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EVALUATION OF RISK FACTORS AND SURGICAL SAFETY OF VAGINAL PELVIC ORGAN PROLAPSE RECONSTRUCTION WITH IMPLANTS

PhD Thesis

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2026

“You can't always get what you want, but if you try sometime you'll find, you get what you need”

- The Rolling Stones: "You Can't Always Get What You Want."

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1. LIST OF ABBREVIATIONS

AC Anterior Colporrhaphy

BSO Bilateral Salpingo-Oophorectomy

BMI Body Mass Index

CI Confidence Interval

DM Diabetes Mellitus

gh Genital Hiatus

HRT Hormone Replacement Therapy

ICS International Continence Society

LH Laparoscopic Hysterectomy

LSC Laparoscopic Sacrocolpopexy

LSH Laparoscopic Supravaginal Hysterectomy

NICE National Institute for Health and Care Excellence

NT Native tissue

OAB Overactive Bladder

OR Odds Ratio

Pb Perineal Body

PC Posterior Colporrhaphy

POP Pelvic Organ Prolapse

QUIPS Quality in Prognostic Studies

RALH Robot-Assisted Hysterectomy

RALSC Robot-Assisted Sacrocolpopexy

RALSH Robot-Assisted Supravaginal Hysterectomy

RCT Randomized Controlled Trial

RoB2 Risk of Bias 2

RF Risk Factor

SUI Stress Urinary Incontinence

TAH Transabdominal Hysterectomy

Tvl Total Vaginal Lenght

U.S. United States

USLS Uterosacral Ligament Suspension

UTI Urinary Tract Infection

vs Versus

VWE Vaginal Wall Erosion

2. STUDENT PROFILE

2.1. Vision and mission statement, specific goals

My mission is to reduce morbidity associated with surgical interventions, and my vision is to formulate rigorous, evidence-based recommendations for surgical indications, contraindications, and patient selection through several focused research objectives. Central to this effort is the systematic evaluation of the safety and efficacy of vaginal implants used in pelvic organ prolapse (POP) surgery, drawing on large-scale meta-analytic data to characterize outcome measures and quantify complication rates with high precision. Additionally, I aim to elucidate the determinants of vaginal wall erosion (VWE), which is the most frequent major complication following transvaginal POP surgery with implant placement, by identifying modifiable and non-modifiable risk factors through comprehensive systematic reviews and meta-analyses. These investigations support the development of refined clinical guidelines regarding surgical indications, implant selection, operative techniques, and individualized patient stratification. By integrating robust statistical evidence with clinical applicability, my work seeks to enhance perioperative decision-making, optimize patient outcomes, and contribute to the standardization of safer and more effective surgical practice.

2.2. Scientometrics

Number of all publications:	9
Cumulative IF:	31,4
Av IF/publication:	3,49
Ranking (SCImago):	D1: 4, Q1: 2, Q2: 2, Q4: 1
Number of publications related to the subject of the thesis:	2
Cumulative IF:	9,5
Av IF/publication:	4,75
Ranking (Sci Mago):	D1: 2
Number of citations on Google Scholar:	110

Number of citations on MTMT (independent):	90
H-index:	4

The detailed bibliography of the student can be found on pages 66-67.

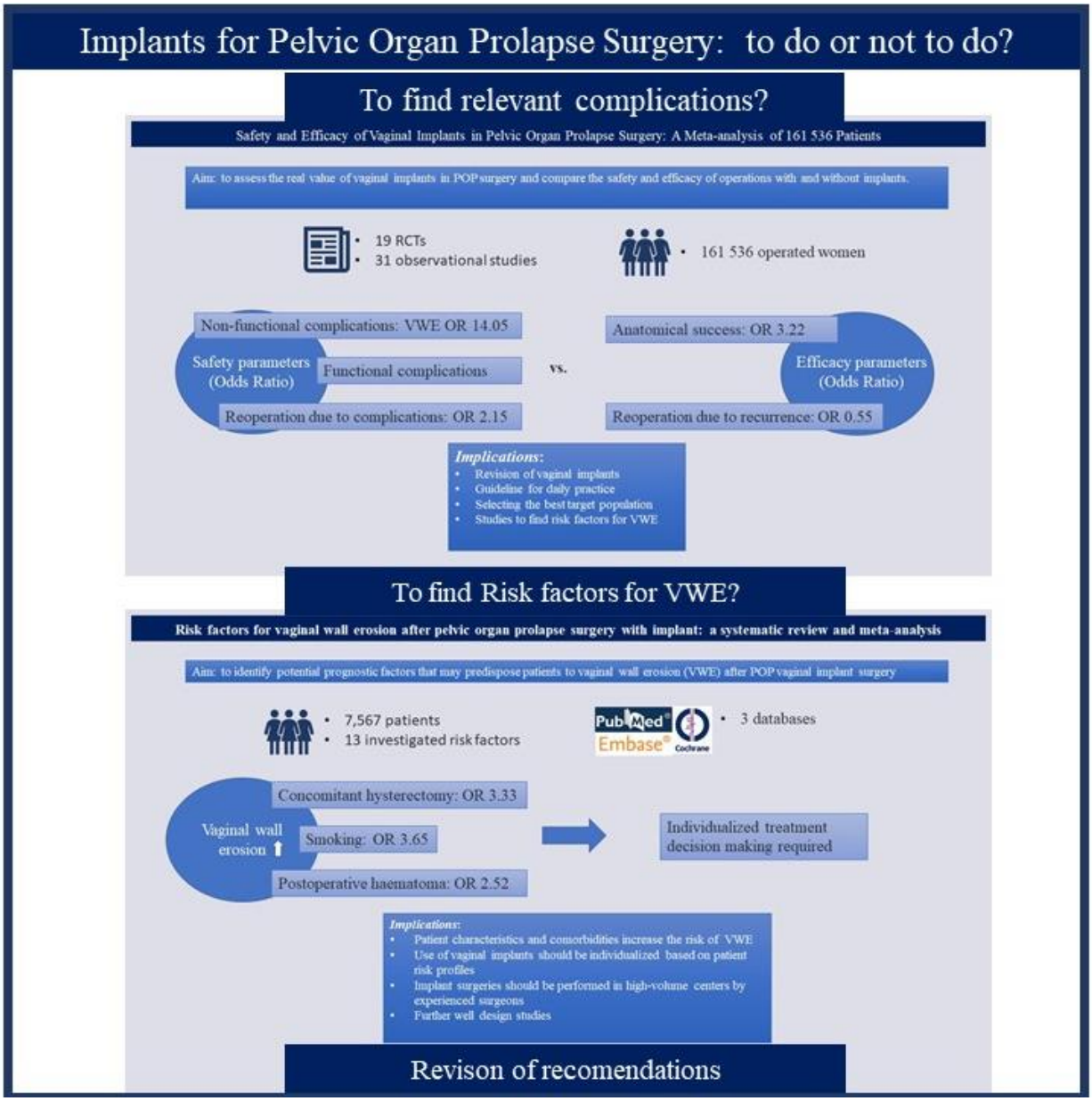
2.3. Future plans

My future plans include completing my residency in urology and subsequently beginning a residency in gynecology to build a strong, dual-specialty foundation in the interdisciplinary field of urogynecology. I aim to become an expert in this border area by integrating clinical training with continued advancement of my scientific career. Drawing on the findings and methodological experience gained from my previous studies, I plan to assess the effectiveness and safety of vaginal POP surgeries performed in Hungary over the last 25 years in a retrospective study and to initiate our own multicentric, randomized controlled trial to further contribute high-quality evidence to the field. I am also committed to mentoring project students, fostering scientific curiosity and supporting the next generation of researchers. Alongside my academic and clinical goals, I intend to continue my athletic career in artistic swimming and strive to compete at the World Championship in Budapest in 2027.

3. SUMMARY OF THE THESIS

The use of vaginal implants in pelvic organ prolapse (POP) surgery nowadays remains a controversial issue (von Theobald, 2011). Approximately 11% of women will undergo surgery for vaginal prolapse during their lifetime, and 30% of these patients will require repeat surgery due to recurrence (Halaska et al., 2012). Traditional surgical procedures using the patient's native tissue (NT) are often insufficient, and POP is likely to recur in such cases. To achieve better outcomes, new procedures using implants have been introduced, offering more durable support (de Tayrac et al., 2022). However, since 2006, the United States (U.S.) Food and Drug Administration (FDA) has issued several warnings regarding the safety of stress urinary incontinence (SUI) and POP surgeries using tapes, meshes, or slings, as these implants have shown high complication rates, particularly vaginal erosion (Halaska et al., 2012; Zacche et al., 2018). Although no detailed causal analysis was conducted, the increase in the number and severity of perioperative complications has limited the use of vaginal implants in POP surgeries in many countries. Therefore, we set ourselves the goal of exploring the causes, and predisposing factors of complications, as we were convinced that, knowing the potential risk factors, vaginal implants can still be used with good success and safety in POP surgery in a selected group of patients based on appropriate indications. Study I evaluated the safety and efficacy of vaginal implants in POP surgeries compared to NT procedures. In study I, we found that vaginal erosion was the most important and frequent, clinically and statistically relevant complication in vaginals POP surgeries using implants. In addition, it provided significantly better anatomical results compared to NT. Consequently, in our second study, we examined the potential risk factors predisposing to vaginal wall erosion (VWE) after POP vaginal implant surgery and identified the patient groups where the implant procedures could be performed safely and where they should be avoided. Study II concluded that smoking and a concomitant hysterectomy were risk factors for the development of VWE when considering vaginal reconstruction with a vaginal implant in cases of POP. Furthermore, postoperative hematoma could also be a potential risk factor for VWE. The findings address key knowledge gaps, support the safe use of vaginal implants in POP surgery, emphasize appropriate patient selection, and inform future development of standardized clinical protocols.

4. GRAPHICAL ABSTRACT



5. INTRODUCTION

5.1. Overview of the topic

5.1.1. What is the topic?

My research focuses on evaluating the safety and effectiveness of vaginal POP surgeries performed with implants compared to procedures that utilize the patient's NT. In addition, the aim was to identify the most frequent, clinically relevant complications and possible risk factors that predispose patients to the most common and clinically relevant complication associated with implant use. By characterizing these predictors, the choice of surgical technique can be better individualized to optimize outcomes and minimize harm.

5.1.2. What is the problem to solve?

The central problem to be addressed is the need to determine whether vaginal implants in POP surgery offer benefits that outweigh their risks, particularly in light of high recurrence rates after native tissue repair and the substantial safety concerns associated with implant-related complications. Despite evidence suggesting that implants provide more durable anatomical support, regulatory warnings, complication reports, and subsequent national bans have created uncertainty regarding their appropriate use (Dabica et al., 2024; Unger & Barber, 2015). As a result, there is a critical lack of evidence-based guidance on which patient subgroups may safely and effectively benefit from implant-based POP surgery. Solving this problem requires clarifying the true risk–benefit profile of vaginal implants and identifying the patients for whom their use is justified.

5.1.3. What is the importance of the topic?

POP is a highly prevalent condition that significantly affects women's quality of life, with approximately half of women over 50 experiencing it, and around 11% undergoing surgery by the age 80 (Halaska et al., 2012). In addition to anatomical complaints (such as a sensation of a vaginal foreign body, a palpable mass in the vagina, pain, etc.), women suffering from vaginal prolapse also experience functional complaints (including urinary incontinence, overactive bladder syndrome, voiding difficulty, etc.) (Doaee et al., 2014). If conservative treatment (pelvic floor muscle training and physiotherapy) fails to achieve results and the patient does not want to use a vaginal pessary, a surgical solution may be recommended.

A variety of conventional surgical techniques using autologous tissue (native tissue repair) have been developed for vaginal reconstruction of POP, however, the high recurrence rate (up to 30 %) and the many surgical techniques show that traditional techniques have not been able to find the ideal surgical type, highlighting the need for surgical approaches that provide more durable and effective anatomical support (de Tayrac et al., 2022).

Between 2016 and 2018, an average of 140,762 POP surgeries were performed annually in the United States, with total national annual costs estimated at $1.523 billion (St Martin et al., 2024). In the United States, more than 100,000 lawsuits have been filed in connection with transvaginal mesh, and manufacturers have paid more than $8 billion in damages (*https://www.millerandzois.com/products-liability/vaginal-mesh-lawsuit-and-settlements/?utm_source=chatgpt.com*, 2025). As a result of international regulatory and health policy decisions, several countries have banned or effectively discontinued the use of vaginal implants in POP surgery. Australia and New Zealand have implemented a complete ban on vaginal implants. In the United States, the FDA ordered the withdrawal of transvaginal mesh devices indicated for POP from the market in 2019, effectively ending their routine clinical use. In the United Kingdom and France, vaginal implants have been suspended, and their use is permitted only under strictly regulated conditions, typically in a research setting. According to the 2019 National Institute for Health and Care Excellence (NICE) guidelines, vaginal implants should be used only in a research setting, which in practice means complete suspension, and routine clinical use is not recommended (Administration, April 29, 2014.; Ng-Stollmann et al., 2020). Current guidelines generally recommend caution regarding the use of vaginal implants, highlighting the risk of complications (e.g., pain, mesh erosion, and infections), and often do not provide specific protocols or technical descriptions for implant use. The International Continence Society (ICS) does not recommend the widespread use of transvaginal mesh in routine POP treatment, particularly as a first-line intervention, but does not provide specific indications or exclusions in all cases (Toozs-Hobson et al., 2012). In contrast, vaginal implants are still used safely in POP surgery in many European countries, such as German-speaking countries. The guidelines in force here do not prohibit the use of implants, but they draw attention to the possibility of increased risk and advise caution (Cardozo L, 2023).

In summary vaginal implants have shown promise in improving long-term outcomes, but their use is complicated by potentially serious implant-related complications, such as VWE. Regulatory warnings, safety concerns, and bans in multiple countries have created uncertainty about the appropriate use of these implants. Despite evidence of potential benefit, there is currently no clear guidance on which patient subgroups are most likely to benefit safely from implant-based surgery. It is crucial to systematically compare the safety and effectiveness of different POP surgical approaches and to identify patient populations in whom procedures using more effective implants can be performed safely.

5.1.4. What would be the impact of our research results?

The findings could transform clinical practice by enabling individualized, evidence-based use of vaginal implants in POP surgeries. We highlight which patient subgroups are at high risk for complications and identify populations likely to benefit from implant-assisted procedures, supporting safer and more effective outcomes. Based on these, the guidelines can be streamlined and updated, which can help provide quality patient care. The results also inform guidelines on surgeon experience and surgical volume, advocate for revision of current implant bans, and emphasize the need for prospective data collection, registries, and long-term RCTs. Additionally, the research may guide development of safer implant materials, ultimately improving patient care and advancing innovation in POP management.

5.2. Description of POP

Pelvic organ prolapse is an anatomical disorder characterized by the caudal descent of the vaginal walls, uterus, or vaginal vault, caused by complex or isolated defects in the fascia–muscle system that support the pelvic floor. POP is a common condition that affects approximately 40–60% of women who have given birth. In the United States, the annual incidence of surgical procedures related to this condition is estimated to be 10–30 cases per 10,000 women; however, minimal descent is usually asymptomatic and therefore does not require treatment (Handa et al., 2004; Smith et al., 2010). The most common symptoms reported by women with prolapse are anatomical in nature: a feeling of a foreign body and/or a visible, palpable bulge in the vagina, dull, pulling pain in the lower abdomen, lower back or vagina. Although functional complaints such as voiding difficulties, incomplete bladder emptying, urinary incontinence, overactive bladder

syndrome, bowel complaints and sexual dysfunction are also frequent. The most important risk factors for the development of pelvic organ prolapse are childbirth, advanced age, and obesity (Cardozo, 2010). POP can also be classified according to the location of the anatomical abnormality and the degree of prolapse. Based on anatomical location, prolapse is categorized into anterior, apical (middle), and posterior compartment prolapses. In cases of anterior vaginal wall prolapse, weakening of the connective tissue and muscle structures that support and stabilize the anterior vaginal wall is observed. Because the bladder is located behind the descended vaginal wall, this condition is referred to as a cystocele (central or lateral). If only the urethra is affected, the condition is termed a urethrocele; when both the urethra and bladder are involved, it is called a cystourethrocele. In posterior compartment prolapse, weakening of the rectovaginal fascia results in descent and protrusion of the posterior vaginal wall. As the rectum is typically situated behind the prolapsed posterior vaginal wall, this condition is termed a rectocele. When the defect is associated with apical compartment descent and the small intestine herniates behind the prolapsed vaginal wall, the condition is referred to as an enterocele. Descent of the apical compartment involves prolapse of the uterus or cervix, or, in patients who have undergone hysterectomy, descent of the vaginal vault. These conditions are referred to as uterovaginal prolapse and vaginal vault prolapse, respectively (Maher et al., 2013). The anterior compartment is the most commonly affected site in vaginal prolapse (Zambon & Badlani, 2016). However, prolapse affecting multiple compartments is much more common than an isolated single-compartment prolapse. The stages describe the anatomical severity of pelvic organ prolapse. In everyday clinical practice, the Baden–Walker classification is most commonly used, which distinguishes between four stages (Belügyminisztérium. Egészségügyi Közlöny, 2024).

Stage 1: POP is only visible above the vaginal orifice

Stage 2: POP reaches the vaginal orifice

Stage 3: POP extends beyond the vaginal orifice

Stage 4: represents complete uterovaginal prolapse or complete vaginal vault prolapse.

The Pelvic Organ Prolapse Quantification System (POP-Q) introduced in 1996 provides a more objective and accurate anatomical description than the pragmatic classification described above. The POP-Q system based on reference points for compartments is not

routinely recommended in everyday practice, but it is an essential method for objective assessment in clinical trials. In the POP-Q system, the topography of the vagina is described by six points measured from the anteroposterior plain of the hymenal ring and the length of three parameters (Figure 1.). There are three reference points anteriorly (Aa, Ba, and C) and three posteriorly (Ap, Bp, and D). Points Aa and Ap are located 3 cm proximal to, or above, the hymenal ring on the anterior and posterior vaginal walls, respectively. Points Ba and Bp are defined as the most distal points of the prolapse between Aa anteriorly or Ap posteriorly and the vaginal apex. Anteriorly, the apex is designated as point C (the cervix), and posteriorly as point D (the pouch of Douglas). In women who have undergone hysterectomy, point C corresponds to the vaginal cuff, and point D is omitted. Three additional measurements are recorded: total vaginal length at rest (tvl), the genital hiatus (gh), measured from the midpoint of the urethral meatus to the posterior hymenal ring, and the perineal body (pb), measured from the posterior margin of the genital hiatus to the mid-anal opening (Persu et al., 2011). The POPQ stages can be established based on the nine measurement points detailed above, which can be used to determine the degree of prolapse objectively, although this staging system is not widely used in clinical practice (Belügyminisztérium. Egészségügyi Közlöny, 2024; Swift et al., 2005).

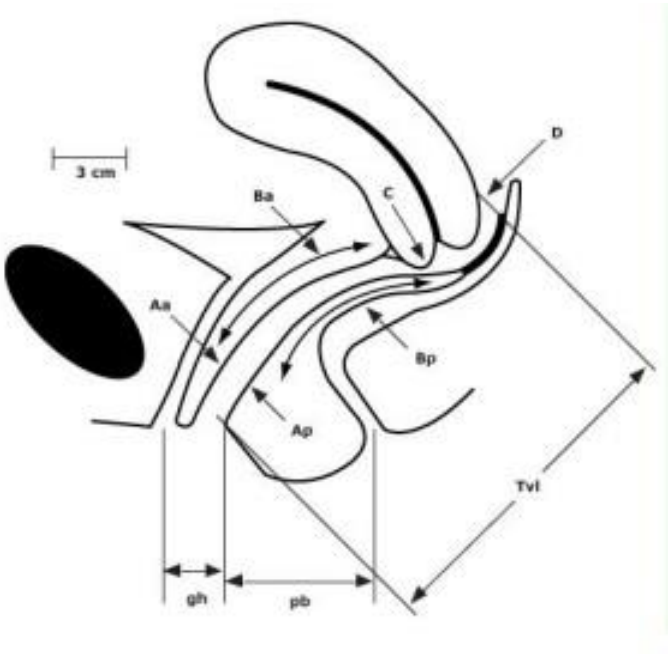


Figure 1.: POP-Q system: The six landmarks (Aa, Ba, C, Ap, Bp, D), the genital hiatus (gh), the perineal body (pb), and the total vaginal length (tvl) are visible (Belügyminisztérium. Egészségügyi Közlöny, 2024).

In the absence of symptoms or complaints, POP does not require treatment. In symptomatic cases, conservative treatment is recommended as first-line therapy, which includes pelvic floor muscle training, adjunctive physical therapy, and/or vaginal pessary therapy. If symptoms persist despite conservative therapy, the patient agrees to surgery and is medically fit, surgical intervention may be considered.

5.3. Description of the surgical interventions

The surgical procedure performed depends on the type and severity of the prolapse identified during the examination, the associated symptoms, the woman's general health, sexual activity and preferences. Women should be aware that the primary aim of surgery is the subjective elimination of the sensation of a vaginal foreign body, that is, the restoration of normal anatomical support. The objective aim of surgical treatment is the reconstruction of prolapsed tissue structures (including fascia, muscles, and connective tissue) or their reinforcement using synthetic implants (such as slings or meshes) or, in selected cases, allo- or xenografts. These goals may be achieved either by elevating the prolapsed structures from below (e.g., traditional anterior vaginal wall repair) or by suspending the most distal point of the prolapse using various fixation techniques to higher, stable anatomical structures. These approaches may also be combined (Barbalat & Tunuguntla, 2012).

There are a number of different surgical techniques available for treating pelvic organ prolapse. In the surgical treatment of POP, vaginal procedures were the first to be applied. Their advantages include easy surgical access, lower operative burden, and the possibility of being performed under regional anaesthesia without the need for general anaesthesia. The first vaginal wall plastic surgery was performed by Sims in 1866 (Pizzoferrato et al., 2023). Although these vaginal procedures based on reconstruction using native tissue elements imposed minimal surgical stress on patients, they were associated with high recurrence rates. For this reason, various implant-free open abdominal reconstructive procedures were introduced in prolapse surgery, among which sacrocolpopexy, first

described in 1957, became particularly prominent (Barbalat & Tunuguntla, 2012). While abdominal procedures provided improved anatomical outcomes, they were associated with greater surgical morbidity, required general anaesthesia, carried higher complication rates, and despite offering more reliable apical suspension were less effective in addressing anterior and posterior compartment prolapse. Consequently, during the 1990s, laparoscopic techniques aimed at reducing the invasiveness of abdominal surgery were introduced into POP surgery, most notably laparoscopic sacrocolpopexy, typically performed using mesh implants. In parallel, vaginal surgery saw the widespread adoption of various synthetic, polypropylene-based tapes and meshes for all three compartments. The passage and, when necessary, fixation of the implant arms were achieved using diverse surgical approaches, including pre- and retropubic, transobturator, sacrospinous, and sacrotuberous techniques (Bechev et al., 2015). To this day, laparoscopic sacrocolpopexy (LSC) remains the most effective and successful minimally invasive procedure recommended by current guidelines for the correction of apical prolapse, and over the past decade it has increasingly been performed using robot-assisted techniques (Gluck et al., 2020). In contrast to vaginal implants, the meshes used in LSC are placed in deeper tissue planes, do not require incision of the vaginal mucosa, and are covered intraperitoneally, which contributes to excellent outcomes and a relatively low rate of complications. Vaginal mesh erosion is therefore infrequently observed in these cases.

The vaginal POP surgeries with implants have significant better efficacy, contrary to the traditional surgical techniques that rely on NT often prove insufficient, and in such cases, POP is likely to recur. The implant material can be synthetic (e.g., durable polypropylene or absorbable polylactic acid mesh), which allows for excellent anatomical correction, however, implant-associated complications may also occur (Jia et al., 2008). Although no comprehensive causal analysis was performed, the increasing frequency and severity of perioperative adverse events initially limited the use of vaginal implants in POP surgery. Unfortunately, these early conclusions led several countries to impose a total ban on the use of vaginal implants not only for POP but also for SUI (Ng-Stollmann et al., 2020). Even in countries where the use of implants is still allowed, there is a lack of clear guidelines on which subgroups of patients with POP can benefit most from implant-based interventions. POP surgeries can be classified according to the surgical approach, the compartment affected, or the type of implant used. The most important POP surgical

approaches are listed below (Ng-Stollmann et al., 2020). Vaginal procedures include anterior and posterior colporrhaphy, paravaginal repair, perineal reconstruction, vaginal hysterectomy, cervical amputation (trachelectomy), Manchester repair (cervical amputation with fixation to the cardinal ligaments of the uterus), sacrospinous colpopexy or hysteropexy, enterocele reconstruction, uterosacral ligament suspension, vaginal obliterative procedures (colpectomy, colpocleisis), vaginal implant based reconstruction using macroporous mesh or tape (anterior, middle, posterior, or multi-compartment prolapse repair). Abdominal procedures include sacrcocolpopexy or sacrocolpohysteropexy, colposuspension, hysterectomy, supravaginal hysterectomy, uterosacral or round ligament fixation. These surgeries can be performed with an open abdominal incision or using minimally invasive techniques, laparoscopy, or robotics with or without implants (mesh, sling) (Yeung et al., 2024). Since multiple compartments are often affected at the same time, several of these techniques are often combined during surgical correction.

5.4. Vaginal wall erosion

Vaginal wall erosion is an implant-associated complication in which the implanted material gradually penetrates, exposes, or disrupts the epithelium covering the vaginal surface. Histologically, it is characterized by thinning or ulceration of the vaginal mucosa, often accompanied by chronic inflammation and tissue transformation. Clinically, it may present with vaginal discharge, bleeding, dyspareunia, pain, or exposure of the underlying material visible or palpable through the vaginal wall. In rare cases, particularly when erosion is not managed surgically, severe infections and local abscesses may occur. Although numerous studies have examined the incidence of VWE following vaginal mesh implantation, no comprehensive study has yet been conducted that specifically evaluated the risk factors for VWE in POP surgery. The reported erosion rates vary widely between studies, ranging from approximately 3% to 20%. The large differences in erosion rates suggest that there are predisposing and protective factors related to the patient, the surgical procedure, and the indications for vaginal POP surgery with implant use (Maher et al., 2013; Zambon & Badlani, 2016). In cases of severe VWE, if there is no extensive infection and the surrounding tissue is calm and unresponsive, the implanted sling or eroded mesh segment must be excised. After refreshing and thoroughly disinfecting the

edges of the wound, the vaginal mucosa covering the implant must be closed without tension. The procedure is performed in conjunction with antibiotic treatment, and if there are no factors that significantly impair wound healing (e.g., poor general condition, severe endocrine disorders, or immunosuppression), complete healing can be expected with a high likelihood of success.

In cases of recurrent erosion or extensive inflammatory lesions, especially if accompanied by symptoms of systemic infection, complete removal of the implant may be necessary.

6. OBJECTIVES

6.1. Study I. – Safety and Efficacy of Vaginal Implants in Pelvic Organ Prolapse Surgery: A Meta-analysis of 161 536 Patients

The objective of our study was to evaluate both the complications and the therapeutic effectiveness of female POP surgeries performed with versus without vaginal implants, in order to determine whether implant use confers an increased risk of adverse events that might outweigh any potential benefits over NT repair. Prevailing expert opinion states that POP procedures utilizing vaginal implants demonstrate superior effectiveness compared with NT techniques, and that associated complications are neither sufficiently severe nor frequent to warrant the exclusion of implants from standard surgical practice. To rigorously assess this hypothesis, we conducted a comprehensive systematic review and meta-analysis to characterize complication profiles and compare the clinical effectiveness of implant-based vaginal POP reconstructions relative to NT approaches.

6.2. Study II. – Risk factors for vaginal wall erosion after pelvic organ prolapse surgery with implant: a systematic review and meta-analysis

A previous meta-analysis assessing the safety and efficacy of implant-based vaginal POP surgery identified VWE as the sole complication of major clinical significance. Given interindividual variability, it was proposed that specific patient- or procedure-related factors may increase susceptibility to this erosive complication. Accordingly, the objective of the present study was to identify prognostic factors associated with VWE following vaginal implant surgery for POP. To address this, we performed a comprehensive systematic review and meta-analysis to quantify the influence of various risk factors on the likelihood of developing VWE.

7. METHODS

Studies I and II were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). To ensure methodological transparency and reproducibility, both study protocols were prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the identifiers CRD42022369386 and CRD42023364171.

7.1. Study I. - Safety and Efficacy of Vaginal Implants in Pelvic Organ Prolapse Surgery: A Meta-analysis of 161 536 Patients

7.1.1. Methodology and Protocol

Our systematic review and meta-analysis followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement PRISMA and the Cochrane handbook (Cumpston et al., 2019; Page et al., 2021). The review protocol was registered on PROSPERO (CRD42022369386).

7.1.2. Eligibility Criteria

The PICO (Population, Intervention, Comparison, Outcome) framework was used to pose our questions. Studies on females with pelvic organ prolapse (P) who underwent vaginal surgery with implants (I) in comparison to surgery without implants (C) were included. All complication types reported (Outcome 1) and the effectiveness (Outcome 2) of the two methods were compared. Complications were reported in terms of number of patients with the complication, the rate of reoperation for complications, and the different complication types. To determine the effectiveness, data on anatomical success (based on definitions used by the authors, Pelvic Organ Prolapse Quantification [POP-Q] stage, POPQ points) and the rate of reoperation for recurrence were collected. Clinical recurrence was defined as POP-Q stage ≥2. To satisfy the inclusion criteria, studies had to report on both patients undergoing vaginal surgery with implants and patients undergoing vaginal surgery with NT. RCTs and prospective and retrospective cohort studies were eligible. No studies were excluded on the basis of language criteria. Studies were excluded if they reported on either implant surgeries or on NT surgeries alone, if the data could not be further processed, or if the publication was a conference abstract, review, case series, or case report.

7.1.3. Information Sources and Search Strategy

Our systematic search was conducted on November 2, 2022 in the Embase, MEDLINE (via PubMed), and Cochrane Central Register of Controlled Trials (CENTRAL) databases. The search key included terms for females who underwent vaginal POP surgery with or without vaginal implants. We did not use filters or other restrictions.

7.1.4. Study Selection and Data Extraction

EndNote version 20.0 (Clarivate Analytics, Philadelphia, PA, USA) and rayyan.ai (Rayyan Systems, Cambridge, MA, USA) were used for the study selection process. After automatic and manual removal of duplicates, the selection was independently performed by two pairs of authors (J.Á. and B.S.; J.Á. and M.T.) at the title and abstract level and then reviewed by full text. Disagreements were resolved at each level by a third author for each pair (N.Á. and P.N.). Cohen's kappa coefficient was calculated after each step to measure inter-rater reliability. Data were collected from the eligible articles by two authors (J.Á. and B.S.) independently and entered into a predetermined data table.

7.1.5. Risk of Bias and Quality of Evidence Assessment

Two review authors (J.Á. and M.T.) assessed the risk of bias independently using the Quality in Prognostic Studies (QUIPS) tool for retrospective and prospective studies, and Risk of Bias 2 (RoB2) tool for randomized trials. For QUIPS, the risk assessment categories were predefined for each domain. Two other authors (P.N. and N.Á.) resolved disagreements. To assess the quality of the evidence, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) recommendations were followed.

7.1.6. Data Synthesis and Analysis

The odds ratios (OR) with 95% confidence intervals (CI) were calculated for the effect size measures. To pool the effect sizes for the sum of intraoperative complications (as reported in the papers), individual intraoperative complication types, total reoperations, reoperations for recurrence, and reoperations for complications, the Mantel-Haenszel method with Hartnung Knapp adjustments was used in random-effect meta-analysis (Harrer, 2021). Heterogeneity was assessed using Higgins and Thompson I 2 statistics. To pool the ORs for various functional complications, nonfunctional complications, and anatomical success outcomes, we used a multivariate model framework (Jackson et al.,

2011). This allowed us to control for intra- and interstudy correlations, and to simultaneously test moderator effects in a model. We used sandwich-type cluster-robust estimates of a variance-covariance matrix of the model coefficients and CIs (Pustejovsky & Tipton, 2022). Small-study publication bias was assessed via visual inspection of funnel plots, while outliers were detected via visual inspection of Baujat plots and leave-one-out analysis according to the recommendations of Harrer et al. (Harrer, 2021).

7.2. Study II. - Risk factors for vaginal wall erosion after pelvic organ prolapse surgery with implant: a systematic review and meta-analysis

7.2.1. Methodology and Protocol

The systematic review and meta-analysis were reported in accordance with the PRISMA 2020 guideline, following the Cochrane Handbook. The study protocol was registered on PROSPERO (registration number CRD42023364171), and was fully adhered to (Cumpston et al., 2019; Page et al., 2021).

7.2.2. Eligibility Criteria

The PFO (Population, Factors, Outcome) framework was used to construct our question. Eligible studies involved adult females who had undergone pelvic organ prolapse vaginal surgery with alloplastic implants (P), and patients with and without risk factors (F) for the odds of vaginal wall erosion (O) were compared. All reported risk factors (F) were compared. Risk factors were reported as the number of patients with and without erosions in terms of all risk factors (RF) or odds ratio (OR) of risk factors predisposing to erosion. In summary, the eligibility criteria included all studies in which women over 18 years of age underwent vaginal surgery with mesh, tape or sling implantation for pelvic organ prolapse and were subsequently assessed for erosion in relation to individual risk factors. Eligible studies reported the event numbers in groups of risk factors or as ORs. Randomized controlled trials and prospective and retrospective cohort studies were eligible. No studies were excluded based on language criteria. Conference abstracts, reviews, case series, and case reports were also excluded.

7.2.3. Information Sources and Search Strategy

Our systematic search was conducted in Embase, MEDLINE (via PubMed), and CENTRAL on June 19, 2023. The search key included terms that focused on females who

underwent vaginal pelvic organ prolapse surgery with vaginal implants and experienced erosions. No filters or other restrictions were applied.

7.2.4. Study Selection and Data Extraction

EndNote 20.0 (Clarivate Analytics, Philadelphia, PA, USA) and rayyan.ai were used for the selection. After automatic and manual removal of duplicates, the selection was performed by two independent review authors (J.Á.-B.S. and J.Á.-M.R.) in pairs at title-abstract and full-text levels of references. Discrepancies on both levels were resolved by two other review authors (N.Á. and P.N.). Cohen's kappa coefficient (κ) was calculated after each step to measure inter-rater reliability. Data from eligible articles were collected independently by two authors (J.Á. and B.S.) into a predefined data table.

7.2.5. Risk of Bias and Quality of Evidence Assessment

Two authors (J.Á. and M.R.) independently assessed the risk of bias using the QUIPS tool for retrospective and prospective studies. For QUIPS, risk assessment categories were pre-defined for each domain. Two other authors (PN and NÁ) resolved any disagreements.

7.2.6. Data Synthesis and Analysis

Considerable between-study heterogeneity was assumed in all cases; therefore, a random-effects model was used to pool effect sizes. ORs with a 95% CI were used as effect size measures. To calculate the study ORs and the pooled OR, the total number of patients and those with the event of interest in each group (referred to as "raw data") were extracted separately or calculated from studies where available. In cases where only ORs without "raw data" were provided, the OR and its 95% CI (assuming Wald type interval if not provided) were used. All statistical analyses were performed with R (R Core Team 2024, v4.4.1) using the meta (Schwarzer 2024, v7.0.0) package for basic meta-analysis calculations and plots, and the dmetar (Cuijpers, Furukawa, and Ebert 2024, v0.1.0) package for additional influential analysis calculations and plots (Cuijpers, 2024; Schwarzer, 2024; Team., 2024). Results were considered statistically significant if the pooled CI did not contain the null value. The findings of the meta-analysis were summarized in forest plots. Where applicable – that is, where the study number was sufficiently large and not too heterogeneous – the prediction intervals of results (i.e., the expected range of effects of future studies) was reported. In addition, between-study

heterogeneity was described using Higgins&Thompson's I2 statistics (Higgins and Thompson 2002) (Higgins & Thompson, 2002). Small study publication bias was assessed by visually inspecting Funnel-plots and calculating the p-value of the Harbord (modified Egger's) test for OR (Harbord, 2009). A possible small study bias was assumed if the p-value was less than 10%. However, it was acknowledged that the test had limited diagnostic assessment below ~10 studies. Potential outlier publications were explored using various influence measures and plots following the recommendations of Harrer et. al (Harrer, 2021).

8. RESULTS

8.1. Study I: Safety and Efficacy of Vaginal Implants in Pelvic Organ Prolapse Surgery: A Meta-analysis of 161 536 Patients

8.1.1. Study Search and Selection

The systematic search yielded 20 005 articles. After duplicate removal, 16 690 articles were screened by title and abstract. Full-text review of 77 reports revealed that 50 studies (19 RCTs, 31 observational studies) involving 161 536 patients were eligible. The screening and selection processes were summarized in a PRISMA flowchart in Figure 2.

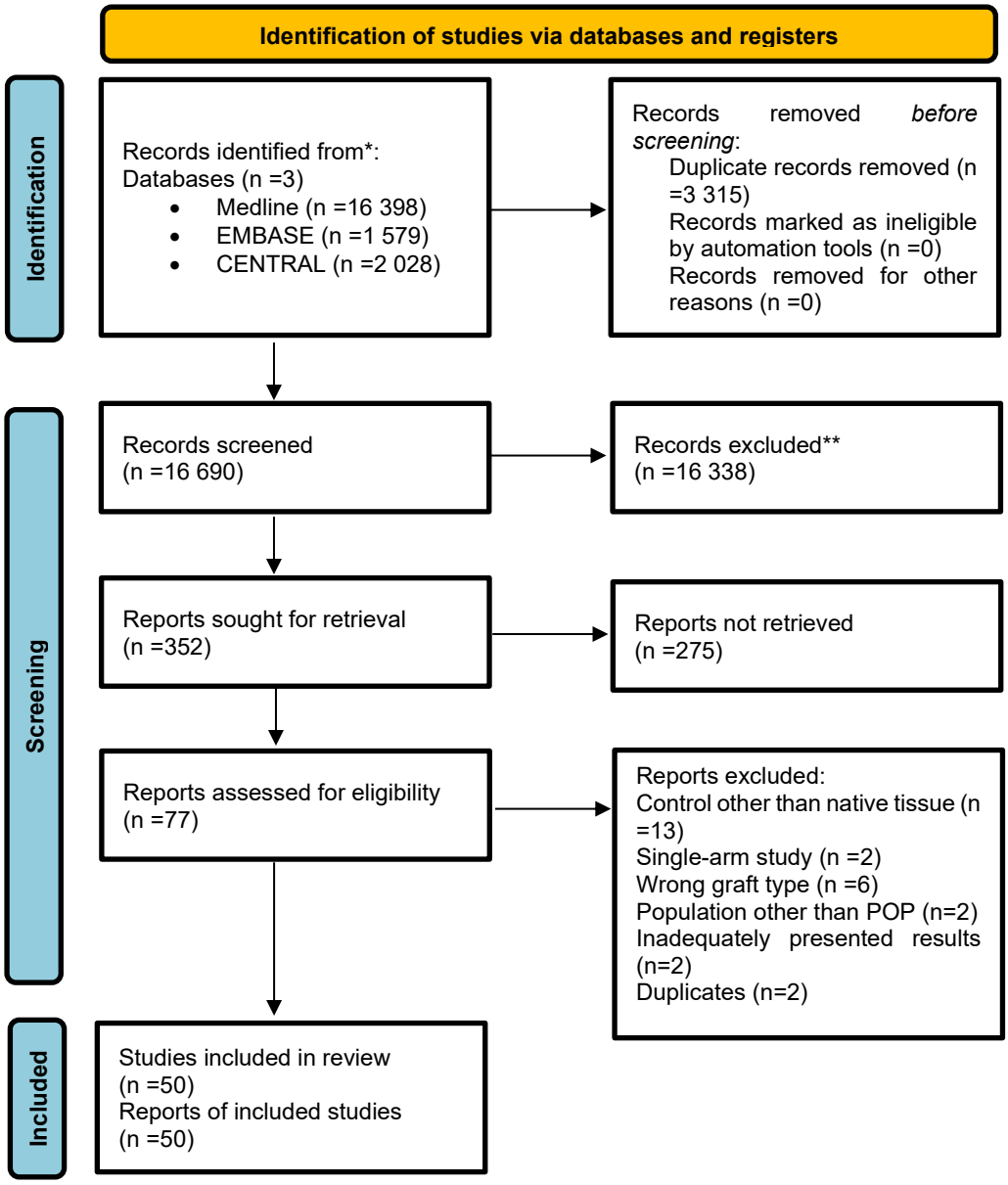


Figure 2.: *I. study PRISMA 2020 flowchart representing the study selection process (Acs et al., 2023).*

8.1.2. Safety Outcomes

In our first study, we examined all complications occurring during and after surgery in regard to safety and also the reoperations due to complications rates. We divided postoperative complications into functional and non-functional groups. **Intraoperative complications** were rare, of these, bladder perforation was the most frequent and the most important one, which occurred significantly more frequently in the implant group (Figures 3–4.).

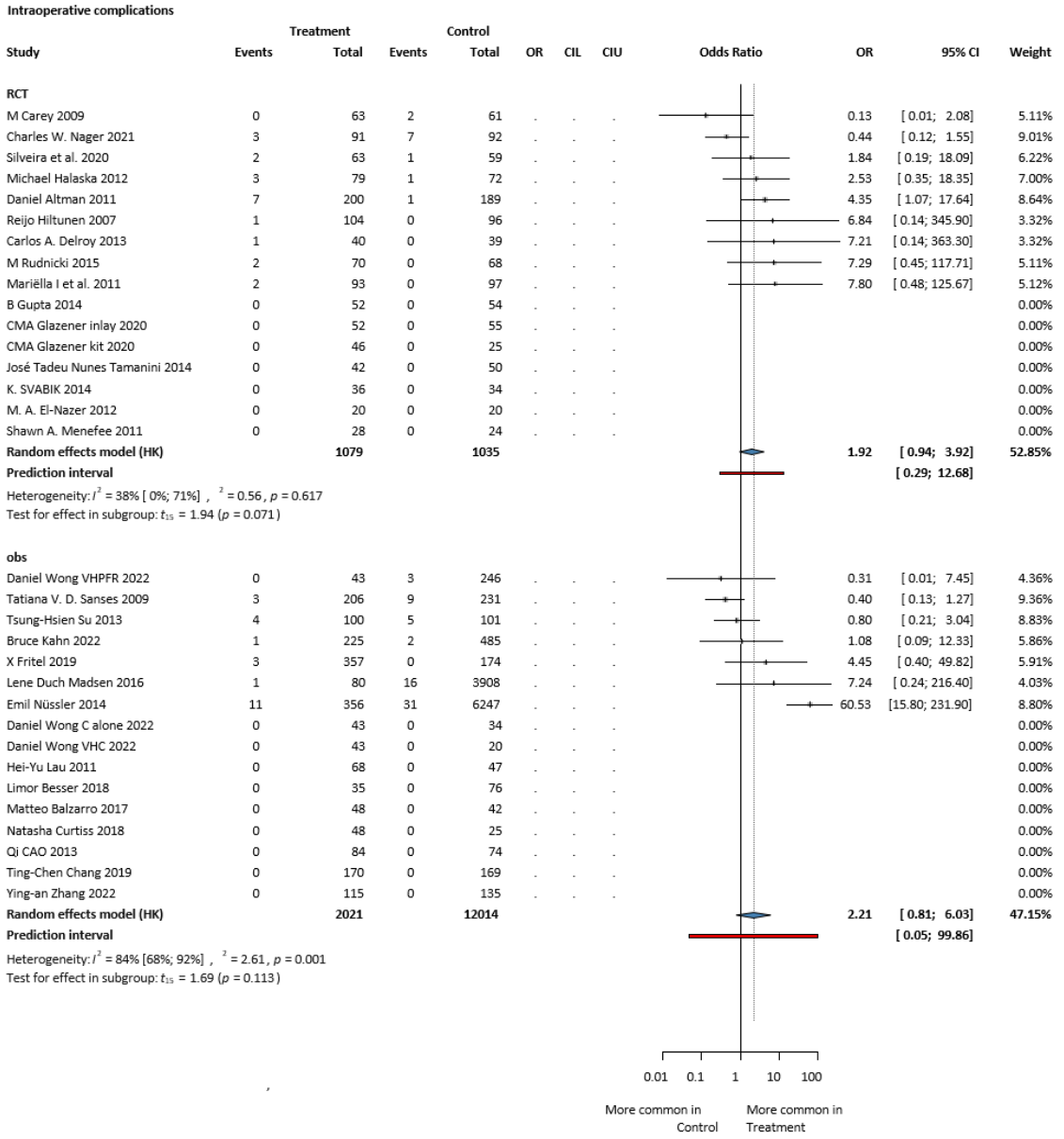


Figure 3.: *Forest plot of the OR with 95% CI of intraoperative complications in the implant (treatment) vs. native tissue (control) groups in randomized controlled trials and observational studies (Acs et al., 2023).*

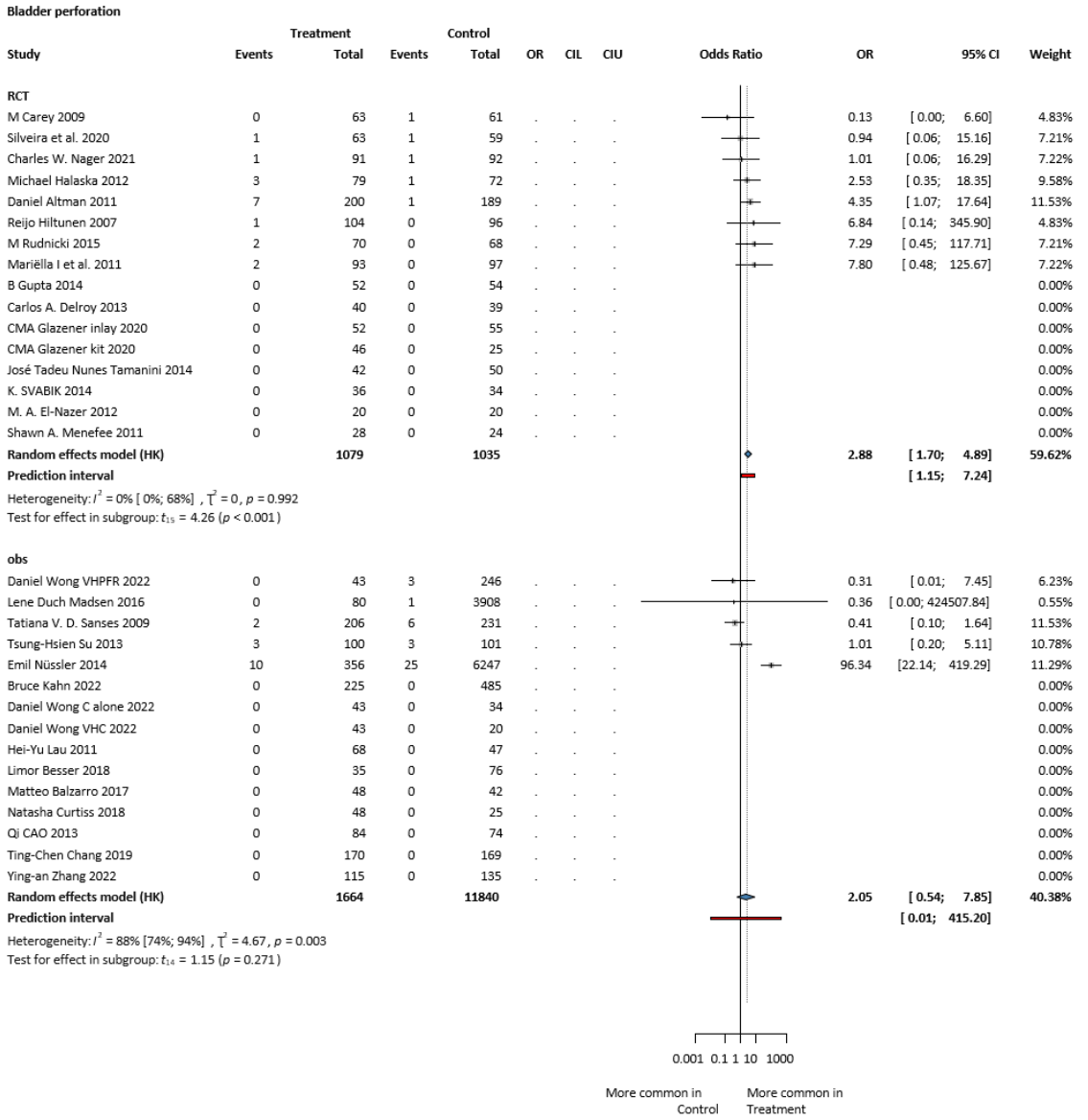


Figure 4.: *Forest plot of the OR with 95% CI of bladder perforations in the implant (treatment) vs. native tissue (control) groups in randomized controlled trials and observational studies (Acs et al., 2023).*

Postoperative complications occurred significantly more frequently in the implant group (OR 1.71, 95% CI 1.19–2.47); however, only one RCT was included in this pooled analysis. There was no significant difference between the groups in overall reoperation rates (OR 1.13, 95% CI 0.79–1.63). Nevertheless, the probability of reoperations due to

complications was significantly higher in the implant group in both randomized trials (OR 2.15, 95% CI 1.20–3.87) and non-randomized trials (OR 3.42, 95% CI 1.28–9.13; Figure 5). In the anterior compartment subgroup, the implant-treated group had a higher incidence of erosion (OR 9.76, 95% CI 4.73–20.15), bleeding (OR 1.71, 95% CI 1.32–2.23), and groin pain (OR 13.74, 95% CI 5.74–32.89).

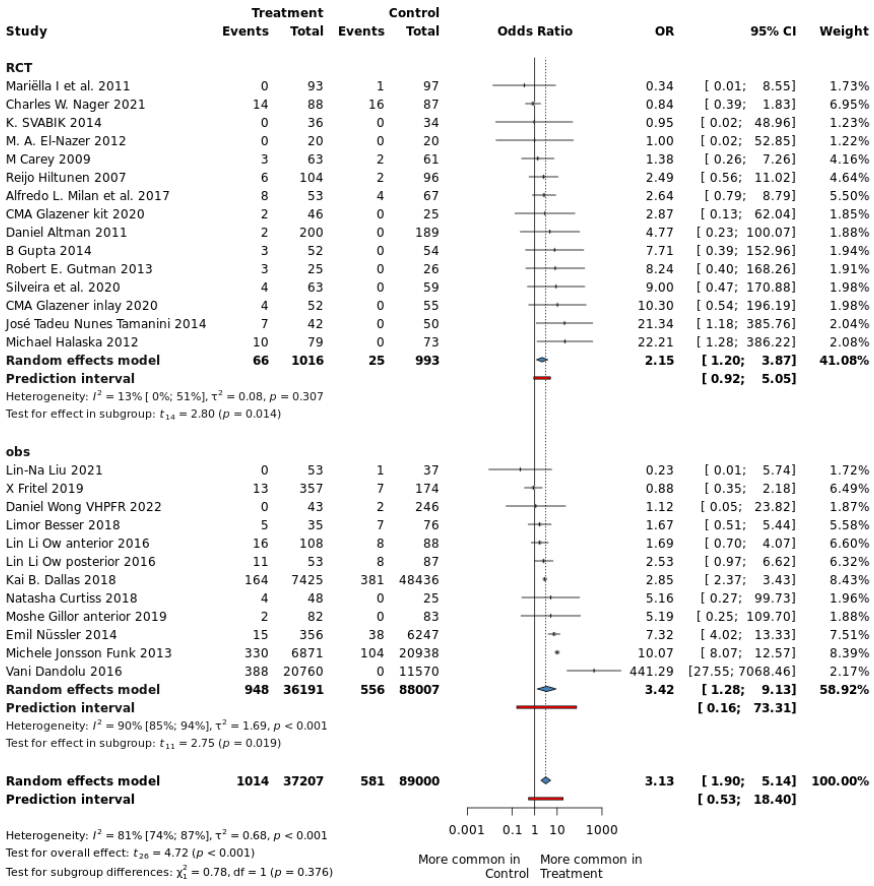


Figure 5.: *Forest plot of the odds ratios (OR) with 95% CI of reoperations due to complications in the implant (treatment) vs. native tissue (control) groups in randomized controlled trials and observational studies (Acs et al., 2023).*

Regarding **non-functional complications** after surgery, vaginal bleeding (OR 1.67, 95% CI 1.15–2.40) and erosion (OR 14.05, 95% CI 7.96–24.80) occurred significantly more frequently in the implant group, while buttock pain occurred more frequently in the NT group (OR 0.34, 95% CI 0.17–0.70). There were no significant differences between the

groups in terms of groin pain, hematoma, pelvic abscess, pelvic pain, fever, thrombosis, urinary tract infection, vaginal adhesions or strictures, or vaginal discharge (Figure 6.).

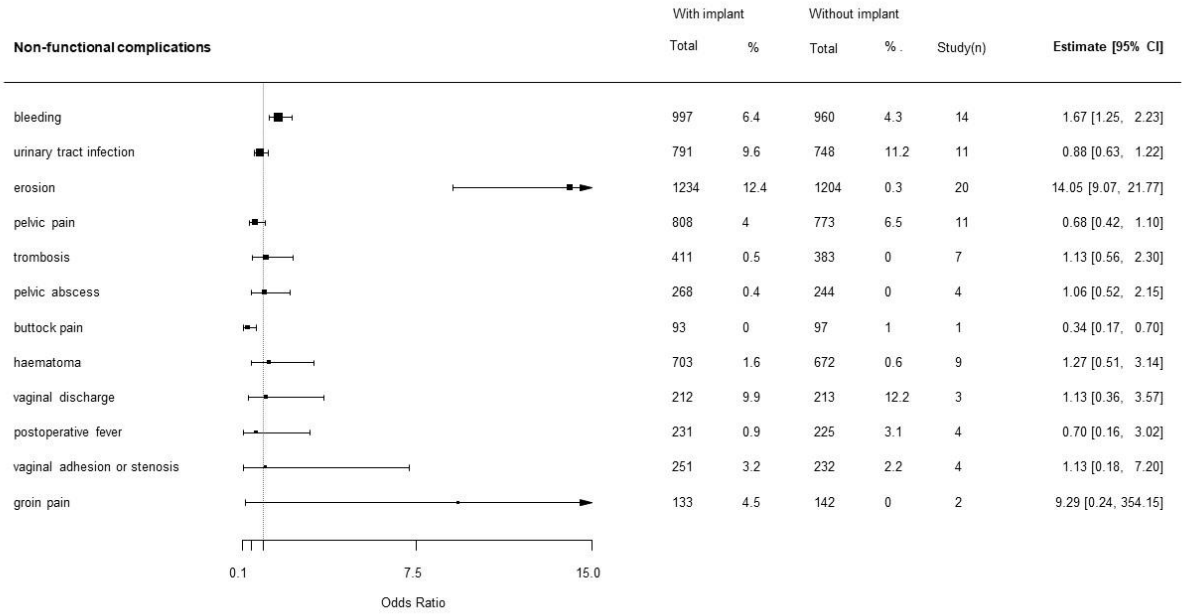


Figure 6.: *Forest plot of the OR with 95% CI of the multivariate analysis for non-functional complications in the implant vs. native tissue (without implant) groups (Acs et al., 2023).*

In terms of **functional complications**, de novo SUI was significantly more common in the implant group (OR 1.44, 95% CI 1.19–1.75), while there were no significant differences in other functional outcomes, including dyspareunia, overactive bladder (OAB), urgency, difficulty with bowel and bladder movements, and urinary retention (Figure 7.). Among functional complications, de novo urgency, de novo stress urinary incontinence (SUI), de novo dyspareunia, and urinary retention all showed a relative frequency of more than 5%. No significant differences were observed regarding the functional complications in the anterior compartment subgroup.

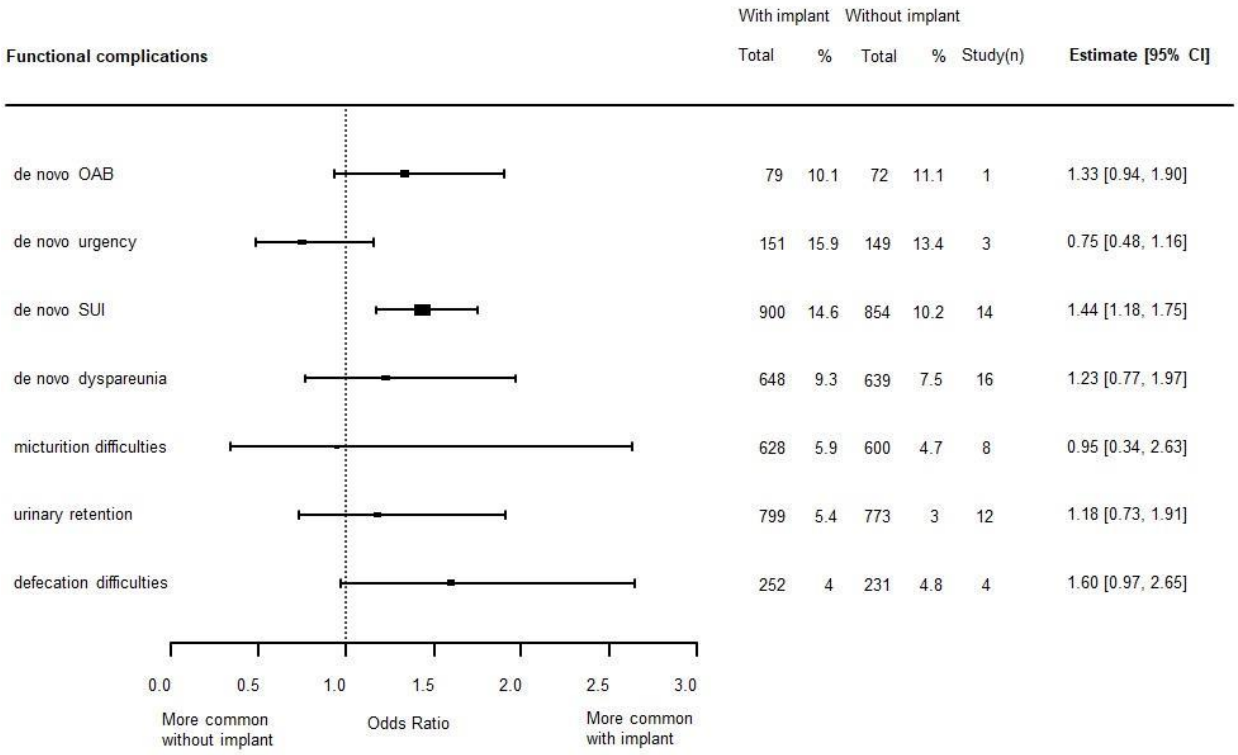


Figure 7.: *Forest plot of the OR with CI 95% of the multivariate analysis for functional complications in the implant vs. native tissue (without implant) groups (Acs et al., 2023).*

8.1.3. Efficacy Outcomes

The odds of anatomically successful reconstruction were 3.22 times higher in the vaginal implant group (95% CI 2.06–5.01), while the occurrence of POP-Q stage 3 during follow-up was 69% higher in the NT group (OR 0.31, 95% CI 0.16–0.62), and these differences between the groups were significant. Although the trend was similar for other POP-Q stages, no significant differences were observed between the groups regarding the occurrence of POP-Q stages 0, 1, 2, or 4 (Figure 8.).

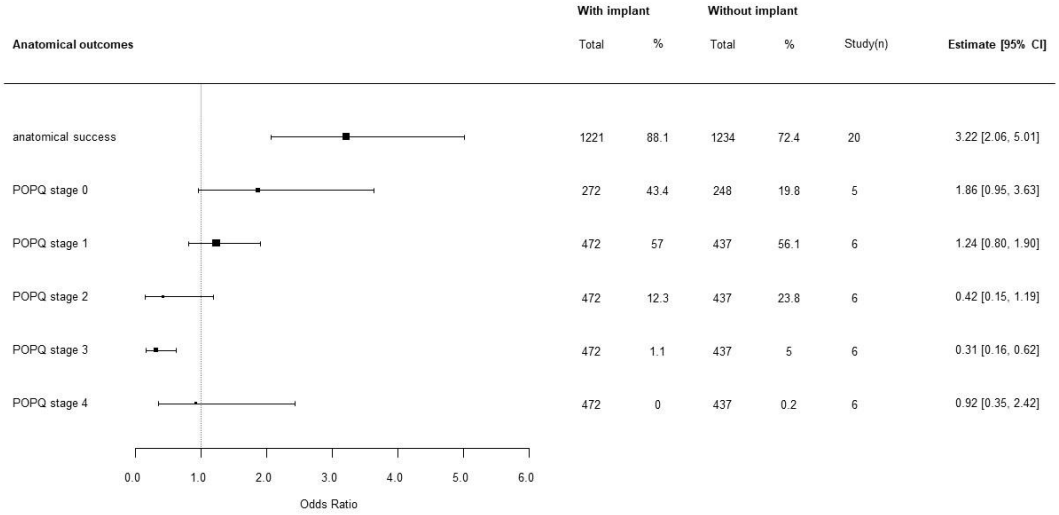


Figure 8.: *Forest plot of the odds ratios of the multivariate analysis for efficacy in the implant vs. native tissue (without implant) groups (Acs et al., 2023).*

In the anterior compartment subgroup the anatomical success was 3.92 times more likely (95% CI 1.87–8.22) and the occurrence of POPQ stage 0 during follow up was also more common (OR 3.18, 95% CI 1.49–6.77) in the implant group, while POPQ stage 2 was more common in the NT group (OR 0.21, 95% CI 0.06–0.73; Figure 9.).

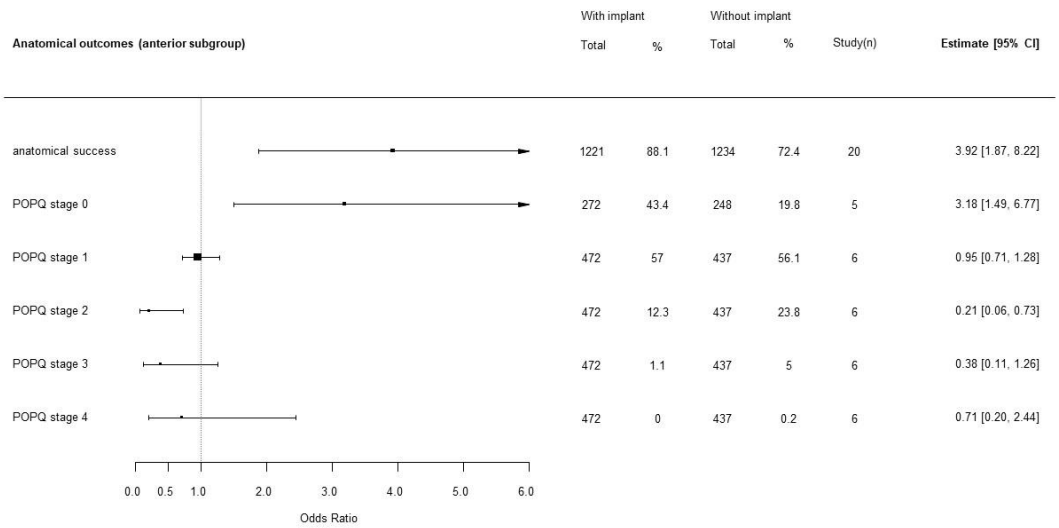


Figure 9.: *Forest plot of the OR with 95% CI of multivariate anterior subgroup analysis for anatomical outcomes in the implant vs. native tissue (without implant) groups (Acs et al., 2023).*

In addition, among RCTs, the rate of reoperation due to recurrence was significantly higher in the NT group (OR 0.55, 95% CI 0.36–0.85; Figure 10.).

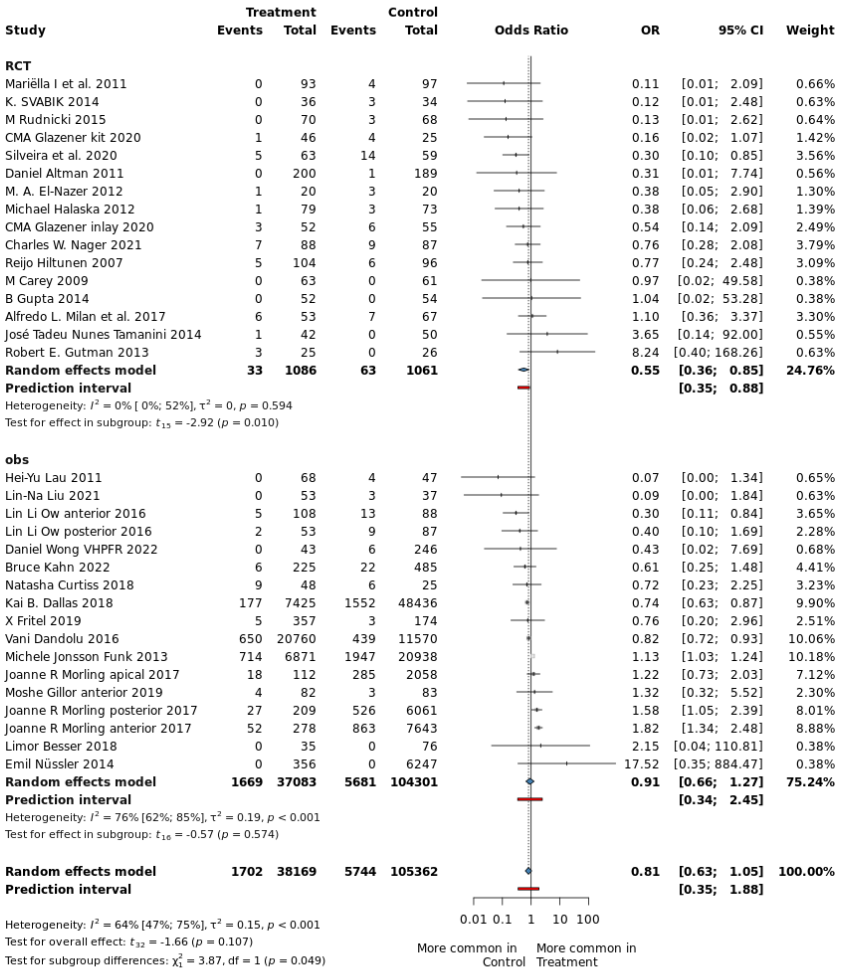


Figure 10.: *Forest plot of the OR with 95% CI of reoperations due to recurrence in the implant (treatment) vs. native tissue (control) groups in randomized controlled trials and observational studies (Acs et al., 2023).*

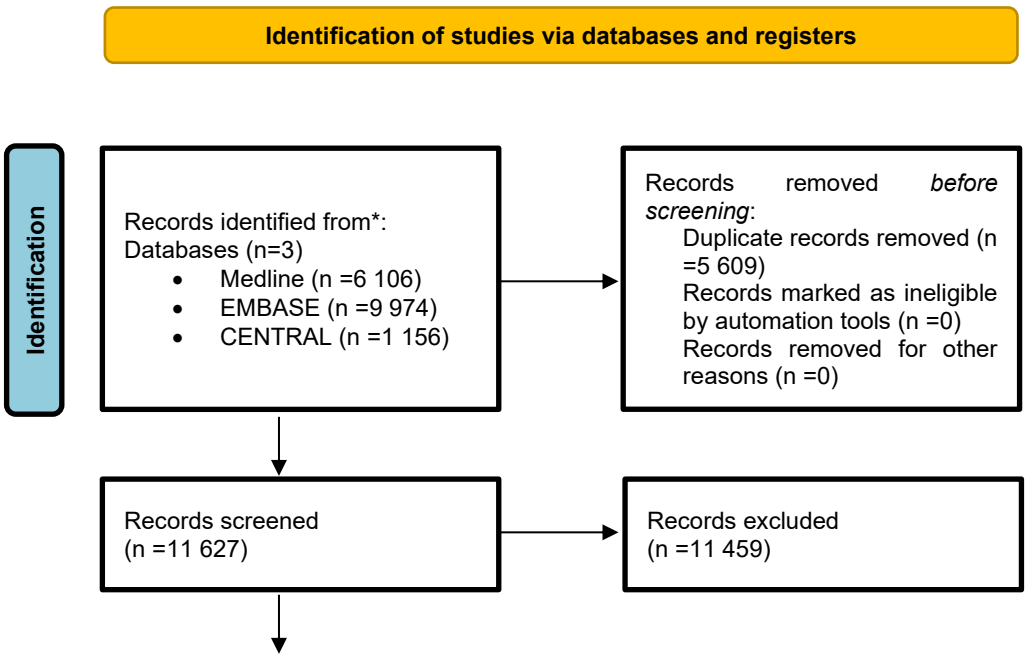
8.1.4. Risk of Bias Assessment

The included studies in the meta-analysis were mainly of moderate risk. Domains for deviations from the planned intervention, missing outcome data and the selection of reported outcome ranges were of low risk of bias. In the multivariate analysis, only randomized trials were used, so overall heterogeneity can be considered low. The heterogeneity was high for most outcomes and this was attributed to different study types, heterogenous populations, and different surgical approaches and expertise.

8.2. Study II: Risk factors for vaginal wall erosion after pelvic organ prolapse surgery with implant: a systematic review and meta-analysis

8.2.1. Study Search and Selection

A total of 17 226 articles were identified during the systematic search. After duplicate removal, 11 627 studies were included, and after title-abstract and full-text screening, 36 articles were eligible. Following data extraction, 25 studies were compared (Figure 11.) Cohen's kappa coefficient (κ) was 0.91 after title and abstract selection and 0.80 after full-text selection.



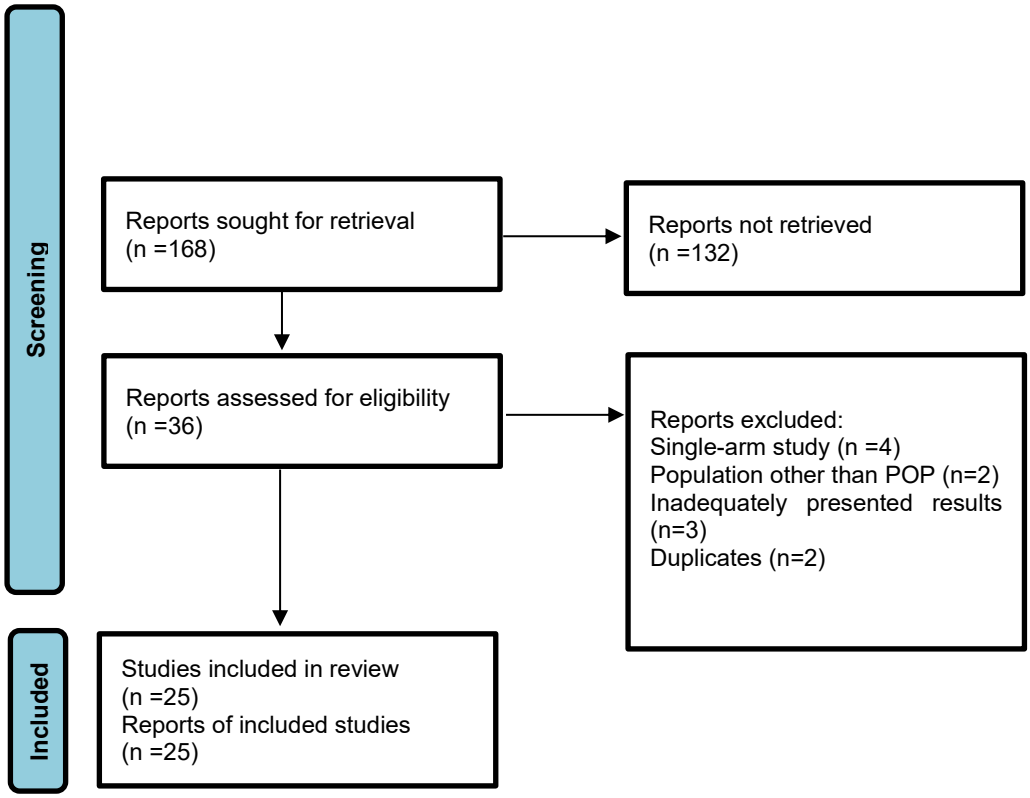


Figure 11.: II. study PRISMA 2020 flowchart representing the study selection process (Acs et al., 2025).

8.2.2. Risk factors

In 60% of the studies (15/25), all three compartments were treated surgically, while six studies focused on only one compartment. Most studies (21) were single-center, involving 1–10 surgeons, and primarily used Prolift implants. The most commonly investigated risk factors were age (n = 10) and concomitant hysterectomy (n = 9). Other factors investigated included body mass index (BMI), smoking, sexual activity, comorbidities, hormone replacement therapy (HRT), previous vaginal surgery, menopausal status, implant type, vaginal compartment operated on and postoperative hematomas.

Age

The included studies assessed age using varying approaches, either as a continuous or categorical variable, with inconsistent age ranges. Three studies (n = 504) were included in the analysis of age as a risk factor. The mean age of women with and without erosion was 59.1 ± 10.6 versus 60.6 ± 10.1, with no clinically relevant or statistically significant difference (OR 1.13, 95% CI 0.46–2.80). Similarly, age >65 years was not associated with increased risk (OR 0.40, 95% CI 0.04–4.07; n = 4), indicating no significant difference between patients above and below 65 years (Figure 12.).

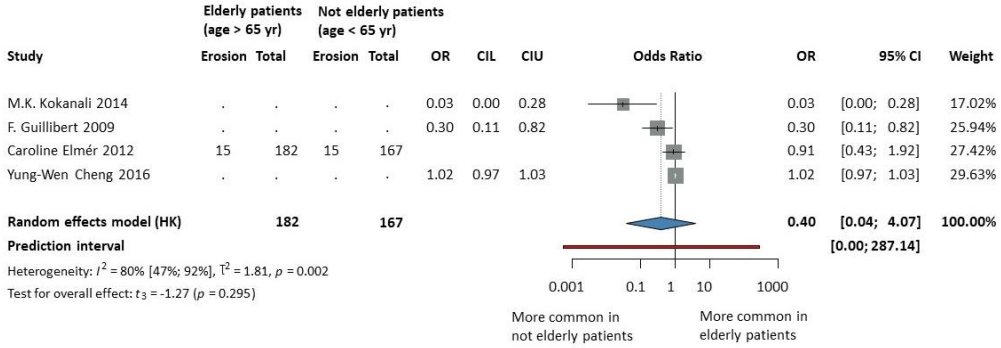


Figure 12.: *Forest plot representing the OR with 95% CI of elderly patients (age above 65 yr) as a risk factor of the patients with vs. without VWE (Acs et al., 2025).*

Comorbidities

VWE was more frequent in patients with diabetes mellitus (OR 2.91, 95% CI 0.67–12.71; n = 6), though this difference was not statistically significant. Also, no significant differences in VWE were observed for patients with versus without hypertension (OR 2.27, 95% CI 0.31–13.78; n = 2) or menopause (OR 0.88, 95% CI 0.11–8.53; n = 7) (Figure 13.).

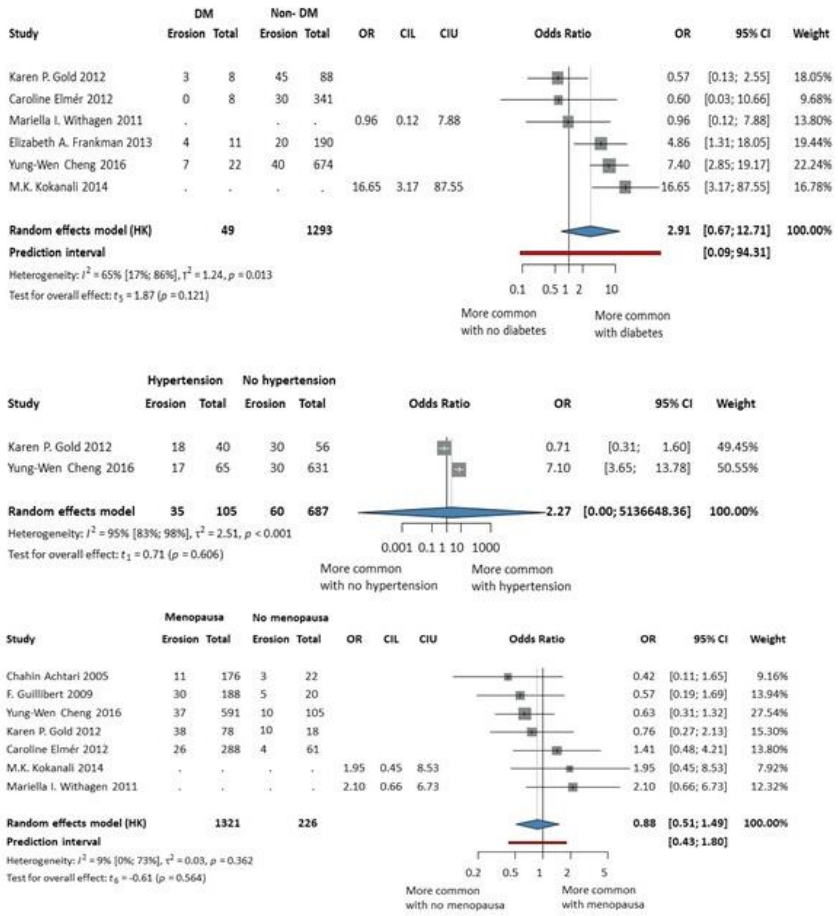


Figure 13.: *Forest plots representing the OR with 95% CI of the occurrence of diabetes mellitus (DM), hypertension and menopausal status as a risk factor of the patients with vs. without VWE (Acs et al., 2025).*

Lifestyle factors

No significant differences were found for BMI (OR 0.96, 95% CI 0.69–1.33; n = 3) or sexual activity (OR 3.07, 95% CI 0.72–13.19; n = 4), although VWE was much more common in sexually active women. However, this difference was not statistically significant, although this observation has strong clinical relevance. VWE was

significantly more frequent in smokers versus non-smokers (OR 3.65, 95% CI 2.56–5.20; n = 7), which has a high clinical relevance (Figure 14.).

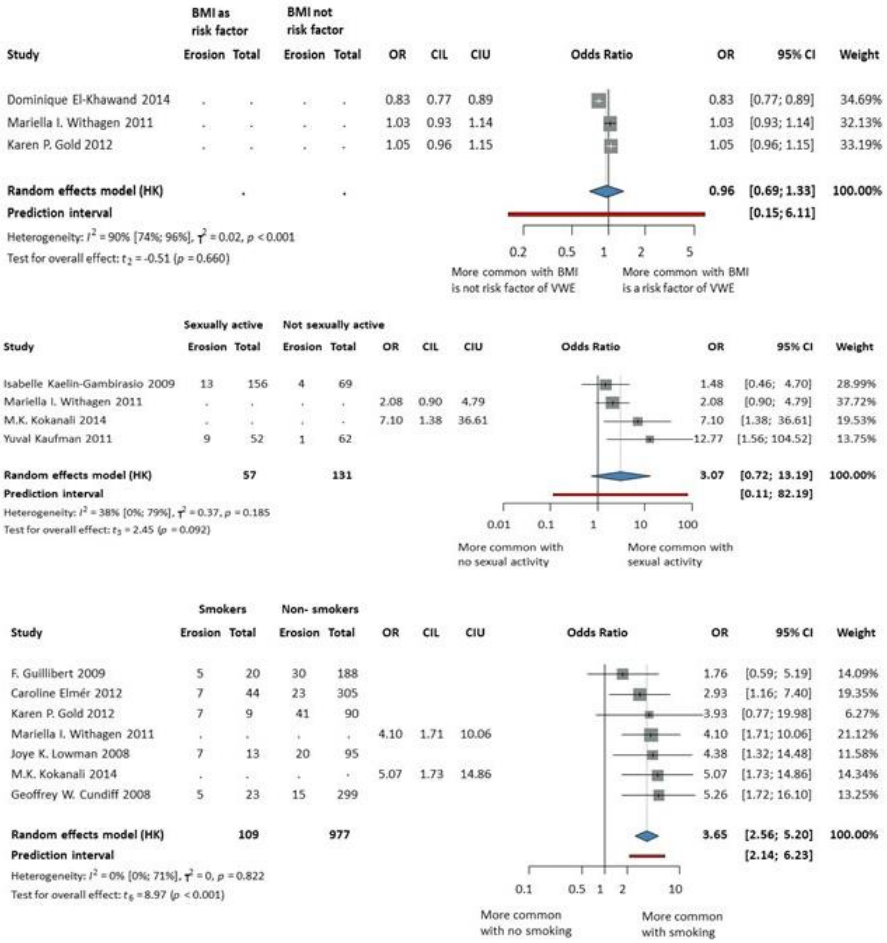


Figure 14.: *Forest plots representing the OR with 95% CI of BMI, sexual activity and smoking status (smoker and non-smoker) as a risk factor of the patients with vs. without VWE (Acs et al., 2025).*

Factors associated with surgical procedures

Concomitant hysterectomy significantly increased the risk of VWE (OR 3.33, 95% CI 1.71–6.48; n = 9), whereas prior hysterectomy did not (OR 1.45, 95% CI 0.54–3.88; n = 2), although previous hysterectomy was only examined in two studies (Figure 15.).

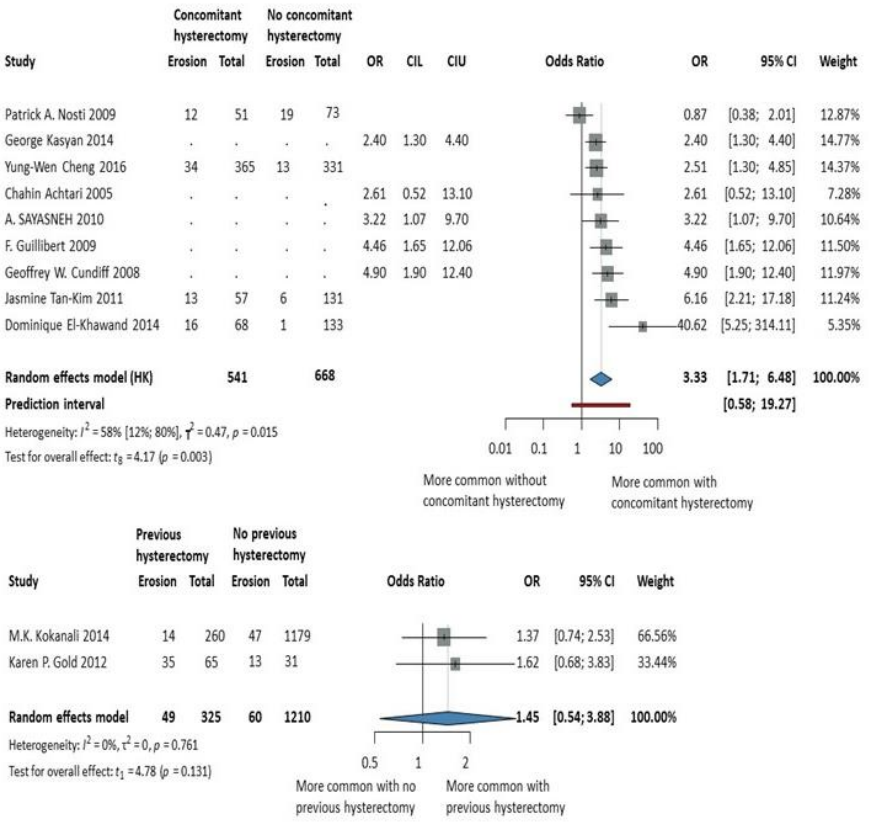


Figure 15.: *Forest plots representing the OR with 95% CI of concomitant hysterectomy and previous hysterectomy as a risk factor of the patients with vs. without VWE (Acs et al., 2025).*

Previous prolapse surgery and HRT had no significant effect on VWE risk (OR 1.74, 95% CI 0.72–4.19; n = 7 and OR 1.29, 95% CI 0.13–12.63; n = 3). Preoperative POP grade and surgical experience were also not associated with VWE, though confidence intervals were very wide (OR 0.98, 95% CI 0.00–442.83; n = 2 and OR 1.85, 95% CI 0.00–24,379,658.30; n = 2) (Figure 16.).

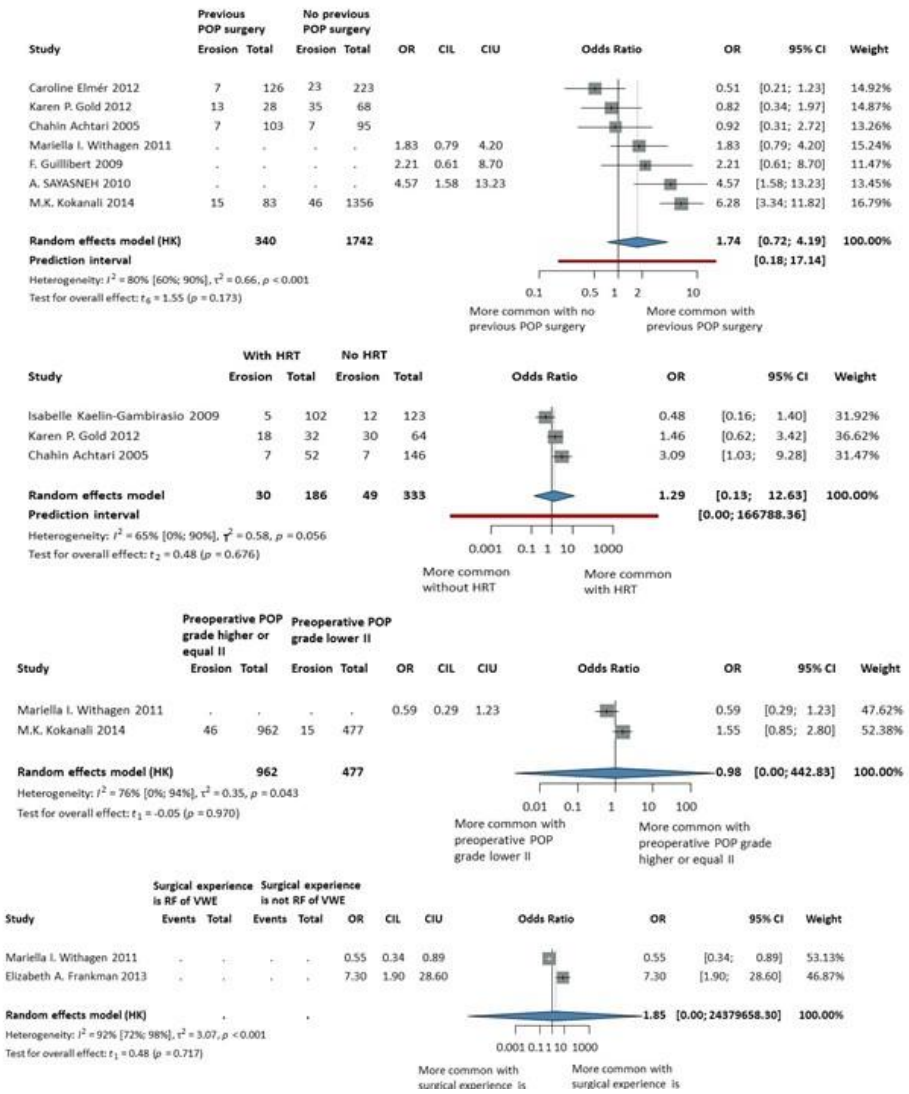


Figure 16.: *Forest plot representing the OR with 95% CI of previous prolapse surgery, HRT, preoperative POP grade and surgical experience as a risk factor (RF) of the patients with vs. without VWE (Acs et al., 2025).*

Postoperative hematomas were significantly associated with higher VWE risk (OR 2.52, 95% CI 1.98–3.20; n = 2) (Figure 17.).

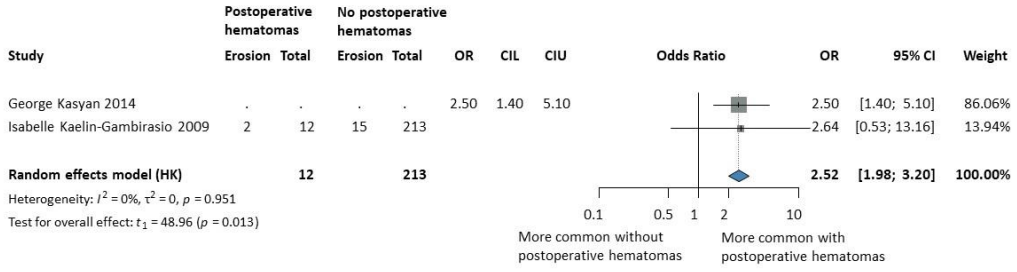


Figure 17.: *Forest plot representing the OR with 95% CI of occurrence of postoperative hematomas as a risk factor of the patients with vs. without VWE (Acs et al., 2025).*

8.2.3. Risk of Bias Assessment

Risk of bias was assessed using the QUIPS tool. Most studies showed a low risk of bias for study participation, while study attrition was generally not applicable due to the retrospective design. Risk factor measurement was also rated as low risk. Statistical analysis presented a moderate risk in most studies, whereas study confounders carried the highest risk of bias. High heterogeneity was observed across nearly all examined risk factors, largely due to inconsistent definitions of these factors.

9. DISCUSSION

9.1. Summary of Findings

In our first study we found that alloplastic implants provide significantly better anatomical corrections and more successful results in the long run than NT repair. One of the most objective measures of effectiveness is the reoperation rate due to recurrence, which was 6.4% in the NT group and 2.5% in the implant group in RCTs. The occurrence and severity of complications in prolapse surgeries performed with implants were clinically acceptable. VWE is the only complication with high clinical relevance, albeit with a wide prevalence (3–20%). According to our meta-analysis, the odds of erosion occurrence were 14 times higher after mesh/sling surgery, although some studies reported substantially lower rates (Song et al., 2016). In the anterior compartment subgroup, the implant group had nine times higher odds of developing erosion. It is important to note that mesh-related complications, particularly VWE, occurred exclusively in the implant group. The high incidence of vaginal erosion was the primary factor in the FDA's decision to impose regulatory restrictions (Administration, April 29, 2014.).

The evaluation of reoperation rates for complications, together with the comparative analysis of specific complication types, provides an objective assessment of the safety profile of POP surgeries. Mesh erosion was the main reason for reoperation, but this complication is primarily influenced by surgical practice and correct indication criteria (Crosby et al., 2014). Our meta-analysis demonstrated a significantly higher rate of reoperation for complications in the implant group; however, the absolute difference in event rates between the groups (6.5% in the implant group vs 2.5% in the native tissue group in RCTs) was clinically irrelevant and it is important to mention that the erosion rate was also higher in these studies (Glazener et al., 2020).

Regarding postoperative nonfunctional complications during the multivariate model analysis we found that the odds of vaginal bleeding (OR 1.67, 95% CI 1.15–2.40) and erosion (OR 14.05, 95% CI 7.96–24.80) were statistically significantly higher in the vaginal implant group. Postoperative bleeding in the anterior compartment subgroup occurred at also a significantly higher rate in the implant group (OR 1.71, 95% CI 1.32–2.23); however, this was generally not clinically relevant, as it did not require intervention in most cases. Vaginal bleeding may be associated with erosion, so we considered this

when developing our statistical model. Buttock pain, which is an unusual complication, was more frequent in the NT group. This pain may be because neurological damage caused by insertion of the sacrospinous ligament suspension suture (Roshanravan et al., 2007). With the exception of erosion, our analysis found no clinically relevant differences between the two groups in terms of other non-functional complications.

Among functional complications, de novo urgency, de novo stress urinary incontinence (SUI), de novo dyspareunia, and urinary difficulties all exceeded a relative frequency of 5%. Statistically significant differences between groups were observed only for de novo stress incontinence. We expected dyspareunia to occur more frequently in the implant group, but there was no significant difference in the occurrence of de novo dyspareunia, which can be partly attributed to the higher age of patients in the implant group (mean age 74.2 ± 8.9 years, compared to 62.7 ± 9.7 years in the NT group).

Based on the results of Study I, we performed our second analysis (Study II), in which we identified the risk factors associated with VWE and determined in which patient populations prolapse surgery could be safely performed with implant placement, achieving greater anatomical efficacy while minimizing the risk of VWE. Several studies have investigated complications associated with mesh surgeries; however, there has been no comprehensive comparative study analyzing all compartments, different implant types, surgical parameters, and anatomical success of implant versus NT POP surgery (de Tayrac et al., 2005; Weintraub et al., 2016). Our second study highlights that smoking and concomitant hysterectomy are risk factors for VWE. Smoking had a significant impact on VWE (OR: 3.65, CIL: 2.56, CIU: 5.20) with its effect being dose-dependent. In terms of surgical procedure-related risk factors, the incidence of concomitant hysterectomy was significantly higher in patients who had developed VWE (OR: 3.33, CI: 1.71–6.48). Overall, it is not advisable to perform hysterectomy at the same time as POP surgery involving implants, especially since our studies show that previous hysterectomy has no significant effect on the incidence of VWE (OR: 1.45, CI: 0.54–3.88).

Besides the previous ones postoperative hematoma was found to be more common in VWE; however, only two studies investigated it, and results should therefore be interpreted with caution.

9.2. International Comparisons

The primary objective of our first study was to evaluate complication rates and effectiveness of the two types of vaginal POP surgery and to determine whether these outcomes substantiate the FDA warnings. Although numerous studies have examined complications associated with mesh-based procedures, no comprehensive comparative analysis has yet assessed all pelvic compartments, different implant types, surgical parameters, and anatomical success in implant versus native tissue POP surgery.

Over the past decade, meta-analyses comparing vaginal mesh and NT surgeries have primarily focused on the anterior compartment (Capobianco et al., 2022; Juliato et al., 2016; Min et al., 2013; Slade et al., 2020), postoperative sexual function (Liao et al., 2019), or potential risk factors for mesh erosion (Deng et al., 2016). However, none of these studies provided a comprehensive assessment of all relevant parameters. To our knowledge, Study I is the most comprehensive analysis to date, providing a detailed assessment of all complications and the effectiveness of implants compared to native tissue surgery in all vaginal compartments, incorporating both randomized controlled trials (RCTs) and observational studies. Given the complexity of the analysis, we developed a multivariate statistical model to account for potential confounding factors. We presented the pooled results separately for RCTs and observational studies; however, due to the high heterogeneity observed among non-randomized studies, only RCTs with more homogeneous patient populations were included in the multivariate analysis. With this new statistical model, which we applied for the first time in Study I, we can consider that individual complications are not independent of each other.

As mentioned above, the reoperation rate due to complications was higher among patients who underwent implant surgery compared to those who underwent surgery using native tissue (randomized trials; OR 2.15, 95% CI 1.20–3.87, non-randomized trials; OR 3.42, 95% CI 1.28–9.13). However, it is worth mentioning that in both cases we are referring to low numbers, altogether, reoperations due to complications did not occur to a clinically relevant extent. Mesh erosion was the main reason for reoperation, but this complication is primarily influenced by surgical practice and correct indication criteria, so in studies where the erosion rate was higher, the reoperation rate due to complications was also higher (Crosby et al., 2014; Glazener et al., 2020). In terms of postoperative non-functional complications, only bleeding, vaginal discharge, urinary tract infection (UTI),

and erosion had an incidence rate above 5%, and therefore these can be considered potentially clinically relevant. It should be noted that complications related to the mesh, particularly erosion of the vaginal wall, occurred only in the implant group, and there were significant differences between the individual studies. The major reason for the FDA imposition of restrictions was the high rate of vaginal erosion. In the multivariate analysis of the anterior subgroup, erosion was nine times more likely to occur in patients who had undergone implant surgery, although there were considerable differences between the individual studies in this case as well (OR: 9.76, 95% CI: 4.73–20.15) (da Silveira et al., 2020; Nussler et al., 2015). Postoperative bleeding occurred at a significantly higher rate in the implant group not only in case of the anterior subgroup, but also in case of all vaginal compartments, however, it was not clinically significant and required intervention in only a minority of cases. It should be noted that vaginal bleeding may be associated with erosion, and this was accounted for in the development of our statistical model. In the majority of previous meta-analyses, only the anterior compartment was investigated in terms of erosion or erosion-associated complications (Capobianco et al., 2022; Maher et al., 2016; Min et al., 2013; Siddiqui et al., 2015). The type of implant material is also an important factor in terms of complications. Among the studies included in our analysis, polypropylene mesh was the most commonly used material. Compared to first-generation meshes, next-generation macroporous, ultra-lightweight meshes are associated with fewer complications. The mechanical and physicochemical properties of polypropylene may hinder complete tissue integration, potentially contributing to erosion and chronic pain. Newly developed advanced materials, such as polycaprolactone, graphene-based nanocomposite copolymers, polycarbonate, polydimethylsiloxane, and polyvinyl plastics, show greater tissue compatibility and may be associated with lower complication rates (Seifalian et al., 2023). Many of these materials are currently under development for vaginal implants, and their evaluation should be prioritized in future studies.

With regard to postoperative functional complications, our results are consistent with previous meta-analyses, which showed no difference in the rates of de novo dyspareunia and de novo urgency between the mesh and non-mesh groups (Capobianco et al., 2022; Maher et al., 2013). The increased incidence of de novo stress urinary incontinence (SUI) is a consequence of the anatomical correction achieved by surgery. More severe prolapse can cause functional lower urinary tract obstruction due to compression of the urethra

(and thus improve urinary sphincter function), which is resolved after the surgical reconstruction of the prolapse and can lead to SUI (Baessler et al., 2018). In older women, the assessment of functional complications is challenging due to age-related changes such as vaginal dryness, narrow vagina, vaginal stenosis, impaired bladder function, and decreased sexual activity, making it difficult to establish a direct causal relationship between vaginal mesh surgery and functional outcomes. Nevertheless, the above-mentioned functional complaints are generally more common in older female patients (Deffieux et al., 2012). The global incidence of de novo dyspareunia following transvaginal mesh surgery was 13.9% (Duraes et al., 2018). Although several studies have demonstrated improved sexual function after POP surgery, the procedure may also lead to dyspareunia in some patients (Jha & Gray, 2015; Lukacz et al., 2020; Wihersaari et al., 2022). Although we expected a higher incidence of dyspareunia in the implant group, no significant difference was observed, which can be partly explained by the higher age of the patients in the cohort (mean 74.2 ± 8.9 years, compared to 62.7 ± 9.7 years in the native tissue group).

The effectiveness was assessed by examining the incidence of reoperations due to recurrence, which was 45% lower among women who underwent implant surgery than NT group. Most of the studies indicate that the number of reoperations for recurrence increases over time and is significantly higher for patients without implants (Dallas et al., 2018; Ow et al., 2016). Altman et al. (Altman et al., 2011) reported that at 1-yr follow-up there were no reoperations for recurrence in the implant group and only one in the NT group. In a study by Milani et al. (Milani et al., 2018) with longer follow-up of 7 year, 7% of implant and 82% of NT cases required reoperations for recurrence. Several studies have determined surgical efficacy in terms of anatomical success, based on POP-Q stage and surgeon-reported POP-Q points (da Silveira et al., 2020; Delroy et al., 2013; El-Nazer et al., 2012; Gillor et al., 2020). Evidence suggests that alloplastic implants achieve significantly better anatomical correction and more durable long-term results compared to native tissue repairs (Chapple et al., 2017). In our univariate analysis, clinical recurrence was defined as POP-Q stage ≥2; using this threshold, the probability of recurrence was 73% higher in the native tissue group (Chang et al., 2019; Halaska et al., 2012). Other studies have also reported high recurrence rates after implant-free surgery,

reaching 19% in cases involving multiple compartments, while reoperation rates due to recurrence exceeded 17% in all compartments (Lavelle et al., 2016; Maher et al., 2013). We conducted our second study based on the results of our first meta-analysis. The most clinically relevant complication of vaginal implant surgery is vaginal erosion, which was also found to occur at a high rate in our first study. However, on the basis of varying erosion rates (3 to 20%) observed in studies, we hypothesized that there are predisposing and protective factors related to the patient, to surgical intervention, and to indications for vaginal POP surgery with implants. In a 2016 meta-analysis, Deng et al. identified younger age, higher parity, premenopausal estrogen replacement therapy, diabetes mellitus, smoking, concomitant hysterectomy, and limited surgical experience as significant risk factors for mesh erosion. However, a substantial proportion of the study population in that analysis underwent implant surgery for stress urinary incontinence rather than POP. Additionally, the study was conducted eight years ago and did not include research published following the implementation of multiple FDA restrictions (Deng et al., 2016). In our second study, we categorized risk factors according to age, comorbidities, lifestyle, and surgical intervention. Age varied significantly between studies, regardless of the prevalence of vaginal wall erosion (VWE). For example, in the study by Kaufman et al., the average age was 61.2 years, ranging from 31 to 84 years. Several studies evaluated the age of women with VWE using different age groups, which made it difficult to compare the studies (Kaufman et al., 2011). This discrepancy may explain why we did not find a significant difference in the prevalence of erosion between younger and older patients, even though we divided our cohort into only two age groups, unlike the analysis by Deng et al., in which patients were divided into three age groups. In our study, the average age of the two groups did not differ significantly, which is consistent with the findings of Kaufman et al. To our knowledge, no study has specifically examined the effect of extreme age (<50 and >75 years) on the development of VWE. In younger patients, VWE is expected to occur more frequently due to higher sexual activity, while in older patients, vaginal wall atrophy associated with genital syndrome of menopause (GSM) may be the main cause. Non-hormonal therapies for maintaining vaginal health in menopausal women are well documented in the literature, facilitating a more detailed examination of risk factors predisposing to VWE (De Franciscis et al.,

2020; Moradi et al., 2023). Further research is needed to clarify the precise etiopathogenic mechanisms between age and VWE.

Regarding comorbidities, diabetes and hypertension were assessed in a limited number of studies, sufficient only for minimal statistical analysis. Although VWE was observed more frequently in patients with these conditions, the differences were not statistically significant, in contrast to the findings reported by Deng et al. This discrepancy may be attributable to the smaller number of data sources available for both conditions in our analysis. Both conditions are associated with peripheral vascular disease, which can compromise the supply of nutrients and oxygen to cells due to denervation and devascularization. This damage can delay wound healing and increase the risk of mesh erosion (Cheng et al., 2017). In contrast, Gold et al. found no association between VWE and diabetes mellitus (Gold et al., 2012). As these results are contradictory, further comprehensive studies are needed to clarify the effect of comorbidities on mesh-related complications. In addition, POP is often associated with recurrent urinary tract infections. In such cases, reconstructive surgery- especially procedures involving vaginal implants- should be postponed until the infections have completely resolved. Thus, effective treatment and prevention of recurrent UTIs are critical components of preoperative optimization for POP surgery (Boeri et al., 2024; Riemma et al., 2025).

Regarding lifestyle factors, smoking was found to have a significant, dose-dependent effect on VWE. Smoking is a well-established risk factor for a wide range of postoperative complications across surgical procedures, adversely affecting both circulation and wound healing processes that are critical during implant surgery (Theadom & Cropley, 2006). Consistent with our findings, Araco et al. reported a fourfold increase in the risk of erosion among smokers (Araco et al., 2009). Although no statistically significant association was observed between sexual activity and VWE in our analysis, it cannot be excluded as a potential risk factor. Some studies suggest that sexual activity may predict late mesh exposure (Barski et al., 2014; Kaufman et al., 2011), while others report no significant effect (Morselli et al., 2019; Withagen et al., 2011). Notably, POP is more prevalent and symptomatic in sexually inactive menopausal women (Stafne et al., 2024), as well as in younger, sexually active women, for whom sacrocolpopexy is often the preferred procedure. POP has a negative impact on sexual function, which typically improves following surgical correction (Mosca et al., 2022). Given the

conflicting evidence, further research is warranted to clarify the relationship between sexual activity and VWE, particularly in younger women, where both intercourse frequency and menopausal status should be considered.

Obesity is a well-known risk factor for surgical site infections and general postoperative complications, and the incidence of wound infections is closely related to tissue perfusion and oxygen supply (Kabon et al., 2004). However, our analysis did not show a statistically significant correlation between VWE and elevated BMI. It should be noted that none of the included studies involved extremely obese patients. Similarly, Deng's 2016 meta-analysis identified smoking and sexual activity as significant risk factors for VWE, but found no significant association between BMI and erosion (Deng et al., 2016). These discrepancies may also reflect the smaller number of cases evaluated in our study. In terms of intervention-related risk factors, the incidence of concomitant hysterectomy was significantly higher among patients who developed VWE (OR: 3.33, 95% CI: 1.71–6.48). However, previous hysterectomy did not prove to be a significant risk factor for erosion. Concomitant hysterectomy may prolong operative time and elevate the risk of bleeding, infection, and other general complications (Selle et al., 2024). The effect of previous prolapse surgery on VWE remains uncertain, as the results reported in the literature are inconsistent. Many studies did not detail the surgical techniques used in previous prolapse surgeries. Although alternative and minimally invasive interventions exist, such as flat magnetic stimulation or laser therapy, these have been studied primarily in the context of treating female stress incontinence (Barba et al., 2023; Ruffolo et al., 2022). In our study, postoperative hematoma was observed more frequently in cases of VWE; however, as only two studies addressed this complication, the results should be interpreted with caution. Large hematomas can increase risk by exerting mechanical tension and potentially compromising microcirculation, which may predispose to infection (Rodrigues et al., 2019). Our study contributes to this ongoing debate by providing real insight into the factors influencing clinicians' decisions regarding implant-based vaginal prolapse surgery, highlighting that clinical experience, institutional protocols, and annual patient volume are likely to shape practice patterns. Future meta-analyses that also consider individual patient data may further refine recommendations regarding for specific risk groups.

9.3. Strengths

A major strength of Study I is the extensive and comprehensive nature of the analysis. This investigation incorporated all complications examined in the existing literature, allowing for a broad and integrated evaluation of outcomes. The study included a large number of studies with high patient numbers which enhances the robustness and overall representativeness of the findings. To our certain knowledge, this is the largest study in this field in terms of patient numbers (more than 160,000 patients). Methodological rigor was a defining feature of Study I. Beyond the use of conventional random-effects models, we implemented an advanced multivariate statistical modelling framework. This approach allowed us to simultaneously account for inter- and intra-study correlations, reducing statistical noise and providing more precise and reliable estimates. Such a methodological advantage is particularly valuable in meta-analyses where data heterogeneity is inherent. The combination of large-scale evidence and sophisticated analytical techniques strengthens the credibility and applicability of the results produced in Study I.

Study II also demonstrates several important strengths. Foremost, this meta-analysis benefits from the inclusion of a substantial number of studies and patients- 25 studies comprising 7,569 patients- making it the largest synthesis conducted to date, which investigates risk factors predisposing to complications of vaginal implants. The extensive sample size significantly increases the generalizability and statistical power of the results, allowing for more confident conclusions regarding risk factors and clinical outcomes. This study was conducted with strict adherence to a pre-registered protocol, ensuring transparency, consistency, and minimization of methodological bias. In addition, Study II evaluated all potential risk factors that may contribute to VWE, offering a comprehensive assessment of the determinants associated with this complication. A notable strength is the inclusion of data from studies published after the FDA warnings, enabling the analysis to reflect the most up-to-date clinical evidence and contemporary practice patterns. This unique feature distinguishes Study II from previous summary studies and enhances the relevance of its findings for current clinical decision-making.

Overall, the large evidence base, rigorous methodology, comprehensive assessment of risk factors, and incorporation of the latest post-regulatory data underscore the strength and reliability of Study II.

9.4. Limitations

Study I presents some limitations that should be considered. One of the notable limitations is the relatively high degree of heterogeneity observed in the included studies. This heterogeneity is likely due to differences in implant types, variations in the vaginal compartments and the diversity of surgical techniques used at the study sites. Because the included publications covered a wide range of mesh materials and surgical approaches but often lacked detailed descriptions of procedural methods, consideration of these sources of variation was inherently limited. Additionally, the follow-up duration varied widely among studies, with some offering relatively short observational periods. This inconsistency restricts the capacity to assess long-term outcomes or delayed complications with confidence. The limited incidence of certain complication types further constrains the interpretability of specific findings; for rare events, statistical estimates become less accurate and less generalizable. However, advanced statistical methods were applied to address heterogeneity, the underlying differences in patient populations, surgical practices, and reporting standards remain an important limitation of Study I.

In terms of the limitations of Study II that, certain risk factors were defined inconsistently across the included studies, and in some cases, the number of reported events was low, which reduces the strength of the comparative analyses. The study populations were heterogeneous, and follow-up durations varied considerably and were often relatively short, limiting the assessment of long-term outcomes. Furthermore, certain risk factors-such as age were reported differently in different studies, either as categorical age groups or as continuous measures for the overall population. This inconsistency limited the number of studies that could be included in specific comparisons. Moreover, there were relatively few well-designed randomized controlled trials with adequate follow-up. In addition, the studies included used very different types of mesh and provided only limited details about surgical procedures. Although we summarized implant types, the operated vaginal compartments, and the number of surgeons performing the procedures the lack of standardized reporting limits the ability to account for these factors fully. These limitations highlight the need for more uniform definitions, consistent reporting practices, and longer-term follow-up in future research.

10. CONCLUSIONS

10.1. Study I.

Vaginal surgery for POP using implants appears to be more effective than procedures performed without implants, with complication rates and severity remaining within clinically acceptable limits. Vaginal wall erosion is the only complication of major clinical concern, yet its incidence may be reduced through improved patient selection and surgery indication, advancements in implant materials, and refined surgical techniques and increased surgical volume. These findings indicate that the current ban on vaginal implants for POP repair may merit reconsideration.

10.2. Study II.

Our findings indicate that smoking and concomitant hysterectomy increase the risk of VWE in POP surgeries involving vaginal implants. Postoperative hematoma may also contribute to this risk, though the evidence is currently limited. Larger, well-designed studies are needed to clarify these associations and additional clinically relevant risk factors. Nonetheless, these considerations highlight the importance of careful patient selection, surgical indications that takes into account known risk factors, minimization of preventable risk factors (e.g., smoking cessation), and continued refinement of implant materials and surgical techniques.

11. IMPLICATIONS FOR PRACTICE

The findings suggest that the use of vaginal implants in POP surgery should not be universally dismissed but rather tailored to the individual patient. Certain patient characteristics and comorbidities- such as smoking, concomitant hysterectomy, and other not yet identified possible risk factors associated with increased risk of VWE- should be carefully evaluated when considering implant-assisted prolapse repair. For appropriately selected “low-risk” patients, vaginal implants may provide superior anatomical outcomes with a low risk of VWE, supporting a reconsideration of current restrictions on implant use. To ensure optimal outcomes and safety, procedures involving vaginal implants should be performed only in high-volume centers by surgeons with substantial experience in POP implant surgery. This would help minimize complications and improve the efficacy of vaginal POP surgery. Until such evidence is available, vaginal implants should be used with great caution, after patients have been thoroughly informed and advised about the complications associated with the implant. The size of the implant should be minimized and its use restricted to patients without confirmed or suspected risk factors. If possible, only in cases use it where no other alternative procedure with similar efficacy is available.

12. IMPLICATIONS FOR RESEARCH

12.1. Methodology and Study Design

Further prospective research is required to more clearly define the contribution of various potential risk factors- such as age, hormone replacement therapy, sexual activity, and surgical volume- to the development of vaginal wall erosion (VWE). Current evidence regarding these factors remains limited or inconsistent, highlighting the need for well-designed studies that can provide more definitive insights. Establishing large-scale data collection efforts, such as an international POP surgical registry or coordinated long-term observational studies, would offer an opportunity to gather comprehensive, standardized information across diverse patient populations and clinical settings. Such initiatives would not only refine risk stratification models but also enhance the ability to identify subgroups of patients who may benefit most from implant-assisted repair. High-quality randomized controlled trials remain critical for advancing the field. Studies with longer follow-up durations, larger patient cohorts, and rigorous comparisons of both established and newly developed mesh materials are needed to thoroughly evaluate surgical outcomes, complication profiles, durability of repairs, and overall patient satisfaction. Such trials would provide the robust evidence necessary to guide clinical decision-making, refine surgical techniques, and ultimately improve the long-term management of POP.

12.2. New Areas

Research efforts should increasingly focus on innovating and evaluating next-generation implant materials. This includes the development of graphene-based nanocomposites and other advanced, tissue-friendly biomaterials that may offer improved biocompatibility, reduced complication rates, and better long-term integration compared with traditional polypropylene meshes. It is worth mentioning tissue engineering, which represents a next-generation approach to POP surgery, aiming to overcome the high recurrence rates associated with NT repair and the complications of synthetic mesh. These new approaches provide temporary mechanical support while promoting host tissue remodeling and eventual scaffold degradation. Few human trials have been conducted; most focus on autologous fascia, combined with stem cells or decellularized ECM scaffolds.

Initial results show encouraging anatomical outcomes and acceptable safety profiles, but long-term data are missing (Gargett et al., 2019; Yang et al., 2021). Although preclinical data are promising, widespread clinical application remains limited, and further research is required to optimize scaffold design, cell therapy strategies, and integration with host tissue.

13. IMPLICATIONS FOR POLICY MAKERS

Based on the results of our study, policymakers should recognize that the complete ban of POP surgical procedures using vaginal implants and their withdrawal from the surgical practice is unjustified. In fact, given their excellent outcomes and, when performed by experienced surgeons, their acceptable rates and severity of complications, such a ban would be particularly detrimental, as it would limit the range of surgical options available. The most important and clinically relevant implant-based POP surgeries' complication is the VWE. Importantly, the incidence of this complication can be minimized through careful patient selection, the establishment of clear and precise surgical indications, and the development of improved implant materials and refined surgical techniques and increased surgical volume. By taking these factors into account, the safety and effectiveness of implant-assisted POP procedures can be substantially enhanced. In conclusion we can say, that the current blanket ban on vaginal implants for POP surgeries warrants reconsideration. Rather than prohibiting the use of these implants outright, policies could focus on promoting evidence-based guidelines that define appropriate patient selection criteria, procedural standards, and follow-up protocols. Encouraging the use of high-quality, tissue-friendly implants and supporting training programs for surgeons in high-volume centers may reduce complication rates and optimize outcomes. Revising current regulations in light of emerging evidence could ultimately expand safe surgical options for patients, improve anatomical and functional outcomes, and contribute to more personalized, patient-centered care in the management of POP.

14. FUTURE PERSPECTIVES

Our primary goal moving forward is to build upon the findings of our current research and to advance the investigation of risk factors associated with VWE in POP surgery. We aim to identify, characterize, and better understand these risk factors in order to improve patient selection and optimize surgical outcomes. Additionally, we seek to establish standardized guidelines for the indications and use of vaginal implants in female pelvic reconstruction, ensuring that these procedures are performed safely and effectively. Another key objective is to contribute to the development and evaluation of novel, biocompatible, and tissue-friendly vaginal implants. By improving the design and materials of these implants, we hope to further reduce the incidence of vaginal erosion and enhance the long-term safety, efficacy, and quality of life for patients undergoing POP surgery. Our focus is on accurately and consistently identifying, measuring, and tracking surgical practice as a potential, yet undetected, risk factors for vaginal wall erosion. To achieve this, we plan to conduct rigorous, well-designed clinical trials that meet the highest standards of scientific methodology. In addition to randomized controlled trials, we intend to use complementary, evidence-based approaches, including prospective observational studies, registries, and long-term follow-up assessments, to collect comprehensive and reliable data.

15. REFERENCES

Acs, J., Szabo, A., Fehervari, P., Harnos, A., Skribek, B., Tenke, M., Szarvas, T., Nyirady, P., Acs, N., Hegyi, P., & Majoros, A. (2023). Safety and Efficacy of Vaginal Implants in Pelvic Organ Prolapse Surgery: A Meta-analysis of 161 536 Patients. *Eur Urol Focus*. https://doi.org/10.1016/j.euf.2023.11.001

Acs, J., Szabo, A., Fehervari, P., Skribek, B., Cavalcante, B. G. N., Vancsa, S., Romics, M., Szarvas, T., Nyirady, P., Acs, N., Hegyi, P., & Majoros, A. (2025). Risk factors for vaginal wall erosion after pelvic organ prolapse surgery with implant: a systematic review and meta-analysis. *Sci Rep*, *15*(1), 40780. https://doi.org/10.1038/s41598-025-24569-5

Administration, U. S. F. a. D. (April 29, 2014.). Med Device Online. FDA issues proposals to address risks associated with surgical mesh for transvaginal repair of pelvic organ prolapse. . *https://www.meddeviceonline.com/doc/fda-risks-surgical-mesh-transvaginal-repair-pelvic-organ-prolapse-0001*.

Altman, D., Vayrynen, T., Engh, M. E., Axelsen, S., Falconer, C., & Nordic Transvaginal Mesh, G. (2011). Anterior colporrhaphy versus transvaginal mesh for pelvic-organ prolapse. *N Engl J Med*, *364*(19), 1826-1836. https://doi.org/10.1056/NEJMoa1009521

Araco, F., Gravante, G., Sorge, R., Overton, J., De Vita, D., Primicerio, M., Dati, S., Araco, P., & Piccione, E. (2009). The influence of BMI, smoking, and age on vaginal erosions after synthetic mesh repair of pelvic organ prolapses. A multicenter study. *Acta Obstet Gynecol Scand*, *88*(7), 772-780. https://doi.org/10.1080/00016340903002840

Baessler, K., Christmann-Schmid, C., Maher, C., Haya, N., Crawford, T. J., & Brown, J. (2018). Surgery for women with pelvic organ prolapse with or without stress urinary incontinence. *Cochrane Database Syst Rev*, *8*(8), CD013108. https://doi.org/10.1002/14651858.CD013108

Barba, M., Cola, A., Rezzan, G., Costa, C., Melocchi, T., De Vicari, D., Terzoni, S., Frigerio, M., & Maruccia, S. (2023). Flat Magnetic Stimulation for Stress Urinary Incontinence: A 3-Month Follow-Up Study. *Healthcare (Basel)*, *11*(12). https://doi.org/10.3390/healthcare11121730

Barbalat, Y., & Tunuguntla, H. S. (2012). Surgery for pelvic organ prolapse: a historical perspective. *Curr Urol Rep*, *13*(3), 256-261. https://doi.org/10.1007/s11934-012-0249-x

Barski, D., Otto, T., & Gerullis, H. (2014). Systematic review and classification of complications after anterior, posterior, apical, and total vaginal mesh implantation for prolapse repair. *Surg Technol Int*, *24*, 217-224. https://www.ncbi.nlm.nih.gov/pubmed/24700225

Bechev, B., Magunska, N., Ivanov, S., & Kovachev, E. (2015). [Laparoscopic Sacrocolpopexy]. *Akush Ginekol (Sofiia)*, *54*(8), 28-32. https://www.ncbi.nlm.nih.gov/pubmed/27032231

Belügyminisztérium. Egészségügyi Közlöny, -. (2024). *Egészségügyi Szakmai Irányelv az Urogynekológiáról (002128).*

Boeri, L., De Lorenzis, E., Lucignani, G., Turetti, M., Silvani, C., Zanetti, S. P., Longo, F., Albo, G., Salonia, A., & Montanari, E. (2024). Oral preparation of hyaluronic acid, chondroitin sulfate, N-acetylglucosamine, and vitamin C improves sexual and urinary symptoms in participants with recurrent urinary tract infections: a randomized crossover trial. *J Sex Med*, *21*(7), 627-634. https://doi.org/10.1093/jsxmed/qdae052

Capobianco, G., Sechi, I., Muresu, N., Saderi, L., Piana, A., Farina, M., Dessole, F., Virdis, G., De Vita, D., Madonia, M., Petrillo, M., & Sotgiu, G. (2022). Native tissue repair (NTR) versus transvaginal mesh interventions for the treatment of anterior vaginal prolapse: Systematic review and meta-analysis. *Maturitas*, *165*, 104-112. https://doi.org/10.1016/j.maturitas.2022.07.013

Cardozo, L., Staskin, D. 3. kiadás. . (2010). *Textbook of Female Urology and Urogynecology.* London: Informa Healthcare UK.

Cardozo L, W. A., Rowner E, Wein A, Abrams P, (eds.). (2023). *Incontinence. 7th International Consultation on Incontinence.*

Chang, T. C., Hsiao, S. M., Wu, P. C., Chen, C. H., Wu, W. Y., & Lin, H. H. (2019). Comparison of clinical outcomes between tailored transvaginal mesh surgery and native tissue repair for pelvic organ prolapse. *J Formos Med Assoc*, *118*(12), 1623-1632. https://doi.org/10.1016/j.jfma.2019.08.034

Chapple, C. R., Cruz, F., Deffieux, X., Milani, A. L., Arlandis, S., Artibani, W., Bauer, R. M., Burkhard, F., Cardozo, L., Castro-Diaz, D., Cornu, J. N., Deprest, J., Gunnemann, A., Gyhagen, M., Heesakkers, J., Koelbl, H., MacNeil, S., Naumann, G., Roovers, J. W. R., . . . Abdel-Fattah, M. (2017). Consensus Statement of the European Urology Association and the European Urogynaecological Association on the Use of Implanted Materials for Treating Pelvic Organ Prolapse and Stress Urinary Incontinence. *Eur Urol*, *72*(3), 424-431. https://doi.org/10.1016/j.eururo.2017.03.048

Cheng, Y. W., Su, T. H., Wang, H., Huang, W. C., & Lau, H. H. (2017). Risk factors and management of vaginal mesh erosion after pelvic organ prolapse surgery. *Taiwan J Obstet Gynecol*, *56*(2), 184-187. https://doi.org/10.1016/j.tjog.2016.02.021

Crosby, E. C., Abernethy, M., Berger, M. B., DeLancey, J. O., Fenner, D. E., & Morgan, D. M. (2014). Symptom resolution after operative management of complications from transvaginal mesh. *Obstet Gynecol*, *123*(1), 134-139. https://doi.org/10.1097/AOG.0000000000000042

Cuijpers, P., Toshi Furukawa, and David Daniel Ebert. (2024). Dmetar: Companion r Package for the Guide Doing Meta-Analysis in r. https://dmetar.protectlab.org.

Cumpston, M., Li, T., Page, M. J., Chandler, J., Welch, V. A., Higgins, J. P., & Thomas, J. (2019). Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev*, *10*(10), ED000142. https://doi.org/10.1002/14651858.ED000142

da Silveira, S., Auge, A. P., Jarmy-Dibella, Z. I., Margarido, P. F., Carramao, S., Alves Rodrigues, C., Doumouchtsis, S. K., Chada Baracat, E., & Milhem Haddad, J. (2020). A multicenter, randomized trial comparing pelvic organ prolapse surgical treatment with native tissue and synthetic mesh: A 5-year follow-up study. *Neurourol Urodyn*, *39*(3), 1002-1011. https://doi.org/10.1002/nau.24323

Dabica, A., Balint, O., Olaru, F., Secosan, C., Balulescu, L., Brasoveanu, S., Pirtea, M., Popin, D., Bacila, I. F., & Pirtea, L. (2024). Complications of Pelvic Prolapse Surgery Using Mesh: A Systematic Review. *J Pers Med*, *14*(6). https://doi.org/10.3390/jpm14060622

Dallas, K. B., Rogo-Gupta, L., & Elliott, C. S. (2018). What Impacts the All Cause Risk of Reoperation after Pelvic Organ Prolapse Repair? A Comparison of Mesh and Native Tissue Approaches in 110,329 Women. *J Urol*, *200*(2), 389-396. https://doi.org/10.1016/j.juro.2018.02.3093

De Franciscis, P., Conte, A., Schiattarella, A., Riemma, G., Cobellis, L., & Colacurci, N. (2020). Non-hormonal Treatments For Menopausal Symptoms and Sleep Disturbances: A Comparison Between Purified Pollen Extracts and Soy Isoflavones. *Curr Pharm Des*, *26*(35), 4509-4514. https://doi.org/10.2174/1381612826666200721002022

de Tayrac, R., Antosh, D. D., Baessler, K., Cheon, C., Deffieux, X., Gutman, R., Lee, J., Nager, C., Schizas, A., Sung, V., & Maher, C. (2022). Summary: 2021 International Consultation on Incontinence Evidence-Based Surgical Pathway for Pelvic Organ Prolapse. *J Clin Med*, *11*(20). https://doi.org/10.3390/jcm11206106

de Tayrac, R., Gervaise, A., Chauveaud, A., & Fernandez, H. (2005). Tension-free polypropylene mesh for vaginal repair of anterior vaginal wall prolapse. *J Reprod Med*, *50*(2), 75-80. https://www.ncbi.nlm.nih.gov/pubmed/15755042

Deffieux, X., Letouzey, V., Savary, D., Sentilhes, L., Agostini, A., Mares, P., Pierre, F., French College of, O., & Gynecology. (2012). Prevention of complications related to the use of prosthetic meshes in prolapse surgery: guidelines for clinical practice. *Eur J Obstet Gynecol Reprod Biol*, *165*(2), 170-180. https://doi.org/10.1016/j.ejogrb.2012.09.001

Delroy, C. A., Castro Rde, A., Dias, M. M., Feldner, P. C., Jr., Bortolini, M. A., Girao, M. J., & Sartori, M. G. (2013). The use of transvaginal synthetic mesh for anterior vaginal wall prolapse repair: a randomized controlled trial. *Int Urogynecol J*, *24*(11), 1899-1907. https://doi.org/10.1007/s00192-013-2092-0

Deng, T., Liao, B., Luo, D., Shen, H., & Wang, K. (2016). Risk factors for mesh erosion after female pelvic floor reconstructive surgery: a systematic review and meta-analysis. *BJU Int*, *117*(2), 323-343. https://doi.org/10.1111/bju.13158

Doaee, M., Moradi-Lakeh, M., Nourmohammadi, A., Razavi-Ratki, S. K., & Nojomi, M. (2014). Management of pelvic organ prolapse and quality of life: a systematic review and meta-analysis. *Int Urogynecol J*, *25*(2), 153-163. https://doi.org/10.1007/s00192-013-2141-8

Duraes, M., Panel, L., Cornille, A., & Courtieu, C. (2018). Long-term follow-up of patients treated by transvaginal mesh repair for anterior prolapse. *Eur J Obstet Gynecol Reprod Biol*, *230*, 124-129. https://doi.org/10.1016/j.ejogrb.2018.09.022

El-Nazer, M. A., Gomaa, I. A., Ismail Madkour, W. A., Swidan, K. H., & El-Etriby, M. A. (2012). Anterior colporrhaphy versus repair with mesh for anterior vaginal wall prolapse: a comparative clinical study. *Arch Gynecol Obstet*, *286*(4), 965-972. https://doi.org/10.1007/s00404-012-2383-6

Gargett, C. E., Gurung, S., Darzi, S., Werkmeister, J. A., & Mukherjee, S. (2019). Tissue engineering approaches for treating pelvic organ prolapse using a novel source of stem/stromal cells and new materials. *Curr Opin Urol*, *29*(4), 450-457. https://doi.org/10.1097/MOU.0000000000000634

Gillor, M., Langer, S., & Dietz, H. P. (2020). A long-term comparative study of Uphold transvaginal mesh kit against anterior colporrhaphy. *Int Urogynecol J*, *31*(4), 793-797. https://doi.org/10.1007/s00192-019-04106-5

Glazener, C., Breeman, S., Elders, A., Hemming, C., Cooper, K. G., Freeman, R. M., Smith, A., Hagen, S., Montgomery, I., Kilonzo, M., Boyers, D., McDonald, A., McPherson, G., MacLennan, G., Norrie, J., Reid, F. M., & Group, P. S. (2020). Mesh inlay, mesh kit or native tissue repair for women having repeat anterior or posterior prolapse surgery: randomised controlled trial (PROSPECT). *BJOG*, *127*(8), 1002-1013. https://doi.org/10.1111/1471-0528.16197

Gluck, O., Blaganje, M., Veit-Rubin, N., Phillips, C., Deprest, J., O'Reilly, B., But, I., Moore, R., Jeffery, S., Haddad, J. M., & Deval, B. (2020). Laparoscopic sacrocolpopexy: A comprehensive literature review on current practice. *Eur J Obstet Gynecol Reprod Biol*, *245*, 94-101. https://doi.org/10.1016/j.ejogrb.2019.12.029

Gold, K. P., Ward, R. M., Zimmerman, C. W., Biller, D. H., McGuinn, S., Slaughter, J. C., & Dmochowski, R. R. (2012). Factors associated with exposure of transvaginally placed polypropylene mesh for pelvic organ prolapse. *Int Urogynecol J*, *23*(10), 1461-1466. https://doi.org/10.1007/s00192-012-1706-2

Halaska, M., Maxova, K., Sottner, O., Svabik, K., Mlcoch, M., Kolarik, D., Mala, I., Krofta, L., & Halaska, M. J. (2012). A multicenter, randomized, prospective, controlled study comparing sacrospinous fixation and transvaginal mesh in the

treatment of posthysterectomy vaginal vault prolapse. *Am J Obstet Gynecol*, *207*(4), 301 e301-307. https://doi.org/10.1016/j.ajog.2012.08.016

Handa, V. L., Garrett, E., Hendrix, S., Gold, E., & Robbins, J. (2004). Progression and remission of pelvic organ prolapse: a longitudinal study of menopausal women. *Am J Obstet Gynecol*, *190*(1), 27-32. https://doi.org/10.1016/j.ajog.2003.07.017

Harbord, R. M., Ross J. Harris, and Jonathan A. C. Sterne. (2009). "Updated Tests for Small-Study Effects in Meta-Analyses." *The Stata Journal: Promoting Communications on Statistics and Stata 9 (2): 197–210.* https://doi.org/10.1177/1536867X0900900202

Harrer, M., Pim Cuijpers, Furukawa Toshi A, and David D Ebert. (2021). Doing Meta-Analysis With R: A Hands-On Guide. 1st ed. *Boca Raton, FL; London: Chapman & Hall/CRC Press.*

Higgins, J. P., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Stat Med*, *21*(11), 1539-1558. https://doi.org/10.1002/sim.1186

https://www.millerandzois.com/products-liability/vaginal-mesh-lawsuit-and-settlements/?utm_source=chatgpt.com. (2025).

Jackson, D., Riley, R., & White, I. R. (2011). Multivariate meta-analysis: potential and promise. *Stat Med*, *30*(20), 2481-2498. https://doi.org/10.1002/sim.4172

Jha, S., & Gray, T. (2015). A systematic review and meta-analysis of the impact of native tissue repair for pelvic organ prolapse on sexual function. *Int Urogynecol J*, *26*(3), 321-327. https://doi.org/10.1007/s00192-014-2518-3

Jia, X., Glazener, C., Mowatt, G., MacLennan, G., Bain, C., Fraser, C., & Burr, J. (2008). Efficacy and safety of using mesh or grafts in surgery for anterior and/or posterior vaginal wall prolapse: systematic review and meta-analysis. *BJOG*, *115*(11), 1350-1361. https://doi.org/10.1111/j.1471-0528.2008.01845.x

Juliato, C. R., Santos Junior, L. C., Haddad, J. M., Castro, R. A., Lima, M., & Castro, E. B. (2016). Mesh Surgery for Anterior Vaginal Wall Prolapse: A Meta-analysis. *Rev Bras Ginecol Obstet*, *38*(7), 356-364. https://doi.org/10.1055/s-0036-1585074

Kabon, B., Nagele, A., Reddy, D., Eagon, C., Fleshman, J. W., Sessler, D. I., & Kurz, A. (2004). Obesity decreases perioperative tissue oxygenation. *Anesthesiology*, *100*(2), 274-280. https://doi.org/10.1097/00000542-200402000-00015

Kaufman, Y., Singh, S. S., Alturki, H., & Lam, A. (2011). Age and sexual activity are risk factors for mesh exposure following transvaginal mesh repair. *Int Urogynecol J*, *22*(3), 307-313. https://doi.org/10.1007/s00192-010-1270-6

Lavelle, R. S., Christie, A. L., Alhalabi, F., & Zimmern, P. E. (2016). Risk of Prolapse Recurrence after Native Tissue Anterior Vaginal Suspension Procedure with Intermediate to Long-Term Followup. *J Urol*, *195*(4 Pt 1), 1014-1020. https://doi.org/10.1016/j.juro.2015.10.138

Liao, S. C., Huang, W. C., Su, T. H., & Lau, H. H. (2019). Changes in Female Sexual Function After Vaginal Mesh Repair Versus Native Tissue Repair for Pelvic Organ Prolapse: A Meta-Analysis of Randomized Controlled Trials. *J Sex Med*, *16*(5), 633-639. https://doi.org/10.1016/j.jsxm.2019.02.016

Lukacz, E. S., Sridhar, A., Chermansky, C. J., Rahn, D. D., Harvie, H. S., Gantz, M. G., Varner, R. E., Korbly, N. B., Mazloomdoost, D., Eunice Kennedy Shriver National Institute of Child, H., & Human Development Pelvic Floor Disorders, N. (2020). Sexual Activity and Dyspareunia 1 Year After Surgical Repair of Pelvic Organ Prolapse. *Obstet Gynecol*, *136*(3), 492-500. https://doi.org/10.1097/AOG.0000000000003992

Maher, C., Feiner, B., Baessler, K., Christmann-Schmid, C., Haya, N., & Brown, J. (2016). Surgery for women with anterior compartment prolapse. *Cochrane Database Syst Rev*, *11*(11), CD004014. https://doi.org/10.1002/14651858.CD004014.pub6

Maher, C., Feiner, B., Baessler, K., & Schmid, C. (2013). Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*(4), CD004014. https://doi.org/10.1002/14651858.CD004014.pub5

Milani, A. L., Damoiseaux, A., IntHout, J., Kluivers, K. B., & Withagen, M. I. J. (2018). Long-term outcome of vaginal mesh or native tissue in recurrent prolapse: a randomized controlled trial. *Int Urogynecol J*, *29*(6), 847-858. https://doi.org/10.1007/s00192-017-3512-3

Min, H., Li, H., Bingshu, L., Yanxiang, C., Lu, C., Qing, S., Xuejiao, Z., Wenying, W., Debin, W., Shasha, H., Wenjuan, D., Jie, M., Xiaohong, Z., Wenjun, G., Jianhua, C., Qian, L., & Yuling, L. (2013). Meta-analysis of the efficacy and safety of the application of adjuvant material in the repair of anterior vaginal wall prolapsed.

Arch Gynecol Obstet, *287*(5), 919-936. https://doi.org/10.1007/s00404-012-2626-6

Moradi, M., Ghavami, V., Niazi, A., Seraj Shirvan, F., & Rasa, S. (2023). The Effect of Salvia Officinalis on Hot Flashes in Postmenopausal Women: A Systematic Review and Meta-Analysis. *Int J Community Based Nurs Midwifery*, *11*(3), 169-178. https://doi.org/10.30476/IJCBNM.2023.97639.2198

Morselli, S., Li Marzi, V., Verrienti, P., Serati, M., Di Camillo, M., Tosto, A., Milanesi, M., & Serni, S. (2019). Transvaginal mesh surgery for pelvic organ prolapse does not affect sexual function at long term follow up. *Eur J Obstet Gynecol Reprod Biol*, *240*, 282-287. https://doi.org/10.1016/j.ejogrb.2019.07.027

Mosca, L., Riemma, G., Braga, A., Frigerio, M., Ruffolo, A. F., Dominoni, M., Munno, G. M., Uccella, S., Serati, M., Raffone, A., Salvatore, S., & Torella, M. (2022). Female Sexual Dysfunctions and Urogynecological Complaints: A Narrative Review. *Medicina (Kaunas)*, *58*(8). https://doi.org/10.3390/medicina58080981

Ng-Stollmann, N., Funfgeld, C., Gabriel, B., & Niesel, A. (2020). The international discussion and the new regulations concerning transvaginal mesh implants in pelvic organ prolapse surgery. *Int Urogynecol J*, *31*(10), 1997-2002. https://doi.org/10.1007/s00192-020-04407-0

Nussler, E., Kesmodel, U. S., Lofgren, M., & Nussler, E. K. (2015). Operation for primary cystocele with anterior colporrhaphy or non-absorbable mesh: patient-reported outcomes. *Int Urogynecol J*, *26*(3), 359-366. https://doi.org/10.1007/s00192-014-2511-x

Ow, L. L., Lim, Y. N., Dwyer, P. L., Karmakar, D., Murray, C., Thomas, E., & Rosamilia, A. (2016). Native tissue repair or transvaginal mesh for recurrent vaginal prolapse: what are the long-term outcomes? *Int Urogynecol J*, *27*(9), 1313-1320. https://doi.org/10.1007/s00192-016-3069-6

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hrobjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., . . . Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*, *372*, n71. https://doi.org/10.1136/bmj.n71

Persu, C., Chapple, C. R., Cauni, V., Gutue, S., & Geavlete, P. (2011). Pelvic Organ Prolapse Quantification System (POP-Q) - a new era in pelvic prolapse staging. *J Med Life*, *4*(1), 75-81. https://www.ncbi.nlm.nih.gov/pubmed/21505577

Pizzoferrato, A. C., Thuillier, C., Venara, A., Bornsztein, N., Bouquet, S., Cayrac, M., Cornillet-Bernard, M., Cotelle, O., Cour, F., Cretinon, S., De Reilhac, P., Loriau, J., Pellet, F., Perrouin-Verbe, M. A., Pourcelot, A. G., Revel-Delhom, C., Steenstrup, B., Vogel, T., Le Normand, L., & Fritel, X. (2023). Management of female pelvic organ prolapse-Summary of the 2021 HAS guidelines. *J Gynecol Obstet Hum Reprod*, *52*(3), 102535. https://doi.org/10.1016/j.jogoh.2023.102535

Pustejovsky, J. E., & Tipton, E. (2022). Meta-analysis with Robust Variance Estimation: Expanding the Range of Working Models. *Prev Sci*, *23*(3), 425-438. https://doi.org/10.1007/s11121-021-01246-3

Riemma, G., Vinci, D., La Verde, M., Caniglia, F. M., Scalzone, G., & Torella, M. (2025). Adding collagen, propolis plus quercetin, bacillus coagulans, hyaluronic acid and chondroitin sulphate to D-mannose avoids symptoms and prevents recurrence in women with recurrent urinary tract infections: a single-blind randomized controlled trial. *Expert Rev Anti Infect Ther*, 1-8. https://doi.org/10.1080/14787210.2025.2487162

Rodrigues, M., Kosaric, N., Bonham, C. A., & Gurtner, G. C. (2019). Wound Healing: A Cellular Perspective. *Physiol Rev*, *99*(1), 665-706. https://doi.org/10.1152/physrev.00067.2017

Roshanravan, S. M., Wieslander, C. K., Schaffer, J. I., & Corton, M. M. (2007). Neurovascular anatomy of the sacrospinous ligament region in female cadavers: Implications in sacrospinous ligament fixation. *Am J Obstet Gynecol*, *197*(6), 660 e661-666. https://doi.org/10.1016/j.ajog.2007.08.061

Ruffolo, A. F., Braga, A., Torella, M., Frigerio, M., Cimmino, C., De Rosa, A., Sorice, P., Castronovo, F., Salvatore, S., & Serati, M. (2022). Vaginal Laser Therapy for Female Stress Urinary Incontinence: New Solutions for a Well-Known Issue-A Concise Review. *Medicina (Kaunas)*, *58*(4). https://doi.org/10.3390/medicina58040512

Schwarzer, G. (2024). Meta: General Package for Meta-Analysis. . https://github.com/guido-s/meta/.

Seifalian, A., Basma, Z., Digesu, A., & Khullar, V. (2023). Polypropylene Pelvic Mesh: What Went Wrong and What Will Be of the Future? *Biomedicines*, *11*(3). https://doi.org/10.3390/biomedicines11030741

Selle, J. M., Hokenstad, E. D., Habermann, E. B., Bews, K. A., & Occhino, J. A. (2024). The effect of concomitant hysterectomy on complications following pelvic organ prolapse surgery. *Arch Gynecol Obstet*, *309*(1), 321-327. https://doi.org/10.1007/s00404-023-07112-7

Siddiqui, N. Y., Grimes, C. L., Casiano, E. R., Abed, H. T., Jeppson, P. C., Olivera, C. K., Sanses, T. V., Steinberg, A. C., South, M. M., Balk, E. M., Sung, V. W., & Society of Gynecologic Surgeons Systematic Review, G. (2015). Mesh sacrocolpopexy compared with native tissue vaginal repair: a systematic review and meta-analysis. *Obstet Gynecol*, *125*(1), 44-55. https://doi.org/10.1097/AOG.0000000000000570

Slade, E., Daly, C., Mavranezouli, I., Dias, S., Kearney, R., Hasler, E., Carter, P., Mahoney, C., Macbeth, F., & Delgado Nunes, V. (2020). Primary surgical management of anterior pelvic organ prolapse: a systematic review, network meta-analysis and cost-effectiveness analysis. *BJOG*, *127*(1), 18-26. https://doi.org/10.1111/1471-0528.15959

Smith, F. J., Holman, C. D., Moorin, R. E., & Tsokos, N. (2010). Lifetime risk of undergoing surgery for pelvic organ prolapse. *Obstet Gynecol*, *116*(5), 1096-1100. https://doi.org/10.1097/AOG.0b013e3181f73729

Song, W., Kim, T. H., Chung, J. W., Cho, W. J., Lee, H. N., Lee, Y. S., & Lee, K. S. (2016). Anatomical and Functional Outcomes of Prolift Transvaginal Mesh for Treatment of Pelvic Organ Prolapse. *Low Urin Tract Symptoms*, *8*(3), 159-164. https://doi.org/10.1111/luts.12090

St Martin, B., Markowitz, M. A., Myers, E. R., Lundsberg, L. S., & Ringel, N. (2024). Estimated National Cost of Pelvic Organ Prolapse Surgery in the United States. *Obstet Gynecol*, *143*(3), 419-427. https://doi.org/10.1097/AOG.0000000000005485

Stafne, S. N., Ulven, S. K. S., Prosch-Bilden, T., & Saga, S. (2024). Pelvic floor disorders and impact on sexual function: a cross-sectional study among non-sexually active

and sexually active women. *Sex Med*, *12*(2), qfae024. https://doi.org/10.1093/sexmed/qfae024

Swift, S., Woodman, P., O'Boyle, A., Kahn, M., Valley, M., Bland, D., Wang, W., & Schaffer, J. (2005). Pelvic Organ Support Study (POSST): the distribution, clinical definition, and epidemiologic condition of pelvic organ support defects. *Am J Obstet Gynecol*, *192*(3), 795-806. https://doi.org/10.1016/j.ajog.2004.10.602

Team., R. C. (2024). R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing. https://www.R-project.org/.

Theadom, A., & Cropley, M. (2006). Effects of preoperative smoking cessation on the incidence and risk of intraoperative and postoperative complications in adult smokers: a systematic review. *Tob Control*, *15*(5), 352-358. https://doi.org/10.1136/tc.2005.015263

Toozs-Hobson, P., Freeman, R., Barber, M., Maher, C., Haylen, B., Athanasiou, S., Swift, S., Whitmore, K., Ghoniem, G., de Ridder, D., International Urogynecological, A., & International Continence, S. (2012). An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for reporting outcomes of surgical procedures for pelvic organ prolapse. *Neurourol Urodyn*, *31*(4), 415-421. https://doi.org/10.1002/nau.22238

Unger, C. A., & Barber, M. D. (2015). Vaginal Mesh in Pelvic Reconstructive Surgery: Controversies, Current Use, and Complications. *Clin Obstet Gynecol*, *58*(4), 740-753. https://doi.org/10.1097/GRF.0000000000000148

von Theobald, P. (2011). Place of mesh in vaginal surgery, including its removal and revision. *Best Pract Res Clin Obstet Gynaecol*, *25*(2), 197-203. https://doi.org/10.1016/j.bpobgyn.2010.11.004

Weintraub, A. Y., Friedman, T., Baumfeld, Y., Neymeyer, J., Neuman, M., & Krissi, H. (2016). Long-term functional outcomes following mesh-augmented posterior vaginal prolapse repair. *Int J Gynaecol Obstet*, *135*(1), 107-111. https://doi.org/10.1016/j.ijgo.2016.04.005

Wihersaari, O., Karjalainen, P., Tolppanen, A. M., Mattsson, N., Nieminen, K., & Jalkanen, J. (2022). Sexual Activity and Dyspareunia After Pelvic Organ Prolapse

Surgery: A 5-Year Nationwide Follow-up Study. *Eur Urol Open Sci*, *45*, 81-89. https://doi.org/10.1016/j.euros.2022.09.014

Withagen, M. I., Vierhout, M. E., Hendriks, J. C., Kluivers, K. B., & Milani, A. L. (2011). Risk factors for exposure, pain, and dyspareunia after tension-free vaginal mesh procedure. *Obstet Gynecol*, *118*(3), 629-636. https://doi.org/10.1097/AOG.0b013e31822ada95

Yang, D., Zhang, M., & Liu, K. (2021). Tissue engineering to treat pelvic organ prolapse. *J Biomater Sci Polym Ed*, *32*(16), 2118-2143. https://doi.org/10.1080/09205063.2021.1958184

Yeung, E., Baessler, K., Christmann-Schmid, C., Haya, N., Chen, Z., Wallace, S. A., Mowat, A., & Maher, C. (2024). Transvaginal mesh or grafts or native tissue repair for vaginal prolapse. *Cochrane Database Syst Rev*, *3*(3), CD012079. https://doi.org/10.1002/14651858.CD012079.pub2

Zacche, M. M., Mukhopadhyay, S., & Giarenis, I. (2018). Trends in prolapse surgery in England. *Int Urogynecol J*, *29*(11), 1689-1695. https://doi.org/10.1007/s00192-018-3731-2

Zambon, J. P., & Badlani, G. H. (2016). Vaginal Mesh Exposure Presentation, Evaluation, and Management. *Curr Urol Rep*, *17*(9), 65. https://doi.org/10.1007/s11934-016-0617-z

16. BIBLIOGRAPHY

16.1. Publications Related to the Thesis

1. Ács J, Szabó A, Fehérvári P, Skribek B, Cavalcante BGN, Váncsa S, Romics M, Szarvas T, Nyirády P, Ács N, Hegyi P, Majoros A. Risk factors for vaginal wall erosion after pelvic organ prolapse surgery with implant: a systematic review and meta-analysis. Sci Rep. 2025 Nov 19;15(1):40780. doi: 10.1038/s41598-025-24569-5.
   IF: 3,9
2. Ács J, Szabó A, Fehérvári P, Harnos A, Skribek B, Tenke M, Szarvas T, Nyirády P, Ács N, Hegyi P, Majoros A. Safety and Efficacy of Vaginal Implants in Pelvic Organ Prolapse Surgery: A Meta-analysis of 161 536 Patients. Eur Urol Focus. 2024 Jul;10(4):525-534. doi: 10.1016/j.euf.2023.11.001.
   IF: 5,6

16.2. Publications not Related to the Thesis

1. Skribek B, Szabó A, Ács J, Cavalcante BGN, Sipos BD, Hegyi P, Mátrai P, Nyirády P, Ács N, Majoros A, Deák PÁ. Oncological Efficacy and Safety of Minimally Invasive Focal and Whole-Gland Interventions in the Treatment of Low- and Intermediate-Risk Prostate Cancer: A Systematic Review and Meta-Analysis. Cancers (Basel). 2025 Aug 30;17(17):2863. doi: 10.3390/cancers17172863.
   IF: 4,4
2. Szabó A, Váncsa S, Hegyi P, Kói T, Ács J, Hermánné RJ, Ács N, Szarvas T, Nyirády P, Kopa Z. Assessing the efficacy of varicocelectomy, antioxidants, FSH treatment, and lifestyle modifications on sperm DNA fragmentation: a systematic review and meta-analysis. Sci Rep. 2025 Mar 24;15(1):10118. doi: 10.1038/s41598-025-93267-z.
   IF: 3,9
3. Filipov T, Teutsch B, Szabó A, Forintos A, Ács J, Váradi A, Hegyi P, Szarvas T, Ács N, Nyirády P, Deák PÁ. Investigating the role of ultrasound-based shear wave elastography in kidney transplanted patients: correlation between non-invasive fibrosis detection, kidney dysfunction and biopsy results-a systematic review and

meta-analysis. J Nephrol. 2024 Jul;37(6):1509-1522. doi: 10.1007/s40620-023-01856-w.

IF: 2,6

4. Skribek B, Szabó A, Ács J, Hegyi P, Mátrai P, Nyirády P, Ács N, Majoros A, Deák PÁ. Ablation and laparoscopic adrenalectomy: Balancing efficacy and safety in the treatment of benign adrenal gland tumors: A systematic review and meta-analysis. Heliyon. 2024 Sep 12;10(19):e37868. doi: 10.1016/j.heliyon.2024.e37868.

   IF: 3,6

5. Ács Júlia, Sonkodi Balázs, Soós Zita, Nyirády Péter, Kopa Zsolt: Az orgazmus nem kívánt hatása: "Orgazmust követő betegség" tünetcsoport (POIS) - új adatok, MAGYAR UROLÓGIA 35: 1 pp. 8-10. (2023)
6. Szabó A, Váncsa S, Hegyi P, Váradi A, Forintos A, Filipov T, Ács J, Ács N, Szarvas T, Nyirády P, Kopa Z. Lifestyle-, environmental-, and additional health factors associated with an increased sperm DNA fragmentation: a systematic review and meta-analysis. Reprod Biol Endocrinol. 2023 Jan 18;21(1):5. doi: 10.1186/s12958-023-01054-0.

   IF: 4,2

7. Sziva RE, Ács J, Tőkés AM, Korsós-Novák Á, Nádasy GL, Ács N, Horváth PG, Szabó A, Ke H, Horváth EM, Kopa Z, Várbíró S. Accurate Quantitative Histomorphometric-Mathematical Image Analysis Methodology of Rodent Testicular Tissue and Its Possible Future Research Perspectives in Andrology and Reproductive Medicine. Life (Basel). 2022 Jan 27;12(2):189. doi: 10.3390/life12020189.

   IF: 3,2

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