse, the absolute risk of requiring subsequent POP surgery within ten years remains modest at 1.6%, and posterior compartment prolapse may be more prevalent.[70,71]

2.2 PELVIC ORGAN PROLAPSE AND ASSOCIATED SYMPTOMS

POP can manifest in various ways. For some women, prolapse is found incidentally during pelvic examinations without any experienced symptoms. Others report multiple concurrent pelvic floor symptoms. Women with the same prolapse stage may exhibit varying degrees of symptom severity, reflecting a poor correlation between anatomy and most of the potentially POP-related symptoms.[6] The hymen appears to be a significant threshold for symptom development; the average number of symptoms per subject increases from fewer than one to more than one when the leading edge extends beyond this level.[19]

The symptoms commonly attributed to POP encompass four categories: tissue protrusion symptoms, lower urinary tract symptoms (LUTSs), anorectal symptoms, and sexual problems. A study involving 308 women

referred for POP treatment found that at least one tissue protrusion, urinary symptom, or anorectal symptom was reported by 85%, 92%, and 59% of these patients, respectively.[72] Severe morbidity is rare, but these symptoms can significantly worsen patients' quality of life, body image, and subjective well-being.[4,73,74]

Except for vaginal bulging, none of the associated symptoms are exclusive to POP; they can also occur with normal pelvic support. Various pelvic floor disorders frequently co-occur.[75] A community-based study found that 80% of women with SUI or OAB, 48% with faecal incontinence (FI), and 69% with POP also reported at least one other pelvic floor disorder.[76] Consequently, differentiating between possible prolapse symptoms and symptoms likely to stem from coexisting lower urinary or gastrointestinal tract dysfunction is challenging.[6]

The following scenarios explain, in most circumstances, the relationship between POP and a specific pelvic floor symptom:[6]

1) POP is the symptom's direct cause.
2) POP contributes to or intensifies the symptom.
3) POP and the condition underlying the symptom share a common pathogenic mechanism.
4) The symptom or its source contributes to POP's development.
5) No causal relationship exists, but both conditions are common and, therefore, often coexist.

2.2.1 Tissue protrusion symptoms

The only symptom that can definitely be directly attributed to POP is the presence of a protrusion, or bulge, outside the vagina, as reported by the patient and confirmed during clinical examination. Two-thirds of women scheduled for POP surgery identify vaginal bulging as their most bothersome symptom.[52] A palpable or visible bulge is also the symptom that most consistently corresponds with clinical examination findings.[20,77–80] However, even this symptom's correlation with the degree of prolapse is moderate at best – 0.38 to 0.58 in populations with urogynaecological conditions.[77,78,80] Although the symptom is specific (86–100%),[78,79,81]

meaning that it is a reliable prolapse indicator, its sensitivity is poor. In the urogynaecological population, 70% of women with POP at or beyond the hymen report bothersome bulges, versus only 16–35% of women in the general population. Even some women with the most severe prolapse degrees do not report this symptom.[78–81] Less specific symptoms, such as pelvic pressure and heaviness, have a much weaker correlation with the degree of vaginal support.[6]

2.2.2 Voiding dysfunction

Voiding difficulty is the LUTS most consistently correlated with worsening POP stages.[7,77,79,82] Around half of women who seek POP treatment at specialist clinics report voiding dysfunction,[7] and around 90% of preoperative voiding dysfunction resolves after POP surgery.[83,84] The anterior vaginal wall's downward displacement, leading to urethral kinking and bladder outlet obstruction, is widely considered the primary mechanism for voiding dysfunction in POP.[85–88]

Voiding dysfunction can present as straining to void, hesitancy in starting to urinate, a slow or intermittent stream, feeling incomplete bladder emptying, and urgency to promptly revoid.[89] A specific POP symptom is urinary splinting, which involves manually supporting the prolapsed tissue to facilitate urination.[78] Voiding difficulty can result in elevated postvoid residual volumes, recurrent urinary tract infections, and, in rare cases, urinary retention.[6] Furthermore, hydronephrosis is found in 10–16% of women presenting with POP, and its risk is higher for those with more severe prolapses.[90]

2.2.3 Overactive bladder symptoms

POP's role in OAB symptoms remains debated. While some researchers have suggested treating even minor POP cases to address OAB symptoms, others have argued that the coexistence of these prevalent conditions is likely coincidental.[7,91,92]

OAB refers to a symptom complex characterised by urinary urgency with or without urgency urinary incontinence (UUI) that is usually

accompanied by urinary frequency and nocturia.[89] The current perspective considers OAB a nonspecific multifactorial symptom syndrome arising from multiple potential pathophysiological mechanisms and contributing factors that likely overlap.[3,93] (Table 1) Its prevalence rises with age, and it is common in both genders; in Finland, 54% of men and 57% of women report urinary urgency.[94]

Table 1. Possible overactive bladder phenotypes, modified from Peyronnet et al.[93]

Phenotyping according to the background mechanism or origin	**Phenotyping according to the pathophysiological cofactors**
Myogenic (detrusor muscle)	Metabolic syndrome
Urotheliogenic (uro- / suburothelium)	Affective disorders
Urethrogenic (urethra)	Functional gastrointestinal disorders
Supraspinal (brain / brainstem)	Sex hormone deficiency
	Alterations in urinary microbiota
	Autonomic nervous system dysfunction

The mechanism through which POP might induce urgency is unclear. Theories include the following: bladder outflow obstruction leading to changes in bladder innervation, detrusor muscle, or spinal micturition reflexes; the stimulation of urothelial stretch receptors due to anterior vaginal wall distension; and downward traction of the urethra causing urine's entry into the proximal urethra and initiating the micturition reflex.[8]

Community-based studies have indicated that women with POP are two to six times more likely to experience OAB symptoms compared to those without POP.[76,95–97] OAB symptoms also tend to improve after surgical POP treatment. A review of 18 studies found the relative risk (RR) range for OAB symptoms after POP surgery to be 0.1–1.0 (post-surgery frequency [including *de novo*] vs. pre-surgery frequency), while frequency reductions ranged from 8% to 69%.[8]

Incomplete symptom relief and the emergence of *de novo* symptoms in 5–22% of cases have prompted efforts to identify predictors for

postoperative OAB.[98] The available data on the prognostic value of age, body mass index (BMI), preoperative prolapse stage, and urodynamic markers are inconclusive.[99–107]

Whether OAB symptoms or their improvement are associated with a specific prolapse compartment has also remained unclear. The pathophysiological hypotheses propose that anterior compartment prolapse involving the bladder might result in more OAB symptoms than posterior compartment prolapse. However, while some studies have suggested a correlation between OAB symptoms and the extent of anterior wall prolapse,[22,97,108,109] others have failed to establish a significant link.[79,80,110–115] Only four studies with relatively small sample sizes have investigated the impact of the operated compartment, and they have not consistently demonstrated differences between anterior and posterior procedures.[99,100,116,117]

2.2.4 Stress urinary incontinence

The relationship between POP and SUI is multifaceted. Around half of the women scheduled for POP surgery report preoperative SUI that may persist or resolve after surgery.[118] Yet, up to half of the women without preoperative SUI develop new-onset, *de novo*, SUI after surgery.[118–122]

The coexistence of POP and SUI makes logical sense. SUI occurs when the urethra cannot maintain closure during elevated intra-abdominal pressure due to an impaired sphincteric system (intrinsic sphincter deficiency) or weakened urethral support (urethral hypermobility). The urethral support system includes the same elements that determine the position of the distal anterior vaginal wall, such as the surrounding muscles and fascial tissues. The pathophysiological mechanisms of (neuro)muscular and connective tissue damage, as well as the risk factors, also overlap.[63]

For 29–52% of women with pre-existing SUI, it resolves after POP surgery without concurrent SUI procedures.[118,123–126] One theory proposes that anterior vaginal repair enhances continence by supporting the hypermobile urethro-vesical junction.[127] Integral theory suggests that correcting lax suspensory ligaments strengthens muscle insertion points,

allowing opposing muscle forces to properly close the urethra.[128] Predictive factors for persistent SUI have not been studied extensively. One study identified high baseline symptom severity as a risk factor, while another found no such correlation.[123,126] One study linked low preoperative maximum urethral closure pressure and a short functional urethral length to persistent urodynamic SUI.[129]

The reported incidence of *de novo* SUI after POP surgery varies widely, from 4% to 49%.[118–122,130] This variability may stem from diverse definitions, populations, baseline continence status, surgical techniques, and follow-up durations.

De novo SUI is thought to be associated with correcting preoperative urethral kinking. Pre-surgery, the mechanical obstruction caused by an advancing anterior wall prolapse might mask SUI.[131,132] When surgical correction resolves the kinking, a potentially weakened continence mechanism may be exposed, resulting in *de novo* SUI.[132] (Figures 4A and 4B) While some studies have supported this theory by demonstrating a negative correlation between increasing degrees of anterior wall prolapse and SUI,[114,133] others have not, failing to establish a clinically significant link between POP anatomy and SUI.[22,79,111]

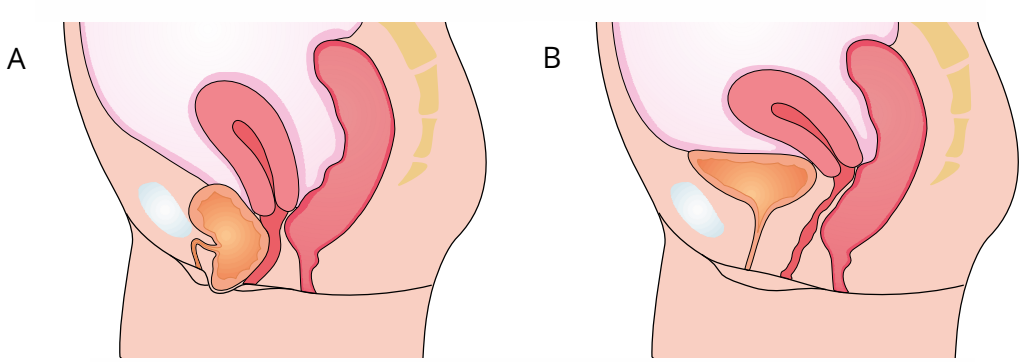


Figure 4. A. Urethral kinking related to specific cystocele types: the proposed mechanism for voiding dysfunction and occult SUI. B. Resolved urethral kinking after POP surgery.[131,132] Copyright Sole Lätti.

To identify patients at risk of *de novo* SUI, international guidelines recommend preoperatively testing continent women with significant anterior or apical prolapses for occult SUI.[13,134] This testing involves a stress test during prolapse reduction,[1] and is found positive in 19–38% of cases.[119,135–137] Its negative predictive value is reasonably good, with a median of 91% (range: 51–100%), but its positive predictive value is no better than chance (median: 40%; range: 0–79%).[138]

A risk calculator assesses an individual patient's risk of *de novo* SUI. Alongside the preoperative reduction stress test, it takes into account the patient's age, BMI, number of vaginal births, UUI symptoms, and diabetes status. The model's internal validation demonstrated a concordance index of 0.73, indicating good discrimination ability, outperforming expert opinion and preoperative stress testing.[139] However, its external validity is questionable, with a concordance index or area under the curve ranging from 0.50 to 0.69.[139–143]

Meta-analyses of randomised controlled trials (RCTs) have shown that combining prolapse surgery with a continence procedure reduces the incidence of postoperative SUI.[11,131] The clearest benefit arises for women with pre-existing SUI; 40% of those who underwent POP surgery alone required further continence surgery compared to 0% for those who underwent combined surgery. For continent women with occult SUI, the rates were 15% versus 1%, compared to 6% versus 2% for those with unknown occult SUI status.[11] (Table 2) Incorporating an SUI procedure into POP surgery for continent women without occult SUI offers no benefit.[131]

Table 2. The need for subsequent SUI surgery after combination surgery (vaginal POP repair and mid-urethral sling) compared to vaginal POP repair alone. Modified from a meta-analysis of RCTs by van der Ploeg et al. [11]

Population	POP and SUI surgery %(*n/N*)	POP surgery only %(*n/N*)	RR (95%CI)	NNT
Preoperative SUI	0% (0/150)	40% (66/165)	0.0 (0–0.2)	2.5
Continent with occult SUI	1% (1/106)	15% (18/123)	0.1 (0.0–0.6)	7.1
Continent with unknown occult SUI status	2% (8/348)	6% (23/360)	0.4 (0.1–1.1)	NS

RR, relative risk; CI, confidence interval; NNT, number needed to treat; NS, non-significant.

Based on these findings, international guidelines recommend a selective strategy combining concomitant continence surgery with POP surgery for women with pre-existing SUI or occult SUI. Conversely, concomitant SUI surgery is not recommended for continent women who test negative for occult SUI.[13,131,134]

Concomitant continence surgery reduces the postoperative SUI risk but is associated with an increased adverse event risk.[11] The meta-analysis reported that serious adverse events – defined as events necessitating an invasive procedure or reoperation or resulting in the failure of at least one organ system or death – were observed in 14% of cases with concurrent SUI surgery versus 8% of those without. The number needed to harm was 17. Serious adverse events that occurred more frequently with combination surgery included bladder perforations, ureteral injuries, mesh exposures, sling-related pain, and long-term voiding difficulties.[11]

Since accurately identifying individuals at risk of postoperative SUI is challenging, some surgeons favour a staged strategy. It entails withholding concurrent continence procedures for all patients and addressing bothersome SUI postoperatively as needed. Thus, unnecessary procedures are avoided, but some patients may require secondary surgeries.[126]

2.2.5 Anorectal symptoms

Women with POP often experience anorectal symptoms, including obstructed defecation and FI. The relationship between POP and these symptoms remains controversial and poorly understood.[144]

When assessing POP's role in anorectal symptoms, understanding the complexity of defecation and faecal continence is essential (Figure 5). These functions rely on a structurally intact gastrointestinal tract and coordinated neural, muscular, hormonal, and cognitive systems.[144,145] Challenges can arise from any disruption to colonic transit, stool consistency, recto-anal sensation, rectal compliance, evacuation completeness, sphincter coordination or strength, or cognitive and neurological function (cerebral, spinal, or peripheral).[145,146]

- Maintaining faecal continence involves the sphincter mechanism: involuntary anal sphincter (IAS), voluntary external anal sphincter (EAS), and puborectalis muscle.
- Defecation begins with colonic peristalsis moving contents into the rectum. Rectal distension triggers the sampling reflex for evaluation of content type. If not ready for defecation, the rectal wall relaxes.
- When ready, the person sits to change the puborectal angle, relaxes EAS and puborectal muscles, and strains to expel faeces. Rectal peristalsis aids in emptying.
- After expulsion, the EAS and puborectalis regain tone for continence at rest.

Figure 5. Overview of defecation physiology, modified from Heitmann et al. [145]

Obstructed defecation

Obstructed defecation is a complaint of difficulty in evacuation marked by symptoms such as straining, the need for manual assistance, and a sensation of incomplete emptying or anorectal blockage.[16] A recent review of cohort studies found obstructed defecation in 53% of women with POP (range: 33–99%); the prevalence was also high in women without POP at 44% (18–59%).[7] The previous literature has not reached a consensus on whether these two conditions co-occur coincidentally due to their high

prevalence or if they share a common cause or have a causal relationship, with POP causing obstructed defecation or vice versa.[9,144]

Plausibly, posterior vaginal wall prolapse could impede rectal emptying by trapping stool in a rectocele pocket. (Figure 1) However, several studies have failed to establish an association between obstructed defecation and the degree of POP generally,[97,147–149] or specifically in the posterior compartment.[97,110,148,150–152] While other studies have suggested a link between obstructed defecation and POP[110,151,153] or posterior POP,[22,77,78,113,133,154–161] these associations have typically been weak.

If anatomical correction resolves obstructed defecation, it could support posterior vaginal wall prolapse as symptoms' cause, but the evidence is inconclusive. In RCTs comparing various surgical methods for rectocele repair, 10–45% of women experienced persistent obstructed defecation.[162–165] Cohort studies have shown varying results, from 87% cure rates to increased symptom levels.[166–168]

The potential causal relationship between POP and obstructed defecation might also be reversed, with straining causing POP. A case-control study provided some evidence for this possibility. Women with POP reported significantly more frequent straining during bowel movements in young adulthood (61%) than women with SUI (30%) and a healthy control group (4%).[169]

Due to this outcome variability and anatomy's unclear link with symptoms, some experts have advocated that surgery has a limited role in correcting obstructed defecation and rectoceles. They stress the importance of thorough differential diagnoses.[170,171] However, causes for difficult defecation are multiple and often overlap, making differentiation challenging.[172] (Figure 6)

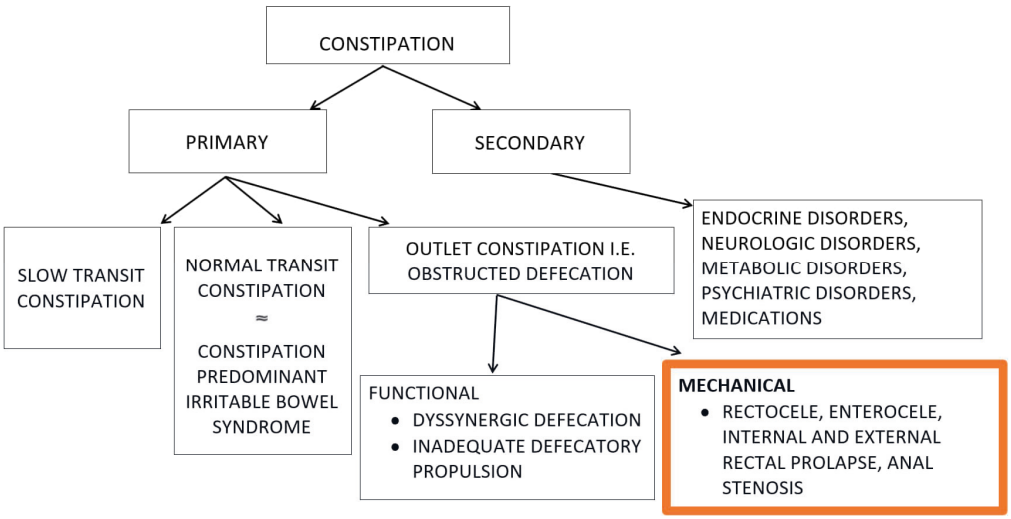


Figure 6. Difficult, infrequent or incomplete defecation (i.e. constipation) can arise from multiple, often overlapping causes. Adapted from [9,171–174]

Highlighting the overlap between constipation disorders, a study involving 90 women with rectoceles and obstructed defecation found that 64% had slow transit times and 45–72% were diagnosed with paradoxical puborectalis contraction. Substantial overlap in structural abnormalities was also observed, with 36% showing signs of intussusception.[170]

Splinting or digitation of stool is the defecation symptom most consistently associated with POP.[175] The terminology is inconsistent, typically referring to pressing on a vaginal bulge, but may also involve rectal digitation or supporting the perineal body or coccygeal area.[1,16] The clinical implications of these manoeuvres may differ, but evidence is lacking; for instance, no studies have compared them between patients with rectocele and intussusception.

Faecal incontinence

The data on POP's relationship with FI are scarce, but they suggest an elevated FI risk in individuals with POP.[151,153,176] FI involves the uncontrolled passage of solid or liquid stool, while anal incontinence includes stool or gas leakage.[177,178] The main types are passive incontinence, urgency

incontinence, and faecal seepage, often with overlapping features.[146] (Table 3) Usually the aetiology is multifactorial, typically a combination of factors that (1) cause diarrhoea, (2) impair colorectal storage capacity, or (3) weaken the sphincter mechanism.[146,174,177,178] (Table 4)

Table 3. Faecal incontinence types and background mechanisms by Bharucha et al.[146]

Category	Symptom	Background mechanisms
Passive	Leakage without awareness	Impaired sensation or internal anal sphincter weakness
Urgency	Marked rectal urgency with an inability to hold stool despite active attempts	External anal sphincter weakness, reduced rectal capacity, or rectal hypersensitivity
Seepage	Staining or a small amount of leakage, often occurring after defecation	*Incomplete evacuation,* impaired rectal sensation, or internal anal sphincter weakness

Table 4. Underlying factors for faecal incontinence. Modified from [146,174,178].

Mechanism	Examples
Anal sphincter complex weakness	Direct trauma: obstetric or iatrogenic injury (haemorrhoidectomy, internal sphincterotomy, fistulotomy)
	Non-traumatic: peripheral neuropathy (pudendal nerve stretch injury, diabetic neuropathy), neurogenic injury higher in the brain–gut axis, internal sphincter thinning of unknown aetiology, myopathies (scleroderma)
Disorders affecting rectal capacity or sensation	Inflammatory (Crohn's disease, ulcerative colitis)
	Iatrogenic: radiation proctitis, anorectal surgery
Altered bowel motility or stool consistency	Diarrhoea (irritable bowel syndrome, medications)
	Overflow due to constipation, *defecatory dysfunction*
Central nervous system disorders	Dementia, stroke, cerebral palsy, spina bifida, spinal cord injury or tumour, multiple sclerosis, Parkinson disease
Structural disorders	Fistula, rectal prolapse, recto-anal intussusception

The co-occurrence of POP and FI is unsurprising given their shared risk factors, such as vaginal delivery and ageing.[51,146] Anal sphincter defects are frequent in individuals with POP, and the puborectalis muscle's impaired function – a risk factor for POP – may also contribute to FI.[179,180] Recto-anal intussusception, common concurrent with prolapse, is also a potential FI cause.[181]

Though it is less likely that POP directly causes FI, a proposed mechanism suggests that a rectocele may result in post-defecation seepage from trapped faeces.[179,182,183] Studies specifically addressing rectocele are lacking, but faecal seepage has been associated with defecatory dysfunction and incomplete emptying due to dyssynergic defecation.[184]

Reports concerning rectocele repair's impact on faecal incontinence have been rare. In a study involving different transvaginal techniques (N=106), most women with preoperative FI experienced resolved symptoms after surgery.[185]

2.2.6 Sexual dysfunction and pain

POP has been associated with a decline in sexual function,[4,186–188] due to factors such as coital urinary incontinence, negative self-perceived body image, and the avoidance of intercourse due to prolapse.[186,189] Meta-analyses have indicated that POP surgery generally enhances sexual function, alleviates dyspareunia, and enables some women to resume sexual activity.[190,191]

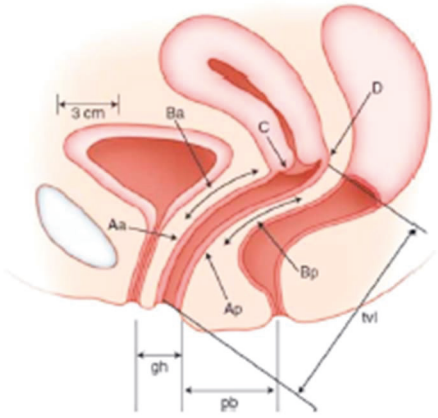
Cohort studies suggest that women with POP tend to report more pain than those without POP, most frequently low back pain. However, the current data are insufficient to establish a causal link between POP and pain.[7]

2.3 EVALUATION OF PELVIC ORGAN PROLAPSE

2.3.1 Quantification

A clinical examination, along with a patient history, is generally sufficient for diagnosing POP and initiating treatment.[192,193] The Pelvic Organ Prolapse Quantification (POP-Q) is the globally accepted standard for measuring and quantifying POP.[1] It has supplanted earlier methods, such as the Baden–Walker halfway system, due to their imprecision and significant inter-examiner variability.[194]

The POP-Q system employs nine distinct measurements in centimetres.[1] These include six points in the vagina during maximal straining in relation to the hymen (Point 0). Negative numbers indicate a point proximal to the hymen, and positive numbers a point distal to the hymen. Additionally, the genital hiatus and perineal body are measured during straining, while the total vaginal length (TVL) is measured at rest.[1,195] (Figure 7)



Anterior wall Aa	Anterior wall Ba	Cervix or Cuff C
Genital hiatus gH	Perineal Body pB	Total Vaginal Length TVL
Posterior wall Ap	Posterior wall Bp	Posterior Fornix D

Figure 7. The Pelvic Organ Prolapse Quantification (POP-Q) system. Re-published with permission from Springer Nature.[1]

Table 5 presents the five stages of pelvic support in POP-Q staging,[1,195] which has been criticised for overlooking the clinical significance of different prolapse types.[196,197] Continuous POP-Q measurements overcome this limitation.[197–199]

Table 5. The Pelvic Organ Prolapse Quantification (POP-Q) staging [1,195]

Stage	Definition
0	Aa, Ap, Ba, Bp = −3 and C or D ≤ −(TVL-2)
1	Stage 0 criteria not met and leading edge < −1
2	Leading edge ≥ −1 but ≤ +1
3	Leading edge > +1 but < + (TVL-2)
4	Leading edge ≥ + (TVL-2)

The POP-Q system has shown good intra- and inter-examiner reproducibility.[200] One drawback is its possible complexity in learning and use.[201] The simplified POP-Q system was developed as a more user-friendly alternative, measuring only four points: Ba for the anterior wall, Bp for the posterior wall, and points C and D for the apex. (Figure 7) The traditional POP-Q staging is otherwise retained, but Stage 0 is incorporated with Stage 1.[1] (Table 5) The inter-examiner agreement ranges from poor to excellent (weighted Kappa: 0.53–1.0),[202–204] and the association with the traditional POP-Q system is substantial (Kendall's tau-b: 0.71–0.80).[205]

2.3.2 Ancillary testing

Ancillary testing – including urodynamic studies, imaging (pelvic floor ultrasound, magnetic resonance imaging [MRI], contrast radiography), and anorectal physiological testing – may be indicated in certain cases, based on symptoms. While imaging can also be employed to confirm prolapse types, quantify POP, and identify muscle injuries, its clinical value in the routine evaluation of uncomplicated POP has not been firmly established.[206]

Urodynamic studies' predictive value for persistent voiding dysfunction and OAB is uncertain.[138] Evaluating SUI in POP patients is complex, involving pre-existing SUI or the prediction of *de novo* SUI, with varying guidance (see Section 2.2.4). In pre-existing SUI, no comparative studies

have evaluated preoperative urodynamic studies' value over office stress tests.[138] Searching for occult SUI through urodynamic assessments reveals more cases than office stress tests but does not appear to improve accuracy in identifying those developing *de novo* SUI.[136]

The clinical significance of obstructed defecation evaluations lacks solid evidence, leading to differing recommendations.[175] Gynaecological guidelines typically suggest additional investigations only if symptoms are disproportionate to physical examination findings or if surgical correction fails to alleviate symptoms.[131,207] Conversely, colorectal guidelines advise special testing (e.g. manometry, balloon expulsion test, transit study, defecography) before invasive treatments; surgery is considered only for patients with confirmed obstructed defecation, normal pelvic floor relaxation during defecation, and a significant structural abnormality in imaging.[171,208] Defecography is considered the reference standard for detecting enteroceles and intussusception, [206,209] with no distinct preference between conventional fluoroscopy or MRI defecography in current literature.[209,210] While pelvic floor ultrasonography is increasingly used, studies have noted inconsistent agreement between defecography and ultrasound.[211]

No definitive evidence shows whether ancillary testing can improve outcomes in the treatment of obstructed defecation. Different tests yield varied results, and the most reliable test is unclear.[209] Moreover, findings do not align well with symptoms and clinical examination.[207,209,212] Finally, testing techniques and diagnostic criteria vary widely across studies, underscoring the need for standardisation.[213–215]

When patients present with POP and FI, additional investigations are generally recommended to identify other underlying conditions, such as sphincter defects or rectal prolapse, which might alter management plans.[131]

2.4 NON-SURGICAL MANAGEMENT OF PELVIC ORGAN PROLAPSE

Optimal POP management considers patients' symptoms and degree of bother, prolapse extent and compartments, previous treatments,

underlying medical conditions, sexual concerns, and patient preferences. Conservative treatment is particularly useful for women who have mild-stage POP, are frail or elderly, refuse or cannot undergo surgery, or want more children.[216]

For some women, *counselling and education* may suffice. POP does not always worsen over time, and current evidence suggests that medical interventions should be considered only at patients' request.[30,32–34,216] However, treatment is necessary even for minimal subjective symptoms in cases of hydronephrosis compromising the kidneys, recurrent urinary infections due to obstructed urinary tract, or severe vaginal erosions that resist conservative treatment.[35,217]

Women with POP are often advised to adopt certain *lifestyle changes*, including weight loss for overweight women, smoking cessation, avoiding heavy lifting or straining, and constipation treatment. Clinical trials have not evaluated their effectiveness, and evidence from observational studies is limited and inconclusive.[193,218] For women with obstructed defecation, the first-line therapy includes dietary modifications, fibre supplementation, and osmotic laxatives, along with appropriate toilet behaviour.[175,219]

RCT evidence has demonstrated the effectiveness of *supervised pelvic floor muscle training* in reducing pelvic floor symptoms among women with Stage I–III POP.[218] While some studies have suggested improved prolapse severity, these results have been inconsistent.[218,220] Biofeedback therapy appears to achieve positive outcomes in managing obstructed defecation even with rectoceles and intussusception.[170,221]

Guidelines recommend considering *vaginal pessaries* for women seeking further therapy.[192,193] Data from few RCTs comparing pessary treatment to no treatment or physiotherapy have been inconclusive, but short-term cohort studies have indicated that pessary treatment improves patients' quality of life.[222,223] A recent RCT showed that initial pessary therapy did not meet noninferiority criteria through patient-reported improvements compared to surgery.[224] Regular follow-up may discourage some women from choosing this option,[225] and pessaries are unsuitable for some patients. A systematic review found a successful fitting rate of 63% at three months,[226] and continuation rates after one year of use have ranged from

42 to 80%.[223,227] Uncommon serious complications are typically related to neglected pessaries.[223]

2.5 SURGICAL TREATMENT OF PELVIC ORGAN PROLAPSE

Women with symptomatic POP who are unresponsive to or decline conservative treatments become candidates for surgery. Surgery aims to enhance quality of life, durably restore anatomy, eliminate protrusion symptoms, normalise bladder, bowel, and sexual function, and prevent complications and new-onset symptoms.[6] Since POP is not life-threatening, assessing its impact on patients' quality of life and understanding individual goals are crucial for tailored management and reasonable postoperative expectations.[228,229]

POP surgery falls into two main categories: reconstructive and obliterative. Reconstructive surgery is the prevailing approach. It can be carried out vaginally or abdominally utilising either native tissue or graft-augmented techniques. In the Finnish Pelvic Organ Prolapse Surgery Survey (FINPOP 2015) cohort, 81% of operations were performed using native tissues, 12% using transvaginal mesh, and 7% using abdominal mesh.[52]

Generally, POP surgery improves prolapse-related symptoms and overall quality of life;[230,231] the FINPOP study found a 90% global improvement and 84% satisfaction two years postoperatively.[230] Additionally, POP surgery is considered relatively safe, with a 3.3% rate of major complications (Clavien–Dindo Grades III–V, indicating complications requiring intervention or worse) and a 0.6% rate of severe complications (Grades IV–V, indicating life-threatening complications or death) within one year post-surgery.[232,233]

Multiple vaginal segments are frequently affected, necessitating a combination of resuspension techniques. The selection of the technique from numerous alternatives is guided by limited evidence comparing their effectiveness.[13] The lack of consensus is reflected in a considerable variation in individual POP procedures across countries and centres; a 2012 study of 15 OECD countries found a difference of > 10 times.[36]

Similarly, nearly a 10-fold difference in transvaginal mesh usage was observed between healthcare districts in Finland in 2015.[52]

One challenge of POP surgery is the high recurrence rate, with reported rates reaching 58% for objective recurrence (at least POP-Q Stage II) one year later.[234] Estimating the exact rate is challenging due to varied definitions and a lack of large-scale studies with long-term follow-ups. Using clinically relevant definitions, a combination of various native tissue procedures found an 18% risk of bothersome vaginal bulge symptom, a 15% risk of prolapse beyond the hymen, and a 5% risk of retreatment (pessary or surgery) within two years post-surgery.[235] In Finland, the 10-year cumulative risk (2000–2009) for further POP operations was 11%, with a median interval of 4.8 years between operations.[39] Of the FINPOP cohort, 25% had undergone previous POP surgery, 69% of whom had undergone prior repairs at the same sites.[52] Risk factors for recurrence, per systematic reviews, include advanced prolapse, young age, family history of POP, levator avulsion, large hiatal area, and previous pelvic floor surgery.[55,236–238]

In response to high objective failure rates after native tissue repairs, transvaginal synthetic mesh gained popularity in the early 2000s. Significant litigation related to adverse outcomes, particularly pain and dyspareunia, followed. Consequently, most manufacturers withdrew their products from the market, and many countries, including the United States and the United Kingdom, prohibited transvaginal mesh. However, it remains available in Finland and most of mainland Europe, Asia, and South America.[239,240]

2.5.1 Outcome assessment

Defining success in POP surgery is complex due to its multifaceted nature, with rates varying dramatically based on chosen definitions.[12,241] In the past, studies focused on anatomical measures.[241,242] However, even despite optimal anatomical corrections, functional problems may persist, and *de novo* symptoms may arise. This possibility underscores the importance of patient-centred approaches prioritising symptom relief and quality of life.[12,14,131,241]

The National Institute of Health's 2001 definition, which considers POP-Q Stage 0 as an optimal *anatomical outcome* and Stage 1 as a satisfactory outcome, has been deemed too strict;[14,242] 40% of women attending annual gynaecological examinations or post-sacrocolpopexy follow-ups do not meet these criteria.[12,20] A more clinically relevant criterion may be at the hymen, as prolapses beyond it are associated with increased symptoms.[12,131]

The ICS and IUGA recommend defining *subjective success* as the absence of vaginal bulge symptoms.[14,131] This definition is more strongly correlated with patients' perceived overall improvement, treatment success, symptom reduction, and enhanced quality of life than any anatomical definition.[12]

To facilitate comparisons in meta-analyses, the current ICS and IUGA consensus is to report multiple outcomes:[13,14]

1) Anatomical outcomes, including all POP-Q points and staging.
2) Patient-reported outcomes:
    a. The presence and absence of vaginal bulge symptoms.
    b. Functional outcomes and quality of life spanning prolapse, urinary, bowel, and sexual function using valid, reliable, and responsive symptom questionnaires and condition-specific quality-of-life instruments.
    c. Patient satisfaction.
3) Further surgery: for primary prolapses of different sites, recurrences at the same sites, complications, or non-prolapse-related conditions (e.g. SUI).
4) Perioperative data (e.g. operative time, blood loss) and short- and long-term complications.

2.5.2 Anterior compartment reconstructive surgery

The anterior compartment is the most frequent site for prolapse surgery and has the highest recurrence rate.[243,244] The most common procedure is anterior repair (colporrhaphy), which involves suture plication of the vesicovaginal fascia in the midline.[245,246] Synthetic mesh is not currently considered the first-line treatment for anterior compartment prolapse; it

may be considered for recurrent prolapse.[13,193,247] Although absorbable mesh and biological grafts are studied as potential solutions, limited data support their use.[13,247]

In a Cochrane review involving nearly 2,000 women with one-to-three year follow-ups, anterior colporrhaphy showed higher rates of prolapse awareness (23% vs 13%), recurrent anterior prolapse on examination, and reoperation for prolapse (4% vs 2%) than transvaginal permanent mesh. *De novo* dyspareunia and SUI rates were not statistically significantly different between groups, but the estimates were imprecise (RR 0.54, 95% confidence interval [CI] 0.27–1.06; RR 0.67, 95% CI 0.44–1.01). Permanent mesh was associated with higher rates of increased blood loss, blood transfusions, cystotomy, and prolapse in the apical or posterior compartments; mesh exposure occurred in 11% of cases, with 7% requiring surgery to address it.[247]

2.5.3 Apical compartment reconstructive surgery

Advanced vaginal wall prolapse often includes the loss of apical support; addressing it adequately is considered essential for successful anterior and posterior repairs.[13,248–250] A national database study in the United States (N = 2,756) with a mean nine-year follow-up provided supporting evidence. It found that women undergoing isolated anterior colporrhaphy had the highest cumulative reoperation rate (20%), exceeding that of women undergoing anterior colporrhaphy combined with apical suspension (12%).[250]

Vaginal apical suspension methods encompass native tissue suspensions, primarily targeting the sacrospinous or uterosacral ligaments, and mesh suspensions, typically directed at the sacrospinous ligament.[13] The predominant abdominal procedure is sacrocolpopexy. It suspends the apex to the sacrum, usually employing mesh, preferably through a minimally invasive approach.[13] The optimal method for an individual patient is selected based on factors such as their surgical history, concomitant pelvic floor disorders, personal goals, and complication and recurrence risks. The vaginal approach is less invasive and does not require

general anaesthesia.[13,131] For uterine prolapses, uterine preservation or hysterectomy must be selected.

For *post-hysterectomy vault prolapse*, sacrocolpopexy is regarded the preferred option; vaginal procedures are considered possible alternatives.[131] A recent Cochrane review associated sacrocolpopexy with lower rates of prolapse awareness, repeat prolapse surgery, and prolapse upon examination compared to vaginal procedures.[251] However, the vaginal group comprised various native tissue and mesh suspensions, and the sacrocolpopexy group included both open and minimally invasive operations. Other systematic reviews have highlighted challenges in comparing data due to the heterogeneity of techniques and outcome measures. While these reviews have noted superior objective success post-sacrocolpopexy, results regarding subjective outcomes remain inconclusive.[252–255]

In Finland in 2015, the prevailing surgical approach for *uterine prolapses* involved vaginal hysterectomy.[52] Recently, uterus-preserving procedures have gained popularity in many countries.[256,257] The reasons for choosing uterine conservation vary, driven by patients' desire or surgeons' preference due to potential advantages. Contraindications include various uterine pathologies. Alongside vaginal and abdominal suspensions (hysteropexies), the Manchester procedure is another option. It shortens and fixes the uterosacral–cardinal ligaments in front of the amputated cervix.[245] Limited evidence from randomised trials comparing uterine preservation to hysterectomy or various preservation methods remains inconclusive, emphasising the need for further data.[13,251,258] Cohort studies suggest that hysteropexy is a viable option for uterine prolapse,[131] and cohort and registry studies on Manchester repair have reported promising results.[259–261]

2.5.4 Posterior compartment reconstructive surgery

Surgical options for posterior compartment prolapse include midline plication (posterior colporrhaphy), site-specific repair, transanal rectocele repair, and sacrocolpopexy with or without concurrent ventral rectopexy.[13]

Perineal repair may be performed in conjunction.[262] Vaginal mesh is not advised due to insufficient evidence supporting its superiority and its higher complication rate.[13,263]

Low- to moderate-quality evidence suggests that repairing rectoceles vaginally outperforms the transanal approach in objective, subjective, and functional outcomes, including obstructed defecation relief.[263] Traditional midline plication may achieve better objective outcomes than site-specific repairs.[13,263] Data on sacrocolpopexy or ventral rectopexy for rectoceles are insufficient.

Enterocele management lacks guidelines. Both vaginal and abdominal techniques have been mentioned, but no comparative studies have been conducted.[264,265]

For combined vaginal and rectal prolapse, sacral colpopexy and rectopexy can be performed together.[266] Surgery for recto-anal intussusception may be considered if conservative treatment fails to alleviate symptoms such as obstructed defecation or FI.[267] The primary approach is abdominal, and minimally invasive ventral mesh rectopexy is gaining popularity.[268] Perineal procedures include Delorme's operation and stapled transanal rectal resection (STARR).[269] No comparative trials have been conducted, but a systematic review of cohort studies reported 77% obstructed defecation and 63% FI improvements after ventral mesh rectopexy.[269]

Overall, high-quality trials that directly compare surgical approaches for obstructed defecation symptoms are lacking.

2.5.5 Obliterative surgery

Obliterative surgery is considered only for women who unequivocally do not wish to preserve their coital function. This surgery, also known as colpocleisis, involves the removal of the vaginal epithelium and suturing the fibromuscular layers of the anterior and posterior vaginal walls together to partially or completely close the vaginal canal.[245] Colpocleisis is suitable for elderly women with significant medical comorbidities due to its low complication risk, quick recovery, and high objective and subjective

success rates.[270,271] In Finland, obliterative surgery represented 0.8% of POP operations in 2015.[52] In the United States, it is slightly more common, at 2.2% in 2012.[271]

2.6 PATIENT-REPORTED OUTCOME MEASURES

A patient-reported outcome (PRO) is a report of a patient's health condition, provided directly by the patient, without any interpretation by clinicians or anyone else.[272] PROs are collected via PROMs, standardized questionnaires that gather information on symptoms, health-related quality of life, and functional status, aiding in understanding the disease burden.[273] These measures are employed to assess treatment effects in research, improve patient-caregiver communication, and evaluate the quality of care, informing health policies and economics.[274] They are intended to complement, rather than replace, clinical data.[275] For pelvic floor disorders, where symptoms play a central role, PROMs present valuable indicators of treatment effects that objective tests or clinical assessment cannot measure.[276]

PROMs can be categorised as generic or condition-specific. Both types are important in enhancing patient care across healthcare systems. For full benefits, both types should be used complementarily.[275] Generic PROMs measure health concepts relevant to diverse patient groups, enabling data compilation and comparison across conditions and settings.[275] Condition-specific PROMs assess the impact of a particular disease, making them more responsive to the post-treatment changes unique to that condition.[275]

Using valid, responsive, and interpretable measures is crucial, and employing consistent PROMs across studies ensures meaningful comparisons.[277] Though multiple PROMs are available for pelvic floor disorders, few have undergone translation and cross-cultural validation.[278]

2.6.1 Pelvic Floor Distress Inventory -20 (PFDI-20)

The Pelvic Floor Distress Inventory (PFDI) is one of the questionnaires recommended by the ICS. Developed for women with all forms of pelvic

floor disorders, it measures lower urinary tract, lower gastrointestinal tract, and prolapse symptoms, gauging their impact on the quality-of-life.[278] The PFDI-20, a shortened version, was created to reduce the respondent burden and has been proven valid, reliable, and responsive in pelvic floor and POP research.[279–281] The Finnish version has also been validated.[282]

The PFDI-20 comprises three scales: the Pelvic Organ Prolapse Distress Inventory -6 (POPDI-6) for POP; the Colorectal-Anal Distress Inventory -8 (CRADI-8) for anorectal function; and the Urinary Distress Inventory -6 (UDI-6) for bladder function. All of these scales have demonstrated responsiveness.[280]

2.6.2 Minimal important difference (MID)

PROMs typically generate summary scores based on responses to multiple questions. Interpreting changes in these scores can be challenging. While any study can theoretically achieve statistical significance by increasing its sample size, the observed difference may lack practical importance for patients.[283]

The minimal important difference (MID) addresses this challenge, representing 'the smallest change in the PROM of interest that patients perceive as important, either beneficial or harmful, and that would prompt the patient or clinician to consider a change in management'.[284] The MID's primary role is to interpret group-level mean differences: if a statistically significant difference in change scores between groups exceeds the MID, it can be considered a clinically meaningful difference in efficacy. It can also be used in responder analysis to compare the proportion of patients experiencing meaningful improvements and in sample size calculations to determine the minimum difference a study must detect.[285,286]

Three studies have determined the MID for PFDI-20; the estimates range from 13.5 to 45 points.[279,287,288] However, no study has specifically evaluated the MID for POP surgery. The MID for a PROM may vary based on the population and clinical context, and a single value may not be universally applicable.[289] The MID for the prolapse-specific subscale, POPDI-6, has not been previously established.

Two main approaches are used to determine the MID. Anchor-based methods correlate PROM score changes with an external criterion (the anchor), such as the patient's global rating of change.[290] Distribution-based methods rely solely on statistical characteristics; a common method involves the 0.5 SD of the baseline PROM score.[291] Since distribution-based methods lack patients' perspectives, they are generally recommended only as supporting evidence or when anchor-based MIDs are unavailable.[289]

Establishing a MID using an anchor-based approach involves choosing an anchor and selecting a MID calculation method. To ensure credible MID estimates, the anchor should be understandable and meaningful to patients, and there should be a substantial correlation between the anchor and the target measure.[290] While multiple MID calculation methods exist, consensus on the best is lacking.[290]

2.6.3 Patient acceptable symptom state (PASS)

The patient acceptable symptom state (PASS) is another useful tool for interpreting PROMs. While the MID indicates the smallest clinically meaningful improvement denoting 'feeling better', PASS represents 'feeling good' and a PROM score 'beyond which patients consider themselves well'.[292] PASS can be used in responder analysis to determine the proportion of patients who achieve acceptable states after treatment, which may be more relevant to patients than experiencing improvements.[293]

PASS is well established in musculoskeletal research,[294] but its application to female pelvic floor disorders is new. One study has determined the PASS for PROMs related to urinary incontinence;[295] no prior studies have defined a PASS for PFDI-20. A recent International Urogynecology Consultation -document listed PASS as a valuable POP surgery outcome.[296]

PASS is determined using an external anchoring method that considers patients' perspectives. Patients respond to a single anchor question, such as, 'When taking into account your daily activities and your symptoms related to the disease, do you consider that your state is good enough?'[292]

Two commonly used statistical methods are the 75th percentile method and the receiver operating characteristic (ROC) curve method; no consensus exists regarding the optimal approach.[297]

2.7 RATIONALE FOR THIS THESIS

This thesis was motivated by the incomplete understanding of the relationship between pelvic anatomy and function. While it is evident that POP involves more than a physical bulge, its exact contribution to bladder and bowel symptoms is undetermined, leading to diverse management approaches.

A prime example is the interplay between posterior vaginal wall prolapse and obstructed defecation; some clinicians view POP as a consequence, rather than the cause, and suggest biofeedback and rectal irrigation, while others recommend surgery. OAB and POP management is similarly divided. Distinguishing between symptoms likely to improve with surgery and those unlikely to improve will facilitate effective counselling and enable realistic expectations.

The optimal approach to address stress continence during POP surgery is not straightforward. Given patients' diverse preferences, choosing a combined or staged SUI strategy necessitates shared decision-making, weighing risks, benefits, and uncertainties. Clinical guidelines are based on RCTs, which inform about the relative risk (between combination surgery and staged approach), but their absolute risks may differ considerably from routine clinical practice. Gaining a realistic picture of absolute risks is paramount for informed decisions. Moreover, identifying predictors for postoperative SUI could refine patient selection for concurrent continence surgery.

3 AIMS OF THE STUDY

The thesis's overarching purpose was to deepen the comprehension of the link between POP and pelvic floor symptoms and to develop tools for accurately assessing how POP surgery affects these symptoms. The specific aims were:

1. To examine whether OAB symptoms depend on the POP compartment (Study I).
2. To describe SUI symptom changes after POP surgery and identify predictors of persistent and *de novo* SUI (Study II).
3. To assess whether posterior vaginal wall prolapse contributes to anorectal symptoms (Study III).
4. To determine the MID and PASS for the PFDI-20 and POPDI-6 measures in POP surgery (Study IV).

4 PARTICIPANTS AND METHODS

4.1 DESIGN, SETTING, AND PARTICIPANTS

The thesis utilised data from the FINPOP 2015, a prospective, observational, multi-centre cohort study involving women who underwent POP surgery in Finland in 2015. Organised by the Finnish Society for Gynecological Surgery, FINPOP aimed to investigate the safety and effectiveness of POP surgery. Of the hospitals performing POP surgery, all five (100%) university hospitals, 17 out of 18 (94%) secondary care hospitals, 15 of 17 (88%) primary care hospitals, and four of five (80%) private hospitals participated.

FINPOP enrolled patients aged 18 years or older who were scheduled for POP surgery. Participants had to be able to communicate in Finnish or Swedish and lack mental or psychological disabilities that would hinder their informed consent. Surgical methods were chosen by individual surgeons according to their usual practice.

The FINPOP cohort included 3,515 women who underwent 3,535 POP operations, accounting for 83% of the 4,240 POP procedures in Finland that year (reported in the Care Register for Health Care). Concomitant SUI surgery was performed for 31 women (0.9%).

4.2 STUDY FLOW

The studies in this thesis included women who completed preoperative patient questionnaires. Figure 8 presents their selection processes, exclusion criteria, and data availability.

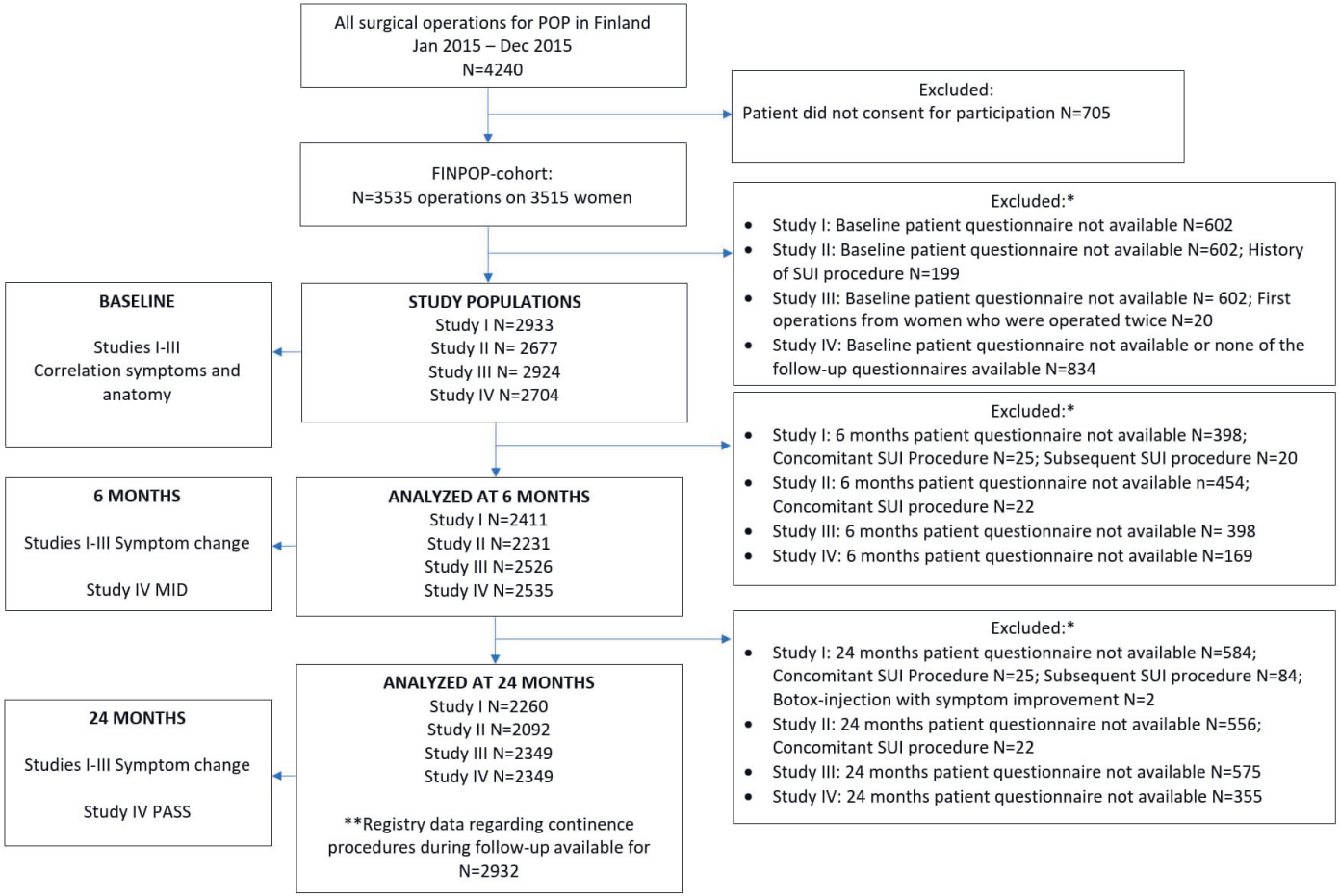


Figure 8. Flowchart depicting the selection of study populations

4.3 DATA SOURCES AND COLLECTION

The studies utilised questionnaire and register data. Surgeons completed a baseline questionnaire, and participants filled out questionnaires at their baseline and six months and two years post-surgery. Data on invasive treatments for urinary incontinence during follow-ups were retrieved from the Care Register for Health Care, a national database maintained by the National Institute of Health and Welfare. The register contains information on inpatient care, day surgeries, and specialised outpatient care at public and private hospitals. Based on mandatory records, it has an over 95% coverage rate.[298] Table 6 describes the studies' data collection.

Table 6. Data collection

Source	Data collected
Surgeon baseline questionnaire	• Surgical history • Type and degree of prolapse (simplified POP-Q) • Operative method (description and the Nordic Classification of Surgical Procedures code)
Participant baseline questionnaire	• Weight, height, parity, and smoking status • Medical history and medications • PFDI-20 (Appendix 1)
Participant follow-up questionnaires, six and 24 months	• PFDI-20 • Patient Global Impression of Improvement (PGI-I; Appendix 2) • PASS question (starting from 24 months; Appendix 3)
Care Register of Health Care	• Further urinary incontinence procedures

4.4 OUTCOME MEASURES AND STATISTICAL ANALYSES

Table 7 presents the outcome measures used in the studies.

Table 7. Outcome measures in Studies I–IV

Study	Outcome measures
I	PFDI-20 Items #15 (urinary frequency) and #16 (UUI)
II	PFDI-20 Item #17 (SUI) Number of subsequent SUI procedures
III	PFDI-20 Items #4 (splinting), #7 (straining), #8 (incomplete emptying), #9 (FI of solid stool), #10 (FI of liquid stool), #11 (flatal incontinence), #12 (pain during defecation), #13 (faecal urgency), #14 (anorectal prolapse)
IV	PFDI-20 score; POPDI-6 score; PGI-I; PASS question

Each PFDI-20 item prompts patients to indicate whether they experience that particular symptom with 'yes' or 'no'. If 'yes', patients then rate the degree of bother using a four-point scale: 1 for 'not at all', 2 for 'somewhat', 3 for 'moderately', and 4 for 'quite a bit'. The PFDI-20 total score ranges from 0 to 300, and each subscale ranges from 0 to 100 points. (Appendix 1)

A symptom was considered present at the baseline if the corresponding PFDI-20 item's baseline score was > 0. Bothersome symptoms were defined as responses 3 and 4. For women with baseline symptoms, these symptoms were considered resolved if their follow-up scores were 0, improved if their bother scores decreased, persistent if their follow-up scores were > 0, and worsened when their bother scores increased. For women with bothersome baseline symptoms, the resolution of these bothersome symptoms was defined as follow-up bother scores of <3.

For women without baseline symptoms, follow-up scores of 1–4 indicated *de novo* symptoms of any degree; scores of 3–4 indicated bothersome *de novo* symptoms.

4.4.1 Study I

In Study I, a generalised linear model (ordinal logistic) was applied to estimate the association between baseline anatomy (Ba, Bp, C) and OAB symptoms' baseline severity (bother scores).

Generalised estimating equations were employed to evaluate whether OAB symptoms' post-surgery improvement differed between operated compartments. The ordinal bother score was used as the dependent variable. The study population was divided into two groups: (1) the anterior/apical group (surgeries for the anterior and/or apical compartment ± the posterior compartment) and (2) the posterior group (surgeries for the posterior compartment only). A sensitivity analysis was performed adjusting for concomitant posterior repair. A secondary analysis was conducted to further explore differences between anterior and apical repair dividing the anterior/apical group into three subgroups: (1) the anterior group, (2) the apical group, and (3) the anterior and apical group.

Multivariable models were fitted to control for prolapse in other compartments and adjust for potential confounders (age, BMI, parity, smoking, previous POP surgery, and previous anti-incontinence surgery). Confounders were selected using the previous literature and clinical expertise with causal diagrams, directed acyclic graphs.[299] Factors associated with both the exposure and the outcome, which were not on the causal pathway, were considered confounders.

4.4.2 Study II

Study II described post-surgery SUI symptom changes and the number of subsequent SUI procedures during follow-up, stratified by the baseline continence status (i.e. incontinent or continent). For women who underwent SUI procedures during the follow-up period, bother scores of 4 (quite a bit bothersome) were recoded after the SUI procedure date, as the aim was to investigate whether women still had SUI after POP surgery.

To assess whether symptoms improved over time, Wilcoxon's signed-rank test was used to compare baseline and 24-month bother scores among women with pre-existing SUI.

A generalised linear model was employed to identify prognostic factors for baseline, persistent (24-month data), and *de novo* (six and 24-month data) SUI; the ordinal bother score was used as the dependent variable. A binary logistic regression model was used to examine prognostic factors for invasive procedures treating persistent SUI during the two-year follow-up. Potential prognostic factors for multivariable models were selected based on the previous literature or clinical interest. These factors included age, BMI, vaginal parity, smoking, diabetes, hysterectomy and POP surgery history, prolapse degree, baseline SUI severity, baseline UUI, and surgery type and compartment. The categories for the compartment of surgery were: (1) anterior group (procedures for the anterior compartment ± procedures for the posterior compartment, but no apical procedures), (2) apical group (any procedure for the apical compartment ± procedures for the anterior or posterior compartments), and (3) posterior group (procedures for the posterior compartment only). Variables with strong collinearity (correlation coefficients >0.4) were not included in the same statistical model.

4.4.3 Study III

In Study III, splinting, straining, and incomplete emptying were classified as obstructed defecation symptoms. Anal incontinence included solid stool, liquid stool, and/or flatus incontinence.

Binary logistic regression was employed to quantify the association between the stage of posterior vaginal wall prolapse and prevalence of bothersome anorectal symptoms at the baseline.

Generalised estimating equations were used to investigate whether anorectal symptoms' post-surgery improvement varied depending on the inclusion of a procedure for the posterior compartment in the surgery. The presence of bothersome symptoms was used as the dependent variable. The sample was divided into two groups: women who underwent posterior

compartment procedures as part of their operations and women who did not. A post-publication sensitivity analysis excluding participants who underwent concurrent surgery for rectal prolapse (n=64 of 2,924, 2.2%) was conducted for this thesis.

Multivariable models were fitted to control for prolapse in other compartments and adjust for potential confounders (age, BMI, parity, previous hysterectomy, and previous POP surgery). Confounders were chosen based on the prior literature and clinical expertise using causal diagrams. Factors that were associated with both the exposure and the outcome but were not on the causal pathway were considered confounders.[299]

4.4.4 Study IV

In Study IV, the MID analysis used baseline and six-month data, while the PASS analysis used baseline and 24-month data.

Four previously established methods were used to determine the MID: three anchor-based methods (the mean change[289,300,301], ROC curve[302], and 75th percentile methods[294,303]) and one distribution-based method (the 0.5 SD method[291]). PGI-I was used as the anchor question. MID's credibility was assessed by calculating Pearson's correlations between the anchor and the PROM change and follow-up scores. To compare the MID estimates with the measurement error, the smallest detectable change was calculated using a separate study population that had been used to validate PFDI-20 in Finnish.[282]

The PASS anchor question was, 'When taking into account your daily activities and symptoms related to prolapse, do you consider your state good enough?' ('yes' or 'no'). The PASS cut-off was determined using two previously established methods: the 75th percentile and ROC curve methods.[297]

4.5 ETHICAL CONSIDERATIONS

The FINPOP study adhered to the ethical standards outlined in the Declaration of Helsinki of 1964 and its 2013 revision. As a survey study, its participants were not subjected to any interventions beyond normal clinical practice. The data were stored and analysed pseudonymously to ensure participant confidentiality. The participants provided their informed consent in writing. The Research Ethics Committee of the Northern Savo Hospital District approved the study on 20 May, 2014, 15 November, 2016, and 19 January, 2021 (283/13.02.00/2015). Authorisation to use the Care Register of Health Care as a data source was obtained from The Finnish Institute for Health and Welfare; the Data Protection Ombudsman was consulted during the process. Institutional approval was also obtained from each participating hospital.

5 RESULTS

5.1 CHARACTERISTICS OF THE STUDY POPULATIONS

The study populations' mean age was 64 (SD ± 11) years, and their mean BMI was 27 (SD ± 4.1) kg/m2. Their median parity and vaginal parity were 2 (interquartile range 1). Table 8 presents additional baseline characteristics.

Table 8. Baseline characteristics

Variable	**Study I**	**Study II**	**Study III**	**Study IV**
Number	2924	2933	2677	2704
Current smoker, n (%)	255 (8.8)	255 (8.7)	236 (8.9)	219 (8.1)
Diabetes, n (%)	283 (10)	283 (10)	249 (9.3)	262 (10)
Prior POP surgery, n (%)	731 (25)	740 (25)	651 (24)	683 (25)
Prior hysterectomy, n (%)	974 (33)	981 (33)	860 (32)	916 (34)
Prior SUI surgery, n (%)	170 (5.8)	170 (5.8)	0	157 (5.8)
POP-Q point Ba ≥ 0, n (%)	1851 (66)	1859 (66)	1706 (66)	1714 (66)
POP-Q point C ≥ 0, n (%)	1134 (41)	1138 (41)	1057 (41)	1047 (41)
POP-Q point Bp ≥ 0, n (%)	1259 (45)	1259 (45)	1143 (44)	1158 (44)
Local/systemic oestrogen, n (%)	2420 (83)	2429 (83)	2206 (83)	2254 (84)
OAB medication, n (%)	97 (3.3)			
Laxative use, n (%)			190 (6.5)	
Type of surgery, n (%)				
Native tissue repair	2355 (81)	2357 (80)	2166 (81)	2160 (80)
Transvaginal mesh	357 (12)	362 (12)	321 (12)	344 (13)
Abdominal mesh	212 (7.3)	214 (7.3)	190 (7.1)	200 (7.4)

5.2 BASELINE SYMPTOM PREVALENCE

Among the women surveyed in the entire FINPOP cohort, 97% (n = 2,725/2,802) reported experiencing at least one symptom related to OAB, SUI, obstructed defecation, or anal incontinence, while 63% found at least one of these symptoms bothersome. Concurrent symptoms were commonly reported. (Figure 9)

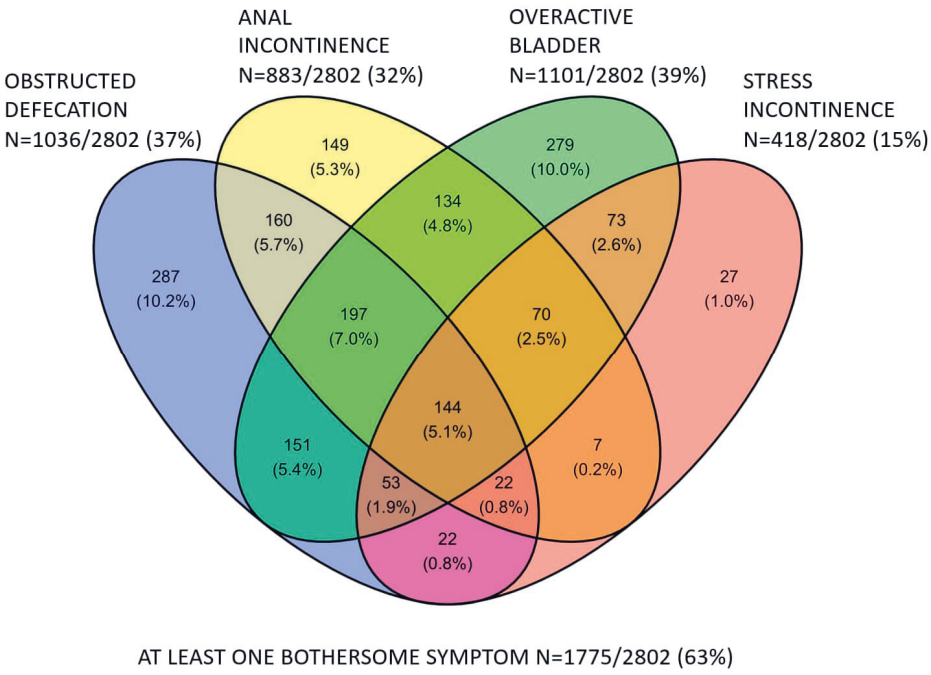


Figure 9. Venn diagram illustrating interrelationships between *bothersome* baseline symptoms. Numbers represent the entire FINPOP study cohort with responses available for all symptoms.

For individual symptoms, the lowest prevalence was observed for solid stool incontinence at 19%, while urinary frequency had the highest prevalence at 67%. Focusing on bothersome symptoms, 6% of women reported bothersome solid stool incontinence, and 31% reported bothersome urinary frequency. (Table 9)

Table 9. Baseline symptom prevalence and changes 6 and 24 months (mo) post-surgery; n/N (%).

Symptom	Any level at baseline	Bothersome at baseline	Persistent bothersome 6 mo [a]	Persistent bothersome 24 mo [a]	Bothersome de novo 6 mo [b]	Bothersome de novo 24 mo[b]
Urinary frequency[c]	1890/2825 (67)	875/2825 (31)	142/687 (21)	168/642 (26)	7/773 (0.9)	16/713 (2.2)
UUI [c]	1759/2845 (62)	744/2845 (26)	154/570 (27)	195/540 (36)	20/922 (2.2)	28/842 (3.3)
SUI [d]	1329/2677 (50)	391/2677 (15)	88/302 (29)	120/282 (43)	18/1139 (1.6)	35/1087 (3.2)
Splinting [e]	1483/2820 (53)	733/2820 (26)	99/602 (16)	129/565 (23)	10/1135 (0.9)	12/1075 (1.1)
Straining [e]	1475/2833 (52)	694/2833 (25)	124/575 (22)	162/539 (30)	12/1170 (1.0)	22/1109 (2.0)
Incompl emptying[e]	1661/2811 (59)	645/2811 (23)	118/539 (22)	134/494 (27)	11/979 (1.1)	17/929 (1.8)
FI, solid stool [e]	545/2854 (19)	181/2854 (6.3)	34/148 (23)	39/145 (27)	13/1959 (0.7)	24/1821 (1.3)
FI, liquid stool [e]	1412/2767 (51)	555/2767 (20)	124/453 (27)	166/428 (39)	20/1151 (1.7)	29/1064 (2.7)
FI, flatus [e]	1743/2814 (62)	634/2814 (23)	190/513 (37)	214/489 (44)	17/894 (1.9)	22/832 (2.6)
Pain defecating [e]	691/2848 (24)	235/2848 (8.3)	42/199 (21)	52/180 (29)	10/1849 (0.5)	24/1734 (1.4)
Faecal urgency [e]	1453/2802 (52)	474/2802 (17)	107/395 (27)	115/372 (31)	14/1140 (1.2)	20/1061 (1.9)
Rectal prolapse [e]	671/2831 (24)	184/2831 (6.5)	34/152 (22)	46/142 (32)	12/1852 (0.6)	23/1735 (1.3)

Calculated among cases [a] with bothersome baseline symptom, [b] without any degree of symptom at baseline, [c] Study I, [d] Study II, [e] Study III.

5.3 OVERACTIVE BLADDER SYMPTOMS (STUDY I)

The urinary frequency severity at the baseline correlated with the increasing anterior wall and apical prolapse degree but not posterior wall degree. UUI's severity at the baseline was associated with an increasing anterior wall prolapse degree but not apical prolapse degree, and an inverse association with posterior wall prolapse was observed. (Table 10) The crude prevalence of symptoms increased by approximately 10% from anterior wall prolapse Stage 0 to Stages 3–4. (Figure 10)

Table 10. Association between overactive bladder symptoms (bother scores) and anatomy of vaginal compartments (*POP-Q points/cm*) at the baseline

POP-Q point	Urinary frequency	UUI
Ba (anterior)	**1.07 (1.03–1.11)**	**1.08 (1.04–1.13)**
Bp (posterior)	0.99 (0.95–1.03)	**0.96 (0.92–0.99)**
C (apical)	**1.04 (1.01–1.06)**	1.01 (0.98–1.03)

The multivariable models' adjusted ORs (95% CI).

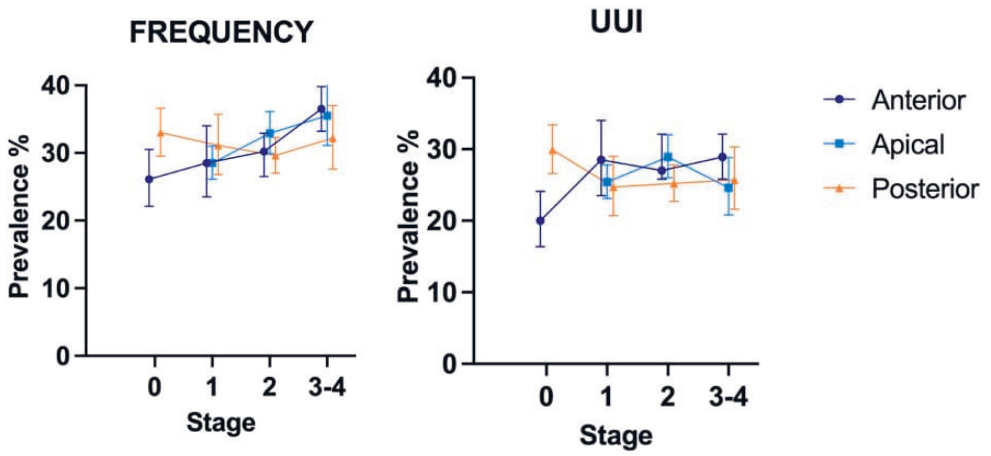


Figure 10. Bothersome overactive bladder symptoms' prevalence (95% CI) at the baseline stratified by the compartment and *stage* of prolapse

Symptom severity improved from the baseline to six months post-surgery for all operated compartments. Women who underwent anterior or apical compartment surgeries presented with more severe symptoms at the baseline than the posterior group. Their symptoms improved more post-surgery, and they achieved symptom levels similar to the posterior group postoperatively. (Figure 11) The sensitivity analysis, adjusting for concomitant posterior repair, produced similar results (data not shown).

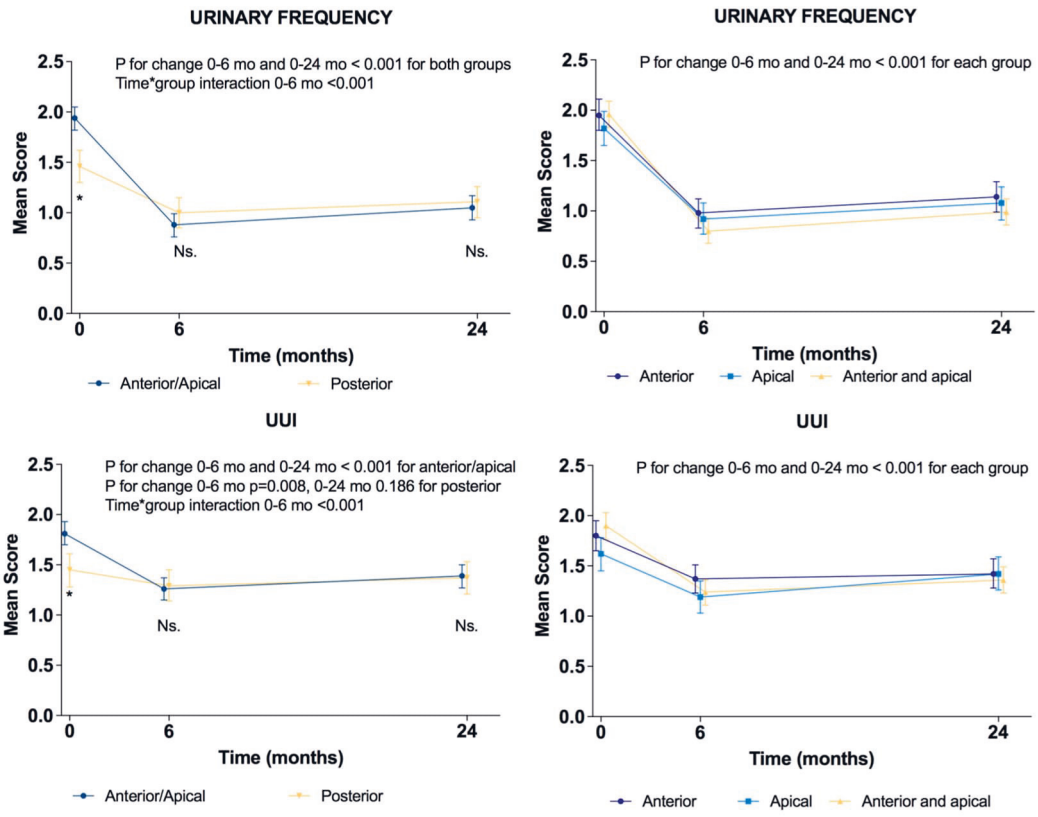


Figure 11. Impact of surgery on overactive bladder symptoms. Y-axis: estimated marginal means (95% CI) from a linear generalised estimating equations multivariable model. X-axis: follow-up points. The left column presents data in two surgical groups. On the right, the anterior/apical group is stratified into three groups. The statistical analyses were performed using ordinal logistic generalised estimating equations. The asterisk indicates $p < 0.05$ and Ns. indicates not significant ($p > 0.05$) in between-group comparisons.

Among those with bothersome baseline OAB symptoms, 21–27% continued to experience bothersome symptoms six months post-surgery. Bothersome *de novo* symptoms developed for 1–2%. (Table 9) Table 11 presents symptom changes stratified by the operated compartment.

Table 11. Overactive bladder symptom changes after prolapse surgery stratified by surgical compartment

	FREQUENCY n/N (%)				UUI n/N (%)			
	Baseline	**Postop**	**6 months**	**24 months**	**Baseline**	**Postop**	**6 months**	**24 months**
Anterior/Apical	1568/2246 (70)	Improved	994/1284 (77)	861/1202 (72)	1462/2263 (65)	Improved	718/1166 (62)	623/1089 (57)
		Resolved	739/1284 (58)	595/1202 (50)		Resolved	390/1166 (33)	331/1089 (30)
		De Novo, any	54/560 (9.6)	70/516 (14)		*De Novo*, any	103/685 (15)	126/626 (20)
		bothersome	5/560 (0.9)	10/516 (1.9)		bothersome	14/685 (2.0)	22/626 (3.5)
Posterior	297/544 (55)	Improved	122/216 (57)	111/202 (55)	273/547 (50)	Improved	99/197 (50)	76/186 (41)
		Resolved	90/216 (42)	82/202 (41)		Resolved	52/197 (26)	49/186 (26)
		De Novo, any	24/205 (12)	28/187 (15)		*De Novo*, any	47/229 (21)	41/205 (20)
		bothersome	2/205 (1.0)	5/187 (2.7)		bothersome	6/229 (2.6)	6/205 (2.9)

5.4 STRESS URINARY INCONTINENCE SYMPTOMS (STUDY II)

At baseline, 50% of the participants reported some level of SUI, while 15% reported bothersome SUI. (Table 9) A younger age, higher BMI, diabetes, and UUI symptoms correlated with increased symptom bother at the baseline. Additionally, a weak inverse correlation was observed between SUI severity and apical prolapse degree. (Table 12)

Table 12. Factors associated with baseline stress urinary incontinence

Variable	Adjusted OR
Age (years)	**0.98 (0.97–0.99)**
BMI (kg/m^2)	**1.03 (1.01–1.05)**
Ba (cm, anterior wall prolapse)	0.99 (0.95–1.04)
C (cm, apical prolapse)	**0.95 (0.92–0.97)**
Bp (cm, posterior wall prolapse)	1.04 (1.00–1.09)
Vaginal parity (number)	1.03 (0.97–1.10)
Smoking	1.22 (0.91–1.65)
Diabetes	**1.40 (1.05–1.85)**
Prior POP surgery	0.99 (0.81–1.20)
Prior hysterectomy	0.93 (0.78–1.12)
Baseline UUI bother score	**2.21 (2.06–2.37)**

Two years post-surgery, 49% reported improved pre-existing SUI; 35% achieved complete resolution. (Table 13) Among the women with bothersome baseline symptoms, 29% reported continued bothersome symptoms at six months, versus 43% at 24 months. (Table 9)

Table 13. Stress urinary incontinence symptom changes after prolapse surgery, n/N (%).

Baseline	**Change at follow-up**	**6 months**	**24 months**
Incontinent N=1329/2677 (50)	Improved	607/1092 (56)	494/1005 (49)
	Resolved	428/1092 (39)	354/1005 (35)
	Worse	78/1092 (7.1)	151/1005 (15)
Continent N=1348/2677 (50)	*De novo*, any bother	166/1139 (15)	218/1087 (20)
	De novo, bothersome	18/1139 (1.6)	35/1087 (3.2)

Strong baseline symptoms were associated with a higher likelihood of persistent symptoms, while advanced baseline apical prolapse and apical compartment surgery predicted positive outcomes. No other variables were associated with persistent SUI symptoms. (Table 14)

During the two-year follow-up period, 5% of women with pre-existing SUI (n=67/1,329) underwent surgical procedures (mid-urethral slings or urethral bulking) for persistent SUI a median of 264 days after their index operations. The factors associated with a higher procedure risk included strong baseline symptom severity and transvaginal mesh surgery, while advanced apical prolapse at the baseline was associated with a lower risk. (Table 14)

Of the women without baseline SUI, 20% developed *de novo* SUI of any degree versus 3% of a bothersome degree, by the two-year follow-up. (Table 13) Eleven of the 1,348 women (0.8%) received surgical procedures for *de novo* SUI a median of 272 days after their index operations.

Table 14. Factors associated with persistent SUI symptoms, procedures for persistent SUI, and *de novo* SUI

Prognostic factor	Persistent SUI [a]	SUI procedure [a]	*De novo* SUI, 6 mo [b]	*De novo* SUI, 24 mo [a]
Baseline SUI bother score	**2.04 (1.65–2.53)**	**1.91 (1.27–2.86)**	N/A	N/A
Age (years)	1.00 (0.98–1.01)	0.98 (0.96–1.01)	**1.03 (1.01–1.05)**	**1.03 (1.01–1.05)**
BMI (kg/m^2)	1.02 (0.99–1.06)	1.01 (0.94–1.07)	**1.05 (1.00–1.09)**	1.02 (0.98–1.06)
Ba (anterior wall)	1.05 (0.98–1.13)	1.08 (0.91–1.27)	1.05 (0.95–1.16)	1.02 (0.93–1.12)
C (apex)	**0.89 (0.85–0.93)**	**0.85 (0.76–0.94)**	0.96 (0.90–1.02)	1.01 (0.96–1.07)
Bp (posterior wall)	1.01 (0.95–1.08)	0.97 (0.82–1.13)	1.07 (0.97–1.18)	1.05 (0.97–1.15)
Vaginal parity (number)	0.96 (0.88–1.06)	0.88 (0.69–1.11)	0.93 (0.79–1.08)	1.04 (0.93–1.16)
Diabetes	1.13 (0.75–1.70)	1.21 (0.52–2.81)	1.58 (0.83–3.01)	1.61 (0.91–2.83)
Smoking	0.77 (0.49–1.22)	0.47 (0.14–1.58)	1.13 (0.54–2.39)	0.73 (0.36–1.47)
Prior POP surgery	1.02 (0.67–1.56)	0.69 (0.23–2.07)	1.01 (0.53–1.93)	0.84 (0.47–1.52)
Prior hysterectomy	0.75 (0.52–1.07)	0.47 (0.18–1.23)	0.93 (0.53–1.64)	1.08 (0.65–1.80)
Baseline UUI bother score	1.07 (0.95–1.19)	1.08 (0.84–1.40)	**1.19 (1.03–1.37)**	**1.21 (1.06–1.38)**
Surgery type				
Native tissue repair	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
Transvaginal mesh	0.90 (0.62–1.30)	**2.80 (1.40–5.59)**	**2.12 (1.29–3.48)**	**1.93 (1.24–3.00)**
Abdominal mesh	1.12 (0.68–1.84)	1.52 (0.43–5.36)	**2.83 (1.57–5.13)**	0.72 (0.35–1.47)
Surgery compartment				
Anterior	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
Apical	**0.58 (0.43–0.80)**	0.73 (0.35–1.49)	0.77 (0.47–1.27)	0.98 (0.63–1.53)
Posterior	0.93 (0.64–1.37)	1.32 (0.58–2.96)	1.01 (0.55–1.83)	1.36 (0.80–2.30)

Adjusted odds ratios (95% CI) from multivariable models [a] 24 months or [b] 6 months postoperatively. N/A, not applicable.

The multivariable models did not identify any significant association between the POP compartment or degree and *de novo* SUI symptoms. Older women, those who underwent transvaginal mesh surgery, and women with baseline UUI symptoms had an increased risk of developing *de novo* SUI symptoms at six and 24 months. Obesity and abdominal mesh surgery were associated with *de novo* SUI at six but not 24 months. (Table 14)

5.5 ANORECTAL SYMPTOMS (STUDY III)

As posterior vaginal wall prolapse progressed from Stage 0 to Stage 2, the likelihood of experiencing bothersome anorectal symptoms increased proportionately for all symptoms ($p \leq 0.007$) except solid stool and flatus incontinence ($p = 0.13$ and 0.05, respectively). The strongest association was observed for splinting. Beyond Stage 2, no further symptom likelihood increases were observed. (Figure 12)

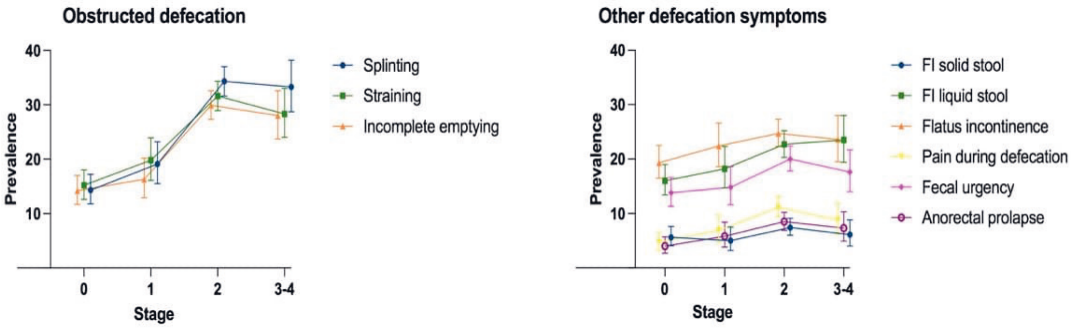


Figure 12. Prevalence (95% CI) of bothersome baseline anorectal symptoms stratified by posterior compartment stage

Each symptom's prevalence decreased over six months, regardless of whether posterior compartment surgery was performed ($p \leq 0.004$). Bothersome obstructed defecation symptoms persisted in 16–22% of cases, and bothersome anal incontinence persisted in 23–37% of cases six months post-surgery. (Table 9)

At baseline, each anorectal symptom was more common among women who underwent posterior compartment surgery than among those who

did not. Obstructed defecation and liquid stool incontinence symptoms improved more after posterior compartment surgery than after surgery for other compartments. Consistent outcomes were observed both among the entire study population and via sensitivity analysis excluding rectopexy cases. (Figure 13)

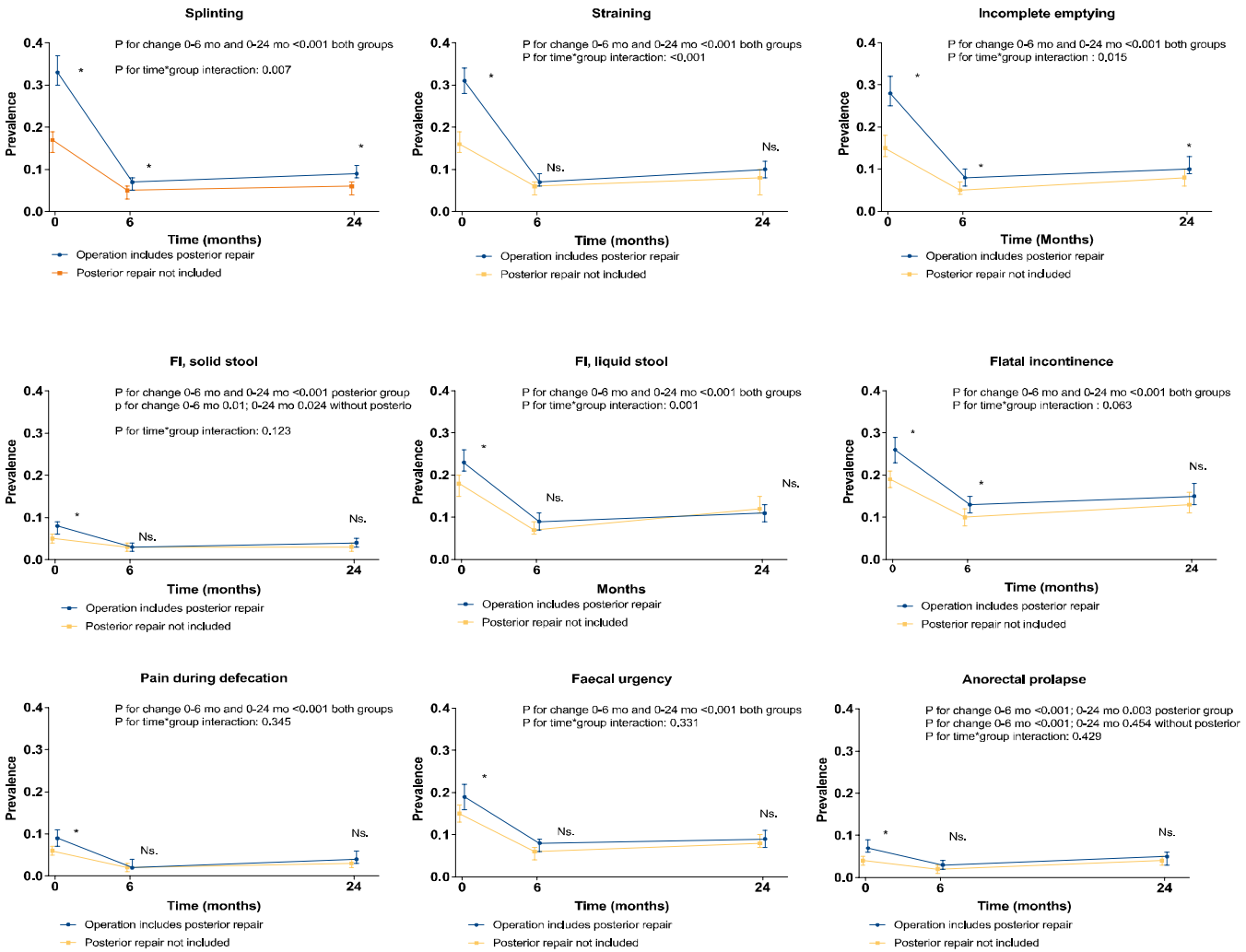


Figure 13. Impact of prolapse surgery on anorectal symptoms. The adjusted prevalences from sensitivity analysis excluding rectopexy cases (n = 64). An asterisk denotes statistical significance ($p < 0.05$), and Ns. indicates insignificance ($p > 0.05$) for between-group comparisons.

5.6 MID AND PASS FOR PFDI-20 (STUDY IV)

The baseline mean PFDI-20 score was 99 (SD ± 50), versus 41 (SD ± 20) for POPDI-6. Table 15 presents the mean change scores from the baseline to six months, categorised according to each global impression of change category.

Table 15. Mean PFDI-20 and POPDI-6 change scores (95% CI) from the baseline to six months for each global impression of change category

PGI-I	n (%)	PFDI-20 change score	POPDI-6 change score
All	2475 (100)	−56 (−58 to −54)	−30 (−31 to −29)
Very much better	842 (34)	−72 (−75 to −69)	−38 (−39 to −36)
Much better	1133 (46)	−56 (−58 to −53)	−30 (−31 to −29)
A little better	335 (14)	−38 (−43 to −33)	−19 (−21 to −17)
No change	95 (3.8)	−14 (−22 to −5.1)	−10 (−15 to −6.0)
A little worse	36 (1.5)	−31 (−49 to −13)	−14 (−22 to −6.3)
Much worse	28 (1.1)	−8.5 (−26 to 9.1)	−9.9 (−19 to −0.6)
Very much worse	6 (0.2)	−17 (−55 to 21)	−5.6 (−26 to 15)

The correlations between PGI-I and PFDI-20 or POPDI-6 change scores at six months were moderate ($r = 0.33$ and $r = 0.35$, respectively; $p < 0.001$). The correlations between PGI-I and PFDI-20 or POPDI-6 six-month postoperative scores were strong ($r = 0.51$ and $r = 0.53$; $p < 0.001$).

The MID estimates' median was 24 points for PFDI-20 and 11 points for POPDI-6. The smallest detectable change exceeded the MID for PFDI-20 at the individual level. (Table 16)

Table 16. Minimal important difference estimates (95% CI) for PFDI-20 and POPDI-6 obtained via different methods

PROM	Mean change	75th percentile	0.5 SD	ROC curve	MID median	SDC group	SDC individual
PFDI-20	−24 (−34 to −15)	−23 (−26 to −20)	−25 (−26 to −24)	−24 (−38 to −10)	−24	5.3	41
POPDI-6	−9.0 (−14 to −4.0)	−13 (−16 to −11)	−10 (−10 to −9.9)	−13 (−21 to −4.4)	−11	0.75	5.8

SDC, smallest detectable change.

Two years post-surgery, 84% of participants (n = 1,902/2,261) considered their state good enough (i.e. had reached PASS). The women who reached PASS had a mean PFDI-20 score of 38 (SD ± 34), while those who did not had a mean score of 103 (SD ± 53). The mean POPDI-6 scores among the women who reached PASS and those who did not were 9.2 (SD ± 11) and 34 (SD ± 22), respectively. Figure 14 depicts the PASS categories' distribution among patients within each PGI-I-category.

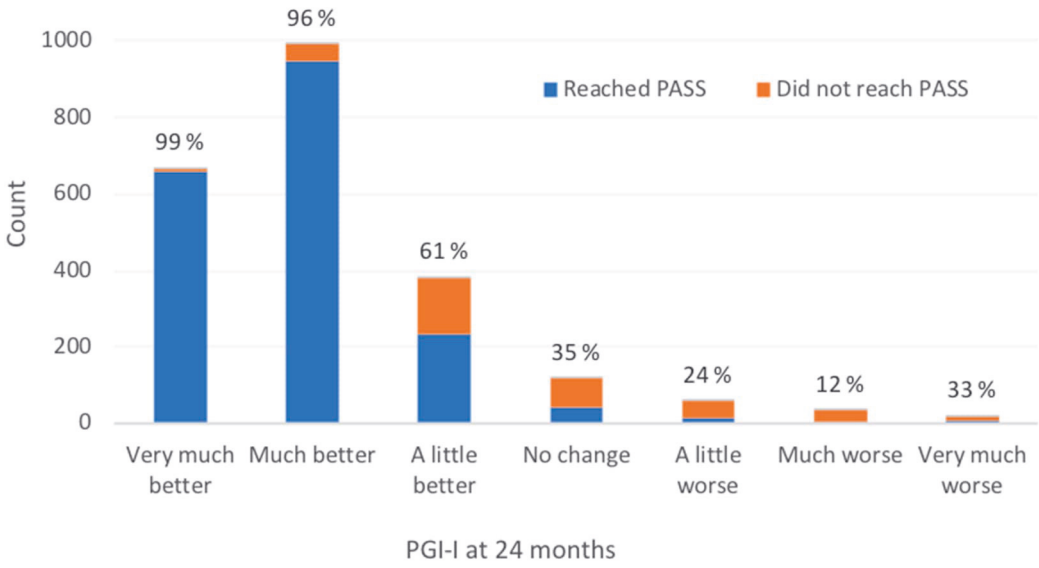


Figure 14. The Patient acceptable symptom state (PASS) category per each global impression of change category at 24-month follow-ups. Percentages indicate the proportion of participants who reached PASS.

The median PASS estimates obtained via different methods were 60 points for PFDI-20 and 17 points for POPDI-6. (Table 17)

Table 17. PASS estimates (95% CI) for PFDI-20 and POPDI-6

PROM	75th percentile	ROC	Median
PFDI-20	58 (55–60)	63 (41–84)	60
POPDI-6	17 (13–19)	18 (13–22)	17

6 DISCUSSION

This thesis highlights the common occurrence of lower urinary tract and anorectal symptoms among women undergoing POP surgery. Nearly all women presented with symptoms related to OAB, SUI, obstructed defecation, or anal incontinence, often concurrently.

In general, surgery favourably influenced each symptom, regardless of the surgical compartment. Nevertheless, residual symptoms occurred; 16–37% of the women with bothersome baseline symptoms still found them bothersome six months after surgery. Although *de novo* symptoms emerged, bothersome symptoms were infrequent.

6.1 THE ROLE OF PROLAPSE IN OVERACTIVE BLADDER SYMPTOMS

This thesis's findings support previous evidence that POP can induce OAB symptoms and that these symptoms improve after POP surgery.

OAB symptoms demonstrated a stronger baseline association and greater postoperative improvement with anterior and apical compartment prolapse compared to the posterior compartment. Conversely, most previous studies have not found a connection between the degree of anterior wall prolapse and OAB severity.[79,80,110–115] Moreover, of the four studies that had investigated surgical compartments' impact on OAB improvements,[99,100,116,117] only one demonstrated any effect, indicating more pronounced improvements after anterior compartment surgery.[100]

Discrepancies between the present study and studies that did not identify associations between baseline anatomy and OAB probably derive from the weakness of the observed correlation. This subtle effect might not have been detectable with smaller samples.[79,110–114] Other reasons include mild or advanced prolapses' inadequate representation,[79,111,112] variables' dichotomization,[79,80,99,100,112,114,115] and the failure to account for prolapse in

other compartments,[22,79,80,112–114] resulting in a lack of contrast in the exposure. Of the three studies that had noted comparable improvements after anterior and posterior compartment surgery, one incorporated multiple predictive factors in its model, possibly leading to overadjustment and collinearity.[116] In the others, all participants underwent concurrent apical repairs, potentially weakening the anterior-posterior comparison.[99,117]

OAB symptoms' association with anterior prolapse supports theories suggesting that POP induces OAB symptoms through bladder outflow obstruction, stretch receptors' activation due to anterior vaginal wall distension, or urethral incompetence.[8] However, symptoms were also prevalent and improved among women with posterior compartment prolapse. The exact mechanism through which posterior compartment surgery might alleviate OAB symptoms remains unclear. However, posterior prolapse could obstruct the bladder or irritate the urothelium via external compression. Alternatively, it could disturb the pelvic floor muscle function, affecting urethral continence mechanisms.

The modest correlation between POP anatomy and OAB symptoms, as well as the incomplete post-surgery symptom relief, indicate that factors beyond prolapse significantly contribute to OAB symptom variability. OAB is a complex, prevalent condition with multiple underlying mechanisms that interact in intricate ways.[93] Since POP surgery does not address other contributing factors, such as urinary microbiota or autonomic nervous system disorders, resolving OAB symptoms entirely through POP surgery alone is inconceivable.

6.2 CHANGES IN STRESS URINARY INCONTINENCE SYMPTOMS AFTER PROLAPSE SURGERY

This thesis's finding of pre-existing SUI's 50% prevalence is in line with the previous literature.[118] Patient-related factors, including anatomy, showed only weak, clinically insignificant associations with preoperative SUI severity. The prior literature has suggested lower SUI rates in advanced

POP,[131,132] based on a Dutch general-population study (N=2,979), which reported 55% concurrent SUI in Stage 2 versus 33% in Stage 4.[22] However, the numbers of advanced prolapses were limited (Stage 3: n=32; Stage 4: n=3), and no statistically significant associations were found. Some studies have found statistically significant negative correlations, but they included women referred for POP *or* SUI, introducing a high risk of selection bias.[114,133]

Pre-existing SUI resolved in one-third of women, aligning with prior research (29–52%).[118,123–126] High baseline symptom severity predicted persistent SUI, as in a Danish study (N = 1,657) with a three-month follow-up.[123] A smaller study (N = 93) did not confirm this finding, but point estimates suggested an increased risk, and wide CIs implied a lack of statistical power.[126] The greatest improvements occurred after surgeries involving the apical compartment. However, both the present study and the Danish study indicated that SUI improvement can follow surgery targeting any compartment.[123] A Swedish RCT comparing perineal repair with pelvic floor physiotherapy for poorly healed perineal injuries provided further evidence: 44% of women with SUI symptoms experienced post-surgery resolution versus no significant improvement post-physiotherapy.[304] The biomechanical rationale for SUI resolution after posterior repair is not immediately apparent; the pelvic floor muscles' and continence mechanism's function might improve after bulges' removal or the perineal body's restoration.

The *de novo* SUI incidence ranges widely in the prior literature (4–49%), primarily due to varying definitions.[118–122,130] The 20% rate of *any de novo* SUI in the current study aligns with a 22% rate in a similar Dutch study.[118] The low incidence of *bothersome de novo* SUI (3%) observed in this study is reassuring.

Except for one study observing a correlation between advanced preoperative cystocele and *de novo* SUI risk,[305] other studies support this thesis's finding that *de novo* SUI develops irrespective of prolapses' degree and compartment.[121,139,306] This result challenges the prevailing linking of *de novo* SUI with the correction of urethral kinking caused by advanced cystoceles.[132] In this context, bladder neck anatomy may be more crucial

than cystocele size.[307] Additionally, posterior compartment prolapses might mask SUI by externally compressing the urethral lumen, rather than inducing urethral kinking.[88,308]

The only consistent risk factors for *de novo* SUI identified in the current study were advanced age, transvaginal mesh surgery, and baseline UUI symptoms. The limited performance of the *de novo* SUI risk calculator is understandable, given weak, non-existent, and even contradictory correlations between its factors and *de novo* SUI across studies.[139–143] For example, both the present study and Lo et al. found *de novo* SUI risk to increase with age,[306] while the study on which the calculator was based reported opposing results.[139]

Varied global rates of *concomitant* SUI surgery imply that international guidelines' recommendations to combine POP and SUI procedures for preoperative overt and occult SUI are not universally accepted.[13,131,134] The reported rates range from 0.2% in Denmark and 0.9% in the FINPOP cohort to 36% in the United States.[309,310]

The present study found notably lower rates of *subsequent* SUI procedures than the systematic review of RCTs (5% vs. 40% for preoperatively incontinent women and 1% vs. 6% for continent women).[11] This disparity may stem from RCTs incorporating SUI procedures into their protocol and involving selected populations. In everyday practice, women receive further treatment only if they actively seek it, and invasive treatment may not be the primary approach.

Among women with preoperative SUI, 65% experienced persistent SUI, yet only 5% underwent subsequent SUI procedures. This finding may imply that many of them managed their symptoms acceptably, as in an RCT in which 21% of participants with persistent symptoms declined planned SUI procedures due to a lack of bother.[124] Cultural factors and concerns about complications may influence patients' decisions. The higher rate of subsequent SUI procedures after transvaginal mesh surgery – despite comparable symptoms – could be attributed to more rigorous follow-ups or patient and surgeon preferences.

6.3 THE ROLE OF PROLAPSE IN OBSTRUCTED DEFECATION AND OTHER ANORECTAL SYMPTOMS

The present study substantiates the role of posterior vaginal wall prolapse in obstructed defecation. These symptoms correlated with the extent of posterior vaginal wall prolapse and improved more after posterior compartment surgery than after surgery excluding this compartment. Previous studies that lacked associations between posterior POP and obstructed defecation often had smaller samples or limited representations of advanced POP stages, resulting in insufficient contrast.[97,110,147–152] Conversely, studies employing standardised measures and well-designed methodologies demonstrated correlations.[78,157]

Greater symptom improvement after posterior compartment repair, compared to cases without repair, implies that prolapse precedes obstructed defecation, not vice versa. Therefore, it is probable that posterior vaginal wall anatomy plays a causal role in obstructed defecation, modifies the effect of an independent anorectal pathology, or both. However, the relationship between these two is not necessarily a simple dichotomy; in some cases, anatomical defects in the posterior compartment may be a consequence of straining.

The reason for the lack of a further increase in symptom prevalence beyond Stage 2 remains unclear. This observation aligns with the work of Tan et al., who investigated 1,912 women with various pelvic floor disorders, noting a linear rise in splinting from POP-Q point Bp −3 to +1 before the prevalence stabilised.[78] A potential explanation is that the POP-Q system, which measures the extent of POP protruding beyond the hymen, might not accurately capture posterior compartment prolapses' size; they often bulge anteriorly within the vagina. Larger posterior wall prolapses might also be more prone to enteroceles, potentially influencing defecation mechanics. In addition, individuals with advanced POP may have a unique neural or psychological makeup, tolerating more severe symptoms and reporting less discomfort.

Obstructed defecation symptoms also improved in women without posterior wall involvement, and at times, symptoms were absent despite

advanced posterior wall prolapse. These findings mirror the complexity of defecation, a coordinated interplay between the nervous system and end organs in which disruptions can lead to intractable interactions.[145]

Prior research on the relationship between POP and FI is scant. The current study revealed a weak correlation between the posterior wall stage and liquid stool incontinence, which also improved more after surgery for the posterior compartment than for other compartments. However, no correlation was found between flatus or solid stool incontinence and baseline anatomy; postoperative improvement was more moderate for these symptoms and unrelated to the treated compartment. These findings suggest that other factors, such as obstetric anal sphincter or nerve injury, likely contribute to FI more, with prolapse potentially intensifying their effects. Nonetheless, it is conceivable that, in some cases, incontinence of liquid stool could be attributed to seepage from the retained stool in the rectocele pocket, as has been proposed.[179,182,183]

Pain during defecation, faecal urgency, and a sensation of anorectal prolapse are not considered typical POP symptoms; rather, they imply anorectal pathology. The current study found a correlation between increasing posterior wall prolapse stages and these symptoms' higher prevalence. However, their post-surgery improvement was less significant than that of obstructed defecation and unrelated to posterior compartment surgery. These symptoms' coexistence with posterior wall prolapse might arise from the same pathogenic mechanism between POP and the conditions leading to these symptoms. For instance, anorectal pain and a sensation of anorectal prolapse have been proposed to indicate intussusception.[311]

6.4 INTERPRETING PFDI-20 SCORES USING MID AND PASS

This thesis complements three previous reports on the MID for PFDI-20 and provides the first MID estimate for POPDI-6. Notably, it defined the MID specifically for women undergoing POP surgery.

Wiegersma et al. established a MID of 13.5 points for women with conservative POP treatments, lower than the current study's 24 points.[287]

This difference can be attributed to their study population's low baseline score of 56 points (vs. 99 points in this study), reflecting a preference for conservative treatments with lower symptom burdens. Prior research has indicated that MIDs are tied to initial symptom severity; individuals experiencing more severe symptoms require greater score changes for meaningful improvements.[303,312]

Barber et al. (MID 45 points) and Utomo et al. (23 points) included women with any pelvic floor dysfunction.[279,288] While Barber et al. focused on women undergoing surgical treatment (baseline score 122), Utomo et al. included both conservative and surgical treatments (baseline score 94). Methodological concerns arise regarding the former study due to its small sample of 45 patients and no participants reporting 'no change' post-surgery.[279]

The smallest detectable change at the group level was lower than the MID, indicating that the measure can distinguish clinically significant changes from measurement error at the group level. However, at the individual level, the smallest detectable change exceeded the MID for PFDI-20. In other words, there is a possibility that an individual patient's PFDI-20 score change as great as the MID could be a measurement error.

The MID determination process is still evolving; questions about method selection, anchors' phrasing and cut-offs, follow-up durations, and confounding factors such as baseline scores are unresolved.[313] Experts have suggested triangulating the MID by combining several anchor- and distribution-based methods and using multiple relevant anchors.[289] Given the lack of a unified perspective, this thesis employed multiple methods, unlike previous reports. The obtained estimates were consistent, enhancing the confidence in the values.

Making patients 'feel better' may not make them 'feel good'. For example: a four-point pain score reduction from 9 on a 0–10 VAS scale can be viewed as a significant improvement, but a score of 5 does not necessarily denote an acceptable condition. PASS addresses this challenge as a threshold indicating patients' likelihood of having reached acceptable symptom states.[292]

The current study introduced PASS into POP research by providing the first estimates for PFDI-20 and POPDI-6. MID and PASS complement each other; patients' conditions may significantly improve, yet remain unsatisfactory from their perspectives. Conversely, even minor improvements might lead patients to deem their conditions acceptable, eliminating the need for further treatment.

Uncertainties persist due to the lack of consensus on optimal methods for establishing PASS thresholds.[297] While baseline scores influence PASS, their impact is not as pronounced as with the MID.[292,293,314] Factors such as previous treatments' success and treatment options' availability could affect the levels at which patients feel they achieve acceptable symptom states.[315] Furthermore, while PASS holds group-level value, considerable variation among individuals is probable; therefore, a single cut-off is likely unsuitable for personalised use.

6.5 METHODOLOGICAL CONSIDERATIONS

An experimental study that randomly exposes women to different degrees of prolapse would be an ideal design to investigate causal relationships between prolapse and symptoms. However, such a study would not be ethical or technically feasible. Longitudinal cohort studies can also address aetiological questions, but validating an observed association as a true cause-and-effect relationship requires considering chance, bias, and confounding.[283]

Chance can influence point estimates in small samples, but inaccuracy due to chance would be unlikely in a study of this magnitude. A large sample also ensures precise estimates (i.e. narrow confidence intervals).

The FINPOP cohort accurately represents the population of interest with a high participation rate. Selection bias is unlikely to have emerged due to participant drop-out at the baseline; the respondents and non-respondents did not significantly differ in age, prior POP surgeries, concomitant or prior incontinence surgeries, or surgery type or compartment ($p > 0.05$ for all).

However, the association between pelvic anatomy and baseline symptoms could have been overestimated because the sample comprised women undergoing POP surgery, implying more pronounced symptoms. The results, therefore, may not directly apply to women with milder conditions.

The follow-up participation rate was acceptable. Non-respondents at two years were more likely to smoke, slightly younger (mean age difference of 1 year), and less likely to have undergone mesh operations.[230] Incomplete questionnaires for various reasons added to the incomplete data, which nevertheless remained at an acceptable level.[230] Importantly, loss to follow-up or unwillingness to answer parts of questionnaires is likely not completely at random. For example, women with poor outcomes may be less willing to respond, potentially distorting satisfaction rate and symptom change estimates during follow-up.

A strength is the available data concerning subsequent SUI procedures from the Care Register for Health Care for all participants but one. However, longer follow-up times might have raised procedure rates. Furthermore, coding errors may have occurred to some extent, although research on Finnish registers' quality suggests they might not have been a major concern.[298]

Objective data on LUTS were not collected; utilising such data could have yielded different results. Although PFDI-20 has been validated overall, its individual items lack standalone validation, posing a potential for misclassification between SUI and UUI. Questionnaires are also vulnerable to participants' capacity and willingness to provide accurate information. Moreover, the absence of data on urinary urgency and nocturia is a limitation regarding the assessment of OAB outcomes.

Multiple doctors quantified POP degrees; confirming consistent adherence to instructions was challenging. Patient-reported covariates – including weight, smoking status, comorbidities, and medication use – may also have involved misclassification. However, these exposure and covariate misclassifications were likely not differential between the comparison groups (i.e. vaginal compartments), allowing for credible comparisons.

Several factors warrant consideration regarding symptom improvement. First, the absence of a non-surgical comparison group hampers the ability to attribute symptom improvements solely to the specific effects of surgery. Non-specific effects, such as regression to the mean and the natural course of the disease, account for considerable part of changes in health status following surgery.[316] However, these factors likely affect various symptoms and compartments uniformly, enabling credible conclusions concerning relative symptom changes. Second, the observed symptom changes should not be generalised to specific procedures. Third, the studies lacked postoperative clinical examinations, hindering the assessment of anatomical recurrences' contributions to persistent symptoms. Finally, the studies did not account for conservative treatments for lower urinary tract symptoms, nor did they consider conservative or surgical treatments for POP recurrence and anorectal symptoms.

The population-based setting, encompassing diverse patients, surgical techniques, and surgeons, enhances the external validity of the findings. Still, the predominantly White and culturally homogenous study population may limit the generalisability of the results to other ethnic groups; cultural aspects might influence psychological dispositions and the perception of symptoms and their severity.

Multivariable regression models were employed to account for potential confounding factors. Building these models is complex, and some variables lack robust supporting evidence. Bias may have arisen from omitting important confounders or adjusting for non-confounders. In Studies I and III, whose models were designed to explain the symptoms, directed acyclic graphs were utilised.[299] In Study II, which focused on prediction, all pertinent prognostic factors derived from existing knowledge or clinical insights were incorporated into the model. Controlling for prolapse in other compartments was feasible, distinguishing this thesis from other studies.

Study IV meets four of the five criteria for a credible MID proposed by Devji et al.[290] However, the correlation between the anchor and the PROM change score is questionable (0.32–0.35). Though correlation thresholds of 0.30–0.35 are commonly considered credible,[289] some researchers

advocate for a higher threshold of 0.5–0.7.[290,317] The anchor's correlation with the postoperative score was stronger than with the change score, highlighting limitations in using the global transition rating as an anchor. Patients may be influenced by their current states when rating and struggle to recall their preoperative states for comparison; shorter periods from their baselines could have increased the correlation.[318] Discrepancies between change scores and PGI-I can also emerge when PFDI-20 fails to accurately represent an individual's perception. For instance, a patient might experience postoperative relief from vaginal bulging, urinary frequency, and obstructed defecation but also encounter distressing *de novo* SUI or dyspareunia - the latter not even included in PFDI-20. Consequently, despite a marked PFDI-20 score improvement, she may perceive her condition as much worse than before the surgery.

6.6 CLINICAL IMPLICATIONS

Clinicians must recognise that the presence of prolapse does not automatically indicate it as the root cause of bladder or bowel symptoms; it could also be an innocent bystander. As pelvic floor disorders often coexist and emerge from diverse origins, expecting POP to account for all symptomology or surgery to universally resolve it would be unrealistic.

Women have a high likelihood to experience OAB symptom improvement after POP surgery. Although OAB was more linked to anterior and apical prolapse, this thesis challenges the conventional view that urinary symptoms are exclusively influenced by the anterior compartment.

Individualising SUI treatments during POP surgery and collaborating with patients is wise. On average, patients with bothersome SUI symptoms face a 24% chance of complete symptom resolution and a 43% chance of persistent bothersome SUI two years after POP surgery alone. Hence, staged strategies are reasonable alternatives for patients hesitant about concurrent continence surgery and open to secondary interventions. On the other hand, given the rarity and unpredictability of bothersome *de novo* SUI, staged strategies may suit most continent women.

This thesis's findings suggest that posterior vaginal wall prolapse can contribute to obstructed defecation, and most patients can anticipate considerable improvement after prolapse surgery. Accordingly, surgery is viable for women with significant posterior vaginal wall prolapse and obstructed defecation refractory to conservative therapies. However, if rectocele is not substantial or symptoms extend beyond obstructed defecation, additional investigations may be prudent.

The importance of comprehensive preoperative counselling cannot be overstated. Clear information about surgery's potential and limitations is essential. While surgery typically alleviates vaginal bulge symptoms, persistent or new bladder or bowel symptoms remain possible. Benefits and risks differ across pelvic floor symptoms; this thesis's findings facilitate personalised counselling.

MID and PASS thresholds lack relevance for individual patients. However, posing the PASS question 'Do you consider your state good enough?' is valuable; sometimes, completely symptom-free states are unrealistic and unlikely to be attained through additional interventions.

6.7 FUTURE CONSIDERATIONS

Further research is needed to explain why some women do not undergo interventions for bothersome postoperative SUI. Additionally, concomitant SUI surgery's effects on patient satisfaction compared to the staged approach should be investigated.

Specific attributions of rectoceles, deficient perineum, enteroceles, intussusception, or dyssynergic defecation to particular anorectal symptoms remain uncertain. Studies should correlate symptoms with various ancillary tests, employing validated questionnaires and standardised testing.

Continued investigations into symptoms' improvement after specific surgical procedures are essential. Studies should apply standardised surgical techniques and include conservative-treatment or waitlist control groups to measure surgery's specific effects. Exploring the correlation between ancillary testing findings – such as urodynamic studies and

defecography – and postoperative outcomes could help identify patients most likely to benefit from surgery. Studies should also involve postoperative clinical assessments to explain the extent to which persistent symptoms stem from residual prolapse.

7 CONCLUSIONS

This thesis supports the following conclusions:

1. OAB symptoms are more related to anterior and apical compartment prolapse than posterior compartment prolapse. Substantial symptom improvement occurs after surgery for any vaginal compartment.
2. Half of women with preoperative SUI experience improvement after POP surgery, and bothersome *de novo* SUI is rare. The rate of subsequent SUI procedures is low. Predicting postoperative SUI remains challenging.
3. Obstructed defecation symptoms depend on the posterior vaginal wall anatomy, and improvements can usually be anticipated after posterior compartment surgery. While anal incontinence, faecal urgency, pain during defecation, and anorectal prolapse symptoms also improve after POP surgery, they are less specific to posterior vaginal wall prolapse and should raise clinical suspicions of underlying anorectal pathology.
4. The MID and PASS thresholds facilitate PFDI-20 and POPDI-6 scores' interpretation in POP surgery. Mean differences of 24 points for PFDI-20 and 11 points for POPDI-6 denote clinically meaningful improvements; postoperative PFDI-20 scores ≤ 60 and POPDI-6 scores ≤ 17 signify the subset of patients who achieve acceptable symptom states.

REFERENCES

1. Haylen BT, Maher CF, Barber MD, Camargo S, Dandolu V, Digesu A, et al. Erratum to: An International Urogynecological Association (IUGA) / International Continence Society (ICS) Joint Report on the Terminology for Female Pelvic Organ Prolapse (POP). Int Urogynecol J. 2016;27(2):655–84.
2. Deprest JA, Cartwright R, Dietz HP, Brito LGO, Koch M, Allen-Brady K, et al. International Urogynecological Consultation (IUC): pathophysiology of pelvic organ prolapse (POP). Int Urogynecol J. 2022;33(7):1699–710.
3. Finazzi Agrò E, Salvatore S, Braga A, Delancey J, Fernando R, Iacovelli V, et al. Pathophysiology of urinary incontinence, pelvic organ prolapse and faecal incontinence. In: Cardozo L, Rovner E, Wagg A, Wein A, Abrams P, editors. Incontinence 7th Edition. 2023. p. 247–396.
4. Robinson D, Prodigalidad LT, Chan S, Serati M, Lozo S, Lowder J, et al. International Urogynaecology Consultation chapter 1 committee 4: patients' perception of disease burden of pelvic organ prolapse. Int Urogynecol J. 2022;33(2):189–210.
5. 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.
6. Barber MD. Symptoms and outcome measures of pelvic organ prolapse. Clin Obstet Gynecol. 2005;48(3):648–61.
7. Harvey MA, Chih HJ, Geoffrion R, Amir B, Bhide A, Miotla P, et al. International Urogynecology Consultation Chapter 1 Committee 5: relationship of pelvic organ prolapse to associated pelvic floor dysfunction symptoms: lower urinary tract, bowel, sexual dysfunction and abdominopelvic pain. Int Urogynecol J. 2021;32(10):2575–94.
8. De Boer TA, Salvatore S, Cardozo L, Chapple C, Kelleher C, Van Kerrebroeck P, et al. Pelvic organ prolapse and overactive bladder. Neurourol Urodyn. 2010;29(1):30–9.
9. Grimes CL, Lukacz ES. Posterior vaginal compartment prolapse and defecatory dysfunction: Are they related? Int Urogynecol J. 2012;23(537–551).

10. Carberry CL. The Effect of Pelvic Organ Prolapse Surgery on Pre-existing Overactive Bladder. Curr Obstet Gynecol Rep. 2016;5:147–51.
11. van der Ploeg JM, van der Steen A, Zwolsman S, van der Vaart CH, Roovers JPWR. Prolapse surgery with or without incontinence procedure: a systematic review and meta-analysis. BJOG. 2018;125(3):289–97.
12. Barber MD, Brubaker LP, Nygaard I, II TLW, Schaffer JI, Chen Z, et al. Defining Success After Surgery for Pelvic Organ Prolapse. Obs Gynecol. 2009;114(3):600–9.
13. de Tayrac R, Antosh DD, Baessler K, Cheon C, Deffieux X, Gutman R, et al. Summary: 2021 International Consultation on Incontinence Evidence-Based Surgical Pathway for Pelvic Organ Prolapse. J Clin Med. 2022;11(20).
14. Toozs-Hobson P, Freeman R, Barber M, Maher C, Haylen B, Athanasiou S, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for reporting outcomes of surgical procedures for pelvic organ prolapse. Int Urogynecol J. 2012;23:527–35.
15. Schünemann HJ, Akl EA, Guyatt GH. Interpreting the results of patient reported outcome measures in clinical trials: The clinician's perspective. Health Qual Life Outcomes. 2006;4:1–8.
16. Sultan AH, Monga A, Lee J, Emmanuel A, Norton C, Santoro G, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female anorectal dysfunction. Int Urogynecol J. 2017;28(1):5–31.
17. Brown HW, Hegde A, Huebner M, Neels H, Barnes HC, Marquini GV, et al. International urogynecology consultation chapter 1 committee 2: Epidemiology of pelvic organ prolapse: prevalence, incidence, natural history, and service needs. Int Urogynecol J. 2022;33(2):173–87.
18. Nygaard I, Bradley C, Brandt D. Pelvic organ prolapse in older women: Prevalence and risk factors. Obstet Gynecol. 2004;104(3):489–97.
19. Swift SE, Tate SB, Nicholas J. Correlation of symptoms with degree of pelvic organ support in a general population of women: what is pelvic organ prolapse? Am J Obstet Gynecol. 2003;189(2):372–7.
20. Swift S, Woodman P, O'Boyle A, Kahn M, Valley M, Bland D, et al. Pelvic Organ Support Study (POSST): The distribution, clinical

definition, and epidemiologic condition of pelvic organ support defects. Am J Obstet Gynecol. 2005;192(3):795–806.
21. Awwad J, Sayegh R, Yeretzian J, Deeb ME. Prevalence, risk factors, and predictors of pelvic organ prolapse: A community-based study. Menopause. 2012;19(11):1235–41.
22. Slieker-Ten Hove MCP, Pool-Goudzwaard AL, Eijkemans MJC, Steegers-Theunissen RPM, Burger CW, Vierhout ME. The prevalence of pelvic organ prolapse symptoms and signs and their relation with bladder and bowel disorders in a general female population. Int Urogynecol J. 2009;20(9):1037–45.
23. Trowbridge ER, Fultz NH, Patel DA, DeLancey JOL, Fenner DE. Distribution of pelvic organ support measures in a population-based sample of middle-aged, community-dwelling African American and white women in southeastern Michigan. Am J Obstet Gynecol. 2008;198(5):548.e1-548.e6.
24. Masenga GG, Shayo BC, Rasch V. Prevalence and risk factors for pelvic organ prolapse in Kilimanjaro, Tanzania: A population based study in Tanzanian rural community. PLoS One. 2018;13(4):1–13.
25. Mäkelä-Kaikkonen J, Karjalainen PK. Lantionpohjan toimintahäiriöt ovat yleisiä [Pelvic floor dysfunction]. Suom Lääkäril. 2021;76:2951–7.
26. Milson I, Altman D, Cartwright R, Lapitan MC, Nelson R, Sjöström S, et al. Epidemiology of urinary incontinence (UI) and other lower urinary tract symptoms (LUTS), pelvic organ prolapse (POP) and anal incontinence (AI). In: Cardozo L, Rovner E, Wagg A, Wein A, Abrams P, editors. Incontinence 7th Edition. Bristol UK: International Continence Society; 2023.
27. Barber MD, Maher C. Epidemiology and outcome assessment of pelvic organ prolapse. Int Urogynecol J. 2013;24(11):1783–90.
28. Nygaard I, Barber MD, Burgio KL, Kenton K, Meikle S, Schaffer J, et al. Prevalence of Symptomatic Pelvic Floor Disorders in US Women. JAMA - J Am Med Assoc. 2008;300(11):1311–6.
29. Slieker-ten Hove MCP, Pool-Goudzwaard AL, Eijkemans MJC, Steegers-Theunissen RPM, Burger CW, Vierhout ME. Symptomatic pelvic organ prolapse and possible risk factors in a general population. Am J Obstet Gynecol. 2009;200(2):184.e1-184.e7.
30. Handa VL, Garrett E, Hendrix S, Gold E, Robbins J. Progression and remission of pelvic organ prolapse: A longitudinal study of menopausal women. Am J Obstet Gynecol. 2004;190(1):27–32.
31. Hendrix SL, Clark A, Nygaard I, Aragaki A, Barnabei V, McTiernan A.

Pelvic organ prolapse in the Women's Health Initiative: Gravity and gravidity. Am J Obstet Gynecol. 2002;186(6):1160–6.
32. Bradley CS, Zimmerman MB, Qi Y, Nygaard IE. Natural History of Pelvic Organ Prolapse in Postmenopausal Women. Obs Gynecol. 2007;109(4):848–54.
33. Miedel A, Ek M, Tegerstedt G, Mæhle-Schmidt M, Nyrén O, Hammarström M. Short-term natural history in women with symptoms indicative of pelvic organ prolapse. Int Urogynecol J. 2011;22(4):461–8.
34. Gilchrist AS, Campbell W, Steele H, Brazell H, Foote J, Swift S. Outcomes of Observation as Therapy for Pelvic Organ Prolapse: A Study in the Natural History of Pelvic Organ Prolapse. Neurourol Urodyn. 2013;32(4):383-6.
35. Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. Lancet. 2007;369(9566):1027–38.
36. Haya N, Baessler K, Christmann-Schmid C, De Tayrac R, Dietz V, Guldberg R, et al. Prolapse and continence surgery in countries of the Organization for Economic Cooperation and Development in 2012. Am J Obstet Gynecol. 2015;212(6):755.e1-755.e27.
37. Smith FJ, Holman CDJ, Moorin RE, Tsokos N. Lifetime Risk of Undergoing Surgery for Pelvic Organ Prolapse. Obs Gynecol. 2010;116(5):1096–100.
38. Løwenstein E, Ottesen B, Gimbel H. Incidence and lifetime risk of pelvic organ prolapse surgery in Denmark from 1977 to 2009. Int Urogynecol J. 2015;26(1):49–55.
39. Kurkijärvi K. Surgery for Stress Urinary Incontinence and Pelvic Organ Prolapse in Finnish Women. In: Doctoral dissertation, University of Turku. 2017. p. https://www.utupub.fi/handle/10024/143988.
40. Corton MM. Anatomy of the pelvis: How the pelvis is built for support. Clin Obstet Gynecol. 2005;48(3):611–26.
41. Shobeiri SA, Delancey JOL. Pelvic Floor Anatomy. In: Santoro GA, Wieczorek AP, Sultan AH, editors. Pelvic Floor Disorders. 2nd ed. Springer; 2021. p. 3–24.
42. Delancey JOL. What's new in the functional anatomy of pelvic organ prolapse. Curr Opin Obs Gynecol. 2016;28(5):420–9.
43. Barber MD. Contemporary views on female pelvic anatomy. Cleve Clin J Med. 2004;72(SUPPL.4):3–11.
44. Dietz HP, Wilson PD, Milsomc I. Maternal birth trauma: Why should it

matter to urogynaecologists? Curr Opin Obstet Gynecol. 2016;28(5):441–8.
45. English EM, Chen L, Sammarco AG, Kolenic GE, Cheng W, Ashton-Miller JA, et al. Mechanisms of Hiatus Failure in Prolapse: A Multifaceted Evaluation. Int Urogynecol J. 2021;32(6):1545–53.
46. Parks AG, Porter NH, Melzak J. Experimental study of the reflex mechanism controlling the muscles of the pelvic floor. Dis Colon Rectum. 1962;5:407–414.
47. Barber MD, Bremer RE, Thor KB, Dolber PC, Kuehl TJ, Coates KW. Innervation of the female levator ani muscles. Am J Obs Gynecol. 2002;187(1):64–71.
48. Wallner C, Maas CP, Dabhoiwala NF, Lamers WH, DeRuiter MC. Innervation of the pelvic floor muscles: a reappraisal for the levator ani nerve. Obs Gynecol. 2006;108(3 Pt 1):529–34.
49. DeLancey JOL, Kane Low L, Miller JM, Patel DA, Tumbarello JA. Graphic integration of causal factors of pelvic floor disorders: an integrated life span model. Am J Obstet Gynecol. 2008;199(6):610.e1-610.e5.
50. Corton MM. Anatomy of Pelvic Floor Dysfunction. Obstet Gynecol Clin North Am. 2009;36(3):401–19.
51. Cattani L, Decoene J, Page AS, Weeg N, Deprest J, Dietz HP. Pregnancy, labour and delivery as risk factors for pelvic organ prolapse: a systematic review. Int Urogynecol J. 2021;32(7):1623–31.
52. Mattsson NK, Karjalainen P, Tolppanen A-M, Heikkinen A-M, Jalkanen J, Härkki P, et al. Methods of surgery for pelvic organ prolapse in a nationwide cohort (FINPOP 2015). Acta Obstet Gynecol Scand. 2019;98(4).
53. Lo T, Jaili S, Uy-patrimonio MC, Karim N, Ibrahim R. Transvaginal management of severe pelvic organ prolapse in nulliparous women. J Obs Gynecol Res. 2017;43(3):543–50.
54. Larsudd-Kåverud J, Gyhagen J, Åkervall S, Molin M, Milsom I, Wagg A, et al. The influence of pregnancy, parity, and mode of delivery on urinary incontinence and prolapse surgery—a national register study. Am J Obstet Gynecol. 2023;228(1):61.e1-61.e13.
55. Schulten SFM, Claas-Quax MJ, Weemhoff M, van Eijndhoven HW, van Leijsen SA, Vergeldt TF, et al. Risk factors for primary pelvic organ prolapse and prolapse recurrence: an updated systematic review and meta-analysis. Am J Obstet Gynecol. 2022;227(2):192–208.
56. Dietz H, Simpson J. Levator trauma is associated with pelvic organ

prolapse. BJOG. 2008;115:979–84.
57. Dietz HP, Franco AVM, Shek KL, Kirby A. Avulsion injury and levator hiatal ballooning: Two independent risk factors for prolapse? An observational study. Acta Obstet Gynecol Scand. 2012;91(2):211–4.
58. Weidner AC, Jamison MG, Branham V, South MM, Borawski KM, Romero AA. Neuropathic injury to the levator ani occurs in 1 in 4 primiparous women. Am J Obstet Gynecol. 2006;195(6):1851–6.
59. Gustavo L, Brito O, Miranda G, Pereira V, Moalli P, Shynlova O, et al. Age and / or postmenopausal status as risk factors for pelvic organ prolapse development : systematic review with meta-analysis. Int Urogynecol J. 2022;33:15–29.
60. Samimi P, Jones SH, Giri A. Family history and pelvic organ prolapse : a systematic review and meta-analysis. Int Urogynecol J. 2021;32:759–74.
61. Jack GS, Nikolova G, Vilain E, Raz S, Rodríguez L V. Familial tranmission of genitovaginal prolapse. Int Urogynecol J. 2006;17:498–501.
62. Allen-Brady K, Chua JWF, Cuffolo R, Koch M, Sorrentino F, Cartwright R. Systematic review and meta-analysis of genetic association studies of pelvic organ prolapse. Int Urogynecol J. 2022;33:67–82.
63. Ashton-miller JA, Delancey JOL. Functional Anatomy of the Female Pelvic Floor. Ann N Y Acad Sci. 2007;1101:266–96.
64. Strohbehn K, Jakary JA, DeLancey JOL. Pelvic Organ Prolapse in Young Women. Obs Gynecol. 1997;90(1):33–6.
65. Veit-Rubin N, Cartwright R, Singh AU, Digesu GA, Fernando R, Khullar V. Association between joint hypermobility and pelvic organ prolapse in women: a systematic review and meta-analysis. Int Urogynecol J. 2016;27(10):1469–78.
66. Carley ME, Schaffer J. Urinary incontinence and pelvic organ prolapse in women with Marfan or Ehlers-Danlos syndrome. Am J Obs Gynecol. 2000;182(5):1021–3.
67. Fitz FF, Bortolini MAT, Pereira GMV, Salerno GRF, Castro RA. PEOPLE: Lifestyle and comorbidities as risk factors for pelvic organ prolapse-a systematic review and meta-analysis PEOPLE: PElvic Organ Prolapse Lifestyle comorbiditiEs. Int Urogynecol J. 2023;34(9):2007–32.
68. Young N, Atan IK, Rojas RG, Dietz HP. Obesity: how much does it matter for female pelvic organ prolapse? Int Urogynecol J. 2018;29:1129–34.
69. Altman D, Falconer C, Cnattingius S, Granath F. Pelvic organ prolapse

surgery following hysterectomy on benign indications. Am J Obstet Gynecol. 2008;198(5):572.e1-572.e6.
70. Kuittinen T, Tulokas S, Rahkola-Soisalo P, Brummer T, Jalkanen J, Tomas E, et al. Pelvic organ prolapse after hysterectomy: A 10-year national follow-up study. Acta Obstet Gynecol Scand. 2023;102(5):556–66.
71. Aagesen AH, Klarskov N, Gradel KO, Husby KR. Hysterectomy on benign indication and risk of pelvic organ prolapse surgery: A national matched cohort study. Acta Obstet Gynecol Scand. 2023;102(6):774–81.
72. Chan SSC, Cheung RYK, Yiu KW, Lee LL, Pang AWL, Chung TKH. Symptoms, quality of life, and factors affecting women's treatment decisions regarding pelvic organ prolapse. Int Urogynecol J. 2012;23(8):1027–33.
73. Jelovsek JE, Barber MD. Women seeking treatment for advanced pelvic organ prolapse have decreased body image and quality of life. Am J Obstet Gynecol. 2006;194(5):1455–61.
74. Ghetti C, Skoczylas LC, Oliphant SS, Nikolajski C, Lowder JL. The Emotional Burden of Pelvic Organ Prolapse in Women Seeking Treatment: A Qualitative Study. Female Pelvic Med Reconstr Surg. 2015;21(6):332–8.
75. Sung VW, Hampton BS. Epidemiology of Pelvic Floor Dysfunction. Obstet Gynecol Clin North Am. 2009;36(3):421–43.
76. Lawrence JM, Lukacz ES, Nager CW, Hsu JWY, Luber KM. Prevalence and co-occurrence of pelvic floor disorders in community-dwelling women. Obstet Gynecol. 2008;111(3):678–85.
77. Ellerkmann RM, Cundiff GW, Melick CF, Nihira MA, Leffler K, Bent AE. Correlation of symptoms with location and severity of pelvic organ prolapse. Am J Obstet Gynecol. 2001;185(6):1332–8.
78. Tan JS, Lukacz ES, Menefee SA, Powell CR, Nager CW, Albo ME, et al. Predictive value of prolapse symptoms: A large database study. Int Urogynecol J. 2005;16(3):203–9.
79. Bradley CS, Nygaard IE. Vaginal wall descensus and pelvic floor symptoms in older women. Obstet Gynecol. 2005;106(4):759–66.
80. Ghetti C, Gregory WT, Edwards SR, Otto LN, Clark AL. Pelvic organ descent and symptoms of pelvic floor disorders. Am J Obstet Gynecol. 2005;193(1):53–7.
81. Barber MD, Neubauer NL, Klein-Olarte V. Can we screen for pelvic organ prolapse without a physical examination in epidemiologic

studies? Am J Obstet Gynecol. 2006 Oct;195(4):942–8.
82. Obinata D, Yamaguchi K, Ito A, Murata Y, Ashikari D, Igarashi T, et al. Lower urinary tract symptoms in female patients with pelvic organ prolapse: Efficacy of pelvic floor reconstruction. Int J Urol. 2014;21(3):301–7.
83. Lo TS, Shailaja N, Hsieh WC, Uy-Patrimonio MC, Yusoff FM, Ibrahim R. Predictors of voiding dysfunction following extensive vaginal pelvic reconstructive surgery. Int Urogynecol J. 2017;28(4):575–82.
84. FitzGerald MP, Kulkarni N, Fenner D. Postoperative resolution of urinary retention in patients with advanced pelvic organ prolapse. Am J Obstet Gynecol. 2000;183(6):1361–4.
85. Richardson DA, Bent AE, Ostergard DR. The effect of uterovaginal prolapse on urethrovesical pressure dynamics. Am J Obs Gynecol. 1983;146(8):901–5.
86. Wong JWH, Ramm O. Urinary Incontinence and Pelvic Organ Prolapse. Clin Obstet Gynecol. 2021;64(2):314–20.
87. Hoffman DS, Nitti VW. Female Bladder Outlet Obstruction. Curr Urol Rep. 2016;17(4):1–7.
88. Marinkovic SP, Stanton SL. Incontinence and voiding difficulties associated with prolapse. J Urol. 2004;171(3):1021–8.
89. Haylen BT, de Ridder D, Freeman RM, Swift SE, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. Int Urogynecol J. 2010 Jan 25;21(1):5–26.
90. Siddique M, Ingraham C, Kudish B, Iglesia CB, Polland A. Hydronephrosis Associated With Pelvic Organ Prolapse: A Systematic Review. Female Pelvic Med Reconstr Surg. 2020;26(3):212–8.
91. Petros P, Quaghebeur J, Wyndaele J-J. An anatomical pathogenesis of lower urinary tract definitions from the 2002 ICS report symptoms, conditions, syndromes, urodynamics. Neurourol Urodyn. 2022;41(3):740–55.
92. Petros P, Quaghebeur J, Wyndaele JJ. Defining urge as an uncontrolled micturition explains pathogenesis, informs cure and helps solve the burgeoning OAB crisis. Neurourol Urodyn. 2022;41(6):1281–92.
93. Peyronnet B, Mironska E, Chapple C, Cardozo L, Oelke M, Dmochowski R, et al. A Comprehensive Review of Overactive Bladder Pathophysiology: On the Way to Tailored Treatment. Eur Urol.

2019;75(6):988–1000.
94. Vaughan CP, Johnson TM, Ala-Lipasti MA, Cartwright R, Tammela TLJ, Taari K, et al. The prevalence of clinically meaningful overactive bladder: Bother and quality of life results from the population-based FINNO study. Eur Urol. 2011;59(4):629–36.
95. Tegerstedt G, Maehle-Schmidt M, Nyrén O, Hammarström M. Prevalence of symptomatic pelvic organ prolapse in a Swedish population. Int Urogynecol J. 2005;16(6):497–503.
96. Fritel X, Varnoux N, Zins M, Breart G, Ringa V. Symptomatic pelvic organ prolapse at midlife, quality of life, and risk factors. Obstet Gynecol. 2009;113(3):609–16.
97. Miedel A, Tegerstedt G, Maehle-Schmidt M, Nyrén O, Hammarström M. Symptoms and pelvic support defects in specific compartments. Obstet Gynecol. 2008;112(4):851–8.
98. De Boer TA, Vierhout ME. Predictors for overactive bladder symptoms after pelvic organ prolapse surgery. Curr Opin Obstet Gynecol. 2011;23(5):366–70.
99. Frigerio M, Manodoro S, Cola A, Palmieri S, Spelzini F, Milani R. Risk factors for persistent, de novo and overall overactive bladder syndrome after surgical prolapse repair. Eur J Obstet Gynecol. 2019;233:141–5.
100. De Boer TA, Kluivers KB, Withagen MIJ, Milani AL, Vierhout ME. Predictive factors for overactive bladder symptoms after pelvic organ prolapse surgery. Int Urogynecol J. 2010;21(9):1143–9.
101. Fletcher SG, Haverkorn RM, Yan J, Lee JJ, Zimmern PE, Lemack GE. Demographic and Urodynamic Factors Associated With Persistent OAB After Anterior Compartment Prolapse Repair. Neurourol Urodyn. 2010;29:1414–8.
102. Miranne JM, Lopes V, Carberry CL, Sung VW. The effect of pelvic organ prolapse severity on improvement in overactive bladder symptoms after pelvic reconstructive surgery. Int Urogynecol J Pelvic Floor Dysfunct. 2013 Aug;24(8):1303–8.
103. Padoa A, Levy E, Fligelman T, Tomashev-Dinkovich R, Tsviban A, Serati M. Predictors of persistent overactive bladder following surgery for advanced pelvic organ prolapse. Int Urogynecol J. 2023;34(3):759–67.
104. Abrar S, Rizvi RM, Zahid N. The association of symptoms of overactive bladder with pelvic organ prolapse and its improvement after pelvic reconstructive surgery. Pakistan J Med Sci.

2021;37(3):897–902.
105. Johnson JR, High RA, Dziadek O, Ocon A, Muir TW, Xu J, et al. Overactive Bladder Symptoms After Pelvic Organ Prolapse Repair. Female Pelvic Med Reconstr Surg. 2020;26(12):742–5.
106. Otsuka A, Watanabe K, Matsushita Y, Watanabe H, Tamura K, Motoyama D, et al. Predictive factors for persistence of preoperative overactive bladder symptoms after transvaginal mesh surgery in women with pelvic organ prolapse. LUTS Low Urin Tract Symptoms. 2020;12(2):167–72.
107. Basu M, Duckett J. Effect of prolapse repair on voiding and the relationship to overactive bladder and detrusor overactivity. Int Urogynecol J. 2009;20(5):499–504.
108. Yuan Z, Shen H. Pelvic organ prolapse quantification in women referred with overactive bladder. Int Urogynecol J. 2010;21:1365–9.
109. Romanzi LJ, Chaikin DC, Blaivas JG. The Effect of Genital Prolapse on Voiding. J Urol. 1999;161:581–6.
110. Groenendijk AG, Birnie E, Roovers JW, Bonsel GJ. Contribution of Primary Pelvic Organ Prolapse to Micturition and Defecation Symptoms. Obstet Gynecol Int. 2012;2012:79803.
111. Teleman P, Laurikainen E, Kinne I, Pogosean R, Jakobsson U, Rudnicki M. Relationship between the Pelvic Organ Prolapse Quantification system (POP-Q), the Pelvic Floor Impact Questionnaire (PFIQ-7), and the Pelvic Floor Distress Inventory (PFDI-20) before and after anterior vaginal wall prolapse surgery. Int Urogynecol J Pelvic Floor Dysfunct. 2014;26(2):195–200.
112. Mouritsen L, Larsen JP. Symptoms, bother and POPQ in women referred with pelvic organ prolapse. Int Urogynecol J. 2003;14(2):122–7.
113. Digesu GA, Chaliha C, Salvatore S, Hutchings A, Khullar V. The relationship of vaginal prolapse severity to symptoms and quality of life. BJOG. 2005;112:971–6.
114. Schimpf MO, Sullivan DMO, Lasala CA, Tulikangas PK. Anterior vaginal wall prolapse and voiding dysfunction in urogynecology patients. Int Urogynecol J. 2007;18:721–5.
115. Salvatore S, Serati M, Siesto G, Cattoni E, Zanirato M, Torella M. Correlation between anatomical findings and symptoms in women with pelvic organ prolapse using an artificial neural network analysis. Int Urogynecol J. 2011;22(4):453–9.
116. Dieter AA, Edenfield AL, Weidner AC, Siddiqui NY. How Does Site of

Pelvic Organ Prolapse Repair Affect Overactive Bladder Symptoms ? Female Pelvic Med Reconstr Surg. 2014;20(4):203–7.
117. Liedl B, Goeschen K, Sutherland SE, Roovers JP, Yassouridis A. Can surgical reconstruction of vaginal and ligamentous laxity cure overactive bladder symptoms in women with pelvic organ prolapse? BJU Int. 2019;123(3):493–510.
118. Lensen EJM, Withagen MIJ, Kluivers KB, Milani AL, Vierhout ME. Urinary Incontinence After Surgery for Pelvic Organ Prolapse. Neurourol Urodyn. 2013;32(5):455–9.
119. Wei JT, Nygaard IE, Richter HE, Nager CW, Barber MD, Kenton KS, et al. A Midurethral Sling to Reduce Incontinence after Vaginal Prolapse Repair. N Engl J Med. 2012;366(25):2358–67.
120. van der Ploeg JM, Rengerink KO, van der Steen A, van Leeuwen JHS, van der Vaart CH, Roovers JPWR. Vaginal prolapse repair with or without a midurethral sling in women with genital prolapse and occult stress urinary incontinence: a randomized trial. Int Urogynecol J. 2016;27(7):1029–38.
121. Khayyami Y, Elmelund M, Lose G, Klarskov N. De novo urinary incontinence after pelvic organ prolapse surgery — a national database study. Int Urogynecol J. 2020;31(2):305–8.
122. Brubaker L, Nygaard I, Richter HE, Visco A, Weber AM, Cundiff GW, et al. Two-Year Outcomes After Sacrocolpopexy With and Without Burch to Prevent Stress Urinary Incontinence. Obs Gynecol. 2008;112(1):49–55.
123. Khayyami Y, Elmelund M, Klarskov N. Urinary incontinence before and after pelvic organ prolapse surgery—A national database study. Int Urogynecol J. 2021;32(8):2119–23.
124. Borstad E, Abdelnoor M, Staff AC, Kulseng-Hanssen S. Surgical strategies for women with pelvic organ prolapse and urinary stress incontinence. Int Urogynecol J. 2010;21(2):179–86.
125. van der Ploeg JM, Oude Rengerink K, van der Steen A, van Leeuwen JHS, Stekelenburg J, Bongers MY, et al. Transvaginal prolapse repair with or without the addition of a midurethral sling in women with genital prolapse and stress urinary incontinence: A randomised trial. BJOG. 2015;122(7):1022–30.
126. Giugale LE, Carter-Brooks CM, Ross JH, Shepherd JP, Zyczynski HM. Outcomes of a Staged Midurethral Sling Strategy for Stress Incontinence and Pelvic Organ Prolapse. Obstet Gynecol. 2019;134(4):736–44.

127. Glazener C, Cooper K, Mashayekhi A. Anterior vaginal repair for urinary incontinence in women (Review). Cochrane Database Syst Rev. 2017;7(7):CD001755.
128. Liedl B, Inoue H, Sekiguchi Y, Gold D, Wagenlehner F. Update of the Integral Theory and System for Management of Pelvic Floor Dysfunction in Females. Eur Urol Suppl. 2018;17(3):100–8.
129. Lo TS, Nawawi EA, Wu PY, bt Karim N, Al-Kharabsheh A. Predictors for persistent urodynamic stress incontinence following extensive pelvic reconstructive surgery with and without midurethral sling. Int Urogynecol J. 2016;27(3):399–406.
130. Ugianskiene A, Kjærgaard N, Inger Lindquist AS, Larsen T, Glavind K. Retrospective study on de novo postoperative urinary incontinence after pelvic organ prolapse surgery. Eur J Obstet Gynecol Reprod Biol. 2017;219:10–4.
131. Maher C, Antosh D, Baessler K, Cheon C, de Tayrac R, Deffieux X, et al. Pelvic Organ Prolapse Surgery. In: Cardozo L, Rovner E, Wagg A, Wein A, Abrams P, editors. Incontinence 7th Edition. Bristol UK: ICI-ICS. International Continence Society; 2023. p. 1727–848.
132. Baessler K, Christmann-Schmid C, Maher C, Haya N, Crawford T, Brown J. Surgery for women with pelvic organ prolapse with or without stress urinary incontinence (Review). Cochrane Database Syst Rev. 2018;8(8):CD013108.
133. Burrows LJ, Meyn L a, Walters MD, Weber AM. Pelvic symptoms in women with pelvic organ prolapse. Obstet Gynecol. 2004;104(5 Pt 1):982–8.
134. Alshiek J, Garcia B, Minassian VA, Iglesia CB, Clark A, Sokol ER, et al. Pelvic Organ prolapse - AUGS practice bulletin. Female Pelvic Med Reconstr Surg. 2017;23(4):218–27.
135. Svenningsen R, Borstad E, Spydslaug AE, Sandvik L, Staff AC. Occult incontinence as predictor for postoperative stress urinary incontinence following pelvic organ prolapse surgery. Int Urogynecol J. 2012;23(7):843–9.
136. van der Ploeg JM, Zwolsman SE, Posthuma S, Wiarda HS, van der Vaart CH, Roovers JPWR. The predictive value of demonstrable stress incontinence during basic office evaluation and urodynamics in women without symptomatic urinary incontinence undergoing vaginal prolapse surgery. Neurourol Urodyn. 2018;37(3):1011–8.
137. Visco AG, Brubaker L, Nygaard I, Richter HE, Cundiff G, Fine P. The role of preoperative urodynamic testing in stress-continent women

undergoing sacrocolpopexy : the Colpopexy and Urinary Reduction Efforts (CARE) randomized surgical trial. Int Urogynecol J. 2008;19(5):607–14.
138. Barbier H, Carberry CL, Karjalainen PK, Mahoney CK, Manriquez Galan V, Rosamilia A, et al. International Urogynecology consultation chapter 2 committee 3: the clinical evaluation of pelvic organ prolapse including investigations into associated morbidity / pelvic floor dysfunction. Int Urogynecol J. 2023;Epub ahead.
139. Jelovsek JE, Chagin K, Brubaker L, Rogers RG, Richter HE, Arya L, et al. A model for predicting the risk of de novo stress urinary incontinence in women undergoing pelvic organ prolapse surgery. Obstet Gynecol. 2014;123(2):279–87.
140. Jelovsek JE, Ploeg JM Van Der, Barber MD. Validation of a Model Predicting De Novo Stress Urinary Incontinence in Women Undergoing Pelvic Organ Prolapse Surgery. Obstet Gynecol. 2019;133(4):683–90.
141. Sabadell J, Salicrú S, Montero-armengol A, Rodriguez-mias N, Gil-moreno A, Poza JL. External validation of de novo stress urinary incontinence prediction model after vaginal prolapse surgery. Int Urogynecol J. 2019;30(10):1719–23.
142. Ross JH, Carter-Brooks CM, Ruppert KM, Giugale LE, Shepherd JP, Zyczynski HM. Assessing the Performance of the De Novo Postoperative Stress Urinary Incontinence Calculator. Female Pelvic Med Reconstr Surg. 2019;27(1):23–7.
143. Yasa C, Gungor Ugurlucan F, Dural O, Yalcın O. External validation of a model predicting de novo stress urinary incontinence after pelvic organ prolapse surgery. Neurourol Urodyn. 2021;40(2):688–94.
144. Hale DS, Fenner D. Consistently inconsistent, the posterior vaginal wall. Am J Obstet Gynecol. 2016;214(3):314–20.
145. Heitmann PT, Vollebregt PF, Knowles CH, Lunniss PJ, Dinning PG, Scott SM. Understanding the physiology of human defaecation and disorders of continence and evacuation. Nat Rev Gastroenterol Hepatol. 2021;18(11):751–69.
146. Bharucha AE, Knowles CH, Mack I, Malcolm A, Oblizajek N, Rao S, et al. Faecal incontinence in adults. Nat Rev Dis Prim. 2022;8(1).
147. Weber AM, Walters MD, Ballard LA, Booher DL, Piedmonte MR, Fenner D. Posterior vaginal prolapse and bowel function. Am J Obstet Gynecol. 1998;179(6 I):1446–50.
148. Jelovsek JE, Barber MD, Paraiso MFR, Walters MD. Functional bowel

and anorectal disorders in patients with pelvic organ prolapse and incontinence. Am J Obstet Gynecol. 2005;193(6):2105–11.
149. Klingele CJ, Bharucha AE, Fletcher JG, Gebhart JB, Riederer SG, Zinsmeister AR. Pelvic organ prolapse in defecatory disorders. Obstet Gynecol. 2005;106(2):315–20.
150. da Silva GM, Gurland B, Sleemi A, Levy G. Posterior vaginal wall prolapse does not correlate with fecal symptoms or objective measures of anorectal function. Am J Obstet Gynecol. 2006;195(6):1742–7.
151. Bradley CS, Zimmerman MB, Wang Q. Vaginal Descent and Pelvic Floor Symptoms in Postmenopausal Women A Longitudinal Study. Obs Gynecol. 2008;111(5):1148–53.
152. Augusto KL, Bezerra LRPS, Murad-Regadas SM, Vasconcelos Neto JA, Vasconcelos CTM, Karbage SAL, et al. Defecatory dysfunction and fecal incontinence in women with or without posterior vaginal wall prolapse as measured by pelvic organ prolapse quantification (POP-Q). Eur J Obstet Gynecol Reprod Biol. 2017;214:50–5.
153. Morgan DM, DeLancey JOL, Guire KE, Fenner DE. Symptoms of anal incontinence and difficult defecation among women with prolapse and a matched control cohort. Am J Obstet Gynecol. 2007;197(5):1–6.
154. Soligo M, Salvatore S, Emmanuel A V., De Ponti E, Zoccatelli M, Cortese M, et al. Patterns of constipation in urogynecology: Clinical importance and pathophysiologic insights. Am J Obstet Gynecol. 2006;195(1):50–5.
155. Collins SA, O'Sullivan DM, Lasala CA. Correlation of POP-Q posterior compartment measures with defecatory dysfunction. Int Urogynecol J. 2012;23(6):743–7.
156. Grimes CL, Tan-Kim J, Nager CW, Dyer KY, Menefee SA, Diwadkar GB, et al. Outcome measures to assess anatomy and function of the posterior vaginal compartment. Int Urogynecol J Pelvic Floor Dysfunct. 2014;25(7):893–9.
157. Erekson EA, Kassis NC, Washington BB, Myers DL. The association between stage II or greater posterior prolapse and bothersome obstructive bowel symptoms. Female Pelvic Med Reconstr Surg. 2010;16(1):59–64.
158. Saks EK, Harvie HS, Asfaw TS, Arya LA. Clinical significance of obstructive defecatory symptoms in women with pelvic organ prolapse. Int J Gynaecol Obstet. 2010;111(3):237–40.
159. Fialkow MF, Gardella C, Melville J, Lentz GM, Fenner DE. Posterior

vaginal wall defects and their relation to measures of pelvic floor neuromuscular function and posterior compartment symptoms. Am J Obstet Gynecol. 2002;187(6):1443–9.
160. Kahn MA, Breitkopf CR, Valley MT, Woodman PJ, O'Boyle AL, Bland DI, et al. Pelvic Organ Support Study (POSST) and bowel symptoms: Straining at stool is associated with perineal and anterior vaginal descent in a general gynecologic population. Am J Obstet Gynecol. 2005;192(5 SPEC. ISS.):1516–22.
161. Bradley CS, Brown MB CG et al. Bowel symptoms in women planning surgery for pelvic organ prolapse. Am J Obs Gynecol. 2006;195(6):1814–9.
162. Paraiso MFR, Barber MD, Muir TW, Walters MD. Rectocele repair: A randomized trial of three surgical techniques including graft augmentation. Am J Obstet Gynecol. 2006;195(6):1762–71.
163. Sung VW, Rardin CR, Raker CA, Lasala CA, Myers DL. Porcine Subintestinal Submucousal Graft Augmentation for Rectocele Repair: A Randomized Controlled Trial. Obs Gynecol. 2012;119(1):125–33.
164. Farid M, Madbouly KM, Hussein A, Mahdy T, Moneim HA, Omar W. Randomized controlled trial between perineal and anal repairs of rectocele in obstructed defecation. World J Surg. 2010;34(4):822–9.
165. Nieminen K, Hiltunen KM, Laitinen J, Oksala J, Heinonen PK. Transanal or vaginal approach to rectocele repair: A prospective, randomized pilot study. Dis Colon Rectum. 2004;47(10):1636–42.
166. Maher CF, Qatawneh AM, Baessler K, Schluter PJ. Midline rectovaginal fascial plication for repair of rectocele and obstructed defecation. Obstet Gynecol. 2004;104(4):685–9.
167. Porter WE, Steele A, Walsh P, Kohli N, Karram MM. The anatomic and functional outcomes of defect-specific rectocele repairs. Am J Obstet Gynecol. 1999;181(6):1353–9.
168. Kahn MA, Stanton SL. Posterior colporrhaphy: Its effects on bowel and sexual function. BJOG An Int J Obstet Gynaecol. 1997;104(1):82–6.
169. Spence-Jones C, Kamm MA, Henry MM, Hudson CN. Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence. BJOG An Int J Obstet Gynaecol. 1994;101(2):147–52.
170. Hicks CW, Weinstein M, Wakamatsu M, Savitt L. In patients with rectoceles and obstructed defecation syndrome , surgery should be the option of last resort. Surgery. 2014;155(4):659–67.

171. Bharucha AE, Dorn SD, Lembo A, Pressman A. American gastroenterological association medical position statement on constipation. Gastroenterology. 2013;144(1):211–7.
172. Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, et al. Bowel disorders. Gastroenterology. 2016;150(6):1393-1407.e5.
173. Tillou J, Poylin V. Functional Disorders : Slow-Transit Constipation. Clin Colon Rectal Surg. 2017;30(1):76–86.
174. Rao SSC, Bharucha AE, Chiarioni G, Felt-Bersma R, Knowles C, Malcolm A, et al. Anorectal disorders. Gastroenterology. 2016;150(6):1430-1442.e4.
175. Brown H, Grimes C. Current Trends in Management of Defecatory Dysfunction, Posterior Compartment Prolapse, and Fecal Incontinence. Curr Obstet Gynecol Rep. 2016;5(2):165–71.
176. Meschia M, Buonaguidi A, Pifarotti P, Somigliana E, Spennacchio M, Amicarelli F. Prevalence of anal incontinence in women with symptoms of urinary incontinence and genital prolapse. Obstet Gynecol. 2002;100(4):719–23.
177. Simren M, Palsson OS, Whitehead WE. Update on Rome IV Criteria for Colorectal Disorders: Implications for Clinical Practice. Curr Gastroenterol Rep. 2017;19(4).
178. Bharucha AE, Dunivan G, Goode PS, Lukacz ES, Markland AD, Matthews CA, et al. Epidemiology, pathophysiology, and classification of fecal incontinence: State of the Science Summary for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) workshop. Am J Gastroenterol. 2015;110(1):127–36.
179. Mathew S, Guzman Rojas RA, Nyhus M, Salvesen K, Volløyhaug II. Prevalence of anal sphincter defects and association with anal incontinence in women scheduled for pelvic organ prolapse surgery. Neurourol Urodyn. 2020;39(8):2409–16.
180. Bharucha AO, Fletcher JG, Harper CM, Hough D, Daube JR, Stevens C, et al. Relationship between symptoms and disordered continence mechanisms in women with idiopathic faecal incontinence. Gut. 2005;54(4):546–55.
181. Yagi Y, Tsunoda A, Takahashi T, Kusanagi H. Rectoanal intussusception is very common in patients with fecal incontinence. J Anus, Rectum Colon. 2018;2(4):162–7.
182. Lee PYH, Steele SR. Complete pelvic floor repair in treating fecal incontinence. Clin Colon Rectal Surg. 2005;18(1):55–9.
183. Wang JY, Abbas MA. Current Management of Fecal Incontinence.

Perm J. 2013;17(3):65–73.
184. Rao SSC, Ozturk R, Stessman M. Investigation of the pathophysiology of fecal seepage. Am J Gastroenterol. 2004;99(11):2204–9.
185. Gustilo-Ashby AM, Paraiso MFR, Jelovsek JE, Walters MD, Barber MD. Bowel symptoms 1 year after surgery for prolapse: further analysis of a randomized trial of rectocele repair. Am J Obstet Gynecol. 2007;197(1):1–5.
186. Athanasiou S, Grigoriadis T, Chalabalaki A, Protopapas A, Antsaklis A. Pelvic organ prolapse contributes to sexual dysfunction: A cross-sectional study. Acta Obstet Gynecol Scand. 2012;91(6):704–9.
187. Novi JM, Jeronis S, Morgan MA, Arya LA. Sexual function in women with pelvic organ prolapse compared to women without pelvic organ prolapse. J Urol. 2005;173(5):1669–72.
188. Tok EC, Yasa O, Ertunc D, Savas A, Durukan H, Kanik A. The effect of pelvic organ prolapse on sexual function in a general cohort of women. J Sex Med. 2010;7(12):3957–62.
189. Lowenstein L, Gamble T, Sanses TVD, Raalte H Van, Carberry C, Jakus S, et al. Sexual Function is Related to Body Image Perception in Women. 2009;2286–91.
190. Jha S, Gray T. A systematic review and meta-analysis of the impact of native tissue repair for pelvic organ prolapse on sexual function. Int Urogynecol J. 2015;26(3):321–7.
191. Wihersaari O, Karjalainen P, Tolppanen AM, Mattsson N, Nieminen K, Jalkanen J. Sexual Activity and Dyspareunia After Pelvic Organ Prolapse Surgery: A 5-Year Nationwide Follow-up Study. Eur Urol Open Sci. 2022;45:81–9.
192. American Urogynecologic Society Best Practice Statement: Evaluation and Counseling of Patients With Pelvic Organ Prolapse. Female Pelvic Med Reconstr Surg. 2017;5:281–7.
193. National Institute for Health and Care. NICE Guidance - Urinary incontinence and pelvic organ prolapse in women: management. BJU Int. 2019;123(5):777–803.
194. Collins SA, O'Shea M, Dykes N, Ramm O, Edenfield A, Shek KL, et al. International Urogynecological Consultation: clinical definition of pelvic organ prolapse. Int Urogynecol J. 2021;32(8):2011–9.
195. Bump RC, Mattiasson A, Bo K, Brubaker LP, DeLancey JOL, Klarskov P, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol. 1996;175(1):10–7.

196. Dietz HP, Mann KP. What is clinically relevant prolapse? An attempt at defining cutoffs for the clinical assessment of pelvic organ descent. Int Urogynecol J Pelvic Floor Dysfunct. 2014;25(4):451–5.
197. Brubaker L, Barber MD, Nygaard I, Nager CW, Varner E, Schaffer J, et al. Quantification of vaginal support: Are continuous summary scores better than POPQ stage? Am J Obstet Gynecol. 2010;203(5):512.e1-512.e6.
198. Toozs-Hobson P, Swift S. POP-Q stage I prolapse: Is it time to alter our terminology? Int Urogynecol J Pelvic Floor Dysfunct. 2014;25(4):445–6.
199. Bump RC. The POP-Q system: Two decades of progress and debate. Int Urogynecol J. 2014;25(4):441–3.
200. Hall AF, Theofrastous JP, Cundiff GW, Harris RL, Hamilton LF, Swift SE, et al. Interobserver and intraobserver reliability of the proposed International Continence Society, Society of Gynecologic Surgeons, and American Urogynecologic Society pelvic organ prolapse classification system. Am J Obstet Gynecol. 1996;175(6):1467–71.
201. Harmanli O. POP-Q 2.0: Its time has come! Int Urogynecol J. 2014;25(4):447–9.
202. Swift S, Morris S, McKinnie V, Freeman R, Petri E, Scotti RJ, et al. Validation of a simplified technique for using the POPQ pelvic organ prolapse classification system. Int Urogynecol J. 2006;17(6):615–20.
203. Parekh M, Swift S, Lemos N, Iskander M, Freeman B, Arunkalaivanan AS, et al. Multicenter inter-examiner agreement trial for the validation of simplified POPQ system. Int Urogynecol J. 2011;22(6):645–50.
204. Lemos N, Korte JE, Iskander M, Freeman R, Arunkalaivanan A, Rizk D, et al. Center-by-center results of a multicenter prospective trial to determine the inter-observer correlation of the simplified POP-Q in describing pelvic organ prolapse. Int Urogynecol J. 2012;23(5):579–84.
205. Manonai J, Mouritsen L, Palma P, Contreras-Ortiz O, Korte JE, Swift S. The inter-system association between the simplified pelvic organ prolapse quantification system (S-POP) and the standard pelvic organ prolapse quantification system (POPQ) in describing pelvic organ prolapse. Int Urogynecol J. 2011;22(3):347–52.
206. Chernyak V, Bleier J, Kobi M, Paquette I, Flusberg M, Zimmern P, et al. Clinical applications of pelvic floor imaging: opinion statement endorsed by the society of abdominal radiology (SAR), American

Urological Association (AUA), and American Urogynecologic Society (AUGS). Abdom Radiol. 2021;46(4):1451–64.
207. Ridgeway BM, Weinstein MM, Tunitsky-Bitton E. American Urogynecologic Society Best-Practice Statement on Evaluation of Obstructed Defecation. Female Pelvic Med Reconstr Surg. 2018;24(6):383–91.
208. Paquette IM, Varma M, Ternent C, Melton-Meaux G, Rafferty JF, Feingold D, et al. The American Society of Colon and Rectal Surgeons' Clinical Practice Guideline for the Evaluation and Management of Constipation. Dis Colon Rectum. 2016;59(6):479–92.
209. Grossi U, Di Tanna GL, Heinrich H, Taylor SA, Knowles CH, Scott SM. Systematic review with meta-analysis: defecography should be a first-line diagnostic modality in patients with refractory constipation. Aliment Pharmacol Ther. 2018;48(11–12):1186–201.
210. Ramage L, Simillis C, Yen C, Lutterodt C, Qiu S, Tan E, et al. Magnetic resonance defecography versus clinical examination and fluoroscopy: a systematic review and meta-analysis. Tech Coloproctol. 2017;21(12):915–27.
211. Jeong HY, Yang SJ, Cho DH, Park DH, Lee JK. Comparison of 3-dimensional pelvic floor ultrasonography and defecography for assessment of posterior pelvic floor disorders. Ann Coloproctol. 2020;36(4):256–63.
212. Tirumanisetty P, Prichard D, Fletcher JG, Chakraborty S, Zinsmeister AR, Bharucha AE. Normal values for assessment of anal sphincter morphology, anorectal motion, and pelvic organ prolapse with MRI in healthy women. Neurogastroenterol Motil. 2018;30(7):1–10.
213. Gurland BH, Khatri G, Ram R, Hull TL, Kocjancic E, Quiroz LH, et al. Consensus Definitions and Interpretation Templates for Magnetic Resonance Imaging of Defecatory Pelvic Floor Disorders. Female Pelvic Med Reconstr Surg. 2021;27(10):e645–56.
214. Paquette I, Rosman D, Sayed R El, Hull T, Kocjancic E, Quiroz L, et al. Consensus Definitions and Interpretation Templates for Fluoroscopic Imaging of Defecatory Pelvic Floor Disorders: Proceedings of the Consensus Meeting of the Pelvic Floor Consortium of the American Society of Colon and Rectal Surgeons, the Society of Abdo. Tech Coloproctol. 2021;25(1):3–17.
215. Alshiek J, Murad-Regadas SM, Mellgren A, Glanc P, Khatri G, Quiroz LH, et al. Consensus definitions and interpretation templates for dynamic ultrasound imaging of defecatory pelvic floor disorders :

Proceedings of the consensus meeting of the pelvic floor disorders consortium of the american society of colon and rectal surgeons, th. Int Urogynecol J. 2023;34(3):603–19.
216. Barber MD. Pelvic organ prolapse. BMJ. 2016;354:1–9.
217. Iglesia CB, Smithling KR. Pelvic organ prolapse. Am Fam Physician. 2017;96(3):179–85.
218. Dumoulin C, Booth J, Cacciari L, Campbell P, Hagen S, Homsi Jorge C, et al. Adult conservative management. In: Cardozo L, Rovner E, Wagg A, Wein A, Abrams P, editors. Incontinence 7th Edition. Bristol UK: International Continence Society; 2023. p. 795–1021.
219. Pratt T, Mishra K. Evaluation and management of defecatory dysfunction in women. Curr Opin Obstet Gynecol. 2018;30(6):451–7.
220. Bø K, Anglès-Acedo S, Batra A, Brækken IH, Chan YL, Jorge CH, et al. International urogynecology consultation chapter 3 committee 2; conservative treatment of patient with pelvic organ prolapse: Pelvic floor muscle training. Int Urogynecol J. 2022;33(10):2633–67.
221. Mimura T, Roy AJ, Storrie JB, Kamm MA. Treatment of impaired defecation associated with rectocele by behavioral retraining (Biofeedback). Dis Colon Rectum. 2000;43(9):1267–72.
222. Bugge C, Adams EJ, Gopinath D, Stewart F, Dembinsky M, Sobiesuo P, et al. Pessaries (mechanical devices) for managing pelvic organ prolapse in women. Cochrane Database Syst Rev. 2020;2020(11).
223. Sansone S, Sze C, Eidelberg A, Stoddard M, Cho A, Asdjodi S, et al. Role of Pessaries in the Treatment of Pelvic Organ Prolapse: A Systematic Review and Meta-analysis. Obstet Gynecol. 2022;140(4):613–22.
224. Van Der Vaart LR, Vollebregt A, Milani AL, Lagro-Janssen AL, Duijnhoven RG, Roovers JPWR, et al. Effect of Pessary vs Surgery on Patient-Reported Improvement in Patients with Symptomatic Pelvic Organ Prolapse: A Randomized Clinical Trial. Jama. 2022;328(23):2312–23.
225. Dwyer L, Dowding D, Kearney R. What is known from the existing literature about self-management of pessaries for pelvic organ prolapse? A scoping review. BMJ Open. 2022;12(7):e060223.
226. Manzini C, Morsinkhof LM, Vaart CH Van Der, Withagen MIJ, Grob ATM. Parameters associated with unsuccessful pessary fitting for pelvic organ prolapse up to three months follow-up : a systematic review and meta-analysis. Int Urogynecol J. 2022;33(7):1719–63.
227. Lamers BHC, Broekman BMW, Milani AL. Pessary treatment for

pelvic organ prolapse and health-related quality of life: A review. Int Urogynecol J. 2011;22(6):637–44.
228. Dunivan GC, Sussman AL, Jelovsek JE, Sung V, Andy UU, Ballard A, et al. Gaining the patient perspective on pelvic floor disorders' surgical adverse events. Am J Obstet Gynecol. 2019;220(2):185.e1-185.e10.
229. Dao A, Dunivan G. Patient-Centered Goals for Treatment of Pelvic Floor Disorders. Curr Bladder Dysfunct Rep. 2022;17(4):210–8.
230. Mattsson NK, Karjalainen PK, Tolppanen A-M, Heikkinen A-M, Sintonen H, Härkki P, et al. Pelvic organ prolapse surgery and quality of life—a nationwide cohort study. Am J Obstet Gynecol. 2020;222(6):588.e1-588.e10.
231. Doaee M, Moradi-Lakeh M, Nourmohammadi A, Razavi-Ratki SK, Nojomi M. Management of pelvic organ prolapse and quality of life: a systematic review and meta-analysis. Int Urogynecol J. 2014;25(2):153–63.
232. Wihersaari O, Karjalainen P, Tolppanen A, Mattsson N. Complications of Pelvic Organ Prolapse Surgery in the 2015 Finnish Pelvic Organ Prolapse Surgery Survey Study. 2020;136(6):1135–44.
233. Dindo D, Demartines N, Clavien P. Classification of Surgical Complications. Ann Surg. 2004;240(2):205–13.
234. Whiteside JL, Weber AM, Meyn LA, Walters MD. Risk factors for prolapse recurrence after vaginal repair. Am J Obs Gynecol. 2004;191(5):1533–8.
235. Siff LN, Barber MD. Native Tissue Prolapse Repairs: Comparative Effectiveness Trials. Obstet Gynecol Clin NA. 2016;43(1):69–81.
236. Vergeldt TFM, Weemhoff M, IntHout J, Kluivers KB. Risk factors for pelvic organ prolapse and its recurrence: a systematic review. Int Urogynecol J. 2015;26(11):1559–73.
237. Friedman T, Eslick GD, Dietz HP. Risk factors for prolapse recurrence: systematic review and meta-analysis. Int Urogynecol J. 2017;29(1):13–21.
238. Shi W, Guo L. Risk factors for the recurrence of pelvic organ prolapse: a meta-analysis. J Obstet Gynaecol (Lahore). 2023;43(1).
239. Iyer S, Botros SM. Transvaginal mesh: a historical review and update of the current state of affairs in the United States. Int Urogynecol J. 2017;28(4):527–35.
240. Ng-Stollmann N, Fünfgeld C, Gabriel B, Niesel A. The international discussion and the new regulations concerning transvaginal mesh implants in pelvic organ prolapse surgery. Int Urogynecol J.

2020;31(10):1997–2002.
241. Kowalski JT, Mehr A, Cohen E, Bradley CS. Systematic review of definitions for success in pelvic organ prolapse surgery. Int Urogynecol J. 2018;29(11):1697–704.
242. Weber AM, Abrams P, Brubaker L, Cundiff G, Davis G, Dmochowski RR, et al. The Standardization of Terminology for Researchers in Female Pelvic Floor Disorders. Int Urogynecol J. 2001;12(3):178–86.
243. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol. 1997;89(4):501–6.
244. Ismail S, Duckett J, Rizk D, Sorinola O. Recurrent pelvic organ prolapse : International Urogynecological Association Research and Development Committee opinion. Int Urogynecol J. 2016;27(11):1619–32.
245. Developed by the Joint Writing Group of the American Urogynecologic Society and the International Urogynecological Association. Joint report on terminology for surgical procedures to treat pelvic organ prolapse. Joint report on terminology for surgical pr. Int Urogynecol J. 2020;31(3):429–63.
246. Halpern-Elenskaia K, Umek W, Bodner-Adler B, Hanzal E. Anterior colporrhaphy: a standard operation? Systematic review of the technical aspects of a common procedure in randomized controlled trials. Int Urogynecol J. 2018;29(6):781–8.
247. Maher C, Feiner B, Baessler K, Haya N, Brown J. Surgery for women with anterior compartment prolapse (Review). Cochrane Database Syst Rev. 2016;11(11):CD004014.
248. Elliott CS, Yeh J, Comiter C V, Chen B, Sokol ER. The Predictive Value of a Cystocele for Concomitant Vaginal Apical Prolapse. J Urol. 2013;189(1):200–3.
249. Lowder JL, Park AJ, Ellison R, Ghetti C. The Role of Apical Vaginal Support in the Appearance of Anterior and Posterior Vaginal Prolapse. Obs Gynecol. 2008;111(1):152–7.
250. Eilber KS, Alperin M, Khan A, Wu N, Pashos CL, Clemens JQ, et al. Outcomes of Vaginal Prolapse Surgery Among Female Medicare Beneficiaries: The Role of Apical Support. Obs Gynecol. 2013;122(5):1–9.
251. Maher C, Yeung E, Haya N, Christmann-Schmid C, Mowat A, Chen Z, et al. Surgery for women with apical vaginal prolapse. Cochrane Database Syst Rev. 2023;7(7):CD012376.

252. Larouche M, Belzile E, Geoffrion R. Surgical Management of Symptomatic Apical Pelvic Organ Prolapse: A Systematic Review and Meta-analysis. Obstet Gynecol. 2021;137(6):1061–73.
253. Siddiqui NY, Grimes CL, Casiano ER, Abed HT, Jeppson PC, Olivera CK, et al. Mesh Sacrocolpopexy Compared With Native Tissue Vaginal Repair A Systematic Review and Meta-analysis. Obs Gynecol. 2015;125(1):44–55.
254. Coolen AWM, Bui BN, Dietz V, Wang R, Montfoort APA Van, Mol BWJ, et al. The treatment of post-hysterectomy vaginal vault prolapse : a systematic review and meta-analysis. Int Urogynecol J. 2017;28(12):1767–83.
255. Zhang W, Cheon WC, Zhang L, Wang X, Wei Y, Lyu C. Comparison of the effectiveness of sacrospinous ligament fixation and sacrocolpopexy: a meta-analysis. Int Urogynecol J. 2022;33(1):3–13.
256. Enklaar RA, van IJsselmuiden MN, IntHout J, Haan SJH, Rijssenbeek OGAM, Bremmer RH, et al. Practice pattern variation: treatment of pelvic organ prolapse in The Netherlands. Int Urogynecol J. 2022;33(7):1973–80.
257. Husby KR, Lose G, Klarsko N. Trends in apical prolapse surgery between 2010 and 2016 in Denmark. Int Urogynecol J. 2020;31:321–7.
258. Meriwether K V., Antosh DD, Olivera CK, Kim-Fine S, Balk EM, Murphy M, et al. Uterine preservation vs hysterectomy in pelvic organ prolapse surgery: a systematic review with meta-analysis and clinical practice guidelines. Am J Obstet Gynecol. 2018;219(2):129-146.e2.
259. Oversand SH, Staff AC, Borstad E, Svenningsen R. The Manchester procedure: anatomical, subjective and sexual outcomes. Int Urogynecol J. 2018;29(8):1193–201.
260. Husby KR, Larsen MD, Lose G, Klarskov N. Surgical treatment of primary uterine prolapse : a comparison of vaginal native tissue surgical techniques. Int Urogynecol J. 2019;30(11):1887–93.
261. Thys SD, Coolen AL, Martens IR, Oosterbaan HP, Roovers JPWR, Mol BW, et al. A comparison of long-term outcome between Manchester Fothergill and vaginal hysterectomy as treatment for uterine descent. Int Urogynecol J. 2011;22(9):1171–8.
262. Kanter G, Jeppson PC, McGuire BL, Rogers RG. Perineorrhaphy: commonly performed yet poorly understood. A survey of surgeons. Int Urogynecol J. 2015;26(12):1797–801.
263. Mowat A, Maher D, Baessler K, Christmann-Schmid C, Haya N, Maher

C. Surgery for women with posterior compartment prolapse (Review). Cochrane Database Syst Rev. 2018;3(3):CD012975.
264. Mege D, Sans A, Maignan A, Duclos J, Frasconi C, Le Huu Nho R, et al. Temporary successful results of ventral rectopexy for enterocele surgical correction, about 138 patients. Int J Colorectal Dis. 2017;32(11):1569–75.
265. Cronjé HS, De Beer JAA, Bam RH. The pathophysiology of an enterocele and its management. J Obstet Gynaecol (Lahore). 2004;24(4):408–13.
266. Weinberg D, Qeadan F, McKee R, Rogers RG, Komesu YM. Safety of laparoscopic sacrocolpopexy with concurrent rectopexy : peri-operative morbidity in a nationwide cohort. Int Urogynecol J. 2019;30:385–92.
267. Mercer-Jones MA, D'Hoore A, Dixon AR, Lehur P, Lindsey I, Mellgren A, et al. Consensus on ventral rectopexy: Report of a panel of experts. Color Dis. 2014;16(2):82–8.
268. Bordeianou L, Hicks CW, Kaiser AM, Alavi K, Sudan R, Wise PE. Rectal Prolapse: An Overview of Clinical Features, Diagnosis, and Patient-Specific Management Strategies. J Gastrointest Surg. 2014;18(5):1059–69.
269. Emile SH, Elfeki HA, Youssef M, Farid M, Wexner SD. Abdominal rectopexy for the treatment of internal rectal prolapse: a Systematic Review and Meta-analysis. Color Dis. 2017;19(1):O13–24.
270. Grzybowska ME, Futyma K, Kusiak A, Wydra DG. Colpocleisis as an obliterative surgery for pelvic organ prolapse: is it still a viable option in the twenty-first century? Narrative review. Int Urogynecol J. 2022;33(1):31–46.
271. Felder L, Heinzelmann-Schwarz V, Kavvadias T. How does colpocleisis for pelvic organ prolapse in older women affect quality of life, body image, and sexuality? A critical review of the literature. Womens Heal. 2022;18:17455057221111068.
272. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. Heal Qual Life Outcomes. 2006;4(79).
273. Sokas C, Hu ÃYF, Edelen ÃM, Sisodia R, Pusic A, Cooper Z, et al. A Review of PROM Implementation in Surgical Practice. Ann Surg. 2022;275(1):85–90.
274. Kluzek S, Dean B, Wartolowska KA. Patient- reported outcome measures (PROMs) as proof of treatment efficacy. BMJ Evid Based

Med. 2022;27(3):153–5.
275. Churruca K, Pomare C, Ellis FLA, Long JC, Suzanna F, Mph BH, et al. Patient-reported outcome measures (PROMs): A review of generic and condition-specific measures and a discussion of trends and issues. Heal Expect. 2021;24:1015–24.
276. Anger JT, Boutros M, Mellgren A, Ph D, Staller K, Vogler SA. Measuring Pelvic Floor Disorder Symptoms Using Patient-Reported Instruments. Female Pelvic Med Reconstr Surg. 2020;26(1):1–15.
277. Guyatt GH, Osoba D, Wu AW, Wyrwich KW, Norman GR, Aaronson N, et al. Methods to explain the clinical significance of health status measures. Mayo Clin Proc. 2002;77(4):371–83.
278. Castro-Diaz D, Robinson D, Arlandis Guzman S, Bosch J, Costantini E, Cotterill N, et al. Patient-reported outcome assessment. In: Cardozo L, Rovner E, Wagg A, Wein A, Abrams P, editors. Incontinence 7th Edition. Bristol UK: International Continence Society; 2023. p. 437–85.
279. Barber MD, Walters MD, Bump RC. Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). Am J Obstet Gynecol. 2005;193:103–13.
280. Barber MD, Chen Z, Lukacz E, Markland A, Wai C, Brubaker L, et al. Further Validation of the Short Form Versions of the Pelvic Floor Distress Inventory (PFDI) and Pelvic Floor Impact Questionnaire (PFIQ). Neurourol Urodyn. 2011;30:541–6.
281. Gelhorn HL, Coyne KS, Sikirica V, Gauld J, Murphy M. Psychometric Evaluation of Health-Related Quality-of-Life Measures After Pelvic Organ Prolapse Surgery. Female Pelvic Med Reconstr Surg. 2012;18(4):221–6.
282. Mattsson NK, Nieminen K, Heikkinen A-M, Jalkanen J, Koivurova S, Eloranta M-L, et al. Validation of the short forms of the Pelvic Floor Distress Inventory (PFDI-20), Pelvic Floor Impact Questionnaire (PFIQ-7), and Pelvic Organ Prolapse / Urinary Incontinence Sexual Questionnaire (PISQ-12) in Finnish. Health Qual Life Outcomes. 2017;15(88).
283. Parfrey PS, Barrett BJ, editors. Clinical Epidemiology (Practice and Methods). 3rd editio. Methods in Molecular Biology. New York: Humana Press; 2016. 1–179 p.
284. Schünemann HJ, Puhan M, Goldstein R, Jaeschke R, Guyatt GH. Measurement Properties and Interpretability of the Chronic Respiratory Disease Questionnaire (CRQ). COPD J Chronic Obstr

Pulm Dis. 2005;2(1):81–9.
285. Johnston BC, Ebrahim S, Carrasco-Labra A, Furukawa TA, Patrick DL, Crawford MW, et al. Minimally important difference estimates and methods: a protocol. BMJ Open. 2015;5(10):e007953.
286. Brozek JL, Guyatt GH, Schünemann HJ. How a well-grounded minimal important difference can enhance transparency of labelling claims and improve interpretation of a patient reported outcome measure. Health Qual Life Outcomes. 2006;4:69.
287. Wiegersma M, Panman CMCR, Berger MY, De Vet HCW, Kollen BJ, Dekker JH. Minimal important change in the pelvic floor distress inventory-20 among women opting for conservative prolapse treatment. Am J Obstet Gynecol. 2017;216(4):397.e1-397.e7.
288. Utomo E, Blok BF, Steensma AB, Korfage IJ. Validation of the Pelvic Floor Distress Inventory (PFDI-20) and Pelvic Floor Impact Questionnaire (PFIQ-7) in a Dutch population. Int Urogynecol J. 2014;25(4):531–44.
289. Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. J Clin Epidemiol. 2008;61(2):102–9.
290. Devji T, Carrasco-labra A, Qasim A, Phillips M, Johnston BC, Devasenapathy N, et al. Evaluating the credibility of anchor based estimates of minimal important differences for patient reported outcomes: instrument development and reliability study. BMJ. 2020;369:m1714.
291. Norman GR, Sloan JA, Wyrwich KW. Interpretation of Changes in Health-related Quality of Life: The Remarkable Universality of Half a Standard Deviation. Med Care. 2003;41(5):582–92.
292. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, et al. Evaluation of clinically relevant states in patient reported outcomes in knee and hip osteoarthritis: the patient acceptable symptom state. Ann Rheum Dis. 2005;64(1):34–7.
293. Tubach F, Dougados M, Falissard B, Baron G, Logeart I, Ravaud P. Feeling good rather than feeling better matters more to patients. Arthritis Care Res. 2006;55(4):526–30.
294. Tubach F, Ravaud P, Martin-Mola E, Awada H, Bellamy N, Bombardier C, et al. Minimum Clinically Important Improvement and Patient Acceptable Symptom State in Pain and Function in Rheumatoid Arthritis, Ankylosing Spondylitis, Chronic Back Pain, Hand Osteoarthritis, and Hip and Knee Osteoarthritis: Results From a

Prospective Multina. Arthritis Care Res. 2012;64(11):1699–707.
295. Sanderson DJ, Zavez A, Meekins AR, Eddib A, Lee TG, Barber MD, et al. The Patient Acceptable Symptom State in Female Urinary Incontinence. Female Pelvic Med Reconstr Surg. 2022;28(1):33–9.
296. Kowalski JT, Barber MD, Klerkx WM, Grzybowska ME, Toozs-Hobson P, Rogers RG, et al. International urogynecological consultation chapter 4.1: definition of outcomes for pelvic organ prolapse surgery. Int Urogynecol J. 2023;34(11):2689–99.
297. Maksymowych WP, Richardson R, Mallon C, Van Der Heijde D, Boonen A. Evaluation and validation of the Patient Acceptable Symptom State (PASS) in patients with ankylosing spondylitis. Arthritis Care Res. 2007;57(1):133–9.
298. Sund R. Quality of the Finnish Hospital Discharge Register: A systematic review. Scand J Public Health. 2012;40(6):505–15.
299. Hernán MA, Hernández-Díaz S, Werler MM, Mitcheil AA. Causal Knowledge as a Prerequisite for Confounding Evaluation: An Application to Birth Defects Epidemiology. Am J Epidemiol. 2002;155(2):176–84.
300. Redelmeier DA, Lorig K. Assessing the Clinical Importance of Symptomatic Improvements. Arch Intern Med. 1993;153:1337–42.
301. Terwee CB, Roorda LD, Knol DL, De Boer MR, De Vet HCW. Linking measurement error to minimal important change of patient-reported outcomes. J Clin Epidemiol. 2009;62(10):1062–7.
302. Turner D, Schünemann HJ, Griffith LE, Beaton DE, Griffiths AM, Critch JN, et al. Using the entire cohort in the receiver operating characteristic analysis maximizes precision of the minimal important difference. J Clin Epidemiol. 2009;62(4):374–9.
303. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, et al. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. Ann Rheum Dis. 2005;64(1):29–33.
304. Bergman I, Westergren Söderberg M, Ek M. Perineorrhaphy Compared With Pelvic Floor Muscle Therapy in Women With Late Consequences of a Poorly Healed Second-Degree Perineal Tear: A Randomized Controlled Trial. Obstet Gynecol. 2020;135(2):341–51.
305. Davenport MT, Sokol ER, Comiter C V, Elliott CS. Does the Degree of Cystocele Predict De Novo Stress Urinary Incontinence After Prolapse Repair? Further Analysis of the Colpopexy and Urinary Reduction Efforts Trial. Female Pelvic Med Reconstr Surg.

2018;24(4):292–4.
306. Lo TS, bt Karim N, Nawawi EA, Wu PY, Nusee Z. Predictors for de novo stress urinary incontinence following extensive pelvic reconstructive surgery. Int Urogynecol J. 2015;26(9):1313–9.
307. Karjalainen P, Gillor M, Dietz H. Predictors for occult stress urinary incontinence. Aust N Z J Obs Gynaecol. 2021;61(2):263–9.
308. Nguyen JN, Yazdany T, Burchette RJ. Urodynamic Evaluation of Urethral Competency in Women with Posterior Vaginal Support Defects. Urology. 2007;69(1):87–90.
309. Husby KR, Gradel KO, Klarskov N. Stress Urinary Incontinence after Operations for Uterine Prolapse: A Nationwide Cohort Study. Urogynecology. 2023;29(2):121–7.
310. Osmundsen B, Gregory WT. De Novo Stress Urinary Incontinence After Prolapse Surgery: Have We Answered the Question? Urogynecology (Phila). 2022;28(8):466–7.
311. Dvorkin LS, Knowles CH, Scott SM, Williams NS, Lunniss PJ. Rectal intussusception: Characterization of symptomatology. Dis Colon Rectum. 2005;48(4):824–31.
312. Frahm Olsen M, Bjerre E, Hansen MD, Tendal B, Hilden J, Hróbjartsson A. Minimum clinically important differences in chronic pain vary considerably by baseline pain and methodological factors: systematic review of empirical studies. J Clin Epidemiol. 2018;101:87-106.e2.
313. Engel L, Beaton DE, Touma Z. Minimal Clinically Important Difference: A Review of Outcome Measure Score Interpretation. Rheum Dis Clin N Am. 2018;44(2):177–88.
314. MacKay C, Clements N, Wong R, Davis AM. A systematic review of estimates of the minimal clinically important difference and patient acceptable symptom state of the Western Ontario and McMaster Universities Osteoarthritis Index in patients who underwent total hip and total knee replacement. Osteoarthr Cartil. 2019;27(10):1408–19.
315. Dekker J. The minimal clinically important difference re-considered. Osteoarthr Cartil. 2019;27(10):1403–4.
316. Karjalainen T, Heikkinen J, Busija L, Jokihaara J, Lewin AM, Naylor JM, et al. Use of Placebo and Nonoperative Control Groups in Surgical Trials A Systematic Review and Meta-analysis. JAMA Netw Open. 2022;5(7):1–12.
317. Guyatt GH, Norman GR, Juniper EF, Griffith LE. A critical look at transition ratings. J Clin Epidemiol. 2002;55(9):900–8.

318. Larsen MD, Lose G, Guldberg R, Gradel KO. Discrepancies between patient-reported outcome measures when assessing urinary incontinence or pelvic- prolapse surgery. Int Urogynecol J. 2016;27(4):537–43.

APPENDICES

APPENDIX 1.

Lantionpohjavaivojen kartoitus (PFDI-20)

Ohjeet: Kysymysten tarkoituksena on kartoittaa mikäli teillä esiintyy tiettyjä tuntemuksia suolen, virtsarakon tai alapään alueelta, ja kuinka paljon nämä oireet teitä vaivaavat. Vastatkaa kysymyksiin laittamalla rasti sopivaan ruutuun. Vastatessanne kysymyksiin ottakaa huomioon oireenne **viimeisten kolmen kuukauden aikana.**

POPDI-6

1. **Onko teillä usein paineen tunnetta alavatsalla?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

2. **Esiintyykö teillä painon tunnetta tai särkyä (jomotusta) alapäässä?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

3. **Esiintyykö teillä pullistuma alapäässä, jonka voitte itse nähdä tai tuntea emättimen ulkosuulla?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

4. **Joudutteko koskaan painamaan emättimestä tai peräaukon läheltä saadaksenne ulostettua?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

5. **Tuntuuko teistä usein siltä, että virtsarakkonne ei tyhjene kokonaan?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

6. **Joudutteko joskus painamaan pullistumaa emättimen sisään aloittaaksenne virtsaamisen tai saadaksenne virtsarakon tyhjenemään?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

POPDI-6 pisteet **x 25=_____**

CRADI-8

7. **Joudutteko ponnistelemaan liikaa saadaksenne ulostettua?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

8. **Tuntuuko teistä ulostamisen jälkeen siltä, ettei suoli ole tyhjentynyt kunnolla?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

9. **Onko teillä vaikeuksia pidättää ulostetta , jos uloste on normaalia?**
   □ Ei □ Kyllä
   Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
   □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

10. **Onko teillä vaikeuksia pidättää ulostetta, jos uloste on löysää?**
    □ Ei □ Kyllä
    Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
    □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

11. **Karkaako teiltä usein kaasu peräsuolesta?**
    □ Ei □ Kyllä
    Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
    □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

12. **Onko ulostaminen teille usein kivuliasta?**
    □ Ei □ Kyllä
    Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
    □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

13. **Tuleeko teille pakottava ulostamistarve ja kiire vessaan ennen ulostamista?**
    □ Ei □ Kyllä
    Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
    □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

14. **Pullistuuko osa peräsuoltanne koskaan ulos peräaukosta ulostamisen aikana tai sen jälkeen?**
    □ Ei □ Kyllä
    Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
    □ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

CRADI-8 pisteet x 25=____

UDI-6

15. Onko teillä tavallisesti tihentynyttä virtsaamistarvetta?
□ Ei □ Kyllä
Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
□ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

16. Karkaako virtsa silloin kun tunnette virtsapakkoa eli hyvin voimakasta virtsaamisen tarvetta?
□ Ei □ Kyllä
Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
□ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

17. Karkaako teiltä tavallisesti virtsaa yskiessä, nauraessa tai aivastaessa?
□ Ei □ Kyllä
Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
□ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

18. Karkaako teiltä tavallisesti pieniä määriä virtsaa (tipoittain)?
□ Ei □ Kyllä
Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
□ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

19. Onko teillä tavallisesti vaikeuksia tyhjentää virtsarakkonne?
□ Ei □ Kyllä
Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
□ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

20. Onko teillä tavallisesti kipua tai epämiellyttävää tunnetta alavatsalla tai alapäässä?
□ Ei □ Kyllä
Jos vastasitte kyllä, kuinka paljon se haittaa teitä?
□ Ei lainkaan □ Jonkin verran □ Melko paljon □ Paljon

UDI-6 pisteet x 25=_____

Pisteyttäminen: Laske kunkin osion pisteiden keskiarvo (0–4) ja kerro se 25:llä saadaksesi kokonaispistemäärän (asteikolla 0 – 100). Vastaamatta jääneitä kysymyksiä ei huomioida pistelaskussa, vaan keskiarvo lasketaan ainoastaan vastattujen kysymysten pisteistä.
PFDI-20 Pisteytyksen yhteenveto: Laske kaikkien kolmen osion pisteet yhteen saadaksesi kokonaispistemäärän (asteikolla 0 – 300).

POPDI-6 / CRADI-8 / UDI-6 **PFDI-20 PISTEET _____**

APPENDIX 2.

Patient Global Impression of Improvement (PGI-I)

Valitkaa numero, joka kuvastaa parhaiten nykyistä, leikkauksen jälkeistä vointianne verrattuna siihen, millainen se oli ennen leikkausta (lähtiessänne mukaan tutkimukseen vuonna 2015)

☐ 1 = hyvin paljon parempi
☐ 2 = paljon parempi
☐ 3 = vähän parempi
☐ 4 = ei muutosta
☐ 5 = vähän huonompi
☐ 6 = paljon huonompi
☐ 7 = hyvin paljon huonompi

APPENDIX 3.

Anchor question for the Patient acceptable symptom state (PASS)

Ottaen huomioon kaikki päivittäiset toimintanne sekä laskeumaan liittyvät oireenne, katsotteko, että nykyinen tilanteenne on riittävän hyvä?

☐ Kyllä ☐ Ei

ORIGINAL PUBLICATIONS (I – IV)

I

Pelvic organ prolapse surgery and overactive bladder symptoms – a population-based cohort (FINPOP)

Karjalainen PK, Tolppanen A-M, Mattsson NK, Wihersaari OAE, Jalkanen JT, Nieminen K

Int Urogyn J. 2022;33(1):95-105

International Urogynecology Journal
https://doi.org/10.1007/s00192-021-04920-w

ORIGINAL ARTICLE

Pelvic organ prolapse surgery and overactive bladder symptoms—a population-based cohort (FINPOP)

Päivi K. Karjalainen[1,2] · Anna-Maija Tolppanen[3] · Nina K. Mattsson[2,4] · Olga A.E. Wihersaari[5,6] · Jyrki T. Jalkanen[6,7] · Kari Nieminen[5,6]

Received: 28 April 2021 / Accepted: 10 June 2021

Abstract

Introduction and hypothesis It is unclear how compartment of pelvic organ prolapse (POP) impacts overactive bladder (OAB) symptom severity or improvement after POP surgery. We hypothesized that anterior and apical prolapse are more strongly associated with OAB symptoms than posterior compartment prolapse.

Methods A total of 2933 POP surgeries from a prospective population-based cohort were divided into two groups: (1) anterior and/or apical compartment surgery (± posterior repair), $N = 2091$; (2) posterior repair only, $N = 478$. Urinary frequency and urgency urinary incontinence (UUI) were evaluated using PFDI-20 (bothersome symptom: score 3–4) at baseline, 6, and 24 months. Association between degree of POP in specific compartments and symptoms at baseline was estimated with generalized linear models and between compartment of surgery and symptom improvement with generalized estimating equations.

Results At least one bothersome symptom was reported by 40% at baseline, 14% at 6, and 19% at 24 months. At baseline, urinary frequency was associated with degree of anterior and apical and UUI with anterior compartment prolapse. Women undergoing surgery for anterior/apical compartment started with worse symptoms and experienced greater improvement than women undergoing posterior compartment surgery. Bothersome frequency resolved in 82% after anterior/apical and in 63% after posterior compartment surgery. Bothersome UUI resolved in 75% after anterior/apical and in 61% after posterior compartment surgery. After surgery, symptom severity was comparable between groups. Bothersome de novo symptoms occurred in 1–3%.

Conclusions OAB symptoms are more strongly related to anterior and apical than to posterior compartment prolapse, but improvement is seen after surgery for any vaginal compartment.

Keywords Overactive bladder · Pelvic organ prolapse · Pelvic organ prolapse surgery · Urgency urinary incontinence · Urinary frequency

✉ Päivi K. Karjalainen
paivikristiina.karjalainen@gmail.com

[1] Department of Obstetrics and Gynecology, Hospital Nova of Central Finland, Hoitajantie 3, 40620 Jyväskylä, Finland

[2] Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland

[3] School of Pharmacy, University of Eastern Finland, Kuopio, Finland

[4] Department of Obstetrics and Gynecology, Kanta-Häme Central Hospital, Hämeenlinna, Finland

[5] Department of Obstetrics and Gynecology, Tampere University Hospital, Tampere, Finland

[6] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

[7] Central Finland Health Care District, Jyväskylä, Finland

Introduction

Overactive bladder (OAB) symptoms are common, affecting around 13% of women of all ages. The prevalence of these symptoms increases with age, and they can have a detrimental impact on the quality of life [1]. Community-based studies show that OAB symptoms are up to six times more frequent among women with pelvic organ prolapse (POP) compared with age-adjusted women without POP [2]. OAB symptoms also improve after POP surgery, implying a connection between the two [2]. Nevertheless, the role of POP as an explanatory pathology behind OAB remains unclear, and current guidelines do not list POP in the diagnostic algorithms for OAB [3, 4].

Proposed mechanisms to explain the co-occurrence of OAB symptoms and POP include detrusor overactivity due to (1) bladder outflow obstruction, (2) bladder wall distension

Published online: 10 July 2021

and stimulation of stretch receptors, and (3) traction and opening of the urethra triggering the emptying reflex [2]. Based on these theories, it is plausible that anterior compartment prolapse (i.e., bladder involvement) has a greater impact on the OAB symptoms than posterior compartment prolapse. However, the majority of studies have not found any correlation among the degree of anterior, apical, or posterior compartment prolapse and severity of OAB symptoms [2]. Furthermore, studies comparing symptom improvement after prolapse surgery for different vaginal compartments conclude comparable improvement regardless of the repaired compartment [5–8]. This lack of association, together with imperfect symptom resolution, challenges the rationale to perform POP surgery to address OAB symptoms [9, 10].

To understand the relationship between OAB symptoms and POP, we [1] quantified the association between the degree of individual POP compartments and OAB symptoms before surgery and [2] examined whether symptom improvement after surgery is dependent on the repaired compartment. We hypothesized that OAB symptoms are more strongly related to the anterior and apical than to the posterior compartment prolapse.

Materials and methods

Setting and participants

We used data from the national, prospective Finnish Pelvic Organ Prolapse Surgery Survey (FINPOP). The study setting, population, and methods of surgery have been reported in more detail previously [11]. All Finnish hospitals performing POP surgery were invited to participate and to recruit all patients scheduled to undergo prolapse surgery during 2015. Women unable to communicate in Finnish or Swedish were excluded. A total of 41 of 45 hospitals (91%) performing POP surgery participated. The FINPOP cohort includes 3535 POP operations representing 83% of POP operations performed nationwide during 2015 (National database: Care Register for Health Care).

The population of this study includes 2933 operations with preoperative clinical examination and symptom questionnaires available. The patient flow, exclusion criteria, and data availability are shown in Fig. 1. We excluded women receiving a procedure for stress urinary incontinence concomitantly ($N = 25$) or during the follow-up ($N = 84$) from the analyses regarding symptom improvement. Of six women receiving intradetrusor injections of botulinum toxin A between 6 and 24 months' follow-up, two were excluded from 24 months' analyses because they reported improvement in the OAB symptom scores. Since usage of OAB medication at baseline did not associate with fewer OAB symptoms (rather the opposite), we did not exclude these women from the analyses.

Data collection

All data in this study were collected prospectively, and information was not retrieved from hospital charts.

The preoperative degree of POP was assessed by the surgeons using the simplified Pelvic Organ Prolapse Quantification (POP-Q) system as a single most distal point (in centimeters from the hymen) for each vaginal compartment (Ba for anterior; Bp for posterior, and C for apical compartment). The stage of POP was determined according to the POP-Q system [12]. Vaginal length was not recorded, and therefore stages 3–4 for all compartments, as well as stages 0–1 for apical prolapse, were combined in the analyses. The surgeons also recorded participants' surgical history and details on the operation performed. The surgeons entered the data in the electronic study registry in a standardized form.

The participants completed standardized, self-administered questionnaires at baseline and at 6 and 24 months after the surgery. This included information on their medical, surgical, and obstetric history. Pelvic floor dysfunction was assessed with a validated, condition-specific quality-of-life instrument, Pelvic Floor Distress Inventory −20 (PFDI-20) [13, 14]. The follow-up questionnaires were mailed to the participants, collected on paper or electronic forms based on participant's preference, and entered in the electronic study registry.

Information on the anti-incontinence procedures during the follow-up were retrieved from the Care Register for Health Care (coverage > 95%) [15].

Outcome measures

OAB symptoms were evaluated using two items in the PFDI-20: Item 15, 'Do you usually experience frequent urination?', assessed urinary frequency; item 16, 'Do you usually experience urine leakage associated with a feeling of urgency, that is, a strong sensation of needing to go to the bathroom?', assessed urgency urinary incontinence [14]. The scale for each symptom is as follows: 0: symptom not present; 1: symptom present but not at all bothersome; 2: symptom somewhat bothersome; 3: symptom moderately bothersome; 4: symptom quite a bit bothersome. We defined answers 3 and 4 as bothersome symptoms. Bothersome symptom was defined as resolved when bother score at follow-up was < 3.

Statistical analyses

We categorized the population into two groups based on the repaired compartment: (1) women who had surgery for anterior and/or apical compartment (± posterior compartment), i.e., anterior/apical group, and (2) women who had surgery for posterior compartment only, i.e., posterior group.

To further explore differences between anterior and apical repairs, we performed a secondary analysis dividing the

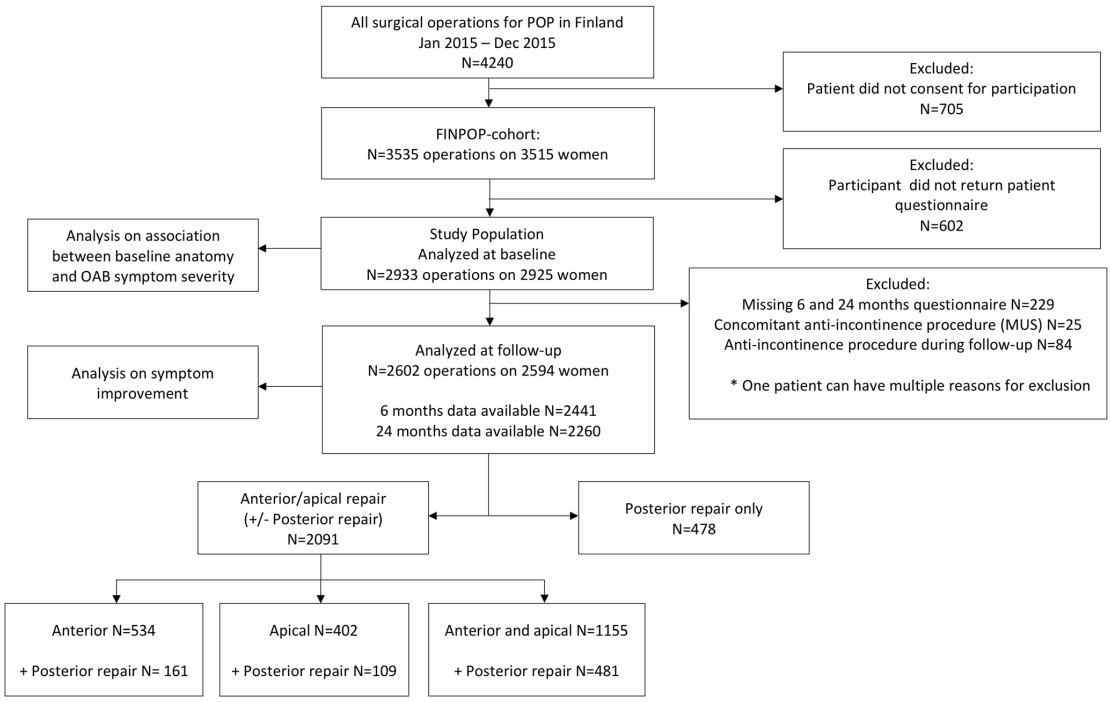


Fig. 1 Flowchart showing the selection of the study population. POP, pelvic organ prolapse; FINPOP, Finnish Pelvic Organ Prolapse Surgery Survey

anterior/apical group into women with (1) a vaginal procedure for anterior wall but not any type of apical procedure (anterior group); (2) any type of apical procedure but no vaginal procedure for anterior vaginal wall (apical group); (3) a vaginal procedure for anterior wall and any type of apical procedure (anterior and apical group).

We used a generalized linear model (ordinal logistic) to estimate the association between the baseline anatomy (Ba, Bp, C in centimeters) and symptom bother (ordinal scale 0 to 4). Multivariable models were fitted to control for prolapse in other compartments (Ba, Bp, C) and to adjust for potential confounders. The confounders (age, BMI, parity, smoking, previous POP surgery, previous anti-incontinence surgery) were selected based on the knowledge from previous literature and from clinical experience using directed acyclic graphs [16]. Spearman's correlation coefficients did not indicate strong collinearity between the variables (all < 0.4). The ordinal logistic model yields odds ratios (OR) with 95% confidence intervals (CI) for a higher bother score with a centimeter increase in the extent of prolapse.

To estimate the association between the site/compartment of surgery and improvement after surgery, we used ordinal generalized estimation equations adjusting for confounders. To assess whether anterior/apical repair improved symptoms more compared with posterior repair, time * repair group interaction was included in the model. We also performed a sensitivity analysis adjusting for concomitant posterior repair.

Estimated marginal means from separate models with continuous dependent variables (instead of ordinal) were used to plot graphs to illustrate the results.

Ethical aspects

The study followed the ethical standards for human experimentation established by the Declaration of Helsinki of 1964, revised in 2013. The Research Ethics Committee of the Northern Savo Hospital District approved the study on May 20, 2014 (reference number 5//2014), and each participating hospital granted an approval for conducting the study. All participants gave written consent.

Results

Characteristics of the study population

The characteristics of the study population ($N = 2933$) are presented in Table 1. Of women with follow-up data ($N = 2602$), 2091 (81%) underwent surgery for the anterior and/or apical (± posterior) compartment and 478 (19%) for the posterior compartment only (Fig. 1). One hundred fifty-seven (6%)

Table 1 Characteristics of the study population

Characteristic	Study population $N=2933$	Data missing n (%)
Age (years), mean±SD	64.0±10.5	2 (0.1)
BMI (kg/m²), mean±SD	26.9±4.1	99 (3.4)
Parity, median (IQR)	2 (1)	47 (1.6)
Current smoker, *n* (%)	255 (8.7)	11 (0.4)
Diabetes, *n* (%)	283 (9.6)	0
Prior hysterectomy, *n* (%)	981 (33.4)	0
Prior POP surgery, *n* (%)	740 (25.2)	0
Prior anti-incontinence surgery, *n* (%)	170 (5.8)	0
POP-Q point Ba ≥ 0, *n* (%)	1859 (65.5)	96 (3.3)
POP-Q point C≥0, *n* (%)	1138 (40.6)	130 (4.4)
POP-Q point Bp≥0, *n* (%)	1259 (44.5)	105 (3.6)
PFDI-20 score, mean±SD	99.1±49.9	5 (0.2)
OAB medication, *n* (%)	97 (3.3)	0
Local or systemic estrogen therapy, *n* (%)	2429 (82.9)	4 (0.1)
Type of surgery, *n* (%)		0
Native tissue repair	2357 (80.4)	
Vaginal mesh	362 (12.3)	
Abdominal mesh	214 (7.3)	

SD, standard deviation; BMI, body mass index; IQR, interquartile range; POP, pelvic organ prolapse; POP-Q, Pelvic Organ Prolapse Quantification System; PFDI-20, Pelvic Floor Distress Inventory-20; OAB, overactive bladder

women self-reported a re-operation for any recurrent prolapse during the 2-year follow-up.

Prevalence of OAB symptoms at baseline

At baseline, 2346 women (82%) reported at least one OAB symptom of any degree and 1135 (40%) at least one bothersome (bother score 3 or 4) OAB symptom (Table 2). Altogether 1303 (46%) women presented with both urinary frequency and urgency urinary incontinence of any degree, and 484 (17%) presented with bothersome urinary frequency and urgency urinary incontinence.

Association between anatomy and OAB symptoms at baseline

The severity of urinary frequency increased with advancing anterior wall and apical prolapse, while posterior wall prolapse was not associated with this symptom. The odds for a higher bother score increased by 7% (95% CI 3–11%) for anterior wall and by 4% (95% CI 1–6%) for apical prolapse per centimeter of additional descent (multivariable model) (Appendix Table 3, Fig. 2). The crude prevalence of bothersome urinary frequency increased from 26% (95% CI 22–31%) to 37% (95% CI 33–40%) and from 29% (95% CI 26–31%) to 36% (95% CI 31–40%) from stage 0 to stage 3–4 of anterior wall and from stage 0–1 to stage 3–4 of apical prolapse, respectively (Appendix Table 4).

The severity of urgency urinary incontinence increased with advancing anterior wall prolapse; the association with the posterior wall prolapse was inverse, and there was no significant association with apical prolapse. The odds for a higher bother score increased by 8% (95% CI 4–13%) for anterior wall and decreased by 4% (95% CI 1–8%) for posterior wall prolapse per centimeter of additional descend (multivariable model) (Appendix Table 3, Fig. 2). The crude prevalence of bothersome urgency urinary incontinence increased from 20% (95% CI 16–24%) for stage 0 to 29% (95% CI 26–32%) for stage 3–4 of anterior wall prolapse and decreased from 30% (95% CI 27–33%) for stage 0 to 26% (95% CI 22–30%) for stage 3–4 of posterior wall prolapse (Appendix Table 4).

Symptom relief after surgery

The severity of urinary frequency and urgency urinary incontinence decreased after surgery for all compartments (anterior, apical, anterior and apical, posterior) during the 6-month follow-up ($p < 0.008$ for all). At 24 months, symptom severity remained better compared with the baseline except for urgency urinary incontinence among women undergoing posterior repair only ($p = 0.186$ for posterior group and < 0.001 for other groups) (Fig. 3).

Table 2 Prevalence of OAB symptoms at baseline and at follow-up

Repair group	Symptom present	Urinary frequency			Urgency incontinence			Either symptom		
		Baseline	6 months	24 months	Baseline	6 months	24 months	Baseline	6 months	24 months
All	**Yes; any degree of bother**	1890 (66.9)	828 (33.7)	910 (39.6)	1759 (61.8)	1186 (48.2)	1158 (50.7)	2346 (82.3)	1422 (57.9)	1451 (63.4)
	Yes, bothersome symptom	875 (31.0)	204 (8.3)	258 (11.2)	744 (26.2)	257 (10.4)	326 (14.3)	1135 (40.4)	331 (13.6)	423 (18.6)
	No	935 (33.1)	1630 (66.3)	1390 (60.4)	1086 (38.2)	1274 (51.8)	1124 (49.3)	504 (17.7)	1035 (42.1)	838 (36.6)
Anterior/Apical	**Yes; any degree of bother**	1568 (69.8)	650 (33.0)	733 (39.8)	1462 (64.6)	958 (48.7)	947 (51.9)	1929 (85.1)	1136 (57.8)	1175 (64.1)
	Yes, bothersome symptom	735 (32.7)	159 (8.1)	198 (10.8)	618 (27.3)	202 (10.3)	261 (14.3)	945 (42.3)	255 (13.1)	333 (18.3)
	No	678 (30.2)	1321 (67.0)	1108 (60.2)	801 (35.4)	1011 (51.3)	878 (48.1)	338 (14.9)	831 (42.2)	657 (35.9)
Posterior	**Yes; any degree of bother**	297 (54.6)	165 (35.8)	164 (38.1)	273 (49.9)	213 (45.7)	197 (45.8)	387 (70.6)	268 (57.8)	260 (60.5)
	Yes, bothersome symptom	129 (23.7)	43 (9.3)	57 (13.2)	114 (20.8)	51 (10.9)	60 (14.0)	175 (32.4)	72 (15.7)	84 (19.7)
	No	247 (45.4)	296 (64.2)	267 (61.9)	274 (50.1)	253 (54.3)	233 (54.2)	161 (29.4)	196 (42.2)	170 (39.5)

Numbers presented as number (%) of data available at each time point

Women undergoing anterior/apical compartment surgery had worse symptom severity at baseline (< 0.001) and experienced greater symptom improvement after surgery than women undergoing surgery for posterior compartment only (time*group interaction < 0.001). There was no difference in the symptom severity after the surgery between the two groups ($p > 0.05$ for all) (Fig. 3). A sensitivity analysis adjusting for concomitant posterior repair yielded similar results (data not shown).

The prevalence of bothersome urinary frequency and urgency urinary incontinence in the total population decreased from 0.31 to 0.08 [relative risk (RR) 0.27] and 0.26 to 0.10 (RR 0.40) during 6 months' follow-up, respectively (Table 2).

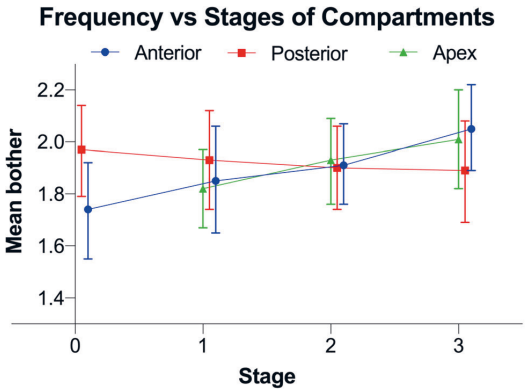
In the anterior/apical group, urinary frequency bother score improved in 994/1284 (77%) women at 6 months and in 861/1202 (72%) at 24 months. Bothersome urinary frequency resolved in 487/597 (82%) women at 6 and in 426/559 (76%) at 24 months. Women with bother score of 0 at baseline reported de novo urinary frequency of any degree in 54/560 (10%) and of bothersome degree in 5/560 (1%) at 6 months. Urgency urinary incontinence bother score had improved in 718/1166 (62%) women at 6 months and in 623/1089 (57%) at 24 months. Bothersome urgency urinary incontinence had resolved in 363/484 (75%) women at 6 and in 301/459 (66%) at 24 months. The risk of de novo urgency urinary incontinence of any degree was 103/685 (15%) and of bothersome degree 14/685 (2%) at 6 months (Fig. 4).

In the posterior group, urinary frequency bother score had improved in 122/216 (57%) women at 6 months and in 111/202 (55%) at 24 months. Bothersome urinary frequency had resolved in 52/83 (63%) women at 6 and in 44/76 (58%) at 24 months. Women with bother score of 0 at baseline reported de novo urinary frequency of any degree in 24/205 (12%) and of bothersome degree in 2/205 (1%) at 6 months. Urgency urinary incontinence bother score had improved in 99/197 (50%) women at 6 months and in 76/186 (41%) at 24 months. Bothersome urgency urinary incontinence had resolved in 48/79 (61%) women at 6 and 39/73 (53%) at 24 months. The risk of de novo urgency urinary incontinence of any degree was 47/229 (21%) and of bothersome degree 6/229 (3%) at 6 months (Fig. 4).

Discussion

Principal findings

OAB symptoms among women undergoing POP surgery are common (urinary frequency or urgency urinary incontinence of any and bothersome degree observed in 82% and 40% of women) and depend on the compartment and severity of prolapse. The symptoms had stronger associations with the anterior and apical compartment than posterior compartment



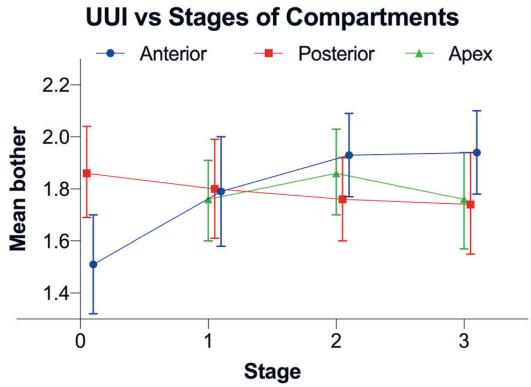
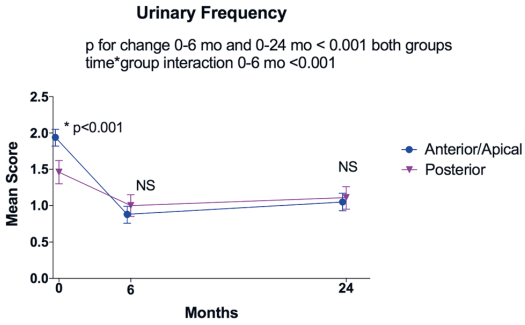
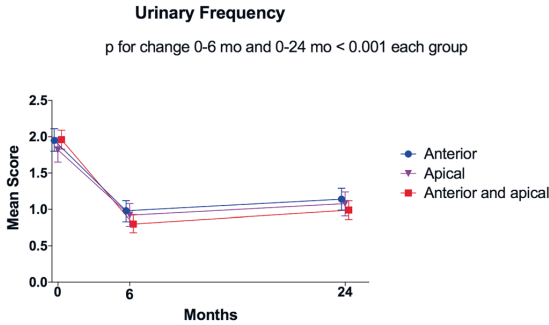
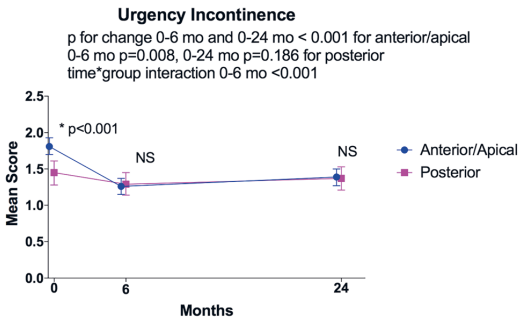


Fig. 2 Association between the severity of overactive bladder symptoms and degree and compartment of prolapse at baseline. UUI, urgency urinary incontinence. Adjusted estimated marginal means with 95% confidence intervals for stages of individual compartments is shown. Stage 3 combines stages 3 and 4 for all compartments. For apical compartment, stage 1 combines stages 0 and 1







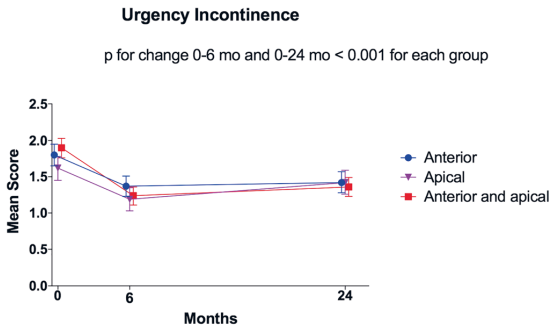


Fig. 3 Impact of surgery on overactive bladder symptoms. Impact of prolapse surgery on the overactive bladder symptom severity during the follow-up is shown. On the Y-axis, estimated marginal means (and their 95% confidence intervals) from linear generalized estimating equations multivariable model (scale 0–4, higher number indicating higher symptom bother: 0: symptom not present, 1: symptom present but not at all bothersome; 2: symptom somewhat bothersome; 3: symptom moderately bothersome; 4: symptom quite a bit bothersome). On the X-axis, follow-up points. On the left column, data stratified into two surgical groups. On the right, anterior/apical group stratified into three groups. The asterisk indicates $P < 0.05$, and NS indicates not significant ($P > 0.05$) for between-group comparison in an ordinal logistic generalized estimated equations model at different time points. *P*-values for within-group improvement and time*group interaction are reported for ordinal models. Between-group comparisons performed only for two groups (i.e., anterior/apical vs. posterior)

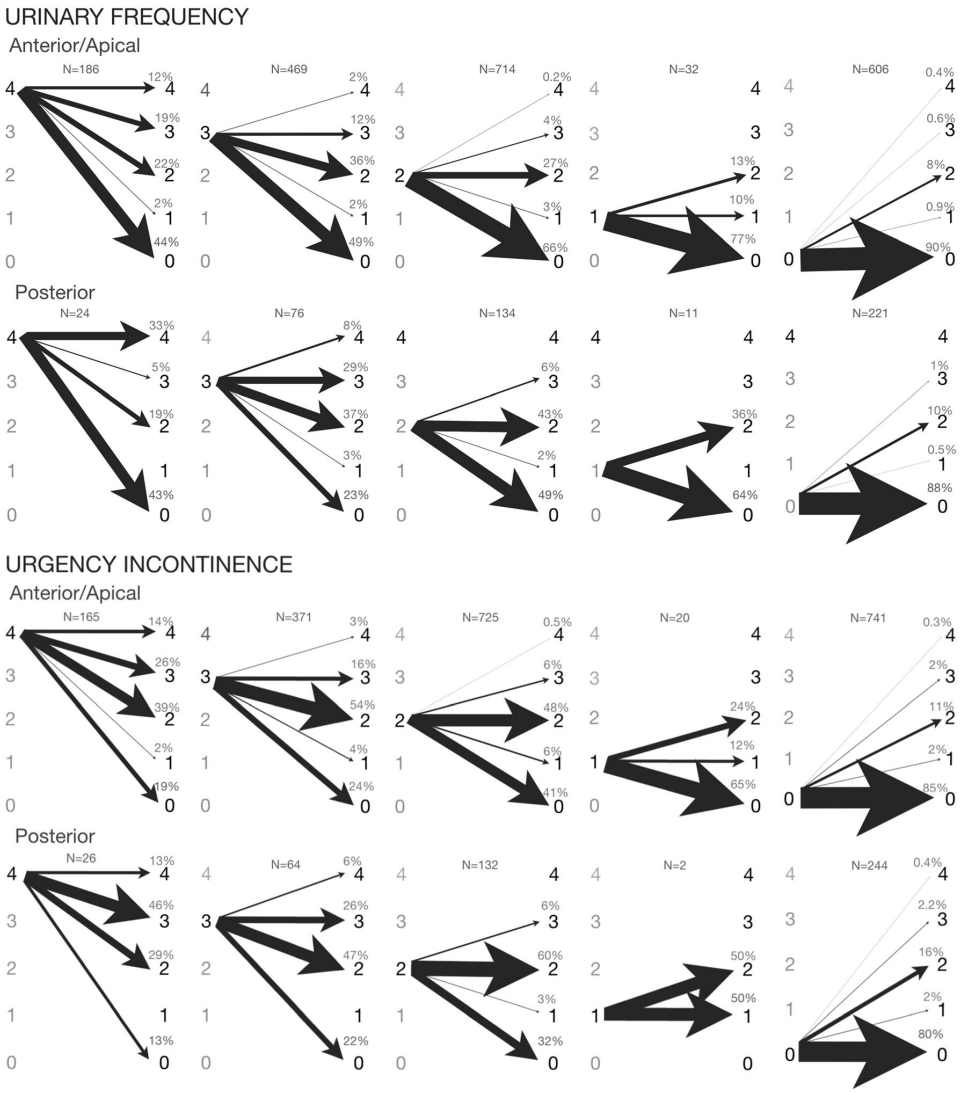


Fig. 4 Change in symptom severity from baseline to 6 months for each overactive bladder symptom stratified by baseline symptom severity in the anterior/apical and the posterior groups. Each image depicts change in symptom severity from baseline to 6 month's follow-up stratified by baseline symptom severity: baseline symptom severity on the left and 6 months' symptom severity on the right. The scale of symptom severity: 4: symptom quite a bit bothersome; 3: symptom moderately bothersome; 2: symptom somewhat bothersome; 1: symptom present but not at all bothersome; 0: symptom not present. The thickness of the arrow is proportional to percentage

prolapse, as hypothesized. Consistent with this finding, surgery for the anterior and/or apical compartment resulted in greater postoperative symptom relief compared to posterior repair. After surgery, women reached a similar level of OAB symptoms regardless of the repaired compartment. At 6 months, 14% of women reported bothersome urinary frequency or urgency urinary incontinence.

The degree of prolapse explained only a small proportion of variation in the symptom severity at baseline (e.g., 11% absolute increase in the prevalence of bothersome urinary frequency from no anterior wall prolapse to stage

3–4). Nevertheless, the correction of anatomy relieved a significant proportion of OAB symptoms. Six months after anterior/apical compartment surgery, urinary frequency bother score had decreased in 77% and urgency urinary incontinence in 62% of women. Although the symptoms did not correlate with the degree of posterior wall prolapse at baseline, OAB symptoms' bother score still decreased after posterior repair in 50-57% of women. Bothersome de novo symptoms were uncommon (1–3% 6 months postoperatively).

Results in the context of what is known

POP and OAB symptoms often coexist, but evidence on the correlation between the specific anatomical defect and symptom severity is conflicting. Results from the majority of studies do not support any correlation between the degree of anterior wall [17–24], posterior wall [19–22, 24], apical [20, 21, 24, 25] or overall [21] prolapse and OAB symptoms [2]. However, some studies report a correlation, and at least four studies agree with our findings reporting more OAB symptoms with advancing degree of anterior wall prolapse [25–28].

A systematic review concludes that OAB symptoms improve after POP surgery [2]. However, it has remained unclear how the improvement relates to surgery for specific vaginal compartments. We identified only four previous studies comparing anterior to posterior involvement, and these studies could not consistently demonstrate a difference between anterior and posterior compartment surgery [5–8].

The reason for the conflicting results may lie in the study populations and methods: small sample size [17–21, 23], lack of contrast due to insufficient numbers of women with small [18, 19] or advanced [21] POP, and dichotomization of variables [5, 7, 19, 21–24] all reduce the ability to detect association [29]. Another common shortcoming is that the analyses are not controlled for prolapse in other compartments [19–23, 28]. This is essential as different anatomic defects likely contribute to different kind of pelvic floor dysfunctions.

Weak association between the degree of prolapse and OAB symptoms as well as incomplete symptom improvement after surgery imply that other factors explain a large part of the variation in OAB symptoms among the POP population. OAB is a nonspecific, complex, and multifactorial symptom syndrome frequent in the general population, and among men as well [1, 2]. There appear to be several distinct subtypes of OAB with multiple different mechanisms. The underlying factors can overlap and have convoluted interactions. Several potential pathophysiological factors, including metabolic syndrome, affective disorders, gastrointestinal functional disorders, sex hormone deficiency, urinary microbiota, and subclinical autonomic nervous system dysfunctions, have been suggested [30]. Since surgery does not address these potential underlying causes, POP surgery will not lead to resolution of OAB symptoms in all cases.

Clinical implications

Patients, as well as clinicians, often assume that POP causes their OAB symptoms. Our data show that while the symptoms are not explained solely by the distorted anatomy, women nevertheless have high probability of symptom improvement without any further intervention.

Based on our results, POP can be considered a contributing factor to OAB symptoms, and it should be evaluated for in the diagnostic workup of women with these symptoms.

Strengths and limitations

To the best of our knowledge, this is the largest study on the topic. A national cohort including all levels of hospital care increases the generalizability of the results. Further strengths include prospective data collection and use of a validated questionnaire. Unlike previous studies [5–7], we excluded women with anti-incontinence procedures. This is important since anti-incontinence surgery may independently affect OAB symptoms [2]. We also analyzed the outcomes on the actual measurement scale instead of dichotomization.

Our study has limitations. The population is comprised of women scheduled for POP surgery. This may lead to referral bias overestimating the effect. Second, we did not use a specific scale for OAB or collect data on urinary urgency and nocturia, two additional symptoms of OAB. Third, we did not obtain frequency volume charts or urodynamic studies and lack objective measures of OAB. Fourth, we did not collect data on OAB medication at follow-up. Finally, the observational nature of the study precludes drawing a definite causal relationship between POP and OAB.

Conclusion

Urinary frequency and urgency urinary incontinence are common among women with POP and more strongly related to anterior and apical than to posterior compartment prolapse. Substantial symptom improvement is seen after surgery for any vaginal compartment, and bothersome de novo symptoms are rare. Residual postoperative symptoms are likely explained by the multifactorial nature of OAB symptoms.

Appendix

Table 3 Association between overactive bladder symptoms and individual vaginal compartments at baseline

Independent variable	Urinary frequency				Urgency urinary incontinence			
	OR[a]	95% CI	aOR[b]	95% CI	OR[a]	95% CI	aOR[b]	95% CI
Ba (anterior wall prolapse)	**1.11**	**1.07–1.15**	**1.07**	**1.03–1.11**	**1.11**	**1.07–1.14**	**1.08**	**1.04–1.13**
Bp (posterior wall prolapse)	0.97	0.93–1.00	0.99	0.95–1.03	**0.94**	**0.91–0.97**	**0.96**	**0.92–0.99**
C (apical prolapse)	**1.05**	**1.03–1.07**	**1.04**	**1.01–1.06**	1.04	1.00–1.05	1.01	0.98–1.03

OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio

[a] Generalized linear models, univariate analysis; [b] generalized linear models, multivariable model. Adjusted for prolapse in other compartments, age, BMI, parity, smoking, history of pelvic organ prolapse and anti-incontinence surgery

Table 4 Prevalence of overactive bladder symptoms at baseline per stages of individual compartments

Symptom	Compartment	Stage	Any degree of bother[a]		Bothersome symptom[b]	
			n with symptom/n total	% (95% CI)	n with symptom/n total	% (95% CI)
Frequency	Anterior	0	264/444	59.5 (54.7–64.1)	116/444	26.1 (22.1–30.5)
		1	184/298	61.7 (56.0–67.3)	85/298	28.5 (23.5–34.0)
		2	785/1157	67.8 (65.1–70.5)	349/1157	30.2 (27.5–32.9)
		3–4	602/831	72.4 (69.3–75.5)	303/831	36.5 (33.2–39.8)
	Posterior	0	492/700	70.3 (66.7–73.7)	231/700	33.0 (29.5–36.6)
		1	312/434	71.9 (67.4–76.1)	135/434	31.1 (26.8–35.7)
		2	759/1183	64.2 (61.4–66.9)	350/1183	29.6 (27.0–32.3)
		3–4	259/404	64.1 (59.2–68.8)	130/404	32.2 (27.6–37.0)
	Apex	0–1	858/1330	64.5 (61.9–67.1)	379/1330	28.5 (26.1–31.0)
		2	633/911	69.5 (66.4–72.5)	300/911	32.9 (29.9–36.1)
		3–4	324/456	71.1 (66.7–75.2)	162/456	35.5 (31.1–40.1)
UUI	Anterior	0	224/449	49.9 (45.2–54.6)	90/449	20.0 (16.4–24.1)
		1	169/298	56.7 (50.9–62.4)	85/298	28.5 (23.5–34.0)
		2	769/1161	66.2 (63.4–69.0)	313/1161	27.0 (25.8–32.1)
		3–4	554/842	65.8 (62.5–69.0)	243/842	28.9 (25.8–32.1)
	Posterior	0	470/709	66.3 (62.7–69.8)	212/709	29.9 (26.6–33.4)
		1	299/438	68.3 (63.7–72.6)	108/438	24.7 (20.7–29.0)
		2	697/1187	58.7 (55.9–61.5)	299/1187	25.2 (22.7–27.8)
		3–4	233/408	57.1 (52.1–62.0)	105/408	25.7 (21.6–30.3)
	Apex	0–1	826/1352	61.1 (58.4–63.7)	343/1352	25.4 (23.1–27.8)
		2	585/903	64.8 (61.6–67.9)	261/903	28.9 (26.0–32.0)
		3–4	278/463	60.0 (55.4–64.5)	114/463	24.6 (20.8–28.8)

CI, confidence interval; UUI, urgency urinary incontinence

[a] Answer 'Yes' in PFDI-20 questionnaire; [b] bothersome symptom defined as answers 3: moderately and 4: quite a bit in PFDI-20 questionnaire (Scale = 0–4)

Acknowledgements Financial support for this project was provided by the Finnish Society for Gynecological Surgery, a nonprofit organization. Dr. Karjalainen has received personal research leave grants from the Finnish Cultural Foundation, Finnish Medical Foundation and State Research Funding/Hospital District of Northern Savo. Funding sources did not have involvement with analysis or interpretation of the data.

Funding Open access funding provided by University of Eastern Finland (UEF) including Kuopio University Hospital.

Declarations

Conflict of interest None.

References

1. Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. Eur Urol. 2006;50:1306–15. https://doi.org/10.1016/j.eururo.2006.09.019.
2. De Boer TA, Salvatore S, Cardozo L, et al. Pelvic organ prolapse and overactive bladder. Neurourol Urodyn. 2010;29(1):30–9. https://doi.org/10.1002/nau.20858.
3. Gormley EA, Lightner DJ, Burgio KL, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment 2019. J Urol. 2019;202(3):558–64. https://doi.org/10.1097/JU.0000000000000309.
4. Nambiar AK, Bosch R, Cruz F, et al. EAU guidelines on assessment and nonsurgical management of urinary incontinence [figure presented]. Eur Urol. 2018;73(4):596–609. https://doi.org/10.1016/j.eururo.2017.12.031.
5. De Boer TA, Kluivers KB, Withagen MIJ, Milani AL, Vierhout ME. Predictive factors for overactive bladder symptoms after pelvic organ prolapse surgery. Int Urogynecol J. 2010;21(9):1143–9. https://doi.org/10.1007/s00192-010-1152-y.
6. Dieter AA, Edenfield AL, Weidner AC, Siddiqui NY. How does site of pelvic organ prolapse repair affect overactive bladder symptoms ? Female Pelvic Med Reconstr Surg. 2014;20(4):203–7. https://doi.org/10.1097/SPV.0000000000000087.
7. Frigerio M, Manodoro S, Cola A, Palmieri S, Spelzini F, Milani R. Risk factors for persistent, de novo and overall overactive bladder syndrome after surgical prolapse repair. Eur J Obstet Gynecol. 2019;233:141–5. https://doi.org/10.1016/j.ejogrb.2018.12.024.
8. Liedl B, Goeschen K, Sutherland SE, Roovers JP, Yassouridis A. Can surgical reconstruction of vaginal and ligamentous laxity cure overactive bladder symptoms in women with pelvic organ prolapse? BJU Int. 2019;123(3):493–510. https://doi.org/10.1111/bju.14453.
9. Sutherland SE. Should asymptomatic anterior pelvic organ prolapse be corrected to treat irritative urinary symptoms? Curr Urol Rep. 2010;11:338–42. https://doi.org/10.1007/s11934-010-0125-5.
10. Carberry CL. The effect of pelvic organ prolapse surgery on preexisting overactive bladder. Curr Obstet Gynecol Rep. 2016:147–51. https://doi.org/10.1007/s13669-016-0153-3.
11. Mattsson NK, Karjalainen P, Tolppanen A-M, et al. Methods of surgery for pelvic organ prolapse in a nationwide cohort (FINPOP 2015). Acta Obstet Gynecol Scand. 2019;98(4):451–9. https://doi.org/10.1111/aogs.13520.
12. Haylen BT, Maher CF, Barber MD, et al. Erratum to: an International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic organ prolapse (POP). Int Urogynecol J. 2016;27:655–84. https://doi.org/10.1007/s00192-016-3003-y.
13. Mattsson NK, Nieminen K, Heikkinen A-M, et al. Validation of the short forms of the pelvic floor distress inventory (PFDI-20), pelvic floor impact questionnaire (PFIQ-7), and pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12) in Finnish. Health Qual Life Outcomes. 2017;15(88). https://doi.org/10.1186/s12955-017-0648-2.
14. Barber MD, Walters MD, Bump RC. Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). Am J Obstet Gynecol. 2005;193:103–13. https://doi.org/10.1016/j.ajog.2004.12.025.
15. Sund R. Quality of the Finnish hospital discharge register: a systematic review. Scand J Public Health. 2012;40(6):505–15. https://doi.org/10.1177/1403494812456637.
16. Hernán MA, Hernández-Díaz S, Werler MM, Mitcheil AA. Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology. Am J Epidemiol. 2002;155(2):176–84.
17. Groenendijk AG, Birnie E, Roovers J-PW, Bonsel GJ. Contribution of primary pelvic organ prolapse to micturition and defecation symptoms. Obstet Gynecol Int. 2012;2012:798035. https://doi.org/10.1155/2012/798035.
18. Teleman P, Laurikainen E, Kinne I, Pogosean R, Jakobsson U, Rudnicki M. Relationship between the pelvic organ prolapse quantification system (POP-Q), the pelvic floor impact questionnaire (PFIQ-7), and the pelvic floor distress inventory (PFDI-20) before and after anterior vaginal wall prolapse surgery. Int Urogynecol J Pelvic Floor Dysfunct. 2014;26(2):195–200. https://doi.org/10.1007/s00192-014-2434-6.
19. Mouritsen L, Larsen JP. Symptoms, bother and POPQ in women referred with pelvic organ prolapse. Int Urogynecol J. 2003;14(2):122–7. https://doi.org/10.1007/s00192-002-1024-1.
20. Digesu GA, Chaliha C, Salvatore S, Hutchings A, Khullar V. The relationship of vaginal prolapse severity to symptoms and quality of life. BJOG An Int J Obstet Gynaecol. 2005;112(7):971–6. https://doi.org/10.1111/j.1471-0528.2005.00568.x.
21. Bradley CS, Nygaard IE. Vaginal wall descensus and pelvic floor symptoms in older women. Obstet Gynecol. 2005;106(4):759–66. https://doi.org/10.1097/01.AOG.0000180183.03897.72.
22. Ghetti C, Gregory WT, Edwards SR, Otto LN, Clark AL. Pelvic organ descent and symptoms of pelvic floor disorders. Am J Obstet Gynecol. 2005;193(1):53–7. https://doi.org/10.1016/j.ajog.2004.12.004.
23. Schimpf MO, Sullivan DMO, Lasala CA, Tulikangas PK. Anterior vaginal wall prolapse and voiding dysfunction in urogynecology patients. Int Urogynecol J. 2007;18:721–5. https://doi.org/10.1007/s00192-006-0227-2.
24. Salvatore S, Serati M, Siesto G, Cattoni E, Zanirato M, Torella M. Correlation between anatomical findings and symptoms in women with pelvic organ prolapse using an artificial neural network analysis. Int Urogynecol J. 2011;22(4):453–9. https://doi.org/10.1007/s00192-010-1300-4.

25. Miedel A, Tegerstedt G, Maehle-Schmidt M, Nyrén O, Hammarström M. Symptoms and pelvic support defects in specific compartments. Obstet Gynecol. 2008;112(4):851–8. https://doi.org/10.1097/AOG.0b013e318187c550.
26. Yuan Z, Shen H. Pelvic organ prolapse quantification in women referred with overactive bladder. Int Urogynecol J. 2010;21:1365–9. https://doi.org/10.1007/s00192-010-1209-y.
27. Romanzi LJ, Chaikin DC, Blaivas JG. The effect of genital prolapse on voiding. J Urol. 1999;161:581–6. https://doi.org/10.1097/00005392-199902000-00062.
28. Slieker-Ten Hove MCP, Pool-Goudzwaard AL, Eijkemans MJC, Steegers-Theunissen RPM, Burger CW, Vierhout ME. The prevalence of pelvic organ prolapse symptoms and signs and their relation with bladder and bowel disorders in a general female population. Int Urogynecol J. 2009;20(9):1037–45. https://doi.org/10.1007/s00192-009-0902-1.
29. Altman DG, Royston P. The cost of dichotomising continuous variables. Br Med J. 2006;332(7549):1080. https://doi.org/10.1136/bmj.332.7549.1080.
30. Peyronnet B, Mironska E, Chapple C, et al. A comprehensive review of overactive bladder pathophysiology: on the way to tailored treatment. Eur Urol. 2019;75(6):988–1000. https://doi.org/10.1016/j.eururo.2019.02.038.

II

Changes in stress urinary incontinence symptoms after pelvic organ prolapse surgery – a population-based cohort (FINPOP)

Karjalainen PK, Tolppanen A-M, Wihersaari O, Nieminen K, Mattsson NK, Jalkanen JT

Manuscript

III

The relationship of defecation symptoms and posterior vaginal wall prolapse in women undergoing pelvic organ prolapse surgery

Karjalainen PK, Mattsson NK, Nieminen K, Tolppanen A-M, Jalkanen JT.

Am J Obstet Gynecol. 2019;221(5):480.e1-480.e10.

IV

Minimal important difference and patient acceptable symptom state for PFDI-20 and POPDI-6 in POP surgery

Karjalainen PK, Mattsson NK, Jalkanen JT, Nieminen K, Tolppanen A-M

Int Urogyn J. 2021;32(12):3169-3176

International Urogynecology Journal
https://doi.org/10.1007/s00192-020-04513-z

ORIGINAL ARTICLE

Minimal important difference and patient acceptable symptom state for PFDI-20 and POPDI-6 in POP surgery

Päivi K. Karjalainen[1,2] · Nina K. Mattsson[2,3] · Jyrki T. Jalkanen[4,5] · Kari Nieminen[5,6] · Anna-Maija Tolppanen[7]

Received: 14 July 2020 / Accepted: 19 August 2020

Abstract

Introduction and hypothesis Patient-reported outcome measures are fundamental tools when assessing effectiveness of treatments. The challenge lies in the interpretation: which magnitude of change in score is meaningful for the patients? The minimal important difference (MID) is defined as the smallest difference in score that patients perceive as important. The Patient Acceptable Symptom State (PASS) represents the value of score beyond which patients consider themselves well. We aimed to determine the MID and PASS for Pelvic Floor Distress Inventory-20 (PFDI-20) and Pelvic Organ Prolapse Distress Inventory-6 (POPDI-6) in pelvic organ prolapse (POP) surgery.

Methods We used data from 2704 POP surgeries from a prospective, population-based cohort. MID was determined with three anchor-based and one distribution-based method. PASS was defined using two different methods. Medians of the estimates were identified.

Results The MID estimates with (1) mean change, (2) receiver-operating characteristic (ROC) curve, (3) 75th percentile, and (4) distribution-based method varied between 22.9–25.0 (median 24.2) points for PFDI-20 and 9.0–12.5 (median 11.3) for POPDI-6. The PASS cutoffs with (1) 75th percentile and (2) ROC curve method varied between 57.7–62.5 (median 60.0) for PFDI-20 and 16.7–17.7 (median 17.2) for POPDI-6.

Conclusion A mean difference of 24 points in the PFDI-20 or 11 points in the POPDI-6 can be used as a clinically relevant difference between groups. Postoperative scores ≤ 60 for PFDI-20 and ≤ 17 for POPDI-6 signify acceptable symptom state.

Keywords Minimal important difference · Patient-acceptable symptom state · Pelvic Floor Distress Inventory-20 · Pelvic Organ Prolapse Distress Inventory-6 · Pelvic organ prolapse surgery

Abbreviations

PROM	Patient-reported outcome measure
MID	Minimal important difference
PASS	Patient-acceptable symptom state
PFDI-20	Pelvic Floor Distress Inventory-20
POP	Pelvic organ prolapse
POPDI-6	Pelvic Organ Prolapse Distress Inventory-6
ROC	Receiver-operating characteristics
SD	Standard deviation
SEM	Standard error of measurement
SDC	Smallest detectable change
ICC	Intraclass correlation coefficient

Presentations Abstract accepted for oral presentation at the 45th Annual Meeting of International Urogynecology Association, Hague, The Netherlands, August 29–September 4, 2020

✉ Päivi K. Karjalainen
paivikristiina.karjalainen@gmail.com

[1] Department of Obstetrics and Gynecology, Central Finland Central Hospital, Keskussairaalantie 19, 40620 Jyväskylä, Finland

[2] University of Eastern Finland, Kuopio, Finland

[3] Department of Obstetrics and Gynecology, Kanta-Häme Central Hospital, Hämeenlinna, Finland

[4] Central Finland Hospital District, Jyväskylä, Finland

[5] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

[6] Department of Obstetrics and Gynecology, Tampere University Hospital, Tampere, Finland

[7] School of Pharmacy, University of Eastern Finland, Kuopio, Finland

Published online: 02 September 2020

CI Confidence interval
AUC Area under the curve

Introduction

The importance of subjective patient-reported outcome measures (PROMs) in assessing the effectiveness of treatments is widely acknowledged [1, 2]. Typically, these PROMs are questionnaires that measure the burden from various symptoms and yield a continuous score, which can then be used to evaluate differences between groups or change within a group. The challenge lies in the interpretation: which magnitude of difference in score is clinically significant. While statistical significance can be reached in theory in any comparative study by increasing the sample size, the observed difference may be so small that it is not meaningful for patients. To address this challenge, two concepts have been introduced: minimal important difference (MID) and patient acceptable symptom state (PASS).

MID represents the smallest difference in score that patients perceive as important [3, 4]. Two primary approaches, anchor-based and distribution-based, are used to determine the MID. Anchor-based methods correlate the change in the target PROM score with an external criterion, which is typically a single global measure of perceived improvement/deterioration rated by the patient [5]. While anchor-based methods reflect patients' personal experience, the distribution-based methods use purely mathematical criteria to determine the MID threshold. Due to this lack of external patient-centered reference point, distribution-based methods have been suggested to be used only as supportive evidence or when an anchor-based MID is not available [6]. Among the various anchor-based methods, none have been demonstrated to be superior to the others [5, 6].

While MID is related to change, typically improvement, PASS is used to interpret whether patients have reached sufficient subjective remission of symptoms (= state). PASS represents "the value of score beyond which patients consider themselves well" [7]. MID and PASS are complementary to one another. When patients rate being improved after a treatment, it does not automatically indicate that their state is satisfactory. On the other hand, after only a modest improvement, patients can assess their state as satisfactory in their normal life and may not be willing to pursue further treatment.

The short form of the Pelvic Floor Distress Inventory (PFDI-20) is a condition-specific health-related quality of life instrument measuring a wide range of symptoms related to pelvic floor dysfunction. It consists of three scales: urinary, colorectal/anal, and pelvic organ prolapse (POP). PFDI-20 has been shown to be a valid, reliable, and responsive instrument in both pelvic floor and POP research [8–10].

Three studies have defined MID for PFDI-20 [8, 11, 12]. These studies included patients with diverse pelvic floor disorders and interventions (Appendix Table 4). Consequently, the estimates differed from each other. MID seems to be disease-specific [6]; therefore, studies defining MID in different patient groups are necessary. Accumulating evidence from multiple studies also creates higher confidence in the MID estimate. MID for PFDI-20 delineated specifically for POP surgery has not been previously defined. Furthermore, unlike for the urinary and colorectal scales of the PFDI-20, MID has not been defined for its prolapse-specific scale (Pelvic Organ Prolapse Distress Inventory, POPDI-6).

Until now, the concept of PASS has been more widely studied and used in musculoskeletal research [7, 13]. To the best of our knowledge, there are no previous reports on PASS for PFDI-20.

The aim of our study was to define MID and PASS for PFDI-20 and POPDI-6 in POP surgery.

Materials and methods

Study population

We used data from the Finnish Pelvic Organ Prolapse Study (FINPOP). FINPOP is an observational, prospective, nationwide cohort including 3535 POP surgeries performed in Finland in 2015. All Finnish hospitals performing POP surgery were invited to participate and to recruit all patients planned to undergo POP surgery. The cohort includes 83% of the operations performed for POP in the whole country during the study period; 81% ($n = 2855$) of the operations were native tissue repairs, 12% ($n = 429$) were vaginal mesh surgeries, and 7% ($n = 251$) were sacrocolpopexies. The study protocol, population, and methods of surgery have been previously described in detail [14].

Measurements

The surgeons filled in questionnaires on the patients' previous gynecological history, degree of prolapse, and details of the surgery at baseline. Participants filled in questionnaires at baseline, 6 months, and 24 months after surgery.

Participants completed PFDI-20 at baseline and at 6 and 24 months after surgery. PFDI-20 consists of three scales: six questions on the inconvenience of POP (POPDI-6), eight questions concerning defecation, and six questions on bladder function. The range of the total score is 0–300 points, and the range for each scale is 0–100, with a higher score indicating higher symptom burden. Missing items are excluded, and the mean from the answered items is used to calculate the total score. The Finnish version of PFDI-20 has been validated [15].

Patients rated their perceived global improvement/deterioration using the Patient Global Impression of Improvement (PGI-I) scale at 6 and 24 months. PGI-I has been validated for use in POP surgery [16]. The wording of the question and choices for answer is as follows: "Check the number that best describes how your postoperative condition is now, compared with how it was before you had the surgery": (1) very much better; (2) much better; (3) a little better; (4) no change; (5) a little worse; (6) much worse; (7) very much worse.

At 24 months, the participants reported their state by answering the PASS anchor question: "When taking into account your daily activities and your symptoms related to prolapse, do you consider that your state is good enough?" ("yes" or "no").

Data handling and statistical analyses

We restricted the analysis to women who had responded to the baseline questionnaire and at least one of the follow-up (6 and/or 24 months) questionnaires ($N = 2704$). We also performed sensitivity analyses on 2623 women after excluding women with concomitant anti-incontinence surgery ($N = 24$) or rectopexy ($N = 57$).

We used baseline and 6 month's data for MID analysis. We calculated the change of PFDI-20 and POPDI-6 scores for each patient by subtracting the PFDI-20/POPDI-6 score at baseline from the PFDI-20/POPDI-6 score at 6 months. Thus, a negative change score indicated improvement of symptom burden and vice versa.

To assess the usefulness of the MID anchor question, PGI-I, we calculated the Pearson's correlations between the PGI-I and PFDI-20/POPDI-6 change score and between the PGI-I and PFDI-20/POPDI-6 score at 6 months. We calculated the mean PFDI-20 and POPDI-6 change scores stratified for each PGI-I category.

We determined MID using four previously established methods: three different anchor-based methods—(1) mean change method, (2) receiver-operating characteristics (ROC) curve method, and (3) 75th percentile method—and (4) one distribution-based method: the half a standard deviation (0.5 SD) method. For the anchor-based methods, 7-point PGI-I was used as the anchor.

As per the mean change method, we calculated MID as the mean change in score of women reporting 'a little better' in PGI-I minus the mean change in score of women reporting 'no change' [6, 17, 18]. As per the ROC curve method, we defined MID as the change score which is associated with the smallest amount of misclassification into improved and not improved according to PGI-I. We included patients reporting 'a little better,' 'much better,' 'very much better,' and 'no change' and then dichotomized the patients into improved ('a little better,' 'much better,' 'very much better') and not improved ('no change'). The MID estimate was determined as the point on the ROC curve maximizing the sum of sensitivity and specificity (the Youden index) [19]. As per the 75th percentile method, we identified the cut-off point corresponding to the 75th percentile of the change score among patients with important improvement (defined as PGI-I answers 'a little better' or 'much better') [20, 21]. Last, using the distribution-based 0.5 SD method, we took the 0.5 standard deviation (SD) of the baseline mean score as the estimate for MID [22].

To compare the MID estimates with the measurement error, we determined the standard error of measurement (SEM) and smallest detectable change (SDC) in a separate study population. This population was previously used to validate the PFDI-20 in Finnish and has been described in detail by Mattson et al. [15]. Briefly, test-retest measures of PFDI-20 and POPDI-6, assessed at a 2-week interval, were available for 60 and 61 women, respectively. Intraclass correlation coefficient (ICC) for PFDI-20 was 0.92, as reported previously, and SD was 52.4. ICC for POPDI-6 was 0.83, and SD was 5.1. SEM was calculated as $SD\sqrt{(1\text{-ICC})}$. The SDC at the group level was calculated as $(1.96 \times SEM \times \sqrt{2})/\sqrt{n}$ [23]. The SDC at the individual level was calculated as $1.96 \times SEM \times \sqrt{2}$ [23].

We used 24 month's data for PASS analysis. We defined PASS with two previously established methods. Based on the response to the PASS anchor question, the patients were dichotomized into those who had or had not reached PASS (i.e., acceptable state). (1) As per the 75th percentile method, we identified the cut-off point corresponding to the 75th percentile of the 24 months' score among those reaching PASS [7, 24]. (2) As per the ROC curve method, we plotted the 24 months' scores against reached/did not reach PASS and then identified the point on the ROC curve that was the best compromise between sensitivity and specificity (= maximized Youden index) [24, 25].

The 95% confidence intervals (CIs) for MIDs and PASSs were derived with bootstrapping based on 1000 replicates.

Ethical aspects

This study followed the ethical standards for human experimentation established by the Declaration of Helsinki in 1964, revised in 2013. The study was approved by the Research Ethics Committee of the Northern Savo Hospital District (reference number 5//2014), and each participating hospital granted an approval for conducting the study. The study was registered prospectively at ClinicalTrials.gov (NCT02716506). All participants gave written consent. The study was organized and funded by the Finnish Society for Gynecological Surgery, a non-profit organization.

Results

The study population consists of 2704 patients with the baseline questionnaire and at least one of the follow-up questionnaires available (6 months $N = 2535$, 24 months $N = 2349$). Of them, 24 (1%) underwent concomitant anti-incontinence surgery (mid-urethral sling), and 57 (2%) underwent concomitant rectopexy. The characteristics of the study population are presented in Table 1.

Minimal important difference for PFDI-20 and POPDI-6

PGI-I and PFDI-20 change score at 6 months correlated moderately ($r = 0.33$; $p < 0.001$). The correlation between PGI-I and 6 month's postoperative PFDI-20 score was strong ($r = 0.51$, $p < 0.001$). PGI-I and POPDI-6 change score at 6 months correlated moderately ($r = 0.35$; $p < 0.001$). The correlation between PGI-I and 6 month's postoperative POPDI-6 score was strong ($r = 0.53$, $p < 0.001$). Table 2 presents the PFDI-20 and POPDI-6 change between baseline and 6 months for each PGI-I category.

The MID estimates (for improvement) for PFDI-20 were as follows: (1) mean change method, −24.4 (95% CI -33.9 to −14.9); (2) ROC curve method, −24.0 (95% CI -37.7 to −10.3) [area under the curve (AUC) 0.79 (95% CI 0.75 to 0.84)]; (3) 75th percentile method −22.9 (95% CI -26.2 to −19.9); 4) 0.5 SD method, −25.0 (95% CI -25.7 to −24.3). The median of the estimates was −24.2. (Fig. 1).

Table 1 Characteristics of the study population ($n = 2704$)

Characteristic	Value
Age, years, mean ± SD	64.2 ± 10.3
BMI, kg/m², mean ± SD	26.9 ± 4.0
Parity, median (IQR)	2 (1)
Prior hysterectomy, *n* (%)	916 (33.9)
Prior prolapse surgery, *n* (%)	683 (25.3)
Prior anti-incontinence surgery, *n* (%)	157 (5.8)
Current smoker, *n* (%)	219 (8.1)
POP-Q point Ba ≥ 0, *n* (%)	1714 (65.5)
POP-Q point Bp ≥ 0, *n* (%)	1158 (44.4)
POP-Q point C ≥ 0, *n* (%)	1047 (40.5)
PFDI-20 baseline score [a], mean ± SD	98.8 ± 49.8
POPDI-6 baseline score [b], mean ± SD	40.8 ± 20.2

[a] The scale of the score is 0–300, higher score indicating higher symptom burden

[b] The scale of the score is 0–100, higher score indicating higher symptom burden

SD standard deviation, *BMI* body mass index, *POP-Q* Pelvic Organ Prolapse Quantification, *PFDI-20* Pelvic Floor Distress Inventory-20, *POPDI-6* Pelvic Organ Prolapse Distress Inventory-6

The MID estimates (for improvement) for POPDI-6 were as follows: (1) mean change method, −9.0 (95% CI -13.8 to −4.0); (2) ROC curve method, −12.5 (95% CI -20.6 to −4.4) [AUC 0.76 (95% CI 0.71 to 0.81)]; (3) 75th percentile method, −12.5 (95% CI -16.1 to −10.6); (4) 0.5 SD method, −10.1 (95% CI -10.4 to −9.9). The median of the estimates was −11.3. (Fig. 1).

SEM for PFDI-20 was 14.8. The SDC at the group level was 5.3. The SDC at the individual level was 41.1. The SEM for POPDI-6 was 2.1. The SDC at the group level was 0.75. The SDC at the individual level was 5.8.

Patient-acceptable symptom state for PFDI-20 and POPDI-6

At 24 months, 84% of the patients reported having reached PASS. The proportion of patients reaching PASS for each PGI-I category is given in Table 3. The mean PFDI-20 score at 24 months among those reaching PASS was 38.4 (95% CI 36.8 to 39.9) and for those not reaching PASS 103.2 (95% CI 97.7 to 108.6). The mean POPDI-6 score at 24 months among those reaching PASS was 9.2 (95% CI 8.7 to 9.7) and for those not reaching PASS 33.9 (95% CI 31.7 to 36.1).

The PASS estimates for PFDI-20 were as follows: (1) 75th percentile method 57.5 points (95% CI 54.9 to 60.4) and (2) ROC curve method 62.5 [95% CI 41.4 to 83.6; sensitivity 78%, specificity 78%; AUC 0.87 (95% CI 0.85 to 0.88)]. The median of the PASS estimates for PFDI-20 was 60.0.

The PASS estimates for POPDI-6 were as follows: (1) 75th percentile method 16.7 (95% CI 12.6 to 18.8) and (2) ROC curve method 17.7 [95% CI 13.1 to 22.3; sensitivity 73%, specificity 84%; AUC 0.86 (95% CI 0.83 to 0.88)]. The median of the PASS estimates for POPDI-6 was 17.2.

The sensitivity analyses excluding the women undergoing concomitant anti-incontinence surgery or rectopexy yielded similar MID and PASS estimates (Appendix Table 5).

Discussion

Our large, population-based study on women undergoing POP surgery showed that a reduction of 24 points in PFDI-20 score and a reduction of 11 points in POPDI-6 score indicate a clinically meaningful improvement within a group or a clinically relevant difference between groups. We used four different methods to define MID, and all methods produced consistent estimates. In addition to MID, we defined PASS estimates for PFDI-20 and POPDI-6. According to our results, a postoperative PFDI-20 score of 60 and a postoperative POPDI-6 score of 17 can be used as a cut-off below which patients are likely to have reached an acceptable state in terms of their symptoms.

Table 2 Mean PFDI-20 and POPDI-6 change scores for each global impression of change category

Patient Global Impression of Improvement	$n = 2475$ [a] p (%)	PFDI-20 change score [b] Mean (95% CI)	POPDI-6 change score [c] Mean (95% CI)
Very much better	842 (34.0)	−71.8 (−74.8 to −68.8)	−37.5 (−38.9 to −36.1)
Much better	1133 (45.8)	−55.7 (−58.1 to −53.3)	−30.0 (−31.1 to −28.9)
A little better	335 (13.5)	−37.9 (−42.5 to −33.4)	−19.4 (−21.3 to −17.4)
No change	95 (3.8)	−13.5 (−21.9 to −5.1)	−10.4 (−14.9 to −6.0)
A little worse	36 (1.5)	−30.5 (−48.5 to −12.6)	−14.2 (−22.1 to −6.3)
Much worse	28 (1.1)	−8.5 (−26.2 to 9.1)	−9.9 (−19.2 to −0.6)
Very much worse	6 (0.2)	−16.8 (−54.8 to 21.2)	−5.6 (−25.8 to 14.7)
All	2475 (100)	−56.2 (−57.9 to −54.4)	−29.8 (−30.7 to −29.0)

[a] Calculated for patients with PFDI-20 change score, POPDI-6 change score, and Patient Global Impression of Improvement available at 6 months

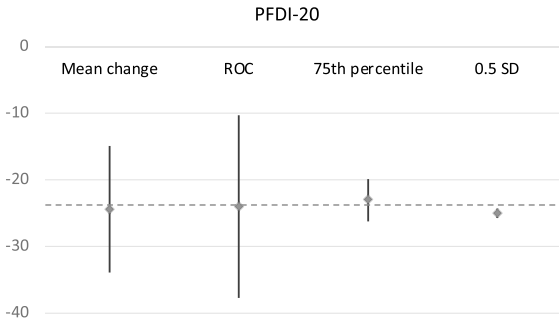
[b] The scale of the score is 0–300, higher score indicating higher symptom burden. Negative value in change score indicates improvement. [c] The scale of the score is 0–100, higher score indicating higher symptom burden. Negative value in change score indicates improvement

PFDI-20 Pelvic Floor Distress Inventory-20, *POPDI-6 CI* Pelvic Organ Prolapse Distress Inventory-6, *CI* confidence interval

Our results complement the three previous reports on MID for PFDI-20 with MID estimates varying between 13.5 and 45 points [8, 11, 12] (Appendix Table 4). None of these studies estimated MID specifically in a POP surgery population. Since MID may vary across clinical conditions [6], it is not reasonable to expect that a single MID would be applicable in all populations. Wiegersma et al. estimated a MID of 13.5 points among women undergoing *conservative* treatment for POP. The lower MID estimate in their study was unsurprising. Their population had a lower baseline score (56 points) than our population (99 points) likely related to the fact that women opt for surgical treatment when the symptom burden is high. Several studies have shown that the MID is dependent on the baseline score, with a higher symptom burden requiring a higher change to be perceived [20, 26]. The studies by Barber et al. (MID 45 points) and by Utomo et al. (23 points) comprised populations with *any* pelvic floor dysfunction. The first included women undergoing surgical treatment, the latter both conservative and surgical treatment. The discrepancy with the estimate of the Barber et al. study may be because they did not subtract the mean change score of the 'no change' group as there were no women who reported 'no change.'

To the best of our knowledge, no previous reports on MID for POPDI-6 exist in the literature. Barber et al. showed that the subscales of PFDI were the most responsive to the respective pelvic floor disorder of primary interest, i.e., responsiveness for the POPDI was the highest when the study population was POP patients and lowest when POP was not the primary condition [9]. POP patients commonly present with various pelvic floor symptoms; thus, it seems sensible to use both PFDI and POPDI in women with POP.

The methods to define MID and PASS are not yet standardized [13]. Open questions include, but are not limited to: the preferred statistical method or combination of methods, wording of the anchors, cut-off in the anchor (a little better for minimal difference or much better for important



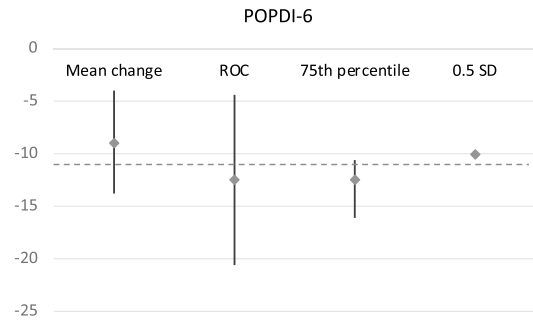


Fig. 1 MID for PFDI-20 and POPDI-6 derived with anchor-based and distribution-based methods. MID estimates defined with four different methods and their 95% confidence intervals. Vertical lines denote 95% confidence intervals. The dashed line indicates the median: - 24 points for PFDI-20 and -11 points for POPDI-6. MID, minimal important difference; PFDI-20, Pelvic Floor Distress Inventory-20; POPDI-6, Pelvic Organ Prolapse Distress Inventory-6; ROC, receiver-operating characteristics; SD, standard deviation

Table 3 Proportion of patients reaching patient acceptable symptom state (PASS) at 2 years' follow-up for each global impression of change category

PGI-I	Patients reporting to have reached PASS [a] N reaching PASS/N patients per PGI-I group	%; 95% CI
Very much better	660/665	99; 98 to 100
Much better	945/990	96; 94 to 97
A little better	233/381	61; 56 to 66
No change	40/116	35; 26 to 44
A little worse	14/58	24; 14 to 37
Much worse	4/33	12; 3 to 28
Very much worse	6/18	33; 13 to 59
All	1902/2261	84; 82 to 85

[a] Calculated for patients with Patient Global Impression of Improvement and Patient Acceptable Symptom State available at 24 months

PASS Patient Acceptable Symptom State, *PGI-I* Patient Global Impression of Improvement, *CI* confidence interval

difference), follow-up time, and adjustment for confounders such as the baseline score. As there is no clear agreement on the best method to define MID and PASS at present, we used multiple methods and provided the medians of the estimates. The estimates for both MID and PASS obtained with different methods were relatively similar, allowing us to select the median as the proposed MID/PASS value.

A recent paper by Devji et at. provides an instrument to critically evaluate the quality of the available MID [27]. Five core items in a credible MID are: anchor and PROM answered by the patients themselves; anchor easily understandable for the patients; good correlation between the anchor and the PROM; precise MID estimate (narrow confidence intervals or large sample); threshold on the anchor reflects a small but important difference (rather than moderate or large). Four of these criteria are met in our study, but the correlation between the anchor and the PROM is suboptimal. The correlation between the anchor and change score in our study was 0.32 for PFDI-20 and 0.35 for POPDI-6. A correlation threshold of 0.30–0.35 for a credible MID is often quoted [6]. However, some authorities have suggested a threshold as high as 0.5 or 0.7 [27, 28]. The anchor correlated more strongly with the postoperative score than with the change score. This phenomenon has been noted previously as well and reflects the shortcoming of the global transition rating as an anchor [29]. It seems that patients are biased by their current state at the time of rating and cannot recall their preoperative state to which they should make a comparison. On the other hand, while PFDI-20 attempts to capture a comprehensive picture of the pelvic floor function, it may fail to capture the individual perspective. For example, a woman may see an improvement in bulge and bladder storage symptoms after POP surgery, but may experience bothersome de novo stress urinary incontinence or dyspareunia (the latter not measured by PFDI-20). She may perceive her state as much worse than before the surgery even though her score improved markedly.

Our MID estimates for PFDI-20 and POPDI-6 can distinguish clinically important change from measurement error with high certainty when used *at the group level*. However, because measurement error (as indicated by SDC) *at the individual level* is larger than the MID, PFDI-20 is not suited to follow up individuals in clinical practice, there is a considerable chance that an observed change of the size of 24 points (= MID) is due to measurement error.

MID and PASS can be used concurrently in interpretation of PROM scores in comparative and observational studies. The principle role of MID is to interpret group-level mean differences: if a statistically significant difference in change score between groups is greater than the MID, it can be interpreted as a clinically meaningful difference in the efficacy. Second, MID and PASS can be used in responder analysis to report or to compare how large a proportion of patients experienced a meaningful improvement and, perhaps more importantly, reached an acceptable state. Since the difference in the PROM score may be difficult to grasp, the proportion of responders provides a useful tool for clinical decision-making and patient counseling. Third, MID can be utilized in sample size calculations to signify the smallest difference the study needs to detect.

We suggest adding the concept of PASS into the armamentarium of gynecological clinical research. PASS may be a more relevant measure for patients compared to MID—after reaching an improvement comparable to MID, one can still suffer from symptom burden that is beyond subjective tolerance. Furthermore, unlike MID, PASS can be used to compare trial results when the baseline PROM score is not available.

Strengths and limitations

The strengths of our study include: a large, population-based sample and wide diversity of surgical methods increase the generalizability of the results; multiple statistical methods yielding consistent MID estimates suggest robustness of the results.

The most important limitation of our study is that the correlation between the anchor (PGI-I) and the PROM change score was only moderate. However, the MIDs detected by the distribution-based method were nearly equal to those detected with the anchor-based methods. Another limitation is that the small number of patients with no change/deterioration prevented us from estimating the MID for deterioration.

Conclusions

We provided MID and PASS estimates to aid the interpretation of PFDI-20 and POPDI-6 scores in POP surgery. A mean difference of 24 points in the PFDI-20 score and 11 points in the POPDI-6 score can be used as a clinically relevant difference between groups. A postoperative PFDI-20 score ≤ 60 and a POPDI-6 score ≤ 17 can be used in responder analysis (acceptable state).

Acknowledgements Financial support for this project was provided by the Finnish Society for Gynecological Surgery, a non-profit organization. Dr. Karjalainen has received grants from the Finnish Cultural Foundation, the Finnish Medical Foundation and State Research Funding/Hospital District of Northern Savo. Funding sources were not involved with analysis or interpretation of the data.

Compliance with ethical standards

Conflict of interest None.

Appendix

Table 4 Characteristics of previous studies estimating the minimal important difference (for improvement) for Pelvic Floor Distress Inventory-20

Author	Year	N	Population	Method to determine MID	Anchor	MID
Barber [8]	2005	45	Surgery for any pelvic floor dysfunction; POP 58%; baseline score 122; follow-up 3–6 months	Anchor based; mean change in score of those being 'a little better' on the global rating scale ($N = 7$)	Global perception of improvement; 7 points	45
Utomo [12]	2014	67	Urinary incontinence, POP (57%), fecal incontinence; Conservative, pharmaceutical, or surgical treatment (66%); baseline score 94; follow-up 6 months	Anchor based; ROC-curve method Question 2 in the RAND 36 was dichotomized: patients reporting to be "a little better" or "much better" were classified as "improved," while "same," "a little worse," or "much worse" were classified as "not improved"	RAND 36; question 2, rating of patient's impression of their general health compared to 1 year ago; 5-point	23
Wiegersma [11]	2017	214	Conservative treatment for POP; baseline score 56; follow-up 12 months	Anchor based; ROC curve method; global perception of improvement was dichotomized to categories "better" and "much better" vs "about the same," "worse", and "much worse"	Global perception of improvement; 5-point	13.5

MID minimal important difference, *POP* pelvic organ prolapse, *TVM* transvaginal mesh, *MUS* mid-urethral sling, *ROC* receiver-operating characteristic

Table 5 MID and PASS for PFDI-20 and POPDI-6 excluding patients with concomitant anti-incontinence surgery or rectopexy $N = 2623$

Method used	MID for PFDI-20 (95% CI)	MID for POPDI-6 (95% CI)	PASS for PFDI-20 (95% CI)	PASS for POPDI-6 (95% CI)
Mean change	−24.1 (−33.9 to −14.9)	−8.7 (−13.8 to −4.0)	NA	NA
ROC curve	−24.0 (−38.7 to −9.2)	−12.5 (−20.1 to −4.9)	57.3 (54.4 to 60.1)	16.7 (11.7 to 18.8)
75th percentile	−22.1 (−26.2 to −19.9)	−12.5 (−16.1 to −10.6)	62.5 (47.9 to 85.4)	17.7 (12.1 to 23.4)
0.5 SD	−24.7 (−25.7 to −24.3)	−10.1 (−10.4 to −9.9)	NA	NA
Median for above estimates	−24.1	−11.3	59.9	17.2

MID and PASS estimates defined with different methods and their medians. Sensitivity analyses excluding women with concomitant anti-incontinence surgery ($N = 24$) and rectopexy ($N = 57$)

MID minimal important difference, *PFDI-20* Pelvic Floor Distress Inventory-20, *CI* confidence interval, *POPDI-6* Pelvic Organ Prolapse Distress Inventory-6, *PASS* Patient Acceptable Symptom State, *ROC* receiver-operating characteristics, *SD* standard deviation, *NA* not applicable

References

1. Barber MD, Brubaker LP, Nygaard I, Wheeler TL 2nd, Schaffer JI, Chen Z, et al. Defining success after surgery for pelvic organ prolapse. Obstet Gynecol. 2009;114(3):600–9.
2. Srikrishna S, Cardozo L. Quality of Life and Patient Reported Outcomes. Glob Libr women's Med. 2014;(ISSN: 1756–2228).
3. Schünemann HJ, Puhan M, Goldstein R, Jaeschke R, Guyatt GH. Measurement properties and interpretability of the chronic respiratory disease questionnaire (CRQ). COPD J Chronic Obstr Pulm Dis. 2005;2(1):81–9.
4. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. Control Clin Trials. 1989;10(4):407–15.
5. Johnston BC, Ebrahim S, Carrasco-Labra A, Furukawa TA, Patrick DL, Crawford MW, et al. Minimally important difference estimates and methods: a protocol. BMJ Open. 2015;5:e007953.
6. Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. J Clin Epidemiol. 2008;61(2):102–9.
7. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, et al. Evaluation of clinically relevant states in patient reported outcomes in knee and hip osteoarthritis: the patient acceptable symptom state. Ann Rheum Dis. 2005;64(1):34–7.
8. Barber MD, Walters MD, Bump RC. Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). Am J Obstet Gynecol. 2005;193:103–13.
9. Barber MD, Chen Z, Lukacz E, Markland A, Wai C, Brubaker L, et al. Further validation of the short form versions of the pelvic floor distress inventory (PFDI) and pelvic floor impact questionnaire (PFIQ). Neurourol Urodyn. 2011;30:541–6.
10. Gelhorn HL, Coyne KS, Sikirica V, Gauld J, Murphy M. Psychometric evaluation of health-related quality-of-life measures after pelvic organ prolapse surgery. Female Pelvic Med Reconstr Surg. 2012;18(4):221–6.
11. Wiegersma M, Panman CMCR, Berger MY, De Vet HCW, Kollen BJ, Dekker JH. Minimal important change in the pelvic floor distress inventory-20 among women opting for conservative prolapse treatment. Am J Obstet Gynecol. 2017;216(4):397.e1–7.
12. Utomo E, Blok BF, Steensma AB, Korfage IJ. Validation of the pelvic floor distress inventory (PFDI-20) and pelvic floor impact questionnaire (PFIQ-7) in a Dutch population. Int Urogynecol J. 2014;25(4):531–44.
13. Tubach F, Ravaud P, Beaton D, Boers M, Bombardier C, Felson DT, et al. Minimal clinically important improvement and patient acceptable symptom state for subjective outcome measures in rheumatic disorders. J Rheumatol. 2007;34(5):1188–93.
14. Mattsson NK, Karjalainen P, Tolppanen A-M, Heikkinen A-M, Jalkanen J, Härkki P, et al. Methods of surgery for pelvic organ prolapse in a nationwide cohort (FINPOP 2015). Acta Obstet Gynecol Scand. 2019;98(4):451–9.
15. Mattsson NK, Nieminen K, Heikkinen A-M, Jalkanen J, Koivurova S, Eloranta M-L, et al. Validation of the short forms of the pelvic floor distress inventory (PFDI-20), pelvic floor impact questionnaire (PFIQ-7), and pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12) in Finnish. Health Qual Life Outcomes. 2017;15:88.
16. Srikrishna S, Robinson D, Cardozo L. Validation of the patient global impression of improvement (PGI-I) for urogenital prolapse. Int Urogynecol J. 2010;21(5):523–8.
17. Redelmeier DA, Lorig K. Assessing the clinical importance of symptomatic improvements. Arch Intern Med. 1993;153:1337–42.
18. Terwee CB, Roorda LD, Knol DL, De Boer MR, De Vet HCW. Linking measurement error to minimal important change of patient-reported outcomes. J Clin Epidemiol. 2009;62(10):1062–7.
19. Turner D, Schünemann HJ, Griffith LE, Beaton DE, Griffiths AM, Critch JN, et al. Using the entire cohort in the receiver operating characteristic analysis maximizes precision of the minimal important difference. J Clin Epidemiol. 2009;62(4):374–9.
20. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, et al. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. Ann Rheum Dis. 2005;64(1):29–33.
21. Tubach F, Ravaud P, Martin-Mola E, Awada H, Bellamy N, Bombardier C, et al. Minimum clinically important improvement and patient acceptable symptom state in pain and function in rheumatoid arthritis, ankylosing spondylitis, chronic Back pain, hand osteoarthritis, and hip and knee osteoarthritis: results from a prospective Multina. Arthritis Care Res. 2012;64(11):1699–707.
22. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care. 2003;41(5):582–92.
23. van Kampen DA, Willems WJ, van Beers LWAH, Castelein RM, Scholtes VAB, Terwee CB. Determination and comparison of the smallest detectable change (SDC) and the minimal important change (MIC) of four-shoulder patient-reported outcome measures (PROMs). J Orthop Surg Res. 2013;8:40.
24. Maksymowych WP, Richardson R, Mallon C, Van Der Heijde D, Boonen A. Evaluation and validation of the patient acceptable symptom state (PASS) in patients with ankylosing spondylitis. Arthritis Care Res. 2007;57(1):133–9.
25. Tubach F, Wells GA, Ravaud P, Dougados M. Minimal clinically important difference, low disease activity state, and patient acceptable symptom state: methodological issues. J Rheumatol. 2005;32(10):2025–9.
26. Frahm Olsen M, Bjerre E, Hansen MD, Tendal B, Hilden J, Hróbjartsson A. Minimum clinically important differences in chronic pain vary considerably by baseline pain and methodological factors: systematic review of empirical studies. J Clin Epidemiol. 2018;101:87–106.e2.
27. Devji T, Carrasco-labra A, Qasim A, Phillips M, Johnston BC, Devasenapathy N, et al. Evaluating the credibility of anchor based estimates of minimal important differences for patient reported outcomes : instrument development and reliability study. BMJ. 2020;369(m1714):1–11.
28. Guyatt GH, Norman GR, Juniper EF, Griffith LE. A critical look at transition ratings. J Clin Epidemiol. 2002;55(9):900–8.
29. Larsen MD, Lose G, Guldberg R, Gradel KO. Discrepancies between patient-reported outcome measures when assessing urinary incontinence or pelvic-prolapse surgery. Int Urogynecol J. 2016;27(4):537–43.

PÄIVI KRISTIINA KARJALAINEN

The exact contribution of pelvic organ prolapse to bladder and bowel symptoms is unclear, resulting in diverse management approaches. This dissertation, involving nearly 3,000 prolapse surgeries, demonstrates that bladder and bowel symptoms are prevalent in women scheduled to prolapse surgery and that these symptoms often improve postoperatively. However, persistent or new-onset symptoms remain possible. The potential and limitations of surgery differ across symptoms; the findings of this thesis aid in providing personalised counselling and setting reasonable treatment expectations.

UNIVERSITY OF
EASTERN FINLAND

uef.fi

**PUBLICATIONS OF
THE UNIVERSITY OF EASTERN FINLAND**
Dissertations in Health Sciences

ISBN 978-952-61-5105-2
ISSN 1798-5706