Merete Kolberg Tennfjord

Pelvic floor muscle function, vaginal symptoms and symptoms of sexual dysfunction in first time mothers: a cohort and a randomised controlled trial

Contents

Acknowledgements

Over three years of work has come to an end and it is time to move on. I must admit, I have truly stepped out of the comfort zone doing this research. But hopefully by bringing more attention to this field of women's health, more openness around common problems during pregnancy and after childbirth could be achieved.

My sincere gratitude goes to all of you who made this dissertation possible, especially to all the women participating in this project.

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Merete Kolberg Tennfjord

List of papers

This thesis is based on the following original papers, which are referred to in the text by their Roman numerals:

I. Tennfjord, M.K., Hilde, G., Stær-Jensen, J. et al. Int Urogynecol J (2014) 25: 1227. doi:10.1007/s00192-014-2373-2. Dyspareunia and pelvic floor muscle function before and during pregnancy and after childbirth.

II. Tennfjord MK, Hilde G, Stær-Jensen J, Siafarikas F, Engh ME, and Bø K. Coital incontinence and vaginal symptoms and the relationship to pelvic floor muscle function in primiparous women at 12 months postpartum: A cross-sectional study. J Sex Med 2015;12:994–1003.

III. Kolberg Tennfjord M, Hilde G, Stær-Jensen J, Siafarikas F, Ellström Engh M, Bø K. Effect of postpartum pelvic floor muscle training on vaginal symptoms and sexual dysfunction— secondary analysis of a randomised trial. BJOG 2016;123:634–642.

IV. Tennfjord, M.K., Engh, M.E. & Bø, K. Int Urogynecol J (2017). doi:10.1007/s00192-017-3290-y. An intra –and interrater reliability and agreement study of vaginal resting pressure, pelvic floor muscle strength and muscular endurance using manometer.

Abbreviations

3D   three dimensional

4D   four dimensional

BMI   body mass index

CI   confidence interval

EMG   electromyography

ICC   intraclass correlation coefficient

ICIQ-VS   International Consultation on Incontinence Questionnaire Vaginal Symptoms

ICIQ-FLUTSsex   International Consultation on Incontinence Questionnaire FLUTSsex

MRI   magnetic resonance imaging

MVC   maximal voluntary contraction

N   Newton

PFD   pelvic floor dysfunction

PFM   pelvic floor muscle

PFMT   pelvic floor muscle training

RCT   randomized controlled trial

RR   relative risk

SD   standard deviation

Note regarding references in background chapter:

In general, references are updated throughout this dissertation. References related to our research area (vaginal symptoms and symptoms of sexual dysfunction during and after pregnancy) reflect our knowledge of the field before project start (January 2010) in the background chapter. Literature related to our research area published during the project period will be included in the discussion chapter in light of the findings from this dissertation.

Summary

Number of women reporting dyspareunia at each time point from pre-pregnancy until 12 months after delivery was 27.8% at pre-pregnancy, 30.5% at gestational 22, 41.4% at gestational week 37, 44.6% at six months and 33.1 % at 12 months after delivery. The majority reported severity of dyspareunia as "a little". There was no difference between women with and without dyspareunia in relation to PFM variables or delivery variables. Longitudinal data showed new cases of dyspareunia during pregnancy and after delivery, but total prevalence of dyspareunia declined throughout the study. Most women with dyspareunia prior to pregnancy and those with new symptoms during pregnancy were symptom free by 12 months after delivery. Other vaginal symptoms were prevalent (73.4%) 12 months after delivery, but few of the symptoms were severe, and 34.5% reported the symptoms to interfere with their sexual life. Overall bother of the vaginal symptoms were low (mean 1.4 out of 10). The women reporting "vagina feels loose or lax" had lower vaginal resting pressure, PFM strength and muscular endurance than women without the symptom; mean difference: 3.6 cmH$_2$O (95%CI 0.7, 6.6), 9.0 cmH$_2$O (95%CI 2.6, 15.4) and 80.0 cmH$_2$Osec (95%CI 32.6, 127.5), respectively. Six months postpartum no significant difference in outcome variables between groups for the total study sample (n=175) or in the stratum with no defects (n=120) were found. In the stratum with major defects of the levator ani muscle (n=55) at post intervention significantly fewer women in the training group had symptoms of "vagina feels loose or lax" than the control group; RR: 0.55 (95% CI: 0.31, 0.95, p=0.03). The results indicate that PFMT may have a preventative effect of "vagina feels loose or lax" in women with major levator ani defects. Bias and minimal detectable change for Camtech AS was found to be -2.44 ±8.7 cmH$_2$O for vaginal resting pressure, -0.22 ±7.6 cmH$_2$O for PFM strength and 0.75 ±59.49 cmH$_2$Osec for muscular endurance (intrarater). Bias and minimal detectable change was 1.36 ±9.0 cmH$_2$O for vaginal resting pressure, 2.24 ±9.0 cmH$_2$O for PFM strength and 15.89 ±69.7 cmH$_2$Osec for muscular endurance (interrater). Camtech AS seems less accurate for the strongest women. A statistically significant improvement in PFM variables needs to exceed the minimal detectable change to be above the error of measurement.

Sammendrag

Dyspareuni er vanlig både før, under og etter graviditet og forekomst var 27.8% før graviditet, 30.5% ved gestasjonsuke 22, 41.4% ved gestasjonsuke 37, 44.6% ved seks måneder og 33.1 % ved 12 måneder etter fødsel. De fleste kvinnene rapporterte graden av dyspareuni som "liten". Ingen statistisk signifikant forskjell mellom bekkenbunnsvariabler og fødselsvariabler mellom kvinner med og uten dyspareuni ble funnet. Longitudinelle analyser viste nye tilfeller av dyspareuni under graviditet og etter fødsel, men den totale forekomsten ble redusert gjennom studiet. 73.4% (130) av kvinnene rapporterte minst et vaginalt symptom, mens 34.5% (61) rapporterte minst et vaginalt symptom som påvirket seksuallivet. Symptomene «ødela» i liten grad seksuallivet. Kvinner som rapporterte "skjede føles romslig/slapp" hadde lavere vaginalt hviletrykk, bekkenbunnsstyrke og muskulær utholdenhet enn kvinner uten symptomet; gjennomsnittforskjell 3.6 cmH$_2$O (95 % KI 0.7, 6.6), 9.0 cmH$_2$O (95 % KI 2.6, 15.4) og 80.0 cmH$_2$Osek (95 % KI 32.6, 127.5), respektivt. Seks måneder etter fødsel var det ingen signifikant forskjell på utfallsvariabler mellom trening og kontroll i den totale gruppen (n=175) eller i stratum uten skade (n=120). I stratum med skade av levator ani muskelen (n=55) ved post intervensjon var det signifikant færre kvinner i treningsgruppen som hadde symptomet "skjede føles romslig/slapp" sammenlignet med kontroll gruppen; RR: 0.55 (95% KI: 0.31, 0.95, p=0.03). Bekkenbunnstrening kan ha en mulig forebyggende effekt på "skjede føles romslig/slapp" hos kvinner med levator ani skade. Bias og minste reelle endring med Camtech AS var for vaginalt hviletrykk: -2.44 ±8.7 cmH$_2$O, for bekkenbunnsstyrke -0.22 ±7.6 cmH$_2$O og for muskulær utholdenhet 0.75 ±59.49 cmH$_2$Osek (intrarater). Bias og minste reelle endring for vaginalt hviletrykk var 1.36 ±9.0 cmH$_2$O, for bekkenbunnsstyrke 2.24 ±9.0 cmH$_2$O og for muskulær utholdenhet 15.89 ±69.7 cmH$_2$Osek (interrater). Camtech AS virker mindre sikkert for de sterkeste kvinnene. En statistisk signifikant forbedring i bekkenbunnsvariabler må overstige den minste reelle forskjell.

Introduction

In 2015, 59 901 deliveries took place in Norway [1]. Pregnancy and childbirth are potential risk periods for developing pelvic floor dysfunctions (PFD), including symptoms of sexual dysfunction [2], which are highly prevalent during this period of life [3]. The pelvic floor muscles (PFM) is thought to be of importance for aspects of female sexual function [4], but this relationship is poorly understood, especially during pregnancy and after childbirth. Several theories exist with lack of supporting evidence leading to hypothesis and "expert advice" about what to do and what not to do [4-7].

As health professionals we see women seeking help with a desire to "get back to normal" after giving birth. There is also an increasing focus into sexual health in media. The need for preventative and treatment alternatives is therefore of most importance. Physiotherapists working in this area, has in-depth knowledge into the pelvic floor and the PFM, with the aim to prevent and treat pain and dysfunctions, and to optimize physical activity and training [8]. Based on current guidelines, pregnant women are encouraged to stay physically active throughout pregnancy and participate in exercises that strengthen and maintain good physical health [9]. In addition, pelvic floor muscle training (PFMT) is recommended as treatment for women with urinary incontinence after childbirth [10]. There are however lack of studies investigating effect of PFMT on symptoms of sexual dysfunction after childbirth.

Background

Anatomy of the female pelvic floor

The term pelvic floor is related to the compound structure, which closes the bony pelvic outlet. The term PFM is related to the muscular layer of the pelvic floor [11]. The pelvic organs (bladder, vagina, urethra, uterus and bowel) are supported by the pelvic floor structures consisting of the vaginal wall, the endopelvic fascia, the arcus tendineus fascia pelvic and the levator ani muscle, and skeletal structure where they attach [12, 13].

Bony pelvis

The bony pelvis consists of the ischium, ilium, sacrum, pubis and the coccyx. These parts are connected by three main joints; the symphysis pubis and the two sacroiliac joints. The bony pelvis is further held together by ligaments; the sacrospinous, sacrotuberous, sacrococcygeal and the sacroiliac ligaments [14]. The pelvis has two basins: the major (greater) pelvic and the minor (lesser) pelvis. The abdominal viscera fill the major pelvis, while the minor pelvis is the narrow continuation of the major pelvis inferiorly and is closed by the pelvic floor [15].

Pelvic floor muscles

The PFM are regular skeletal muscles [16]. There are some literature claiming that the PFM consists predominantly of type I (slow twitch) fibers together with a small number of type II (fast twitch) fibers [13, 17, 18]. However, the literature is controversial. The PFM comprise a superficial layer including: ischiocavernosus, bulbospongiosus and the transverse perineal muscles and a deep layer including the levator ani muscles [12]. The levator ani muscle consists of three parts: the pubococcygeus, the puborectalis, and the iliococcygeus muscles [19]. The pubococcygeus muscle can further be divided into the puboanal, puboperineal and the pubovaginal muscle [19]. Some authors are in favour of the term puboviseralis for this portion of the muscle [20-22] (Figure 1). Different muscle fibre directions, origins and insertions makes up the subdivisions of the levator ani muscle [21, 22]. The puboviseralis and the puborectalis muscles form a U-shape as they originate from the pubic bone on either side of the midline and pass behind the rectum to form a sling. The iliococcygeus muscle arises laterally from the arcus tendineus levator ani and forms a horizontal sheet that spans the opening in the posterior region of the pelvis, thereby providing support which the pelvic organs rest [21, 23, 24]. The connective tissue (fascia) covering the superior and the inferior surfaces of the levator ani muscle and the levator ani muscles make up the pelvic

diaphragm [24]. The anterior-posterior midline cleft of these muscles is called the levator hiatus, and is the location of which the urethra, vagina and rectum pass [25].

Innervation

The levator ani -and coccygeus muscles are innervated through direct branches coming from spinal level S3 to S4 [26] (S5) [27]. The pudendal nerve originates from S2 to S4 and includes sensory and motor fibres and innervates the external urethral -and anal sphincters, the superficial perineal muscles, labial skin and clitoris [26-28]. The structures responsible for the sexual arousal responses are largely a product of spinal cord reflex mechanisms. The afferent reflex arm is primarily through the pudendal nerve, whereas the efferent reflex arm is a coordinated somatic and autonomic activity [29].
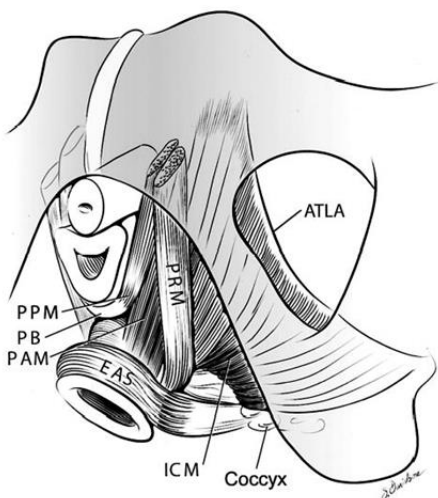
Figure 1. The levator ani muscles from below showing the arcus tendineus levator ani (ATLA); puboanal muscle (PAM); perineal body (PB); puboperineal muscle (PPM); iliococcygeal muscle (ICM); puborectal muscle (PRM). Copyright © DeLancey 2003.

From: Kearney,R.; Sawhney,R.; Delancey,J.O. 2004. Levator ani muscle anatomy evaluated by origin-insertion pairs. Obstet.Gynecol., 104,168-173.

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Pelvic floor muscle function

The PFM together with the supportive ligaments and fascia contribute to maintain continence for urine, flatus and faces while allowing voiding, defecation, sexual intercourse and childbirth, in addition to the overall function to support the abdominal and the pelvic viscera [23, 30-33]. The function of the PFM is performed by contraction and relaxation. In its resting state, the pelvic floor gives support to the pelvic organs [11]. A normal PFM is a situation in which the PFM can voluntarily and involuntary contract and relax. Voluntary contraction will be normal or strong and voluntary relaxation complete (back to or below the resting line after contraction) [11]. Both contraction and relaxation must be present and are needed to allow adequate function of the PFM [11]. A voluntary PFM contraction can be described as an inward lift and a squeeze

around the urethra, vagina and the rectum, resulting in urethral closure, stabilization, and resistance to downward movement. It is the levator ani muscles (the puboviseral muscle and the puborectal muscle) that are primarily responsible for this squeeze and lift function [13, 24, 34-38]. Using transperineal ultrasound and during a PFM contraction, the displacement of the bladder neck was recorded in the cranio-anterior directions [39]. The iliococcygeus muscle acts in a similar manner as the puboviseral muscle [13, 37, 38].

The levator ani adapts to changes in posture and activity when needed; during rest, during voluntary and involuntary contractions and during defecation [32]. The mean inward lift of the PFM during maximum contraction in a magnetic resonance imaging (MRI) study of 16 continent and incontinent women has shown to be 10.8 mm (SD 6.0). During straining, the mean movement among the same women was 19.1mm (SD 7.4) [35]. During a PFM contraction it has also been shown that mean incremental increase in maximum urethral closure pressure may range from 8 [40] to 23.2 (SD 8.4) [41] to 47.3 cmH$_2$O [42].

A PFM contraction of the levator ani has been found upon clitoral and cervical stimulation [6]. This contraction is thought to be mediated through the vaginolevator reflex [6]. During contraction ballooning of the upper vagina and a drop in vaginal pressure is seen, while the lower two-thirds of the vagina narrow with a pressure increase. These changes are thought to enhance the sexual response and prepare for the reproductive process [6]. Both involuntary and voluntary contractions of the PFM (levator ani, bulbocavernosus and ischicavernosus) has been said to contribute to and intensify sexual arousal and orgasm [5]. The involuntary contractions has been described as a product of spinal cord reflex mechanisms [6, 29], but if and how a voluntary PFM contraction may contribute to further arousal or intensify orgasm is not clear. One theory is that during a strong voluntary PFM contraction, the bulbocavernosus may further exacerbate erection of the clitoris [6] equivalent to the penile erection [19], intensifying orgasm. The increased blood flow to the clitoris, vagina and labia leads to engorgement of these organs [6, 29, 43].

Examination of pelvic floor muscle function

Vaginal resting pressure is the resting condition of the muscle with no voluntary muscle contraction [11]. PFM strength is the force-generating capacity of a muscle and is often expressed as maximal voluntary contraction (MVC). MVC is the attempt of a muscle to recruit as many muscle fibers as possible in order of developing force [44]. Local muscular endurance is twofold; the ability of a muscle to sustain near maximal or maximal force, assessed by the time a person is

able to maintain a maximal static or isometric contraction, and the ability to repeatedly develop near maximal or maximal force determined by the number of repetitions [45]. Vaginal resting pressure, PFM strength and muscular endurance may be assessed in several ways; visual observation and palpation, electromyography (EMG), dynamometry, imaging, such as MRI and ultrasonography, and vaginal pressure measurements (manometry). It is difficult to measure and no gold standard exists [11, 46].

Visual observation and palpation

A correct PFM contraction has been described as an inward lift and a squeeze around the urethra, vagina and rectum that could be observed at the perineum and felt by vaginal examination of the PFM [34, 47]. Palpation of the PFM is relatively easy to perform and may be used to assess the PFM and surrounding areas at rest, during contraction and relaxation [11], but inter-observer variability has reported to be high [48]. The modified Oxford 6 point scale is commonly used amongst physiotherapists to quantify PFM strength [49]. However, the ability to discriminate between weak, moderate, good or strong contractions has been questioned [50, 51], although contradictory findings have been reported [52, 53]. Visual observation and vaginal palpation has been recommended to qualitatively determine if a contraction is present or not, rather than to quantify degree of PFM strength [46, 50, 51].

Electromyography

EMG has shown to be reasonable reliable, responsive, sensitive and specific to differentiate between normal, denervated and reinnervated and myopathic muscles, but its validity is questioned [54]. It is a measure of recruitments of motor units and not PFM strength [55]. The use of vaginal probes with electrodes embedded on their surfaces has been used as a convenient way to measure surface EMG from the PFM [56]. Reliability studies show conflicting results [56, 57].

Dynamometry

Dynamometry measures forces produced by a muscle contraction, and consists of an upper fixed speculum branch with an adjustable lower branch. It measures PFM strength, endurance, speed of contraction and passive forces expressed as newton (N). There are several dynamometers being developed [58], the first being the Michigan dynamometer [59]. Reliability studies on different dynamometers has concluded good reliability for maximum strength; Intraclass correlation coefficient (ICC)>0.80 [60] [61-63]. The Montreal dynamometer has shown acceptable intrarater reliability for the passive properties of the PFM (dependability indices of 0.75-0.93) [64] and

promising construct and convergent validity [51, 65]. Poorer intrarater reliability has been found for muscular endurance (dependability indices of 0.10) [62]. However, the device is not commercially available and its use is restricted to research purposes [58].

Imaging

MRI is capable of providing anatomical details of the pelvic floor, both normal anatomy and levator trauma [24], but due to cost, access and contraindications the adoption into clinical practice has been difficult [66]. The use of ultrasound has therefore emerged and three dimensional (D) ultrasound has shown to be well suited for pelvic floor imaging and biometric measurements [66, 67]. 3D/4D ultrasound gives real-time imaging of maneuvers such as a PFM contraction in any user-definable plane and gives access to the plane of the levator hiatus [68]. The method has been tested showing good reliability for assessment of pelvic floor anatomy and function [69-71], and for diagnosis of major levator ani muscle defects [72, 73]. It has also shown to be able to quantify squeeze and lift during a PFM contraction [39] and may be used as biofeedback during teaching and training and as an outcome measure after PFMT and rehabilitation [68, 74].

Manometer

In physiotherapy practices, manometer is the most common method of assessing PFM function; vaginal resting pressure, PFM strength and muscular endurance [46, 75]. There is a variety of devices in use, but they all measure squeeze pressure in either mmHg, hPa or cmH_2O. In general manometer has been established as a reliable assessment method for PFM strength [76-79] if there is a simultaneous inward movement of the perineum seen by observation and palpation [80]. Measurement of vaginal resting pressure using Peritron has also shown good reliability (ICC 0.74-0.77), while muscular endurance measured as multiple repeated muscle contractions (20 fast contractions) concluded poor reliability (ICC 0.05-0.42) [77]. Due to different manometers being tested with different measurement properties, comparing results across studies are difficult [81]. While good reliability and validity for PFM strength has been concluded using Camtech AS [78, 80], the reliability and agreement of vaginal resting pressure and muscular endurance has not been assessed, nor has interrater reliability and agreement for PFM strength.

Female pelvic floor dysfunction

PFD are listed as urinary incontinence symptoms, bladder storage and sensory symptoms of the bladder, voiding and post micturition symptoms, pelvic organ prolapse symptoms, symptoms of sexual dysfunction and anorectal dysfunction, lower urinary tract pain and/or other pelvic pain, and lower urinary tract infection [82]. However, some authors do not acknowledge symptoms of

sexual dysfunction and pelvic pain as part of PFD [83, 84]. Most common in clinical practice and clinically definable conditions are urinary incontinence, anal incontinence and pelvic organ prolapse [85].

The understanding of the cause of the above PFD is far from complete, probably due to the complexity of their multifactorial nature and the overlapping of symptoms [86]. Rather than a single underlying factor, it is more probable a combination of anatomical, physiological, genetic, lifestyle, and reproductive factors that interact throughout a woman's life span to contribute to PFDs [85, 86]. The underlying factors have been described as a three phased model: (Figure 2)

Predisposing factors (e.g. growth and development, genetics, nutritional factors).

Inciting factors (e.g. birth induced changes, surgery)

Intervening factors (e.g. age-related changes, occupational lifting, obesity, medications) [86].
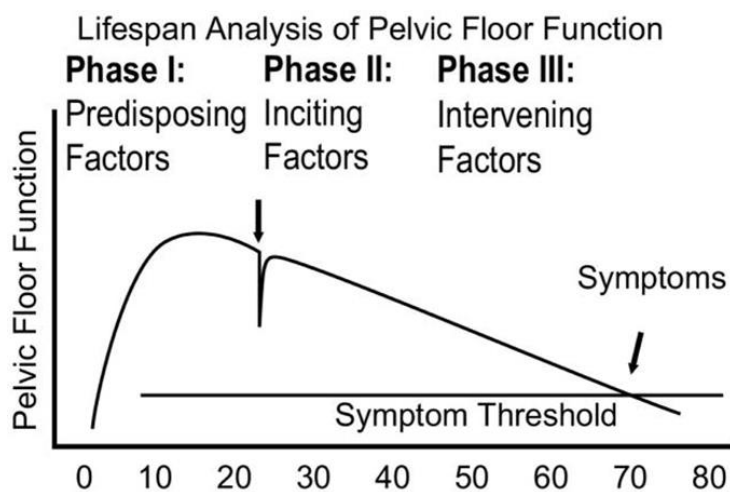
Figure 2. *Integrated lifespan analysis of pelvic floor function*

This graphical display of the abstract concept of pelvic floor function tracks the functional reserve throughout different phases of a woman's lifespan. Initially, pelvic floor structure growth in late teens leads to a fully developed pelvic floor. Vaginal birth affects pelvic floor function. Finally, age-related deterioration occurs until a symptom threshold is reached where the functional reserve present earlier in life is lost. (© DeLancey 2007)

From: DeLancey,J.O; Kane,Low L.; Miller,J.M.; Patel,D.A.; Tumbarello,J.A. 2008. Graphic integration of causal factors of pelvic floor disorders: an integrated life span model. Am.J.Obstet.Gynecol, 199,610-61. With permission from J.O.DeLancey

Diagnosis

The use of validated questionnaires assures that data are responsive, reliable and quantifiable. Validated questionnaires utilized to assess female sexual function may be generalized or condition-specific [87]. Generalized questionnaires focuses on evaluating sexual function in a general population and not specifically in women with PFD. These types of questionnaires may not be sensitive enough to detect differences in sexual function due to e.g. incontinence and pelvic organ prolapse. There are several general questionnaires focusing on sexual function [88-90]. Sexual History Form 12 (SHF-12) is a short version of a 24 item questionnaire [89]. The Female Sexual Function Index (FSFI) is a validated 19-item self-report measure of female sexual function, which gives scores on six domains and measures sexual desire, arousal, lubrication, orgasm, satisfaction and pain [88, 91, 92]. The GRISS-questionnaire is a self-administered questionnaire covering sexual satisfaction, pain, interest in and satisfaction with sex, arousal, ability to orgasm, adequacy of vaginal tone and general feeling [90]. Prior to project start, we were not aware of any studies undertaken to validate generalized questionnaires during pregnancy or in women after childbirth.

There are several condition-specific questionnaires focusing on sexual function for use in women with PFDs [93-98]. The questionnaires differ in type of questions and focus on sexual function. The International Consultation on Incontinence Questionnaire Vaginal Symptoms (ICIQ-VS) has shown good validity, reliability and is sensitivity to change and includes 14 items on vaginal symptoms and the impact of vaginal symptoms on quality of life and sexual life [94]. International Consultation on Incontinence Questionnaire FLUTSsex (ICIQ-FLUTSsex) has been established as a reliable, valid and responsive assessment tool to address sexual issues in women with urinary symptoms/incontinence [96]. Questionnaires assessing sexual function and pelvic organ prolapse are that developed by Mouritsen et al [97], the original long form of the Pelvic Organ Prolapse Urinary Incontinence Sexual Questionnaire (PISQ) [95] and the validated short form of the PISQ (PISQ-12) [99]. The Australian Pelvic floor questionnaire is an interviewer-administered pelvic floor questionnaire that integrates bladder, bowel and sexual function, pelvic organ prolapse, severity, bothersomeness and condition-specific quality of life in an urogynecologic population [93]. Prior to project start, we were not aware of any studies undertaken to validate the condition specific questionnaires during pregnancy or in women after childbirth. ICIQ-FLUTSex has been translated and validated into Norwegian language [100].

Definition and classification

The symptoms addressed in this thesis are listed below as defined in current terminology papers [82, 101].

Prolapse symptoms: "A departure from normal sensation, structure or function, experienced by the woman in reference to the position of her pelvic organs" [101].

More specific terminology:

Vaginal bulging: "complaint of a bulge or something coming down towards or through the vaginal introitus. The woman may state she can either feel the bulge by direct palpation or see it aided with a mirror" [101].

Pelvic pressure: "complaint of increased heaviness or dragging in the suprapubic area and/or pelvis" [101].

Urinary incontinence symptoms:

More specific terminology:

Coital incontinence: "complaint of involuntary loss of urine with coitus" [101]. This present thesis does not separate coital incontinence during penetration or during orgasm.

Symptoms of sexual dysfunction

"A departure from normal sensation and/or function experienced by a woman during sexual activity" [101].

More specific terminology:

Dyspareunia: "complaint of persistent or recurrent pain or discomfort associated with attempted or complete vaginal penetration" [101].

Vaginal laxity: "complaint of excessive vaginal laxity" [101].

Other vaginal symptoms that may influence sexual function [94]

- Dragging pain in lower abdomen [94]

- Vaginal soreness [94]

- Reduced sensation in or around the vagina [94]

- Vaginal dryness [94]

- Vagina feeling tight [94]

Prevalence

There are several large population based studies on PFD and sexual disorders with prevalence rates up to 40% in women of all ages [84, 102, 103]. Most common reported symptoms have been urinary incontinence, followed by faecal incontinence and pelvic organ prolapse, of which proportion of women reporting symptoms have shown to increase with parity [84] and age [84, 103].

Other PFD and symptoms of sexual dysfunction have been dyspareunia with a prevalence between 3.9-7% [102, 103], and vaginal laxity (5.2%) [103]. Coital incontinence in incontinent women has been reported to range between 10% and 27% [104, 105]. However, it has been suggested that the numbers of women with PFD and symptoms of sexual dysfunction might be underreported as women seldom report symptoms of sexual dysfunction or that women have less often sex due to problems [106, 107].

Vaginal symptoms and symptoms of sexual dysfunction during pregnancy and after childbirth

PFD, including symptoms of sexual dysfunction, are prevalent among women after delivery [3, 108-113], ranging from 30-60% in the first three months [108, 110, 111, 113]. Six months after delivery, symptoms have shown to gradually decline, with numbers ranging from 17-27% [3, 108-111]. Studies performed in primiparous women report dyspareunia as most common with similar rates [108, 110, 111]. Despite the high prevalence rates, few studies address bother of those symptoms [3, 114]. Overall impression from published research prior to project start in 2010 was that symptoms of sexual dysfunction, especially dyspareunia, is most common six months after delivery before it gradually declines [3, 114]. Few studies have confirmed this [109], whereas women seven months after delivery reported high pain levels as compared to early pregnancy (p-value <0.01) [115]. Other symptoms reported have been lack of vaginal lubrication, vaginal tightness and lack of muscle tone with prevalence of 26, 20, 12% six months after delivery, respectively [108]. Coital incontinence has been reported between 1-7% in pregnant and postpartum women [109, 116, 117], with a risk of underreported numbers [105, 107, 117].

There is reason to believe that symptoms of sexual dysfunction at pre-pregnancy and pregnancy may influence the situation after childbirth, but yet there are few longitudinal studies investigating

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this relationship [3]. Serati et al [109] investigated de novo PFD six and 12 months after delivery in women with mixed parity, were almost half (46%) were excluded due to incontinence and sexual dysfunction.

Etiology and pathophysiology

PFD, especially urinary incontinence and pelvic organ prolapse seem to increase with age, parity and obesity [84, 103, 118]. Symptoms of sexual dysfunction, however, have found to decrease with increasing age [102] and the aetiology is often more diverse and complex than that of urinary incontinence and pelvic organ prolapse [4]. Further, having one or more PFD [29, 107, 119], not being in a relationship and having lower education have increased odds of experiencing symptoms of sexual dysfunction, such as dyspareunia [102, 119]. Symptoms of sexual dysfunction may be an end-product of a vicious circle and reveal little about the cause or pathophysiology [43, 107, 120].

Vaginal symptoms and symptoms of sexual dysfunction during pregnancy

Increases in PFM resting state and a reduction in PFM activity on straining, indicative of alterations in the contractile power of the muscle, has been found as a possible mechanism of the increasing weight and size of the uterus during pregnancy [121]. Further, hormones (relaxin, progesterone and estrogen) affect the biochemical composition of the pelvic floor tissue and leads to changes in the organization, orientation, and diameter of the collagen fibers, affecting the viscoelastic properties of the vaginal wall, the levator ani and the perineal body [122-124]. Physiological changes with increases in hiatal dimensions and bladder neck mobility has also been demonstrated by our study group [125].

A review on female sexual function during pregnancy concluded that sexual function had a significant global decline during pregnancy, particularly in the third trimester [114]. Of symptoms studied, vaginal pain was a barrier to sexual activity during the 3rd trimester (p<0.001), while symptoms of vaginal looseness and dryness was not [115]. Vaginal discomfort and dryness were significantly higher at the 3rd trimester compared to earlier in pregnancy in another study [126]. Closely linked factors studied have been sexual desire, frequency of intercourse and sexual satisfaction which have found to be influenced by fatigue and depression during pregnancy (p<0.05) [127].

Vaginal symptoms and symptoms of sexual dysfunction after childbirth

Review articles report an association between assisted vaginal delivery and degree of perineal trauma with sexual dysfunction [3, 43, 128]. However studies included in the reviews differ in type of questionnaires used to study sexual problems, study design (retrospective, prospective or cross-sectional), number of study participants, parity and length of follow up, making it difficult to draw overall conclusions. This reflects the conflicting evidence of the role of childbirth on sexual function, were some studies find an association with mode of delivery/delivery variables [108, 111, 112, 129-131] and others do not [109, 110, 113, 132-135]. Dyspareunia has by far received most attention in the above cited studies. Literature focusing on other vaginal symptoms and symptoms of sexual dysfunction are scarce.

Two years after the first delivery no association between dyspareunia and mode of delivery were found [132]. Six years after the index delivery, among 4214 women, women who had caesarean section reported better vaginal tone and sexual satisfaction compared to those having vaginal births or instrumental deliveries (p=0.002) [136].

Hormonal factors

At three months [110] and at six months after delivery [108, 111] breastfeeding has found to be associated with dyspareunia. Other studies show contradictory results [113, 115, 131]. Breastfeeding has a profound effect on postpartum hormonal levels [2]. In lactating women, high levels of prolactin suppress ovarian androgen and oestrogen production. Lower androgen levels may be a factor in lower sexual desire and lower estrogen levels may influence negatively on vaginal lubrication [5, 127]. Plausible, it may be that breastfeeding also indirectly affect PFM function [5]. Breastfeeding has also been found as an influencing factor on interest in sex [130], sexual desire, frequency of intercourse and sexual satisfaction [127]. Use of hormonal contraceptives seem to increase the risk of dyspareunia [137], but results are inconsistent [108].

Weakening of the pelvic floor muscles

Vaginal delivery is a risk factor for weakening of the PFM [24, 138, 139]. There is now a body of literature showing that soon after childbirth, decreases in levator ani resting pressure [121, 140, 141] and PFM strength occur [121, 135, 140-144]. Although PFM function seems to return to pre-pregnancy levels after some months [121, 135], Elenskaia et al [140] found that after one year, vaginal resting pressure was lower one year after delivery in primiparous women compared to pregnancy levels.

Weakening of the PFM may have a negative impact on sexual function [4, 145]. One theory is that "sagging" of the levator ani pull on the pudendal nerve, resulting in pelvic or perineal pain [6]. Another theory is that laxity or weakness of the PFM following childbirth cause vaginal hypoesthesia, coital incontinence and coital anorgasmia [5, 145]. The exact mechanism behind these theories is unclear.

A PubMed search prior to project start (January 2010) found two studies on PFM function and symptoms of sexual dysfunction in relation to childbirth [133, 146]. The study by de Souza Caroci et al [146] included 226 primiparous women during pregnancy and followed the women 30 days after delivery. The study found no association with weak PFM strength (assessed by perineometry and vaginal palpation) and dyspareunia. However, about half of the study population was lost to follow up. The study by Baytur et al [133] included 68 women >two years after delivery and found no association between low PFM strength and symptoms of sexual dysfunction, including dyspareunia.

Nerve injury

Vaginal delivery has shown to cause nerve denervation and alter PFM morphology and function [138, 139, 147, 148]. Lien et al [149] showed in a 3D computer simulation that the inferior rectal nerve branch of the pudendal nerve exhibited the maximum strain of 35% during the second stage of labour. Branches to the labia (the posterior labial nerve) exhibited far less strain (14.7%), mainly due to the lateral course of the branch along the pelvic sidewall. Increased duration of the second stage of labour and high fetal birth weight seems to be associated with pudendal nerve damage [139, 147, 148]. There is scant knowledge into studies investigating effect of nerve damage on symptoms of sexual dysfunction. However, due to the course of the nerve, damage to the pudendal nerve may lead to sensory, arousal and orgasm difficulty [150], and pelvic or perineal pain (dyspareunia and vulvodynia) [6]. The levator ani muscles are not innervated by the pudendal nerve, but through direct branches coming from spinal level S3 to S4 [26] (S5) [27]. Most likely there is an interaction between compression and strain during the second stage of labour as nerves within the pelvis are not so frequently injured [122, 149].

Role of connective tissue, ligaments and fascia

The connective tissue plays an important part in pelvic organ support [30, 33]. It may be alterations in the composition of ligaments and fascia during pregnancy, stretching and tearing of the connective tissue during delivery, as well as levator ani muscle weakness following childbirth that may lead to connective tissue abnormalities and possible loss of support [30, 33, 122, 123]. There are

limited knowledge into the link between connective tissue weakness and symptoms of sexual dysfunction. However, loss of pelvic organ support may result in PFD [30], further influencing female sexual function.

Levator ani muscle defects

Vaginal delivery may stretch and load the PFM beyond their physiological properties. Lien et al [151] showed that the medial part of the PFM (pubovisceral muscle) may be stretched three times their resting length during crowning of the foetal head. Other biomechanical studies have confirmed their findings [152, 153]. All women sustain stretching of their pelvic floor during birth, but only some experience injuries [122]. Several mechanisms for injury to the levator ani muscles have been proposed; neuropathy, tearing and stretching of the muscle, and compression [24]. Such defects of the levator ani muscles may occur unilateral or bilateral, and has shown to appear on imaging as an abnormal insertion of the muscle towards the pubic bone [72, 154]. Major levator ani defects have been found in 20-36% of women after delivery [154, 155]. The use of forceps and having a long second stage of labour has been associated with major defects of the levator ani [24, 156, 157]. Levator avulsion has shown to impact on PFM strength [158-160]. Levator avulsion may also alter pelvic floor anatomy and function [161], but not sexual activity three months after delivery [162].

Pelvic floor muscle training

Strength training

PFMT was introduced as early as 1948 by Kegel [47] with the focus on treating urinary incontinence and pelvic organ prolapse [34]. Based on results from updated Cochrane reviews, PFMT is recommended to be included in first-line conservative management programs for women with stress, urge, or mixed, urinary incontinence [10, 163] and pelvic organ prolapse [164]. The theory behind the rationale for strength training of the PFM is that the PFM, like other skeletal muscles, respond to strength training by improved neuromuscular function, increased muscular cross-sectional area, increased number of activated motor neurons and excitation, and improved muscle tone [165]. Strength training may also build up the structural support of the pelvic floor by elevating the levator plate inside the pelvis to a higher location and by enhancing hypertrophy and stiffness of the PFM and adjacent connective tissue [36].

Progressive overload embedded into the program design is a key component for maximizing strength, power, hypertrophy, and local muscular endurance [165, 166]. The key component is further

specific targeted training [167, 168]. This is achieved by performing a close to maximal contraction of the PFM as possible, without straining or the use of extra-pelvic musculature, and involves a squeeze and a lift of the PFM [11, 34, 80, 167]. Proper teaching of a correct PFM contraction is essential to achieve the desired effect of PFMT [34, 80, 169].

In PFMT the load may be altered in several ways; perform maximal contractions, lengthen the holding periods, increase the number of repetitions and sets completed, and reduce rest intervals [167]. The recommendations for strength training for novice adult trainers is; 8-12 repetitions maximum (60-70%), 1-3 set, 1-2 min rest in between sets, 2-3 days per week [166]. Training to improve local muscular endurance is recommended using high-volume and short rest interval workouts [165, 166]. Specific recommendations for local muscular endurance is using light to moderate load (40-60%) performed at a high number of repetitions >15, with short rest periods in between sets (<1 min), 2-3 days per week [166]. However, to improve muscular endurance, fatigue is a necessary component, and improvement in maximum strength usually improves local muscular endurance but not the other way around [16].

There is a significant interplay between neural and muscular adaptations during strength and power training [165]. In the initial phases of strength training, the gains in strength seem to be due to neural adaptions [170]. Later on, muscle hypertrophy becomes dominant [16, 170]. Recommended duration of training has been a minimum of 15-20 weeks [168], and Bø et al [171] found a significant effect after PFMT on PFM strength throughout a six months period of intensive training.

The physiological effects of strength training work directly on pelvic floor anatomy and function [36, 74] and may directly or indirectly influence female sexual function [172]. It has been demonstrated that women with stronger PFM has better orgasm and arousal potentials [173-175], better lubrication [174, 175] and report higher frequency of intercourse [176, 177]. It is not known whether this relationship exists amongst pregnant women or in women after childbirth.

Effect of pelvic floor muscle training on vaginal symptoms and symptoms of sexual dysfunction

Physical therapy, including PFMT, has been described as promising in treating aspects of sexual dysfunction in women [4, 145]. Combination therapy, including PFMT for certain pelvic floor pain conditions, has received Grade B recommendations [120].

Prior to project start in 2010, we identified six RCTs on the effect of PFMT for sexual dysfunction and symptoms of sexual dysfunction in women after delivery [178-180], in women with stress urinary incontinence [181] and in women with orgasmic disorders [182, 183]. After project start seven new RCTs were published in women with pelvic organ prolapse [184-187], in women with stress urinary incontinence [188, 189], and in gynecological cancer patients [190]. There were no new RCTs conducted during pregnancy or after childbirth after 2010. Results from all trials are summarized in Table 1. The RCTs varied in study population, type of intervention, training dosage, length and type of follow up, outcome measures and assessment methods of the PFM. Citak et al [178] was the only study investigating effect of PFMT in a healthy population. The search strategy revealed three non-randomized trials in women with urinary incontinence [191-193], showing some effect after pelvic floor rehabilitation, including PFMT. The PEDro score assessing quality [194] of the 13 RCTs ranged from four to eight and are summarized in Table 2.

Effect of pelvic floor muscle training on vaginal symptoms and symptoms of sexual dysfunction in the general female population

Six studies reported an overall positive effect of physical therapy for different aspects of sexual dysfunction: improved arousal, lubrication and orgasm, less problems with sex-life spoilt by urinary symptoms, increased control and stronger PFM, "tighter vagina", increased libido, less pain, increased sensibility and awareness around the pelvic floor, improved confidence and partner's sexual satisfaction [181, 184-186, 189, 190]. Of these, three studies included PFMT as the only treatment option [181, 184, 185]. Four studies showed contradictory results [182, 183, 187, 188].

Effect of pelvic floor muscle training on vaginal symptoms and symptoms of sexual dysfunction during pregnancy and after delivery

Two RCTs assessed the effect of PFMT after delivery [178, 179] and one study assessed the effect of PFMT during pregnancy [180]. Citak et al [178] reported improved arousal, lubrication and orgasm in favour of the intervention group seven months after childbirth, whereas the study by Mørkved et

al [180] found improved satisfaction with sexual life six years after the intervention. The RCT by Wilson and Herbison [179] showed no effect after PFMT on pain, interest in and satisfaction with sex, arousal, ability to orgasm, adequacy of vaginal tone and general feeling. The latter study had almost 37% loss to follow up with over twice as many in the intervention group. Differences in dosage, follow-up and start of the intervention period may also explain the conflicting results.

PFM strength improved in the study by Citak et al [178] and Mørkved et al [180], but not in the study by Wilson and Herbison [179]. There were no report of any association with improved PFM strength and improvement in sexual function.

Table 1. Randomised controlled trials evaluating the effect of pelvic floor muscle training on female sexual function. From Tennfjord MK, Ellström Engh M, Bø K. Role of physical therapy in the treatment of female sexual dysfunction. In: Costantini E, Villari D, Filocamo M, eds., editors. Female sexual function and dysfunction: Springer, Cham; 2017.

Author/year	Design	Study population	Intervention period	Dosage	Follow-up	Loss to follow up	Outcome measures	Results
During pregnancy and after childbirth								
Citak et al, 2010	Single blinded RCT	118 primiparous women (mean age 22.6)	4th-7th month postpartum	*PFMT*: 10 reps increasing to 15 reps daily, 2 sec contraction increasing to 5 and 10 sec *Control*: no treatment	*PFMT*: Telephone and meeting with nurse twice in the first month and once in the following months	Total: 43 (36.4%) Training:21 (17.8%) Control:22 (18.6%)	FSFI. PFM strength assessed by digital palpation and manometer	Positive effect in favor of training group on arousal, lubrication and orgasm. Improvement in PFM strength
Wilson and Herbison, 1998	RCT	230 incontinent primi/multi-parous women (mean age 28.4)	3-12 months postpartum	*PFMT*: 80-100 reps x 8-10 daily *Cones*: 20-100 g 15 min daily *PFMT and cones*: see above *Control Group:* standard treatment as recommended at hospital, but no	*PFMT and cones*: PT meeting 3, 4, 6 and 9 months after delivery	Total: 85 (36.9%) Intervention: 59 (25.7%) Control:26 (11.3%)	Postal questionnaire: pain, interest in and satisfaction with sex, arousal, ability to orgasm, adequacy of vaginal tone and general feeling. PFM strength and endurance assessed by	No between group difference

				follow up			perinometer	
Mørkved et al 2007	Single blind RCT (Abstract)	280 primiparous women with and without UI followed up after 6 years (mean age at inclusion 27.5)	Btw 20th and 36th months of pregnancy for 12 weeks	*PFMT*: 6–8 sec hold near maximum contraction with 3-4 fast contractions in 4 series. Resting period was about 6 seconds. Home training 8-12 repsx2 daily *Control*: no treatment	*PFMT*: Weekly group training led by PT	Total: 106 (38%)	Postal questionnaire: satisfaction with sex after delivery	Improved satisfaction in favor of training group
General female population								
Bø et al 2000	RCT	59 women with SUI (mean age 50.7)	6 months	*PFMT*: 8-12 x 3 daily (near maximum PFM contractions) *Control*: no treatment	*PFMT*: Weekly group training with PT	Total: 4 (6.8%) Training: 4 (6.8%) Control: 0	QoLS-N and B-FLUTS. PFM strength assessed with manometer	Fewer problems with sex-life spoilt by urinary symptoms in favor of training group. Improved PFM strength
Brækken et al 2014	Partially blinded RCT	109 women with POP (mean age 48.9)	6 months	*PFMT*: 8-12 x 3 daily (near maximum PFM contractions) *Control*: no	*PFMT*: Individual training weekly/every other week with PT	Total: 2 (1.8%) Training: 1 (0.9%)	POP-specific questionnaire, semi-structured interview, PFM function assessed	Improvement in sexual function in favor of training group. Improved PFM strength and

				treatment		Control: 1 (0.9%)	by manometer.	endurance, not vaginal resting pressure
Liebergall-Wischnitzer et al, 2012	RCT	187 women with SUI (mean age 46.7)	3 months	*PFMT*: 25 min exercises daily, rapid/prolonged/gradual contractions *Paula method*: 45 min exercises daily	*PFMT*: 6 group sessions with PT *Paula method:* Weekly private session with instructor	Total: 61 (32.6%) PFMT: 38 (20.3%) Paula: 23 (12.3%)	I-QOL and PISQ-12	Sexual function improved in both groups, no between group differences
Yang et al 2012	RCT (pilot)	34 women with gynecological cancer (mean age 52.4)	4 weeks	*Biofeedback*: 20 min with 40 cycles with 10 sec of maximum activity followed by 20 sec of relaxation. 20 min with an intensive core exercise session. Home training 10 reps x 2 daily *Control*: no treatment	*Biofeedback*: 45-min exercise session and a 30-min counseling session per week for 4 weeks led by PT	Total: 10 (29.4%) Training: 5 (14.7%) Control: 5 (14.7%)	Australian Pelvic floor questionnaire on sexual function. PFM strength assessed with perineometer	Improved sexual function, numbers being sexually active and PFM strength increased in favor of the training group. Improved PFM strength
Hagen et al 2014	parallel-group, multicenter	477 women with symptomatic POP (mean age 56.8	16 weeks	*PFMT*: Individualized: 10 sec maximum hold x 10	*PFMT*: 5 individualized	6 months:	PISQ-12	Sexual scores (interference of prolapse symptoms

	RCT	years)		and 50 fast contractions x 3 daily *Control*: no treatment	sessions led by PT	Training: 36 (16%) Control: 36 (16%) 12 months: Training: 75 (33.3%) Control: 77 (34.7%)		with sex life) improved at 6 months after intervention in favor of training group. 12 months after intervention no difference
Eftekhar et al 2014	RCT	90 women with grade <3 POP (mean age 36.5 years)	8 weeks	*Treatment:* Vaginal and anal biofeedback, infra-red, reinforcement exercises and relaxation including PFMT. PFMT included 6-8 sec of contractions with 6 sec rest in between for 15 min x 3 daily	*Treatment*: Home training taught by PT	Total: 0%	FSFI	Physical therapy improved orgasm and severe dyspareunia compared to surgical group. Libido and arousal improved in both groups with no between group differences

				Surgery: rectocele repair				
Wiegersma et al 2014	RCT	287 women with symptomatic, mild POP (mean age 64.3 years)	3 months	*Treatment:* PFMT, myofeedback, electrical stimulation, the knack, lifestyle advice (diet, body weight, toilet habits), PFM relaxation and general relaxation. PFMT: 2-3 times daily, 3-5 x per week *Control:* no treatment	*Treatment*: Once a week with PT at first, then every 2nd and 3rd week with an average of 7 visits.	Total: 48 (16.7%) Training: 31 (10.8%) Control: 17 (5.9%)	PISQ 12 PFM function (ability to contract and relax) measured by digital palpation	No effect and no improvement of PFM function
Chambless et al 1984	RCT	36 women with orgasmic disorder (mean age 27.4 years)	6 weeks	*PFMT:* 10 min daily *Placebo*: 10 nonsexual images concerning vaginal sensations 10 min daily *Control:* no treatment	*PFMT and placebo*: Weekly mail and telephone contact	Total: 21(58.3%) PFMT: 8 (22.2%) Placebo: 10 (27.7%)	SAI-E (arousal, anxiety, satisfaction), WSQ (orgasmic responsiveness, frequency of orgasm, stimulation) and expectancy due to treatment or assessment only. PFM strength	Higher expectancy scores in PFMT and placebo, but no between group differences. All groups improved in orgasm, but no between group differences. No improvement in strength.

					Control: 3 (8.3%)	assessed with perineometer	
Trudel and Saint-Laurent 1983	RCT	12 women with orgasmic disorder (mean age not stated)	8 weeks	*PFMT:* 3 sec contract and 3 sec relax with increasing intensity for 20 min daily *Sexual awareness, relaxation, breathing (SARB):* different exercises for 20 min daily	*Both groups*: Home training with weekly phone contact with experimenter	0%	SAI, SII, clinical questionnaire (sexual reactions, stimuli needed to reach orgasm)	No effect in main outcome: orgasmic responsivity between groups. Higher scores for SARB group on sexual satisfaction, self-acceptance and perceptual accuracy scale, but no between group differences
Handa et al 2011	RCT	445 women with SUI, mean age 49.8 years	8 weeks (analysis done 3 months after intervention)	*Group 1:* continence pessary *Group 2:* behavioral therapy (pelvic floor muscle training and continence strategies) *Group 3:* combination therapy	*Group 1*: pessary fitted and used as desire to decrease UI *Group 2 and 3*: four visits over 8 weeks + home training with increasing difficulty over time	Total: 100 (22.5%)	Personal Experiences Questionnaire (SPEQ) (libido, arousal and dyspareunia) Pelvic Organ Prolapse-Urinary Incontinence Sexual Function Questionnaire	Change in measured aspects of sexual function did not differ among treatment groups. In those with improved SUI the combined therapy group had improved sexual

							(PISQ-12) PFM function measured with palpation	function compared to pessary group. In those with improved SUI the behavioral therapy had improved sexual function compared to pessary group. In those with no improved SUI, groups were similar. Change in PFM strength associated with improved SUI but not improved sexual function

Table 2. Methodological quality score (PEDro Scale) of controlled trials evaluating effect of pelvic floor muscle training in the general female population and during pregnancy and after childbirth. From Tennfjord MK, Ellström Engh M, Bø K. Role of physical therapy in the treatment of female sexual dysfunction. In: Costantini E, Villari D, Filocamo M, eds., editors. Female sexual function and dysfunction: Springer, Cham; 2017.

Study	E	1	2	3	4	5	6	7	8	9	10	Total score
Citak et al 2010	+	+	-	+	-	-	+	-	-	+	+	5
Wilson and Herbison, 1998	+	+	-	+	-	-	+	-	-	+	+	5
Mørkved et al 2007 Abstract	+	+	+	+	-	-	+	-	-	+	+	6
Bø et al 2000	+	+	+	+	-	-	+	+	-	+	+	7
Brækken et al 2014	+	+	+	+	-	-	-	+	+	+	+	7
Liebergall-Wischnitzer et al, 2012	+	+	+	+	-	-	+	-	-	+	+	6
Yang et al 2012	+	+	-	+	-	-	+	+	-	+	+	6

	E	1	2	3	4	5	6	7	8	9	10	Total
Pilot												
Hagen et al 2014	+	+	+	+	-	-	+	-	+	+	+	7
Eftekhar et al 2014	+	+	-	+	-	-	-	+	+	+	+	6
Wiegersma et al 2014	+	+	+	+	-	-	+	+	+	+	+	8
Chambless et al 1984	+	+	-	-	-	-	+	-	-	+	+	4
Trudel and Saint-Laurent 1983	+	+	-	+	-	-	-	+	-	+	+	5
Handa et al 2011	+	+	+	+	-	-	+	-	-	+	+	6

E-eligibility criteria specified,1-subjects randomly allocated to groups, 2-allocation concealed, 3-groups similar at baseline, 4-subjects blinded, 5-therapist administering treatment, 6-assesors blinded, 7-measures of key outcomes obtained from >85% of subjects, 8-data analyzed by intention to treat, 9-statistical comparison between groups conducted, 10-point measures and measures of group variability provided.

+, criterion clearly satisfied, - criterion is not satisfied, ? not clear if criterion is satisfied. Total score is determined by counting the number of criteria satisfied, except "eligibility criteria satisfied" score is not used to generate the total score. Total scores are out of 10.

*point 4 and 5 are unable to meet satisfactory criteria in all studies as subjects allocated to PFMT and therapists administering the treatment are aware of the intervention

Gaps of knowledge

Before project start there was lack of studies on:

1) Incidence and prevalence of dyspareunia and the relationship with PFM variables during pregnancy until 12 months after delivery. Presence of dyspareunia following childbirth has been well described, but there is lack of longitudinal studies on dyspareunia from before pregnancy till after childbirth, including level of bother. The evidence regarding PFM variables and dyspareunia are scarce. Furthermore the relationship with delivery variables and hormonal factors are conflicting.

2) The relationship between PFM variables and vaginal symptoms and coital incontinence 12 months after childbirth.

3) Conservative management on prevention or treatment of vaginal symptoms, coital incontinence and dyspareunia in primiparous women with and without major defect of the levator ani.

4) Intra –and interrater reliability and agreement of vaginal resting pressure, PFM strength and muscular endurance using Camtech AS, Sandvika, Norway.

Aims

Overall aims

The overall aims of this dissertation were: 1) to study presence of vaginal symptoms and symptoms of sexual dysfunction from before and during pregnancy and after childbirth, and study possible associations to PFM function, delivery variables and hormonal factors, 2) to evaluate effect of PFMT six months after delivery on vaginal symptoms and symptoms of sexual dysfunction in primiparous women with and without major levator ani defects, 3) to evaluate intra-and interrater reliability and agreement of vaginal resting pressure, PFM strength and endurance using manometer (Camtech AS).

Specific aims

Paper I: To study incidence and prevalence of dyspareunia cross-sectional and longitudinal, and level of bother from before pregnancy until 12 months after delivery. 2) To compare PFM variables in women with and without dyspareunia. 3) To compare delivery variables, numbers breastfeeding and numbers using hormonal contraceptives in women with and without dyspareunia.

Paper II: To study prevalence and bother of coital incontinence, vaginal symptoms and sexual matters 12 months after delivery, and whether coital incontinence and vaginal symptoms were associated with PFM variables.

Paper III: To study effect of PFMT on vaginal symptoms and sexual matters, dyspareunia and coital incontinence in primiparous women stratified by major or no defects of the levator ani muscle. To investigate whether a possible effect of PFMT was associated with a change in PFM variables.

Paper IV: To evaluate the intra- and interrater reliability and agreement of vaginal resting pressure, PFM strength and muscular endurance using manometer (Camtech AS).

Materials and methods

Study design and sampling

The papers were based on a prospective cohort study (Paper I-II), and a RCT (Paper III) (Figure 3) and an intra –and interrater reliability and agreement study (Paper IV). Paper I and II were a planned part of a prospective cohort study on pelvic floor changes and symptoms related to pelvic floor dysfunction during and after pregnancy [125, 195]. Data collection for paper I-III was performed at Akershus University Hospital in collaboration with the Norwegian School of Sport Sciences. The intra- and interrater reliability and agreement study was performed at a physiotherapy center (Vest-Helse) in Sandvika, Norway from March 2015 to April 2015. Women scheduled for delivery at Akershus University Hospital, Norway, from January 2010 until April 2011 were invited to participate when they attended their routine ultrasound examination at mid-pregnancy (N=2621).

In the RCT 175 primiparous were included six weeks after delivery (baseline). Follow up was at six months after delivery (post-intervention) (Figure 3). Paper III was a planned part of the RCT with the primary aim to assess the effect of PFMT on urinary incontinence after childbirth [196]. 2621 women (of all primiparous women scheduled for delivery between January 2010 until April 2011) were eligible for participation. From the cohort study (Paper I and II), 277 women who delivered vaginally and did not have a tear ≥3b were asked to participate in the RCT. Two-hundred-twenty-one women were eligible for participation (45 women had a caesarean section, six women had tears ≥3b, three had a stillborn delivery and two preterm delivery), of which 139 women agreed to participate. Thirty-six women were additionally recruited from the maternity ward at the hospital or from the community primary health care clinics within the same geographical area as the hospital.

The four papers had the following study design and samples:

Paper I: A cross-sectional study of 300 nulliparous women seen at four different time-points from mid-pregnancy until 12 months after delivery, including retrospective data from before pregnancy, and a longitudinal study based on the sample of 177 women attending all time points

of the data collection. Data on dyspareunia from six weeks postpartum were excluded due to few women resuming sexual intercourse.

Paper II: A cross-sectional study 12 months after delivery of 177 primiparous women attending all time-points of the data collection.

Paper III: A two-armed assessor blinded parallel group RCT starting from six weeks to six months after delivery. One-hundred-seventy-five primiparous women were stratified on major levator ani muscle defects or not verified by transperineal ultrasound before randomization into either PFMT or control group.

Paper IV: An intra -and interrater reliability and agreement study of 23 women. Participants were tested twice on the same day by two independent assessors (intrarater). One week later MKT re-tested the same group of women at the same time-point as test one (interrater).

Figure 3. *Flowchart of study participants in the cohort study and RCT*

Prospective cohort starting at gestational week 22, including 300 first time mothers
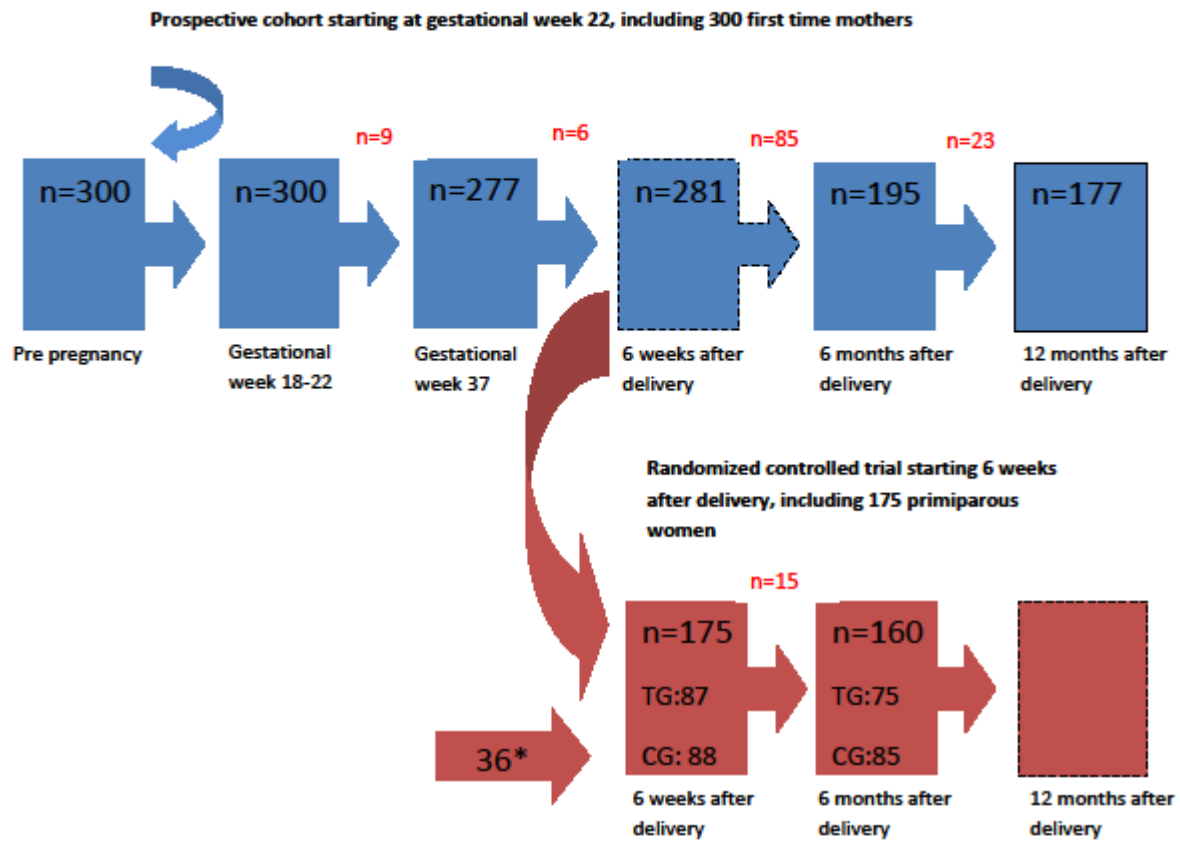
Figure illustrating the prospective cohort study (blue boxes) and the randomized controlled trial (red boxes), with numbers of participants at each stage of the data collection. Blue arrow indicating retrospective data for pre-pregnancy asked at gestational week 18-22. Red numbers is participants lost to follow up.

Paper I: Cross-sectional study including all time points of data collection (blue box with solid line), except six weeks after delivery (blue box with broken line). Longitudinal study following 177 women attending all time points of the data collection (blue box with solid line). Six weeks after delivery is not included (blue box with broken line).

Paper II: Cross-sectional study 12 months after delivery: n= 177 (blue box with solid line).

Paper III: Randomized controlled trial, n=175, starting six weeks after delivery with a follow up at six months after delivery (red boxes with solid lines). 12 months after delivery is not included in this thesis (red box with broken line).TG=training group, CG=control group. *36 women were additionally recruited from the maternity ward at the hospital or from the community primary health care clinics.

Inclusion criteria and clinical visits

Inclusion criteria

Paper I-II: Nulliparous, singleton pregnant woman able to speak and understand Scandinavian language were included. Exclusion criteria were multiple pregnancies and previous miscarriage after week 16 of pregnancy. Ongoing exclusion criteria were premature birth < week 32, stillbirth, serious illness to mother or child and subsequent pregnancies after six weeks of gestation. Women recruited to PFMT in the RCT (Paper III) were also excluded.

Paper III: Primiparous women able to understand Scandinavian languages who have had a vaginal delivery to a singleton infant after more than 32 weeks of gestation including normal or instrumental assisted deliveries were included. Women with and without vaginal symptoms were included. Exclusion criteria were caesarean section, ≥3b degree perineal tears and serious illness to mother or child. At the project hospital women with third or fourth degree perineal tears are routinely referred to physiotherapy for PFMT and could ethically not be allocated to a control group. Intrauterine foetal deaths/stillborn were also excluded.

Paper IV: Inclusion criterion was ability to contract the PFM correctly, defined as an inward movement and squeeze around the pelvic openings assessed by observation and vaginal palpation [34, 80]. Exclusion criterion was the inability to understand instructions given in any of the Scandinavian languages.

Clinical visits

The participating women came for appointed visits based on convenience with the routine controls at mid-pregnancy and six weeks after delivery. Further follow-up was scheduled six and 12 months after delivery (Figure 3)

Sample size

Inclusion of 300 nulliparous women into the cohort study (Figure 3) was based on sample size calculations for detecting changes in levator hiatus dimensions [125, 195].

Paper I-II: No specific sample size calculations were done to investigate presence of dyspareunia (Paper I) or for vaginal symptoms or sexual matters (Paper II). There were no sample size calculations to study associations between symptoms and vaginal resting pressure, PFM strength and muscular endurance during or after pregnancy. This present study was larger than the two studies on PFM function and dyspareunia available at project start [133, 146].

Paper III: Power calculation was done for the primary analyses on urinary incontinence [197] and was based on the results from a former study [198]. Since the study included stratified analysis on women with and without major levator ani defects, a sample size of 80 per group was estimated to be required. No specific power calculation was done for the planned secondary analysis on vaginal symptoms and symptoms of sexual dysfunction, but the trial aimed to include as many women as possible beyond what was estimated to be required. The small number of RCTs, variations in sample size and focus on different PFD in women after delivery [178-180], made it difficult to make sample size calculations for the present RCT during planning of the trial.

Paper IV: A convenient sample of 23 women was recruited to evaluate the intra –and interrater reliability and agreement of PFM function measured by manometer (Camtech AS). This was based on previous reliability studies in the field [76-79].

Data collection

Pelvic floor muscle function

For all studies (Paper I-IV) all participating women were given a short anatomy lecture and taught how to correctly contract the PFM using observation and palpation [34, 80] before measurement was taken. Vaginal resting pressure, PFM strength and muscular endurance were measured using a high precision pressure transducer connected to a vaginal balloon (Camtech AS, Sandvika, Norway) (Figure 4). The balloon catheter was compressed 10-20% to allow for air expansion at body temperature, before it was connected to the fibertip. A lubricating gel was applied to the balloon catheter. The device was positioned with the middle of the balloon 3.5 cm internal to the introitus in the vaginal high pressure zone [38, 199], a method found to be reliable an valid for assessment of PFM strength, with simultaneous observation of an inward movement of the catheter and no use of extra-pelvic muscle contraction [78, 80]. The atmospheric pressure on the balloon was calibrated to zero cmH$_2$O for each subject before it was placed in the vagina. Vaginal resting pressure was measured as the difference between the atmospheric pressure and the vaginal high pressure zone at rest, with no voluntary PFM activity, and was registered as cmH$_2$O. The measurement was taken before the first contraction and registered as a flat curve while the women was instructed to relax and given time to slowly breathe in and out. PFM strength was measured from the resting pressure line till the peak, not including the resting pressure, reported as the mean of three maximum voluntary contractions, and registered as cmH$_2$O. Local muscular endurance was defined as a sustained maximum contraction [45], and was quantified as the area

under the curve during ten seconds, measured during one attempt and registered as cmH$_2$Osec (Figure 5). The measurements were standardized and performed by two trained physiotherapists blinded to the questionnaire data and recorded with the woman in supine position, with legs bent and one leg resting against the wall on a flat bench with a small pillow underneath the head (Figure 4a). The physiotherapists involved in the cohort study (Paper I-II) and RCT (Paper III) were different than the ones involved in the reliability and agreement study (Paper IV), but the same procedure were followed.
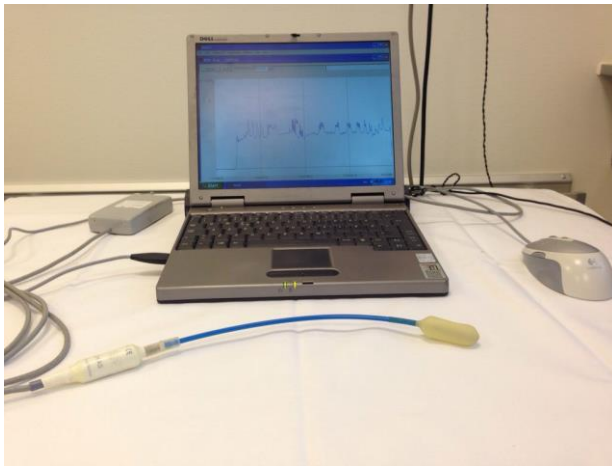
Figure 4. Camtech AS, Sandvika, Norway. From: Tennfjord, M.K., Engh, M.E. & Bø, K. Int Urogynecol J (2017). doi:10.1007/s00192-017-3290-y. An intra –and interrater reliability and agreement study of vaginal resting pressure, pelvic floor muscle strength and muscular endurance using manometer. Used with permission from Springer.

Manometry analysis

Data showing pressure values and pressure curves was stored at the apparatus' hard disk using the unique ID number for each woman. Each assessor analyzed their own measurement. The ID number of each woman was the only link to the clinical data. Questionnaire data and recordings from prior assessments were not available during analysis.
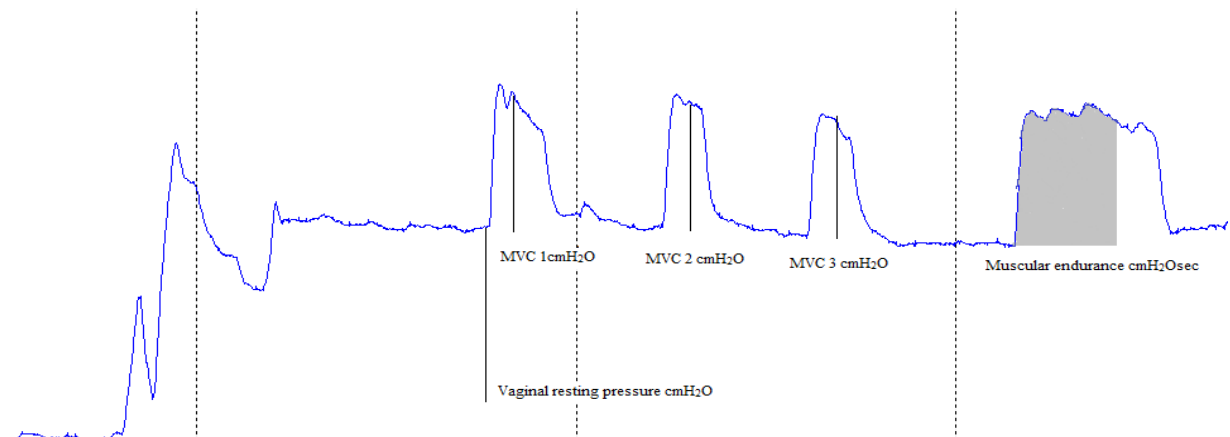
Figure 5. Manometer assessment showing vaginal resting pressure, PFM strength and muscular endurance. From Tennfjord, M.K., Engh, M.E. & Bø, K. Int Urogynecol J (2017). doi:10.1007/s00192-017-3290-y. An intra –and interrater reliability and agreement study of vaginal resting pressure, pelvic floor muscle strength and muscular endurance using manometer. Used with permission from Springer.

Questionnaire data

Electronic questionnaire, including background data and symptoms, were sent out prior to the clinical visits (Figure 3). The participating women were asked to fill in the questionnaire and recall the last four weeks for all time points. For pre-pregnancy symptoms the women were asked to recall the last three months before the pregnancy when they received the questionnaire at the first clinical visit at mid-pregnancy. Data from the electronic questionnaire were used for paper I-III. For paper IV the women were asked background questions when they met for their scheduled appointment.

ICIQ-VS [94] were used to assess vaginal symptoms and sexual matters. Level of bother was assessed on a scale from 0-10, were 0 were no bother and 10 were major bother. For paper II all questions were included, but no sum score was used. For paper III all questions were used except for question 5a:" Are you aware of a lump or bulge coming down in your vagina?" and question 6a: "Do you feel a lump or bulge coming out of your vagina, so that you can feel it on the outside or see it on the outside?". These questions were not the focus of this dissertation and published by Bø et al [200]. ICIQ-VS has shown good validity, reliability and is sensitivity to change [94], but has not undergone linguistic validation into Norwegian. This was done by our study group during planning of the study.

A Norwegian validated version of ICIQ-FLUTSsex was used to address symptoms of dyspareunia with question 4a: "Do you have pain when you have sexual intercourse?" (Paper I)

and coital incontinence with question 5a: "Do you leak urine when you have sexual intercourse?" (Paper II). Level of bother was asked for both questions [96, 100]. ICIQ-FLUTSsex has been established as a reliable, valid and responsive assessment tool to address sexual issues. [96]

Obstetric data

Data on delivery mode and other delivery variables were gathered from the women's electronic medical record (PARTUS) (Paper I-III). Data was anonymised and stored safely with the unique ID number of each woman as the only link to the data.

Ultrasound assessment of major levator ani muscle defects

Tomographic ultrasound imaging was performed by two trained gynaecologists using three and four-dimensional transperineal ultrasound (GE Kretz Voluson E8 - RAB4-8) in a standardized lithotomy position after voiding [67, 69]. The method was used to identify major defects of the levator ani muscle which allowed for stratification of major defects or not in the RCT (Paper III). The participating women were asked to perform three maximum PFM contractions, taught by the physiotherapists involved in the study. All three PFM contractions were recorded. The volume with the best contraction, defined as the volume with the largest reduction in the anterior-posterior diameter of the levator hiatus during contraction, was used for assessment of major levator ani defects [73]. Major defects of the levator ani muscle were diagnosed using the axial plane at maximal PFM contraction. For reference, the plane of minimal hiatal dimensions was used [73, 201, 202], described by Dietz et al 2005 [203]. Tomographic slices were taken at 2.5 mm slice intervals starting from 5 mm caudal to 12.5 mm cranial to the reference plane, giving eight slices [73, 201, 202]. Major defects were diagnosed when there was an abnormal insertion of the medial part of the levator ani muscle into the pubic bone, present in all three central slices [201]. The method has shown very good intra- and inter-rater reliability six weeks after childbirth [73].

Randomisation and blinding

The participants were randomised in blocks of ten to either PFMT or control with usual care after being stratified according to major or no defects of the levator ani muscle at the very end of the baseline assessment (paper III). The randomization sequence was computer-generated and opaque, sealed envelopes were used. All investigators were blinded to the participants' answers on the questionnaire when performing the clinical measurements. The project coordinator

(midwife) administered the allocation process outside the clinical assessment room. Blinding of investigators to group allocation during the clinical measurements was therefore possible throughout the study.

Intervention

The training group attended a weekly PFMT class led by one of three trained physiotherapists at three different locations for four months, starting six weeks after delivery. The exercise protocol has been described previously by Bø et al [204, 205] and Mørkved and Bø [206] and follows recommendations for strength training [166, 207]. In between sets of PFM exercises, body awareness, breathing, relaxation, and strength exercises for the abdominals, back, arms and thigh muscles were done. In addition, the intervention group was instructed to perform three sets of 8–12 close to maximum PFM contractions daily at home. The intervention group also received an additional booklet and a DVD for further instructions on PFMT. Participants recorded adherence to the home program in a training diary, and the physiotherapists registered class participation. The control group received no intervention beyond the written information received at discharge from the hospital containing information about postpartum PFMT and the individual assessment of how to perform a correct PFM contraction.

Statistics

Demographic data and descriptive variables were given as mean values with standard deviations (SD), or in case of categorical data as frequencies with percentages. For all paper the level of significance was set to ≤ 0.05. Normality tests were performed. Data for all papers were analysed using SPSS, version 15 (SPSS, Inc., Armonk, NY, USA).

Paper I: Data from PFM variables were reasonable normally distributed. Both parametric and nonparametric analysis were performed and showed equal results (no difference), thus Independent samples t-test was used to analyze differences in PFM variables (vaginal resting pressure, PFM strength and muscular endurance) between groups of women with and without dyspareunia. This was done to ease comparisons with previous research on this topic [133, 146]. The relationship with dyspareunia and breastfeeding, use of hormonal contraceptives, and data on delivery variables, were analysed using Chi-squared test for independence and independent samples t-test potential were appropriate. To assess whether breastfeeding influenced PFM variables, independent samples t-test was used. An additional effect size calculation was done using the Cohen's criteria [208].

Paper II: Spearman's rank order correlation was used to analyze the relationship between PFM variables and coital incontinence and vaginal symptoms and was used because there was categorical data in the analysis. We were interested in the relationship between PFM function and vaginal symptoms at 12 months after childbirth. PFM variables were reasonable normally distributed, and both parametric and non-parametric tests showed equal results, thus Independent sample t-test was used. Differences between symptomatic and asymptomatic women on delivery mode were analysed separately using chi-square test. The effect of use of hormonal contraceptives and breastfeeding on vaginal symptoms was analyzed using Chi-square test. An additional effect size calculation was done using the Cohen's criteria [208].

Paper III: Between-group comparisons on categorical data for vaginal symptoms, sexual matters, coital incontinence and dyspareunia were analysed by chi-square and the Mantel-Haenszel risk ratio (relative risk, RR). For continuous data, an Independent sample t-test was used, and was chosen as these data were reasonable normally distributed. No within-group analysis was done due to different number of women having intercourse at baseline and post-intervention.

Data was analysed as intention-to-treat. In principle, when there were missing values post intervention, the method of last observation carried forward was used for categorical data. For continuous data the baseline value plus the added average change observed in the corresponding control group was used. Assumptions using intention-to-treat were explored through sensitivity analysis. An additional per protocol analysis was performed based on women completing the trial and adhering to more than 80% of the prescribed training sessions (at home and during group training) who did not have a new pregnancy post intervention at six months after delivery.

A sub-analysis was performed using multiple regression on the effect of PFMT (a difference in symptoms between training and control group seen at post intervention), to the possible change in PFM variables (assessed as the change in vaginal resting pressure, PFM strength or muscular endurance from six weeks to six months postpartum). Before change score was calculated, baseline comparability of PFM variables was ensured [209]. An interaction effect was tested across stratum groups (major or no defect of the levator ani muscle), symptom variables, and between training and control groups. The treatment effect was estimated using independent sample t-test.

Paper IV: intra-class correlation coefficient (ICC, average measures) using a two-way mixed model for absolute agreement with 95% confidence interval (CI). Common ICC values suggested were used; ICC <0.20 were considered poor, 0.21– 0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good and 0.81–1.00 very good. One sample t-test was used to calculate the mean difference (bias) between measurements and the corresponding SD and 95% CI. The Bland-Altman approach was

used to assess for systematic bias and random error using the mean difference and 95% limits of agreement (1.96 SD) [210]. Data from PFM variables were right-skewed as shown in The Bland-Altman plot. We did not proceed with further adjustments of the data [211] as this would make comparisons to other studies more difficult. Minimal detectable change was calculated to identify the smallest amount of change above the threshold of error using the SD of the mean difference (bias) multiplied with 1.96 SD [211].

Ethics

- The study procedures were in accordance with the World Medical Association, Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects (updated 2013) [212].

- The cohort study (Paper I-II) was approved by The Regional Medical Ethics Committee (REK South East 2009/170) and Data Protect Officer at Akershus University hospital (2799026) was informed. (Appendix I)

- The RCT (Paper III) was approved by The Regional Medical Ethics Committee (REK South East 2009/289a) and the Data Protect Officer at Akershus University hospital (2799004) was informed about the study. The study was registered at ClinicalTrials.gov (NCT01069484). (Appendix II)

- Information about the study was given and written consent was taken for all participants before entering the study (Appendix III including Paper I-III).

- For the intra –and interrater reliability and agreement study (Paper IV) The Regional Medical Ethics Committee (2014/1768) approved the study and the Data Protection Officer at Akershus University hospital (15-018) was informed about the study. Change in location was approved by the The Regional Medical Ethics Committee (2014/1768). Information about the study was given and written consent was taken for all participants before entering the study (Appendix IV)

Results

The following section summarizes the main findings from paper I-IV. For details, the reader is referred to the original papers included at the end of the thesis.

Paper I

Three hundred nulliparous women (mean age 28.7 mean 4.3, mean BMI 23.9 (SD 3.9)) were seen at four different time-points from gestational week 18-22 until 12 months postpartum, including retrospective data from before pregnancy (Figure 3). Presence of all severity dyspareunia was 27.8% at pre-pregnancy, 30.5% at gestational 22, 41.4% at gestational week 37, 44.6% at six months postpartum and 33.1 % at 12 months postpartum. Most women reported dyspareunia as "a little". Mean level of bother was lowest at pre-pregnancy: 3.4 out of 10, SD 2.5 and highest at 12 months after delivery: mean 5.1 out of 10, SD 2.9. No statistically significant difference in PFM variables was found between women with and without dyspareunia. A borderline significant difference in numbers with dyspareunia was found for women breastfeeding (>once daily) at six months after delivery 65/132 (49.2 %) versus those not breastfeeding (<once daily) 13/43 (30.2 %) (p=0.05). The effect size was considered low (Phi 0.165). No difference was found for women breastfeeding or not at 12 months after delivery, use of contraceptives at six or 12 months after delivery or in delivery variables between women with and without dyspareunia. Results from the longitudinal analysis showed new cases of dyspareunia both during pregnancy and after delivery, but total prevalence declined throughout the study.

Paper II

One-hundred-seventy-seven primiparous women were included for analysis 12 months after delivery. No significant differences was found in background characteristics for the total study sample at 12 months postpartum (n=177) or between women with no vaginal symptoms (n=47), with vaginal symptoms (n=130) and vaginal symptoms interfering with sexual life (n=61) (p>0.05).

Two (1.2%) out of the 166 women having sexual intercourse complained of coital incontinence. Overall, 73.4% (130) of all participants reported at least one vaginal symptom, whereas 34.5% (61) reported at least one vaginal symptom interfering with sexual life. At 12 months after delivery, 166 (93.8%) women had sexual intercourse. Of those eleven not having sexual intercourse at the time, two was due to vaginal symptoms and nine were due to "other reasons".

Symptoms of "vagina feels dry" were most prevalent (41.2%) followed by "vagina feels sore" (26%) and "vagina feels loose or lax" (26%). Thirty-two percent reported worries that the vaginal symptoms affected their sexual life and 23% reported that the relationship with their partner was affected as a result of the vaginal symptoms. The overall bother given by the question "how much do you feel that your sex life has been spoilt by vaginal symptoms?" was low (1.4 out of 10 SD 2.5).

Breastfeeding (>once daily) was associated with "vagina feels sore" compared to those not breastfeeding (<once daily); 24/64 (37.5%) versus 22/113 (19.5%) (p=0.01). A borderline significant difference was found for "vagina feels dry" in women breastfeeding versus those not breastfeeding; 33/64 (51.6%) versus 40/113 (35.4%) (p=0.05), respectively. No difference was found for use of hormonal contraceptives (p>0.05).

Vaginal resting pressure, PFM strength and muscular endurance showed a weak negative correlation with the symptom "vagina feels loose or lax": vaginal resting pressure: r_s=-0.16, p=-0.03, PFM strength, r_s=-0.20, p=0.007 and endurance, r_s=-0.21, p=0.005. The mean difference for women with and without the symptom was 3.6 cmH$_2$O (95%CI 0.7, 6.6) for vaginal resting pressure, 9.0 cmH$_2$O (95%CI 2.6, 15.4) for PFM strength and 80.0 cmH$_2$Osec (95%CI 32.6, 127.5) for muscular endurance.

There was no difference between women with no vaginal symptoms, with vaginal symptoms, and with vaginal symptoms interfering with sexual life when grouped by delivery mode. Looking at each vaginal symptom separately, "vagina feels loose or lax" was the only symptom associated with delivery mode (Table 3). When comparing women with and without the symptom, more women with the symptom had a normal vaginal delivery and an instrumental delivery versus caesarean section (p-value=0.02).

Table 3. *Distribution of symptom ("vagina feels loose or lax") with delivery mode.*

	No loose or lax	Loose or lax	Total
NVD	80 (68.4%)	37 (31.6%)	117
IVD	19 (73.1%)	7 (26.9%)	26
CS	32 (94.1%)	2 (5.9%)	34
Total	131	46	177

Paper III

One-hundred-seventy-five primiparous women were included at six weeks after delivery (mean 6.1 weeks, SD 0.9, range 3.9-8.7). Of these, 55 women were diagnosed with major levator ani muscle defect and 120 women with no defect of the levator ani muscle. Women in the control group had significantly higher education level than women in the training group (p=0.01). There was no association between education and any of the outcome variables of interest, so no further adjustments were done. No other differences in demographic variables were seen between groups at inclusion.

Among the 15 women lost to follow up, a higher percentage with lower education (46.7%) was found when compared with the 160 women completing the trial (15.6%) p=0.01 [196]. Ninety-six percent (72/75) of women in the training group adhered to 80% of the required attendance both for class sessions and for daily home training [196]. Two women from the control group were pregnant with their second child at six months after delivery.

No baseline differences were found for the outcome variables for vaginal symptoms, sexual matters, dyspareunia and coital incontinence except for "vagina feels sore" (p = 0.04). At follow-up six months after delivery no significant difference in outcome variables between groups for the total study sample (n=175) or in the stratum with no defects (n=120) were found. In the stratum with major defects (n=55) at post intervention significantly fewer women in the training group had symptoms of "vagina feels loose or lax" than the control group; RR: 0.55 (95% CI: 0.31, 0.95, p=0.03). Results from the multiple regression analysis showed that the effect of PFMT on the symptom "vagina feels loose or lax" in the stratum with major defects was not related to changes in PFM variables between training and control group. No difference was found between groups in relation to the question "how much do you feel that your sex life has been spoilt by vaginal symptoms?" (95% CI: -1.0, 0.6, p=0.59). The bother was considered low: mean 1.3 (SD 2.4) versus 1.1 (SD 2.1) for training and control, respectively. Similar results were found for all outcomes when performing a per-protocol analysis. There was no difference between groups in number of women not having intercourse at six months postpartum: 9/72 (12.5%) versus 10/83 (12%) (p=0.81) for the training group and control group, respectively.

Paper IV

Twenty-three women were recruited to the study. One woman was excluded due to inability to insert the probe (owing to restricted vaginal opening) and one woman did not meet for her scheduled appointment. Furthermore, one had to be excluded owing to poor quality of the pressure curves, leaving 20 women for analysis (mean age 56.2 years (range 27-71), mean parity 1.7 (range 0-3) and mean body mass index 23.6 (range 18.4-27.2, SD 2.4). The majority, 18 (85.7%), had a college/university degree and 10 (47.6%) reported having strenuous physical work. All participants were familiar with PFMT and they were all able to perform a correct PFM contraction after instructions. Fourteen (66.7%) reported that they sometimes experienced minor symptoms from the pelvic floor. Two were pregnant with their second child, second and third trimester.

Results from the intra -and interrater analysis showed considerable intervariation and the distribution of scores was right-skewed. ICC values were very good for all measurements for both intra -and interrater assessments (ICC >0.90).

Results from the one-sample t-test showed some systematic bias, only statistically significant for vaginal resting pressure (mean difference -2.44 (95% CI -0.36, -4.51) in the intrarater assessment and PFM strength (mean difference 2.24 (95% CI 0.03, 4.45) in the interrater assessment. The Bland-Altman plot showed random error to be present for all assessments as indicated by relatively wide limits of agreement. The results were more or less the same for both the intra – and interrater analysis. Outliers were observed in all measurements, representing the strongest women. Bias and minimal detectable change for intrarater agreement were; vaginal resting pressure: -2.44 ±8.7 cmH_2O, PFM strength -0.22 ±7.6 cmH_2O and muscular endurance 0.75 ±59.49 cmH_2Osec. Interrater agreement for vaginal resting pressure was: 1.36 ±9.0 cmH_2O, for PFM strength 2.24 ±9.0 cmH_2O and for muscular endurance 15.89 ±69.7 cmH_2Osec.

Discussion

Summary of main findings

Number of women reporting dyspareunia at each time point from pre-pregnancy until 12 months after delivery was close to or above 30%. The majority reported severity of dyspareunia as "a little". There was no difference between women with and without dyspareunia in relation to PFM variables or delivery variables. Longitudinal data showed new cases of dyspareunia during pregnancy and after delivery, but total prevalence of dyspareunia declined throughout the study. Other vaginal symptoms were prevalent (73.4%) 12 months after delivery, but few of the symptoms were severe, and 34.5% reported the symptoms to interfere with their sexual life. Overall bother of the vaginal symptoms were low (mean 1.4 out of 10). Significantly lower vaginal resting pressure, PFM strength and muscular endurance were found for women reporting "vagina feels loose or lax" 12 months after delivery compared to women with no symptoms. In the RCT, no effect of PFMT was seen in the total group (n=175) or in the group with no defects (n=120) on vaginal symptoms or the questions related to sexual function. However, the results indicate that PFMT may have a preventative effect of "vagina feels loose or lax" in women with major levator ani defects. Bias and minimal detectable change for manometer (Camtech AS) were; vaginal resting pressure: -2.44 $\pm$8.7 cmH$_2$O, PFM strength -0.22 $\pm$7.6 cmH$_2$O and muscular endurance 0.75 $\pm$59.49 cmH$_2$Osec (Intrarater). Interrater agreement for vaginal resting pressure was: 1.36 $\pm$9.0 cmH$_2$O, for PFM strength 2.24 $\pm$9.0 cmH$_2$O and for muscular endurance 15.89 $\pm$69.7 cmH$_2$Osec. Camtech AS seems less accurate for the strongest women in this sample, and a statistically significant improvement in PFM variables needs to exceed the minimal detectable change to be above the error of measurement.

Methodological considerations

Paper IV

Strengths and limitations

The use of Camtech AS, Sandvika, Norway (Figure 4b) has found to be reliable and valid for assessment of PFM strength, with simultaneous observation of an inward movement of the catheter and no use of extra-pelvic muscle contraction [78, 80]. This measurement was used in the data collection of PFM function and is included in all papers in this dissertation. Performing this

study last was probably not optimal as all the measurements had already been done, but the results and discussions concerning PFM function in Paper I-III in this dissertation, inspired us to carry out this study. In order to have a meaningful interpretation of the results from Paper I-III, Paper IV will be discussed first.

Strengths of paper IV was the study design, standardisation of test procedures (including vaginal resting pressure, PFM strength and muscular endurance) and the use of recommended statistical methods for assessing reliability and agreement [80, 199, 211, 213, 214]. Appropriate checklists were used [214]. The testers were trained by the main supervisor of the project and both testers had extensive experience in use of the method. The testers were also blinded to each other's results and results from the first test were unavailable during the second test.

A limitation was that we did not perform an apriori sample size calculation, but based the number of participants on previous studies assessing reliability of manometer measurements in this field [76-79]. Although this dissertation is on first time mothers, we choose a heterogeneous study population with the aim to be able to generalize the findings into everyday clinical life. This was also done for comparison with the previous reliability study by Bø et al [78]. We could still question the generalizability of the results. Our results indicate that the apparatus seem less accurate for the strongest women in this sample. We could perhaps have included more women into the study to give better estimates to the limits of agreement [213], but this would probably not changed the overall outcome, because of the large differences between those being weak and strong. Increasing sample size would not change the SD (measure of variability) in this sample which was used for calculating the limits of agreement [215].

Another limitation is that there were no predefined cut-off values for what is clinically significant. Ideally it should be defined a head of the study to help with the interpretation of the data and calculate sample size [210]. However, defining clinical cut-off values would be difficult to estimate, as there are no known "normal" values [11].

Interpretation

Our results show ICC values >0.90 for all measurements. This indicates high reliability [211]. However ICC values are not a robust measure of reliability, as it is largely sample dependent [210]. The large variation in scores amongst the participants would probably explain the high ICC values [210]. Whether the cut-off for determining good ICC values used in this present study and others [76, 77] are appropriate can be discussed as they are equal to that of other correlational studies like Pearson's r [211].

Including Bland and Altman plots with limits of agreement showed relatively large random errors. This was more or less the same for all measurements. Other studies report of some variation around their test differences [76, 78, 79]. Bø et al [78] test-retest study on PFM strength using Camtech AS concluded reproducible results, but with wide confidence intervals. This is in accordance with our results. To our knowledge, no studies on reliability or agreement of vaginal resting pressure and muscular endurance have been performed using Camtech AS. Using Peritron, Frawley et al [77] found ICC values for resting pressure to be 0.74 and for endurance 0.05. This indicates moderate and poor reliability, respectively [211]. However, our results are not directly comparable due to the use of different devices and probes [81, 216]. Further, Frawley et al [77] tested muscular endurance as multiple repeated muscle contractions (20 fast contractions). Our approach for testing muscular endurance was using the area under the curve (Figure 5) as this will include the force applied during a specific time (10 sec). To ensure maximal tension in the muscle it is commonly recommended that the contraction is held >six sec [170]. Local muscular endurance may also be defined as the ability to repeatedly develop near maximal or maximal force determined by number of repetitions [45], but using time in seconds will not give details on the exact force.

We were surprised that vaginal resting pressure had the same amount of error as did PFM strength and muscular endurance. Guaderrama et al [38] described the vaginal pressure profile during rest and squeeze and found the highest pressure in the mid zone of the vagina. Anatomic correlates of this pressure zone are not known, but Bø et al [199] found the highest squeeze pressure when the vaginal balloon was 3.5 cm inside from the vaginal introitus. There were however individual differences [199] and it has also been found marked asymmetry in both rest and squeeze pressure recordings from left to right and from anterior to posterior [38]. It comes to stand that measurement of vaginal resting pressure and squeeze pressure may be inheritably problematic due to the above considerations.

Indication of bias was seen for vaginal resting pressure and PFM strength for the intra –and interrater measurements, respectively, but the relatively large amount of random error may have precluded bias [217]. Bias could be a result of a learning effect, although we tried to rule out this by changing order of testers and giving the women opportunity to practice a few contractions before measurement was taken. Previous studies in this field have not found bias in their measurements [76, 78, 79].

Measurements recorded for the strongest women were more problematic than measurements recorded for the weakest women. The vaginal balloon may be pulled more inside the vagina during contraction, and may not have been in the high pressure zone [38], a possible explanation

for the outliers seen in our sample. For the balloon to stay in the high pressure zone [199], the assessors had to control the movement of the balloon which could yield a potential source of error. This may have led to the limits of agreement being wider apart than they should for the lowest scores and narrower than they should for the highest scores [210].

Clinical implications

As seen from our results on intra –and interrater agreement there were some random error present. Using Camtech AS, we emphasize that recordings should preferably be done by one tester, minimum two, and careful attention should be paid to a standardised procedure with placement of the probe. Probably, the use of Camtech AS would be more reliable in research settings as there is an average of results rather than individual results as we see in the clinic. However, to transfer data into clinical practice, examiners must be aware that a statistically significant improvement in PFM variables needs to exceed the minimal detectable change to be above the error of measurement [210]. Our results highlight a need to continue developing new instruments which is reliable and valid for the measurement of PFM function. The use of dynamometry might be more reliable and less sensitive to the movement of the apparatus during contraction as the device is more fixed inside the vagina [62]. However, this device is not commercially available [58]. Regarding vaginal resting pressure, vaginal surface EMG might be a more reliable tool to assess the resting condition of the PFM as no voluntary muscle activation is present and the measurement would be less biased by cross-talks from nearby muscles at rest than during contraction [11, 55].

Paper I-III

Strengths and limitations

All women scheduled for delivery at Akershus University Hospital (N=2621) were invited to participate in this study. The women in the cohort (Paper I and II) and RCT (Paper III), were similar to that of the total population (N=2621) with respect to age, marital status and body mass index (BMI), except that they had a higher level of education (75.3% versus 47%, respectively p<0.001) (non-published data). However, the inclusion criteria were the ability to understand Scandinavian languages, which make generalization to all primiparous women difficult.

Another strength is the low variation in time for attendance for each of the four visits minimizing possible bias due to the altered pelvic floor function during pregnancy and the natural remission after childbirth [218].

Few women were lost to follow up throughout the cohort study (11.6%). However, 71 women were excluded from the cohort to participate in the planned parallel ongoing RCT, leaving 177 women for analysis at 12 months after delivery. This was done because these women would have had a different intervention than the women remaining in the cohort. At 12 months after delivery, there were no significant differences regarding age, education or marital status amongst those women lost to follow up and those excluded, or for the women recruited to PFMT in the RCT compared to the women participating in the study at 12 months postpartum. In the RCT, (Paper III) more women in the training group versus the control group were lost to follow up. Differential lost to follow up may have biased the results [219], but sensitivity analysis (intention-to-treat and per-protocol) showed similar results, making bias less likely. Intention-to-treat analysis maintain the groups similar apart from the random variation, but the approach with imputation of missing data may be a limitation as it may give a biased estimate of the treatment effect [220]. However, few women were lost to follow up and reasons for loss to follow up were not related to the intervention itself.

The randomization procedure adds strength, and is vital for the internal validity of the trial [221-223]. Triple blinding is considered the strongest design in the RCT [224], but this was not possible in our exercise trial. There was imbalance at baseline where the control group had statistically higher educational level than the treatment group, which may have underestimated our results.

Appropriate checklists for the observational studies Paper I and II (STROBE) [225] and for the RCT Paper III (CONSORT) [221] were used and helps secure transparency.

Lack of a-priori sample size calculations is a limitation (Paper I-III). This may give insufficient statistical power and lead to a type 2 error [226]. This may have been the case regarding less common variables not reaching statistical significance in Paper II and III. However, the finding "vaginal feels loose or lax" was seen as common and clinically relevant (26% 12 months after delivery). Paper I was larger than the studies finding no difference between women with and without dyspareunia in relation to PFM function after childbirth [133, 146, 227]. All these studies had performed an apriori sample size, but differences in study design and follow-up make comparisons with our study difficult.

Neither the ICIQ-VS [94] nor the ICIQ-FLUTSsex [96] covered all aspects of sexual function, e.g.; satisfaction, orgasm, desire, partner, social life. However, the questionnaires allowed us to study a

range of vaginal symptoms that was thought to be relevant in this group of women, how the symptoms affected sexual life, including bother of the problem, which adds strength. Another limitation was that the questionnaires were not validated amongst pregnant women or in women after childbirth. The validation of ICIQ-VS into Norwegian done by our study group may also add a limitation, although these questions were thought to be relatively easy to interpret.

The cross-sectional analysis in Paper I and II does not allow us to determine the time order of events between PFM function and symptoms, or evidence of causation [228]. We therefore included the longitudinal analysis in paper I looking into incidence and prevalence of dyspareunia among the same women in the cohort. Pre-pregnancy dyspareunia was asked retrospectively, which could bias the results [228]. Although ideal, following women from before their first pregnancy is a well known difficulty.

P-values were reported for all tests without adjusting for multiple testing (Paper II-III). This involves a risk of making a type 1 error [229]. If the outcome variables were independent of each other an adjustment for multiple testing would perhaps had been more appropriate [229, 230]. A possibility could be to exclude some questions that correlated with each other, but the use of sexual matters (the questions covering all vaginal questions) made us use all vaginal symptoms in the questionnaire. The results of statistically significance were therefore judged upon clinical relevance and left unadjusted.

Paper I

Interpretation

No difference in PFM variables were found for women with and without dyspareunia in our study. Our findings confirm the results from existing literature on associations with dyspareunia and PFM strength after childbirth [133, 146, 227]. Studies from the general female population assessing women with sexual pain disorders (superficial) compared to asymptomatic controls, suggestions of lower PFM strength [231, 232] and muscular endurance [233] have been found. Reasons for these conflicting results may be that we did not differentiate dyspareunia as superficial or deep, which was a diagnostic criteria in those studies from the general female population. Distal vaginal palpation may elicit vaginisimus, which are reflex contractions of the superficial PFM and levator ani muscle. With deeper vaginal palpation other pelvic floor disorders may be triggered [234].

Vaginal resting pressure has been though to be a factor in relation to dyspareunia [11]. We did not find any difference in vaginal resting pressure among women with and without

dyspareunia, and vaginal resting pressure was not included in the other studies investigating dyspareunia in women after childbirth [133, 146, 227]. Using vaginal palpation [232], EMG [233, 235] and transperineal ultrasound [231] in women with sexual pain disorders compared to asymptomatic controls from the general population PFM hyper tonicity have been found. However, it has not been clearly established whether it is the pain that causes the PFM hyper tonicity or if it is the hyper tonicity that causes the pain [236]. There are no gold standard for measurement of PFM function [11] and no consensus for cut-off points for determining PFM hyper tonicity [236]. Recent ultrasound studies have shown alterations in vaginal anatomy and function during pregnancy [125] and after childbirth [195, 237, 238]. This may make measurement of PFM function, especially vaginal resting pressure, problematic. A larger sample including more women with more severe dyspareunia could have been appropriate in our study, as there may be different findings in PFM function according to severity of pain and diagnosis. Dyspareunia gradually declined throughout pregnancy. Still, at 12 months after delivery 34 (19%) reported dyspareunia. Although most cases were mild, bother was 5.1 out of 10 (cross-sectional data from 12 months). The relatively large SD at the different time-points indicates however a wide range in bother of dyspareunia. From the longitudinal analyses 18% were new cases from six months after delivery. This is in contrast to previous literature [2, 3, 114], were dyspareunia seems to be a problem within the first six months before women resume intercourse. After this project started in 2010 a few longer-term studies have been found reporting dyspareunia as bothersome and that it may impact on quality of life 18 months [239, 240] and five years after delivery [238]. De Souza et al [241] reported of improved pain levels (FSFI score) one year after delivery [241].

In our study, women breastfeeding reported more dyspareunia at six months after delivery, but the finding was only borderline significant; 65 (49 %) amongst those breastfeeding versus 13 (30%) of those not breastfeeding (p=0.05). It is difficult to draw overall conclusions on the impact of breastfeeding on dyspareunia due to the conflicting results from previous research finding an association [108, 110, 111] and not finding this association [113, 115, 131].

There was no difference between women with and without dyspareunia in relation to delivery variables in our study. There may be several reasons for this. From the longitudinal analysis numbers with dyspareunia prior to pregnancy was 27.1%. This means that dyspareunia was not simply a "product" of the delivery, as confirmed by other studies [240, 242]. Second, the question of dyspareunia was not differentiated as pain on first vaginal intercourse after childbirth or subsequent intercourse. MacDonald et al [239] reported that 85.7% of primiparous women experienced pain on first vaginal intercourse and that 23.3% of those described the pain as

severe. In our cohort most women resumed intercourse between six weeks and six months after delivery. Asking about dyspareunia the last four weeks at six months after delivery may not have captured those with pain on first sex and/or those with more intense dyspareunia. Furthermore, the literature on delivery mode and dyspareunia is conflicting [243]. Operative vaginal deliveries has been found to be associated with dyspareunia in large studies on postnatal women [111, 112, 129, 130, 240]. However, conflicting results exists [109, 110, 113, 132, 133, 135]. These latter findings may partly be explained by lower sample size, which could also be a reason for the lack of association in our study. Literature on associations with episiotomy and dyspareunia is also conflicting, were some studies find an association [131, 240], and others don't [113]. Since dyspareunia is a symptom it may be an end-product of a complex circle and reveal little about the cause or pathophysiology [43, 107, 120].

Paper II

Interpretation

The focus on vaginal symptoms in relation to sexual function during pregnancy and after childbirth has emerged since this project started in 2010 [143, 238, 242, 244-247]. Before this project started only a few studies had looked into symptoms other than dyspareunia, but there was lack of data beyond six months after childbirth [108, 111]. A few other studies have been published since then, assessing vaginal symptoms 12 months after delivery [131, 242]. Prevalence of vaginal symptoms (e.g. vaginal tightness and vaginal laxity) has been found more or less in the same range as our study.

One literature review from 2012 [2] as well as previous reviews [3, 114] have concluded with lack of studies addressing bother in relation to symptoms of sexual dysfunction. Roos et al [248] found that only half of the women reporting a sexual complaint reported it to be bothersome. This underlies the importance of addressing sexual problems in the clinic, as well as the bother of the complaint. We addressed nine questions related to vaginal symptoms and found that the overall bother of symptoms on sexual life was low. This was supported by van Delft et al [143, 244]. Twelve months after delivery, 93.8% of the women had sexual intercourse in our study. Our questionnaire does not address frequency of intercourse, which we acknowledge as an important factor. However, low mean overall bother of vaginal symptoms support our findings that vaginal symptoms 12 months after childbirth does not seem to affect the sexual life of primiparous women to a great extent. However, the 2.5 SD indicates some range in bother.

Breastfeeding was found to be associated with vaginal dryness and soreness 12 months after childbirth. Although vaginal dryness was barely significant (P-value=0.05), vaginal soreness and

breastfeeding was a stronger finding (P-value=0.01). Vaginal soreness and dryness was found to correlate in our study (p<0.01). Dyspareunia correlated with vaginal soreness and dryness (p<0.01). Since breastfeeding has shown to have a profound effect of postpartum hormonal levels [2], affecting negatively on vaginal lubrication [5, 127], this finding may be clinically relevant.

The only symptom that correlated significantly with PFM function was "vagina feels loose or lax". Differences in PFM strength and muscular endurance between women with and without the symptom were also above the error of measurement and thought to be clinically significant (9.0 cmH$_2$O and 80.0 cmH$_2$Osec, respectively). Differences in vaginal resting pressure was however low (3.6 cmH$_2$O). From clinical experience and previous research [245] women may have a feeling of increased vaginal laxity. It may that this feeling is more subjective than objective. Most likely the finding of reduced PFM strength and muscular endurance in women with loose or lax vagina was mediated through mode of delivery as more women with this symptom had had a vaginal delivery and instrumental delivery compared to caesarean delivery in our study. This finding was supported by Thibault-Gagnon et al [245]. We did not control for delivery mode as we were interested in the situation between PFM function and vaginal symptoms 12 months after childbirth.

There are several studies reporting on the relationship with delivery mode and levator avulsion on various vaginal symptoms [143, 238, 242, 244-246]. An association between levator avulsion and vaginal laxity has been found [143, 244, 245]. However, Laterza et al [249] found no difference among women with and without levator avulsion on the sum score of different sexual function domains, including vaginal laxity. The main focus in this present paper was the relationship between PFM variables and vaginal symptoms 12 months postpartum and no analysis regarding the effect of defects was performed. Further discussion related to defects is below related to Paper III.

Paper III

Interpretation

From Table 1, 13 RCTs on PFMT for prevention and treatment of symptoms related to sexual dysfunction were found. These were in either postpartum women [178-180], in women with pelvic organ prolapse (POP) [184-187], in women with stress urinary incontinence (SUI) [181, 188, 189], in women with orgasmic disorders [182, 183] and in gynecological cancer patients [190]. No new RCTs were found for women during or after pregnancy after project start. The three RCTs in women after delivery published prior to project start [178-180] will therefore be discussed in light of the findings from our study.

The only symptom that had effect after PFMT was on "vagina feels loose or lax". This effect was seen in the stratum with major defects only. This finding may be relevant as several studies find an association with levator avulsion and PFM strength [143, 158-160, 247, 250] and vaginal laxity [143, 244, 245]. Although diagnosing major levator ani defects has shown good reliability [72, 73], we cannot rule out false positives due to haematoma early after birth [251]. None of the other RCTs in women after delivery [178-180] studied the effect of PFMT on vaginal laxity.

We did not find an association with effect after PFMT and change in PFM strength. There was a low overall difference in change between the training and control group in PFM strength from baseline to follow-up (3.6 cmH$_2$O) in favour of the training group [200]. From the results of Paper IV this is well below the minimal detectable change of 9.0 cmH$_2$O for PFM strength. The same training program has been utilized previously demonstrating a change above the minimal detectable change for PFM strength [204, 205, 252]. It may be that timing of our trial was not optimal to study vaginal symptoms and symptoms of sexual dysfunction as there seems to be a natural resolution after delivery until six months [195]. This may also explain the lack of findings from the same trial on urinary incontinence [196] and pelvic organ prolapse [200]. Furthermore, women may have less often sex during this period, a possible explanation for the lack of findings for the questions on sexual matters in our study. Since there are no normative data to assess PFM function in general, a non-statistically significant improvement in PFM variables after PFMT does not mean lack of a clinical significant improvement in symptoms [253]. A positive effect of PFMT may also influence on psychosocial aspects such as improved self-esteem and self-acceptance, body awareness and satisfaction [184]. Both Citak et al [178] and Mørkved et al [180] showed an increase in PFM strength and symptoms studied after PFMT. However, none of the studies reported on any correlation with improvement in sexual function and improvement in PFM strength.

Paper I-III

Clinical implications

Despite the high prevalence of dyspareunia (Paper I) and other vaginal symptoms (Paper II) during pregnancy and after childbirth the overall bother of symptoms affecting sexual life was low. This should be reassuring to the majority of women. Openness and understanding regarding women expressing bothersome symptoms is important.

From clinical experience some postpartum women and health professionals fear that PFMT may create and exacerbate PFM pain and dyspareunia. Some literature also suggest that PFMT should

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be avoided in women with hypertonic PFM, described as "short" or "tight" PFM [4, 7]. This present RCT did not show any effect of PFMT on dyspareunia, or adverse effects. Other RCTs in women after delivery did not find effect of PFMT on dyspareunia [178, 179]. One observational study in women after delivery [254] found no adverse effect of PFM contractions on pain early after delivery. Amongst nulliparous women with provoked vestibulodynia [255] a PFM contraction indicated lower vaginal resting pressure. In general, therapists should be careful giving recommendations based on theories with poor supporting evidence.

We have shown that women reporting "vagina feels loose or lax" had lower PFM strength and muscular endurance than those not reporting this symptom (Paper II). We have also shown that PFMT may have a preventative effect of "vagina feels loose or lax" in women with major levator ani defects, although no effect of PFMT was seen for other vaginal symptoms or the questions related to sexual function (Paper III). From a clinically point of view the findings of effect after PFMT is important. There has been an increasing amount of women wanting surgical help for this problem (loose or lax vagina) [68]. This corresponds to what we have seen in the clinic. In addition there are limited data on prevention of PFD [256], and evidence of changes in pelvic floor physiology already during pregnancy [125]. Whether or not vaginal laxity is a sexual problem remains unknown. Some studies include vaginal symptoms as a sexual dysfunction [242, 249], whereas others describe the vaginal symptoms as separate from a sexual dysfunction [143, 238, 244, 245]. The fact that few women were bothered by their vaginal symptoms makes this unlikely, although individually, symptoms may be more bothersome.

To date, there are no clinical guidelines for prevention or treatment of symptoms of sexual dysfunction, and due to the large heterogeneity of studies related to women's sexual function, recommendations through pooled effects in systematic reviews are challenging [223, 257]. One systematic literature review from 2015 on PFMT in women with sexual dysfunction [258] concluded that PFMT gave an overall improvement of at least one sexual variable which was studied. The authors emphasized that the results needs to be interpreted with caution due to methodological limitations of the studies included. It may be that women would benefit from a variety of interventions, including PFMT, and a multidisciplinary approach for their problems [259]. The results from the present thesis should be followed up in future studies [229].

Studies investigating long-term effects after pregnancy and childbirth would be of importance. Recent studies have shown that delivery mode impact on dyspareunia and various sexual complaints 18 months [240] and five years [238] after the first birth. The reported complaints are probably not solely due to mode of delivery due to the multifactorial picture of women's sexual function [4, 256].

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Conclusions

I.   Numbers with dyspareunia was high before, during and after pregnancy. New cases of dyspareunia were seen throughout pregnancy and postpartum, but numbers with dyspareunia decreased throughout the study. The severity of dyspareunia was described as a "little". No relationship with dyspareunia and PFM variables or delivery variables was found.

II.   12 months after delivery prevalence of vaginal symptoms was high, but the overall bother of symptoms affecting sexual life was low. Women reporting "vagina feels loose or lax" had lower vaginal resting pressure, PFM strength and muscular endurance.

III. Six months after delivery, no effect of PFMT was seen in the total group or in the stratum with any defects on vaginal symptoms or symptoms of sexual dysfunction. However, the results indicate that PFMT may have a preventative effect of "vagina feels loose or lax" in women with major levator ani defects.

IV.   Clinical reference values for PFM variables were found for: intrarater agreement for vaginal resting pressure: -2.44 $\pm$8.7 cmH$_2$O, for PFM strength -0.22 $\pm$7.6 cmH$_2$O and for muscular endurance 0.75 $\pm$59.49 cmH$_2$Osec. Interrater agreement for vaginal resting pressure was found to be: 1.36 $\pm$9.0 cmH$_2$O, for PFM strength 2.24 $\pm$9.0 cmH$_2$O and for muscular endurance 15.89 $\pm$69.7 cmH$_2$Osec. Manometry (Camtech AS) seems less accurate for the strongest women in this sample, and a statistically significant improvement in PFM variables needs to exceed the minimal detectable change to be above the error of measurement.

Further research

I.   Further research into studies assessing PFM variables in relation to various severity types of dyspareunia, differencing dyspareunia as superficial or deep and dyspareunia at first or subsequent intercourse after delivery. Follow-up studies years after first delivery is needed and knowledge into factors influencing dyspareunia before, during and after childbirth would be important.

II. Further research into factors influencing vaginal symptoms and symptoms of sexual dysfunction are needed. To study less common symptoms e.g. coital incontinence, large epidemiologic studies are needed. Follow-up studies years after the first delivery would be important.

III. There is need for well powered high quality RCTs with the primary focus into vaginal symptoms and symptoms of sexual dysfunction. The start of the intervention should preferably be after six months after delivery as most women resume intercourse at this point. The use of validated questionnaires is important, and a more qualitative approach to capture in-depth knowledge into women's sexual function.

IV. To continue further improvement of reliable and valid methods for measurements of the PFM to be used in clinic and research.

References

1. Health NIoP. Medical Birth Registry of Norway 2017 [Available from: https://statistikk.fhi.no/mfr/.

2. Leeman LM, Rogers RG. Sex after childbirth: postpartum sexual function. Obstet Gynecol. 2012;119(3):647-655.

3. Abdool Z, Thakar R, Sultan AH. Postpartum female sexual function. Eur J Obstet Gynecol Reprod Biol. 2009;145(2):133-137.

4. Graziottin A. Female sexual dysfunction. In: Bø K, Berghmans B, Mørkved S, Van Kampen M, editors. Evidence based physical therapy for the pelvic floor Bridging science and clinical practice. 1 ed. Philadelphia: Churchill Livingstone Elsevier; 2015. p. 243-270.

5. Berman J, Berman L, Kanaly K. Female sexual dysfunction: new perspectives on anatomy, physiology, evaluation and treatment. EAU Update Series. 2003;1(3):166-177.

6. Shafik A. The role of the levator ani muscle in evacuation, sexual performance and pelvic floor disorders. International urogynecology journal and pelvic floor dysfunction. 2000;11(6):361-376.

7. FitzGerald MP, Kotarinos R. Rehabilitation of the short pelvic floor. II: Treatment of the patient with the short pelvic floor. Int Urogyn J. 2003;14:269-275.

8. Bø K. Overview of physical therapy for pelvic floor dysfunction. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 1 ed. Philadelphia: Churchill Livingstone elsevier; 2015. p. 1-8.

9. Gynecologists TACoOa. Committee opinion: Physical activity and exercise during pregnancy and the postpartum period. 2015;650.

10. Boyle R, Hay-Smith EJ, Cody JD, Morkved S. Pelvic floor muscle training for prevention and treatment of urinary and faecal incontinence in antenatal and postnatal women. Cochrane database of systematic reviews. 2012;10:CD007471.

11. Messelink B, Benson T, Berghmans B, Bo K, Corcos J, Fowler C, et al. Standardization of terminology of pelvic floor muscle function and dysfunction: report from the pelvic floor clinical assessment group of the International Continence Society. Neurourol Urodyn. 2005;24(4):374-380.

12. Healey CH, Borley NR, Mundy A. True pelvis, pelvic floor and perineum. In: Standring S EH, Healy J.C, Johnson D, Williams A, editors., editor. Gray's anatomy: The anatomical basis of clinical practice. Edinburgh: Elsevier Churchill Livingstone; 2005. p. 1357-1371.

13. Ashton-Miller JA, DeLancey JO. Functional anatomy of the female pelvic floor. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 2 ed. Philadelphia: Churchill Livingstone Elsevier 2015. p. 19-34.

14. Dietz HP, Hoyte L, Steensma AB. Atlas of Pelvic Floor Ultrasound. Dordrecht: Springer; 2008.

15. Herschorn S. Female Pelvic Floor Anatomy: The Pelvic Floor, Supporting Structures, and Pelvic Organs. Reviews in urology. 2004;6(5).

16.   Bø K, Aschehoug A. Strength training. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 2 ed. Philadelphia: Churchill Livingstone elsevier; 2015. p. 117-130.

17.   Critchley HOD, Dixon JS, Gosling JA. Comparative Study of the Periurethral and Perianal Parts of the Human Levator ani Muscle. Urol Int. 1980;35:226–232

18.   koelbl H, Strassegger H, Riss PA, Gruber H. Morphologic and functional aspects of pelvic floor muscles in patients with pelvic relaxation and genuine stress incontinence. Obstet Gynecol. 1989;47(5):789-195.

19.   Hoffman BL, Schorge JO, Schaffer JI, Halvorson LM, Bradshaw KD, Cunningham FG. Williams Gynecology. 2 ed. Texas: McGraw-Hill Medical; 2012.

20.   Delancey JOL. The anatomy of the pelvic floor. Curr Opin Obstet Gynecol. 1994;6:313-316.

21.   Kearney R, Sawhney R, DeLancey J. Levator ani muscle anatomy evaluated by origin-insertion pairs. Obstet Gynecol. 2004;104(1):168-173.

22.   Margulies RU, Hsu Y, Kearney R, Stein T, Umek WH, DeLancey JOL. Appearance of the Levator Ani Muscle Subdivisions in Magnetic Resonance Images. Obstet Gynecol. 2006;107:1064–1069.

23.   Ashton-Miller JA, Howard D, DeLancey JO. The functional anatomy of the female pelvic floor and stress continence control system. Scand J Urol Nephrol Suppl. 2001(207):1-7; discussion 106-125.

24.   DeLancey JO, Ashton-Miller JA. MRI of intact and injured female pelvic floor muscles. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 1. 2 ed. Philadelphia: Churchill Livingstone Elsevier 2015. p. 97-109.

25.   Tunn R, DeLancey JO, Howard D, Thorp JM, Ashton-Miller JA, Quint LE. MR imaging of levator ani muscle recovery following vaginal delivery. International urogynecology journal and pelvic floor dysfunction. 1999;10(5):300-307.

26.   Percy JP, Swash M, Neill ME, Parks AG. Electrophysiological Study Of Motor Nerve Supply Of Pelvic Floor. The Lancet. 1981;1(8210):16-17.

27.   Barber MD, Bremer RE, Thor KB, Dolber PC, Kuehl TJ, Coates KW. Innervation of the female levator ani muscles. American journal of obstetrics and gynecology. 2002;187(1):64-71.

28.   Vodusek DB. Neuroanatomy and neurophysiology of pelvic floor muscles. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 1. 2 ed. Philadelphia: Churchill Livingstone Elsevier; 2007. p. 35-43.

29.   Achtari C, Dwyer PL. Sexual function and pelvic floor disorders. Best practice & research Clinical obstetrics & gynaecology. 2005;19(6):993-1008; quiz A1001-1008.

30.   Ashton-Miller JA, DeLancey JO. Functional anatomy of the female pelvic floor. Ann N Y Acad Sci. 2007;1101:266-296.

31.   Delancey JOL. Anatomy and biomechanics of genital prolapse. Clin Obstet Gynecol. 1993;36(4):897-909.

32.   Taverner D, Smiddy FG. An electromyographic study of the normal function of the external anal sphincter and pelvic diaphragm. Dis Colon Rectum. 1959;2(2):153-160.

33.   Norton PA. Pelvic floor disorders: the role of fascia and ligaments. Clin Obstet Gynecol. 1993;36(4):926-938.

34.   Kegel AH. Stress incontinence and genital relaxation; a nonsurgical method of increasing the tone of sphincters and their supporting structures. Ciba clinical symposia. 1952;4(2):35-51.

35.   Bo K, Lilleas F, Talseth T, Hedland H. Dynamic MRI of the pelvic floor muscles in an upright sitting position. Neurourol Urodyn. 2001;20(2):167-174.

36.   Bø K. Pelvic floor muscle training is effective in treatment of female stress urinary incontinence, but how does it work? International urogynecology journal. 2004;15:76-84.

37.   Betschart C, Kim J, Miller JM, Ashton-Miller JA, Delancey JOL. Comparison of muscle fiber directions between different levator ani muscle subdivisions: in vivo MRI measurements in women. International urogynecology journal. 2014;25:1263–1268.

38.   Guaderrama NM, Nager CW, Liu J, Pretorius DH, Mittal RK. The vaginal pressure profile. Neurourol Urodyn. 2005;24(3):243–247.

39.   Brækken IH, Majida M, Engh ME, Bø K. Test-retest reliability of pelvic floor muscle contraction measured by 4D ultrasound. Neurourol Urodyn. 2008;28(1):68-73.

40.   Colstrup H. Voluntary contractions in the female urethra. J Urol. 1985;134:902-906.

41.   Bø K, Talseth T. Change in urethral pressure during voluntary pelvic floor muscle contraction and vaginal electrical stimulation. International urogynecology journal. 1997;8:3-7.

42.   Ruo H. The relationships of urethral and pelvic floor muscles and the urethral pressure measurements in women with stress urinary incontinence. Eur Urol. 2000;37:149-155.

43.   Jha S, Thakar R. Female sexual dysfunction. Eur J Obstet Gynecol Reprod Biol. 2010;153:117-123.

44.   Knuttgen HG, Kraemer WJ. Terminology and measurment in exercise performance. Journal of strength and conditioning research / National Strength & Conditioning Association. 1987;1(1):1-10.

45.   Wilmore JH, Costill DL. Physiology of sport and exercise. 2 ed. Leeds: Human Kinetics; 1999.

46.   Bø K, Sherburn M. Evaluation of female pelvic-floor muscle function and strength. Phys Ther. 2005;85(3):269-282.

47.   Kegel AH. Progressive Resistance Exercise to the Functional Restoration of the Perineal Muscles. Am J Obst Gynec. 1948;56:238-248.

48.   Slieker-ten Hove MC, Pool-Goudzwaard AL, Eijkemans MJ, Steegers-Theunissen RP, Burger CW, Vierhout ME. Face validity and reliability of the first digital assessment scheme of pelvic floor muscle function conform the new standardized terminology of the International Continence Society. Neurourol Urodyn. 2009;28(4):295-300.

49.   Laycock J. Clinical evaluation of the pelvic floor. In: Schussler B, Laycock J, Norton PA, Stanton SL, (eds), editors. Pelvic floor re-education, Principles and Practice. London: Springer-Verlag; 1994. p. 42–48.

50.   Bø K, Finckenhagen HB. Vaginal palpation of pelvic floor muscle strength: inter-test reproducibility and comparison between palpation and vaginal squeeze pressure. Acta Obstet Gynecol Scand. 2001;80:883–887.

51.   Morin M, Bourbonnais D, Gravel D, Dumoulin C, Lemieux MC. Pelvic floor maximal strength using vaginal digital assessment compared to dynamometric measurements. Neurourol Urodyn. 2004a;23(4):336-341.

52.   Devreese A, Staes F, De Weerdt W, Feys H, Van Assche A, Penninckx F, et al. Clinical Evaluation of Pelvic Floor Muscle Function in Continent and IncontinentWomen. Neurourol Urodyn. 2004;23:190-197.

53.   van delft K, Thakar R, Sultan AH. Pelvic floor muscle contractility: digital assessment vs transperineal ultrasound. Ultrasound Obstet Gynecol. 2015;45:217–222.

54.   Flury N, Koenig I, Radlinger L. Crosstalk considerations in studies evaluating pelvic floor muscles using surface electromyography in women: a scoping review. Arch Gynecol Obstet. 2017;295(4):799-809.

55.   Vodusek DB. Electromyography. In: Bø K, Berghmans B, Mørkved S, Van Kampen M, editors. Evidence based physical therapy for the pelvic floor Bridging science and clinical practice. 2 ed. Philadelphia: Churchill Livingstone Elsevier; 2015. p. 53-60.

56.   Auchincloss CC, McLean L. The reliability of surface EMG recorded from the pelvic floor muscles. J Neurosci Methods. 2009;182(1):85-96.

57.   Glazer HI, Romanzi L, Polaneczky M. Pelvic floor muscle surface electromyography: reliability and clinical predicitive validity. J Reprod Med. 1999;44:779-782.

58.   Dumoulin C, Morin M. Pelvic floor dynamometry. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 2 ed. Philadelphia: Churchill Livingstone Elsevier 2015. p. 66-76.

59.   Sampselle CM, Miller JM, Mims BL, Delancey JOL, Ashton-miller JA, Antonakos CL. Effect of Pelvic Muscle Exercise on Transient Incontinence During Pregnancy and After Birth. Obstet Gynecol. 1998;91(3):406-412.

60.   Miller JM, Ashton-Miller JA, Perruchini D, al. E. Test-retest reliability of an instrumented speculum for measuring vaginal closing force. Neurourol Urodyn. 2007;26(6):858-863.

61.   Dumoulin C, Bourbonnais D, Lemieux MC. Development of a Dynamometer for Measuring the Isometric Force of the Pelvic Floor Musculature. Neurourol Urodyn. 2003;22:648-653.

62.   Dumoulin C, Gravel D, Bourbonnais D, Lemieux MC, Morin M. Reliability of Dynamometric Measurements of the Pelvic Floor Musculature. Neurourol Urodyn. 2004;23:134-142.

63.   Ashton-Miller JA, Zielinski R, Miller JM, DeLancey JOL. Validity and Reliability of an Instrumented Speculum Designed to Minimize the Effect of Intra-abdominal Pressure on the Measurement of Pelvic Floor Muscle Strength. Clin Biomech. 2014;29(10):1146–1150.

64.   Morin M, Gravel D, Bourbonnais D, Dumoulin C, Ouellet S. Reliability of Dynamometric Passive Properties of the Pelvic Floor Muscles in Postmenopausal Women With Stress Urinary Incontinence. Neurourol Urodyn. 2008;27:819–825.

65.   Morin M, Bourbonnais D, Gravel D, Dumoulin C, Lemieux MC. Pelvic floor muscle function in continent and stress urinary incontinent women using dynamometric measurements. Neurourol Urodyn. 2004b;23(7):668-674.

66.   Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol. 2005;25(6):580-585.

67.   Majida M, Braekken IH, Bo K, Benth JS, Engh ME. Validation of three-dimensional perineal ultrasound and magnetic resonance imaging measurements of the pubovisceral muscle at rest. Ultrasound Obstet Gynecol. 2010;35(6):715-722.

68.   Dietz HP. Ultrasound in the assessment of pelvic floor muscle and pelvic organ descent. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 2 ed. Philadelphia: Churchill Livingstone Elsevier 2015. p. 84-97.

69.   Majida M, Braekken IH, Umek W, Bo K, Saltyte Benth J, Ellstrom Engh M. Interobserver repeatability of three- and four-dimensional transperineal ultrasound assessment of pelvic floor muscle anatomy and function. Ultrasound Obstet Gynecol. 2009;33(5):567-573.

70.   Brækken IH, Majida M, Ellstrøm-Engh M, Dietz HP, Umek W, Bø K. Test–retest and intra-observer repeatability of two-, three- and four-dimensional perineal ultrasound of pelvic floor muscle anatomy and function. International urogynecology journal and pelvic floor dysfunction. 2007;19:227-235.

71.   Siafarikas F, Staer-Jensen J, Braekken IH, Bo K, Engh ME. Learning process for performing and analyzing 3D/4D transperineal ultrasound imaging and interobserver reliability study. Ultrasound Obstet Gynecol. 2013;41(3):312-317.

72.   Dietz HP. Quantification of major morhological abnormalities of the levator ani. Ultrasound Obstet Gynecol. 2007;29:329-334.

73.   Staer-Jensen J, Siafarikas F, Hilde G, Braekken IH, Bo K, Engh ME. Pelvic floor muscle injuries 6 weeks post partum-an intra- and inter-rater study. Neurourol Urodyn. 2013;32(7):993-997.

74.   Braekken IH, Majida M, Engh ME, Bø K. Morphological changes after pelvic floor muscle training measured by 3-dimensional ultrasonography: a randomized controlled trial. Obstet Gynecol. 2010;115(2 Pt 1):317-324.

75.   Bø K. Vaginal squeeze pressure measurement. In: Bø K, Berghmans B, Mørkved S, Van Kampen M, editors. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 2 ed. Philadelphia: Churchill Livingstone Elsevier; 2015. p. 61-66.

76.   Sigurdardottir T, Steingrimsdottir T, Arnason A, Bø K. Test-retest intra-rater reliability of vaginal measurement of pelvic floor muscle strength using myomed 932. Acta Obstet Gynecol Scand. 2009;88:939-943.

77.   Frawley HC, Galea MP, Phillips BA, Sherburn M, Bø K. Reliability of pelvic floor muscle strength assessment using different test positions and tools. Neurourol Urodyn. 2006;25(3):236-242.

78.   Bø K, Hagen R, Kvarstein B, Larsen S. Pelvic floor muscle exercise for the treatment of female stress urinary incontinence: I. Reliability of vaginal pressure measurements of pelvic muscle strength. Neurourol Urodyn. 1990;9(5):471-477.

79.   Ferreira CH, Barbosa PB, de Oliveira Souza F, Antonio FI, Franco MM, Bø K. Inter-rater reliability study of the modified Oxford Grading Scale and the Peritron manometer. Physiotherapy. 2011;97(2):132-138.

80.   Bø K, Hagen RR, Kvarstein B, Larsen S. Pelvic floor muscle exercise for the treatment of female stress urinary incontinence. II. Validity of vaginal pressure measurements of pelvic muscle strength and the necessity of supplementary methods for control of correct contraction. Neurourol Urodyn. 1990;9(5):479-487.

81.   Bø K, Raastad R, Finckenhagen HB. Does the size of the vaginal probe affect measurement of pelvic floor muscle strength? Acta Obstet Gynecol Scand. 2005;84:129-133.

82.   Bo K, Frawley HC, Haylen BT, Abramov Y, Almeida FG, Berghmans B, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint

report on the terminology for the conservative and nonpharmacological management of female pelvic floor dysfunction. International urogynecology journal. 2016.

83.   Weber AM, Abrams P, Brubaker L, Cundiff G, Davis G, Dmochowski RR, et al. The Standardization of Terminology for Researchers in Female Pelvic Floor Disorders. International urogynecology journal. 2001;12:178-186.

84.   Nygaard I, Barber MD. Prevalence of Symptomatic Pelvic Floor Disorders in US Women. JAMA. 2008;17:1311-1316.

85.   Bump RC, Norton PA. Epidemiology and natural history of pelvic floor dysfunction. Obstet Gynecol Clin North Am. 1998;25(4):723-746.

86.   Delancey JO, Kane Low L, Miller JM, Patel DA, Tumbarello JA. Graphic integration of causal factors of pelvic floor disorders: an integrated life span model. American journal of obstetrics and gynecology. 2008;199(6):610 e611-615.

87.   Kammerer-Doak D. Assessment of sexual function in women with pelvic floor dysfunction. International urogynecology journal. 2009;20 (suppl 1):45-50.

88.   Rosen RC, Brown C, Heiman J, Leiblum S, Meston CM, Sabsigh R, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000;26:191–208.

89.   Creti L, Fichten CS, Libman E, Amsel R, Brender W. Female sexual functioning: a global score for Nowinski and Lopiccolo's sexual history form. Canadian Psychological Association; Montreal, Quebec1988.

90.   Rust J, Golombok S. The GRISS: a psychometric instrument for the assessment of sexual dysfunction. Arch Sex Behav. 1986;15(2):157-165.

91.   Verit FF, Verit A. Validation of the female sexual function index in women with chronic pelvic pain. The journal of sexual medicine. 2007;4(6):1635-1641.

92.   Meston CM. Validation of the Female Sexual Function Index (FSFI) in women with female orgasmic disorder and in women with hypoactive sexual desire disorder. J Sex Marital Ther. 2003;29:36-46.

93.   Baessler K, O'Neill SM, Maher CF, Battistutta D. Australian pelvic floor questionnaire: a validated interviewer-administered pelvic floor questionnaire for routine clinic and research. International urogynecology journal and pelvic floor dysfunction. 2009;20:149–158.

94.   Price N JS, Avery K, Brookes ST, Abrams P Development and psychometric evaluation of the ICIQ Vaginal Symptoms Questionnaire: the ICIQ-VS. BJOG : an international journal of obstetrics and gynaecology. 2006;113:700-712.

95.   Rogers RG, Kammerer-Doak DN, Villarreal A, Coates K, Qualls C. A new instrument to measure sexual function in women with urinary incontinence or pelvic organ prolapse. American journal of obstetrics and gynecology. 2001;184:552–558.

96.   Jackson S, Donovan J, Brookes S, Eckford S, Swithinbank L, Abrams P. The Bristol Female Lower Urinary Tract Symptoms questionnaire: development and psychometric testing. Br J Urol. 1996;77(6):805-812.

97.   Mouritsen L, Larsen JP. Symptoms, bother and POPQ in women referred with pelvic organ prolapse. Int Urogyn J pelvic floor dysfunction. 2003;14:122-127.

98.   Barber MD, Kuchibhatla MN, Pieper CF, Bump RC. Psychometric evaluation of 2 comprehensive condition-specific quality of life instruments for women with pelvic floor disorders. American journal of obstetrics and gynecology. 2001;185(6):1388-1395.

99.   Rogers RG, Coates KW, Kammerer-Doak DN, Khalsa S, Qualls C. A short form of the pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12). Int Urogyn J pelvic floor dysfunction. 2003;14:164–168.

100.   Abrams P, Avery K, Gardener N, Donovan J, Board IA. The International Consultation on Incontinence Modular Questionnaire: www.iciq.net. J Urol. 2006;175(3 Pt 1):1063-1066; discussion 1066.

101.   Haylen BT, de Ridder D, Freeman RM, Swift SE, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. International urogynecology journal. 2010;21(1):5-26.

102.   Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. JAMA. 1999;281(6):537-544.

103.   MacLennan AH, Taylor AW, Wilson DH, Wilson D. The prevalence of pelvic floor disorders and their relationship to gender, age, parity and mode of delivery. BJOG : an international journal of obstetrics and gynaecology. 2000;107:1460-1470.

104.   Moran PA, Dwyer PL, Ziccone SP. Urinary leakage during coitus in women. J Obstet Gynaecol. 1999;19(3):286-288.

105.   Serati M, Salvatore S, Uccella S, Nappi RE, Bolis P. Female urinary incontinence during intercourse: a review on an understudied problem for women's sexuality. The journal of sexual medicine. 2009;6(1):40-48.

106.   Shaw C. A systematic review of the literature on the prevalence of sexual impairment in women with urinary incontinence and the prevalence of urinary leakage during sexual activity. Eur Urol. 2002;42(5):432-440.

107.   Mouritsen L. Pathophysiology of sexual dysfunction as related to pelvic floor disorders. International urogynecology journal. 2009;20:19-25.

108.   Barrett G, Pendry E, Peacock J, Victor C, Thakar R, Manyonda I. Women's sexual health after childbirth. BJOG : an international journal of obstetrics and gynaecology. 2000;107(2):186-195.

109.   Serati M, Salvatore S, Khullar V, Uccella S, Bertelli E, Ghezzi F, et al. Prospective study to assess risk factors for pelvic floor dysfunction after delivery. Acta Obstet Gynecol Scand. 2008;87(3):313-318.

110.   Connolly A, Thorp J, Pahel L. Effects of pregnancy and childbirth on postpartum sexual function: a longitudinal prospective study. International urogynecology journal and pelvic floor dysfunction. 2005;16(4):263-267.

111.   Signorello LB, Harlow BL, Chekos AK, Repke JT. Postpartum sexual functioning and its relationship to perineal trauma: a retrospective cohort study of primiparous women. American journal of obstetrics and gynecology. 2001;184(5):881-890.

112.   Brown S, Lumley J. Maternal health after childbirth: results of an Australian population based survey. Br J Obstet Gynaecol. 1998;105(2):156-161.

113.   Andrews V, Thakar R, Sultan AH, Jones PW. Evaluation of postpartum perineal pain and dyspareunia-A prospective study. Eur J Obstet Gynecol Reprod Biol. 2008;137:152-156.

114.   Serati M, Salvatore S, Siesto G, Cattoni E, Zanirato M, Khullar V, et al. Female sexual function during pregnancy and after childbirth. The journal of sexual medicine. 2010;7(8):2782-2790.

115. Pauls RN, Occhino JA, Dryfhout VL. Effects of pregnancy on female sexual function and body image: a prospective study. The journal of sexual medicine. 2008;5:1915-1922.

116. Dolan LM, Walsh D, Hamilton S, Marshall K, Thompson K, Ashe RG. A study of quality of life in primigravidae with urinary incontinence. International urogynecology journal. 2004;15(3):160-164.

117. Ege E; Akin B; Altuntug K; Benli S AA. Prevalence of urinary incontinence in the 12-months postpartum period and related risk factors in Turkey. Urol Int. 2008;80:355-361.

118. Delancey JOL. The hidden epidemic of pelvic floor dysfunction: Achievable goals for improved prevention and treatment. AJOG. 2005;192:1488-1495.

119. Handa VL, Cundiff G, Chang HH, Helzlsouer KJ. Female sexual function and pelvic floor disorders. Obstet Gynecol. 2008;111(5):1045-1052.

120. Basson R, Wierman ME, Van Lankveld J, Brotto L. Summary of the recommendations on sexual dysfunctions in women. The journal of sexual medicine. 2010;7(1 Pt 2):314-326.

121. Shafik A, El-Sibai O. Levator ani muscle activity in pregnancy and the postpartum period: a myoelectric study. Clin Exp Obstet Gynecol. 2000;27(2):129-132.

122. Ashton-Miller JA, Delancey JOL. On the Biomechanics of Vaginal Birth and Common Sequelae. Annu Rev Biomed Eng. 2009;11:163–176.

123. Lavin JM, Smith ARB, Anderson J, Grant M, Buckley H, Critchley H, et al. The effects of the first pregnancy on the connective tissue of the rectus sheath. Neurourol and Urodyn. 1997;16:381-382.

124. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics. 23 ed: McGraw-Hill Medical; 2010.

125. Stær-Jensen J, Siafarikas F, Hilde G, Bø K, Engh ME. Ultrasonographic evaluation of pelvic organ support during pregnancy. Obstet Gynecol. 2013;122(2):329-336.

126. Erol B, Sanli O, Korkmaz D, Seyhan A, Akman Ta, Kadioglu A. A cross-sectional study of female sexual function and dysfunction during pregnancy. The journal of sexual medicine. 2007;4(5):1381–1387

127. DeJudicibus MA, McCabe MP. Psychological factors and the sexuality of pregnant and postpartum women. J Sex Res. 2002;39(2):94-103.

128. Hicks TL, Goodall SF, Quattrone EM, Lydon-Rochelle MT. Postpartum Sexual Functioning and Method of Delivery: Summary of the Evidence. Journal of midwifery & women's health. 2004;49(5):430–436.

129. Thompson JF, Roberts CL, Currie M, Ellwood DA. Prevalence and persistence of health problems after childbirth: associations with parity and method of birth. Birth. 2002;29(2):83-94.

130. Glazener CMA. Sexual function after childbirth: women's experiences, persistent morbidity and lack of professional recognition. BJOG : an international journal of obstetrics and gynaecology. 1997;104:330-335.

131. Fodstad K, Staff AC, Laine K. Sexual activity and dyspareunia the first year postpartum in relation to degree of perineal trauma. Int Urogyn J. 2016;10:1513-1523.

132. Klein K, Worda C, Leipold H, Gruber C, Husslein P, Wenzl R. Does the mode of delivery influence sexual function after childbirth? Journal of women's health. 2009;18(8):1227-1231.

133.   Baytur YB, Deveci A, Uyar Y, Ozcakir HT, Kizilkaya S, Caglar H. Mode of delivery and pelvic floor muscle strength and sexual function after childbirth. Int J   Gynaecol Obstet. 2005;88(3):276-280.

134.   Brubaker L, Handa VL, Bradley CS, Connolly AM, Moalli P, Brown MB, et al. Sexual Function 6 Months After First Delivery. Obstet Gynecol. 2008;111(5):1040-1044.

135.   Meyer S, Hohlfeld P, Achtari C, Russolo A, De Grandi P. Birth trauma: short and long term effects of forceps delivery compared with spontaneous delivery on various pelvic floor parameters. BJOG : an international journal of obstetrics and gynaecology. 2000;107:1360-1365.

136.   Dean N, Wilson D, Herbison P, Glazener C, Aung T, Macarthur C. Sexual function, delivery mode history, pelvic floor muscle exercises and incontinence: A cross-sectional study six years post-partum. Aust N Z J Obstet Gynaecol. 2008;48:302–311.

137.   Champaneria R, D'Andrea RM, Latthe PM. Hormonal contraception and pelvic floor function: a systematic review. Int Urogyn J. 2016;27:709-722.

138.   Snooks SJ, Setchell M, Swash M, Henry MM. Injury to innervation of pelvic floor sphincter musculature in childbirth. Lancet. 1984;2(8402):546-550.

139.   Allen RE, Hosker GL, Smith AR, Warrell DW. Pelvic floor damage and childbirth: a neurophysiological study. Br J Obstet Gynaecol. 1990;97(9):770-779.

140.   Elenskaia K, Thakar R, Sultan AH, Scheer I, Beggs A. The effect of pregnancy and childbirth on pelvic floor muscle function. International urogynecology journal. 2011;22(11):1421-1427.

141.   Hilde G, Staer-Jensen J, Siafarikas F, Engh ME, Braekken IH, Bo K. Impact of childbirth and mode of delivery on vaginal resting pressure and on pelvic floor muscle strength and endurance. American journal of obstetrics and gynecology. 2013;208(1):51-57.

142.   Peschers UM, Schaer GN, DeLancey JOL, Schuessler B. Levator ani function before and after childbirth. BJOG : an international journal of obstetrics and gynaecology. 1997;104:1004-1008.

143.   van Delft KWM, Thakar R, Sultan AH. The natural history of levator avulsion one year following childbirth: a prospective study. BJOG : an international journal of obstetrics and gynaecology. 2014;122:1266-1273.

144.   Sigurdardottir T, Steingrimsdottir T, Arnason A, Bø K. Pelvic floor muscle function before and after first childbirth. International urogynecology journal. 2011;22:1497-1503.

145.   Rosenbaum TY. Pelvic floor involvement in male and female sexual dysfunction and the role of pelvic floor rehabilitation in treatment: a literature review. The journal of sexual medicine. 2007;4:4-13.

146.   de Souza Caroci A, Riesco MLG, da Silva Sousa W, Cotrim AC, Sena EM, Rocha NL, et al. Analysis of pelvic floor musculature function during pregnancy and postpartum: a cohort study: (a prospective cohort study to assess the PFMS by perineometry and digital vaginal palpation during pregnancy and following vaginal or caesarean childbirth). J Clin Nurs. 2010;19:2424-2433.

147.   Snooks SJ, Swash M, Henry MM, Setchell M. Risk factors in childbirth causing damage to the pelvic floor innervation. Int J Colorectal Dis. 1986;1(1):20-24.

148.   Sultan AH, Kamm MA, Hudson CN. Pudendal nerve damage during labour : prospective study before and after childbirth. BJOG : an international journal of obstetrics and gynaecology. 1994;101:22-28.

149.   Lien KC, Morgan DM, DeLancey JOL, Ashton-Miller JA. Pudendal nerve stretch during vaginal birth: A 3D computer simulation. AJOG. 2005;192:1669-1676.

150.   Wohlrab KJ, Rardin CR. Impact of Route of Delivery on Continence and Sexual Function. Clin Perinatol. 2008;35:583–590.

151.   Lien KC, Mooney B, DeLancey JO, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol. 2004;103(1):31-40.

152.   Hoyte L, Damaser MS, Warfield SK, Chukkapalli G, Majumdar A, Choi DJ, et al. Quantity and distribution of levator ani stretch during simulated vaginal childbirth. American journal of obstetrics and gynecology. 2008;199(2):198-205.

153.   Parente MP, Jorge RM, Mascarenhas T, Fernandes AA, Martins JA. Deformation of the pelvic floor muscles during a vaginal delivery. Int Urogyn J pelvic floor dysfunction. 2008;19(1):65-71.

154.   DeLancey JO, Kearney R, Chou Q, Speights S, Binno S. The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery. Obstet Gynecol. 2003;101(1):46-53.

155.   Dietz HP, Lanzarone V. Levator Trauma After Vaginal Delivery. Obstet Gynecol. 2005;106(4):707-712.

156.   Kearney R, Miller JM, Ashton-Miller JA, Delancey JOL. Obstetrical factors associated with levator ani muscle injury after vaginal birth. Obstet Gynecol. 2006;107(1):144-149.

157.   Kearney R, Fitzpatrick M, Brennan S, Behan M, Miller JM, Keane D, et al. Levator ani injury in primiparous women with forceps delivery for fetal distress, forceps for second stage arrest, and spontaneous delivery. 111. 2010;1:19-22.

158.   Dietz HP, Shek C. Levator avulsion and grading of pelvic floor muscle strength. International urogynecology journal. 2008;19:633–636.

159.   DeLancey JOL, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of Levator Ani Muscle Defects and Function in Women With and Without Pelvic Organ Prolapse. Obstet Gynecol. 2007;109(2).

160.   Rogers RG, Leeman LM, Migliaccio L, Albers LL. Does the severity of spontaneous genital tract trauma affect postpartum pelvic floor function? International urogynecology journal. 2008;19:429–435.

161.   Clark NA, Brincat CA, Yousuf AA, al. e. Levator defects affect perineal position independently of prolapse status. American journal of obstetrics and gynecology. 2010;203(595):17-22.

162.   Rogers RG, Leeman LM, Migliaccio L, Albers LL. Does the severity of spontaneous genital tract trauma affect postpartum pelvic floor function? Int Urogynecol J Pelvic Floor Dysfunct. 2008;19(3):429-435

163.   Hay-Smith EJ, Herderschee R, Dumoulin C, Herbison GP. Comparisons of approaches to pelvic floor muscle training for urinary incontinence in women. Cochrane database of systematic reviews. 2011(12):CD009508.

164.   Hagen S, Stark D. Conservative prevention and management of pelvic organ prolapse in women. Cochrane database of systematic reviews. 2011(12):CD003882.

165.   Kraemer WJ, Ratamess NA. Fundamentals of resistance training: progression and exercise prescription. Med Sci Sports Exerc. 2004;36(4):674-688.

166.   American College of Sports M. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. Med Sci Sports Exerc. 2009;41(3):687-708.

167.   Bø K. Pelvic Floor Muscle Exercise for the Treatment of Stress Urinary Incontinence An Exercise Physiology Perspective. International urogynecology journal. 1995;6:282-291.

168.   Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee I-M, et al. ACSM Position Stand: Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory, Musculoskeletal, and Neuromotor Fitness in Apparently Healthy Adults: Guidance for Prescribing Exercise. Med Sci Sports Exerc. 2011:1334-1359.

169.   Bø K, Mørkved S. Motor learning. In: Bø K, Berghmans B, Mørkved S, Van Kampen M, editors. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 1 ed. Philadelphia: Churchill Livingstone Elsevier; 2007. p. 113-119.

170.   Åstrand PO, Rodahl K, Dahl HA. Textbook of work physiology; physiological basis of exercise: Human Kinetics, Champaign, IL; 2003.

171.   Bø K, Hagen RH, Kvarstein B, Jørgensen J, Larsen S. Pelvic floor muscle exercise for the treatment of female stress urinary incontinence. III. Effects of two different degrees of pelvic floor muscle exercises. Neurourol Urodyn. 1990;9:489-502.

172.   Bø K. Pelvic floor muscle training in treatment of female stress urinary incontinence, pelvic organ prolapse and sexual dysfunction. World J Urol. 2012;30(4):437-443.

173.   Lowenstein L, Gruenwald I, Gartman I, Vardi Y. Can stronger pelvic muscle floor improve sexual function? International urogynecology journal. 2010;21(5):553-556.

174.   Martinez CS, Ferreira FV, Castro AAM, Gomide LB. Women with greater pelvic floor muscle strength have better sexual function. Acta Obstetrica et Gynaecologica Scandinavia. 2014;93:457-502.

175.   de Menezes Franco M, Driusso P, Bø K, de Abreu DCC, da Silva Lara LA, de Sá Rosa ACJ, et al. Relationship between pelvic floor muscle strength and sexual dysfunction in postmenopausal women: a cross-sectional study. International urogynecology journal. 2016:1-6.

176.   Chambless DL, Stern T, Sultan FE, Williams AJ, Goldstein AJ, Lineberger MH, et al. The pubococcygens and female orgasm: a correlational study with normal subjects. Arch Sex Behav. 1982;11(6):479-490.

177.   Kanter G, Rogers RG, Pauls RN, Kammerer-Doak D, Thakar R. A strong pelvic floor is associated with higher rates of sexual activity in women with pelvic floor disorders. International urogynecology journal. 2015;26(7):991-996.

178.   Citak N, Cam C, Arslan H, Karateke A, Tug N, Ayaz R, et al. Postpartum sexual function of women and the effects of early pelvic floor muscle exercises. Acta Obstet Gynecol Scand. 2010;89(6):817-822.

179.   Wilson PD, Herbison GP. A randomized controlled trial of pelvic floor muscle exercises to treat postnatal urinary incontinence. International urogynecology journal and pelvic floor dysfunction. 1998;9(5):257-264.

180.   Mørkved S, Rømmen K, Schei B, Salvesen KA, Bø K. No difference in urinary incontinence between training and control group six years after cessation of a randomized controlled trial, but improved sexual satisfaction in the training group. Neurourol Urodyn. 2007;26(5):667.

181.   Bo K, Talseth T, Vinsnes A. Randomized controlled trial on the effect of pelvic floor muscle training on quality of life and sexual problems in genuine stress incontinent women. Acta Obstet Gynecol Scand. 2000;79(7):598-603.

182.   Chambless DL, Sultan FE, Stern TE, O'Neill C, Garrison S, Jackson A. Effect of pubococcygeal exercise on coital orgasm in women. J Consult Clin Psychol. 1984;52(1):114-118.

183.   Trudel G, Saint-Laurent S. A comparison between the effects of Kegel's exercises and a combination of sexual awareness relaxation and breathing on situational orgasmic dysfunction in women. J Sex Marital Ther. 1983;9(3):204-209.

184.   Braekken IH, Majida M, Ellstrom Engh M, Bo K. Can Pelvic Floor Muscle Training Improve Sexual Function in Women with Pelvic Organ Prolapse? A Randomized Controlled Trial. The journal of sexual medicine. 2014.

185.   Hagen S, Stark D, Glazener C, Dickson S, Barry S, Elders A, et al. Individualised pelvic floor muscle training in women with pelvic organ prolapse (POPPY): a multicentre randomised controlled trial. Lancet. 2014;383(9919):796-806.

186.   Eftekhar T, Sohrabi M, Haghollahi F, Shariat M, Miri E. Comparison effect of physiotherapy with surgery on sexual function in patients with pelvic floor disorder: A randomized clinical trial. Iranian journal of reproductive medicine. 2014;12(1):7-14.

187.   Wiegersma M, Panman CM, Kollen BJ, Berger MY, Lisman-Van Leeuwen Y, Dekker JH. Effect of pelvic floor muscle training compared with watchful waiting in older women with symptomatic mild pelvic organ prolapse: randomised controlled trial in primary care. BMJ. 2014;349:g7378.

188.   Liebergall-Wischnitzer M, Paltiel O, Hochner Celnikier D, Lavy Y, Manor O, Woloski Wruble AC. Sexual function and quality of life of women with stress urinary incontinence: a randomized controlled trial comparing the Paula method (circular muscle exercises) to pelvic floor muscle training (PFMT) exercises. The journal of sexual medicine. 2012;9(6):1613-1623.

189.   Handa VL, Whitcomb E, Weidner AC, Nygaard I, Brubaker L, Bradley CS, et al. Sexual function before and after non-surgical treatment for stress urinary incontinence. Female pelvic medicine & reconstructive surgery. 2011;17(1):30–35.

190.   Yang EJ, Lim JY, Rah UW, Kim YB. Effect of a pelvic floor muscle training program on gynecologic cancer survivors with pelvic floor dysfunction: a randomized controlled trial. Gynecol Oncol. 2012;125(3):705-711.

191.   Beji NK, Yalcin O, Erkan HA. The effect of pelvic floor training on sexual function of treated patients. International urogynecology journal and pelvic floor dysfunction. 2003;14(4):234-238; discussion 238.

192.   Zahariou AG, Karamouti MV, Papaioannou PD. Pelvic floor muscle training improves sexual function of women with stress urinary incontinence. International urogynecology journal and pelvic floor dysfunction. 2008;19(3):401-406.

193.   Rivalta M, Sighinolfi MC, Micali S, De Stefani S, Bianchi G. Sexual function and quality of life in women with urinary incontinence treated by a complete rehabilitation program (biofeedback, functional electrical stimulation, pelvic floor muscle exercises, and vaginal cones). The journal of sexual medicine. 2010;7:1200-1208.

194.   Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003;83(8):713-721.

195.   Staer-Jensen J, Siafarikas F, Hilde G, Benth JS, Bo K, Engh ME. Postpartum recovery of levator hiatus and bladder neck mobility in relation to pregnancy. Obstet Gynecol. 2015;125(3):531-539.

196.   Hilde G, Staer-Jensen J, Siafarikas F, Ellstrom Engh M, Bo K. Postpartum pelvic floor muscle training and urinary incontinence: a randomized controlled trial. Obstet Gynecol. 2013;122(6):1231-1238.

197.   Hilde G, Staer-Jensen J, Ellstrom Engh M, Braekken IH, Bo K. Continence and pelvic floor status in nulliparous women at midterm pregnancy. International urogynecology journal. 2012;23(9):1257-1263.

198.   Mørkved S, Bø K. The effect of postpartum pelvic floor muscle exercise in the prevention and treatment of urinary incontinence. International urogynecology journal and pelvic floor dysfunction. 1997;8(4):217-222.

199.   Bø K. Pressure measurements during pelvic floor muscle contractions: the effect of different positions of the vaginal measuring device. Neurourol Urodyn. 1992;11(2):107-113.

200.   Bo K, Hilde G, Staer-Jensen J, Siafarikas F, Tennfjord MK, Engh ME. Postpartum pelvic floor muscle training and pelvic organ prolapse-a randomized trial of primiparous women. American journal of obstetrics and gynecology. 2015;212(1):38 e31-37.

201.   Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. International urogynecology journal. 2011;22(6):699-704.

202.   Dietz HP, Shek KL. Tomographic ultrasound imaging of the pelvic floor: which levels matter most? Ultrasound Obstet Gynecol. 2009;33(6):698-703.

203.   Dietz HP, Shek K, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound Ultrasound Obstet Gynecol. 2005;25:580-585.

204.   Bø K, Talseth T, Holme I. Single blind, randomised controlled trial of pelvic floor exercises, electrical stimulation, vaginal cones, and no treatment in management of genuine stress incontinence in women. BMJ. 1999;318:487–493.

205.   Bø K, Hagen RH, Kvarstein B, Jørgensen J, Larsen S. Pelvic Floor Muscle Exercise for the Treatment of Female Stress Urinary Incontinence: III. Effects of Two Different Degrees of Pelvic Floor Muscle Exercises. Neurourol Urodyn. 1990;9:489-502.

206.   Morkved S, Bo K. The effect of postpartum pelvic floor muscle exercise in the prevention and treatment of urinary incontinence. International urogynecology journal and pelvic floor dysfunction. 1997;8(4):217-222.

207.   DiNubile NA. Strength training. Clin Sports Med. 1991;10(1):33-62.

208.   Cohen J. Statistical power analysis for the behavioural sciences. 2 ed. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988.

209.   Vickers AJ, Altman DG. Statistical notes. Analysing controlled trials with baseline and follow up measurements. BMJ. 2001;323:1123-1124.

210.   Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. The Lancet 1986;8:307-310.

211.   Atkinson G, Nevill AM. Statistical Methods For Assessing Measurement Error (Reliability) in Variables Relevant to Sports Medicine. Sports Med. 1998:217-238.

212.   WMA. Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects Fortaleza Brazil 2013 [Available from: www.wma.net/en/30/publictions/10policies/b3/.

213.   De Vet HCV, Terwee CB, Mokkink LB, Knol DL, editors. Measurement in medicine a practical guide. United States of America, New York: Cambridge University Press; 2011.

214.   Kottner JA, Audige L, Brorson S, Donner A, Gajewski BJ, Hròbjartsson A, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. Int J Nurs Stud. 2011;48:661–671.

215.   Altman DG, Bland JM. Statistics Notes Standard deviations and standard errors. BMJ. 2005;331:903.

216.   Barbosa PB, Franco MM, Souza FO, Antônio FI, Montezuma T, Ferreira CHJ. Comparison between measurements obtained with three different perineometers. Clinics. 2009;64(6):527-533.

217.   Bland JM, Altman DG. Comparing two methods of clinical measurement: a personal history. Int J Epidemiol. 1995;24:7-14.

218.   Koelbl H, Nitti V, Baessler K, Salvatore S, Sultan A, Yamaguchi O. Pathophysiology of urinary incontinence, faecal incontinence and pelvic organ prolapse. In: Abrams P, Cardozo L, Khoury S, Wein A, editors., editors. Incontinence: 4th International Consultation on Incontinence. Paris: Health Publication Ltd; 2009. p. 255-330.

219.   Morshed S, Tornetta P, Bhandari M. Analysis of Observational Studies: A Guide to Understanding Statistical Methods. Bone Joint Surg Am. 2009;91(3):50-60.

220.   Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. BMJ. 1999;319:670-674.

221.   Moher D HS, Schulz K.F, Montori V, Gøtzsche P.C, Devereaux P.J, Elbourne D, Egger M, Altman D.G. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. International Journal of Surgery. 2012;10:28-55.

222.   Bø K, Herbert RD. When and how should new therapies become routine clinical practice? Physiotherapy. 2009;95:51–57.

223.   Herbert R. Critical appraisal of randomized trials and systematic reviews of the effects of physical therapy interventions for the pelvic floor. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence-based physical therapy for the pelvic floor Bridging science and clinical practice. 2 ed. Philadelphia: Churchill Livingstone Elsevier 2015. p. 9-17.

224.   Brubaker L, Nygaard I, Bø K, Tincello DG, Homma K, Cook J, et al. Research methodology. In: Abrams P, Cardozo L, Khoury S, Wein A, editors. Incontinence 5th International Consultation on Incontinence. 5th ed. Paris: European Association of Urology; 2013. p. 1865-1893.

225.   von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies J Clin Epidemiol. 2008;61(4):344-349.

226.   Jennie A. Freiman JA, Chalmers TC, Smith Jr H, Kuebler RR. The Importance of Beta, the Type II Error and Sample Size in the Design and Interpretation of the Randomized Control Trial — Survey of 71 Negative Trials. N Engl J Med. 1978;299:690-694.

227.   Mendes EPB, Oliveira SMJV, Caroci AS, Francisco AA, Oliveira SG, Silva RL. Pelvic floor muscle strength in primiparous women according to the delivery type: cross-sectional study. Rev Latino-Am Enfermagem. 2016;24.

228.   Rothman KJ, Greenland S, Lash TL. Modern epidemiology. 3 ed. Philadelphia: Lippincott Williams & Wilkins; 2008.

229.   Bendera R, Lange S. Adjusting for multiple testing—when and how? J Clin Epidemiol. 2001;54 343–349.

230.   Bland JM, Altman DG. Multiple significance tests: the Bonferroni method. BMJ. 1995;310:170.

231.   Morin M, Bergeron S, Khalife S, Mayrand MH, Binik YM. Morphometry of the pelvic floor muscles in women with and without provoked vestibulodynia using 4D ultrasound. The journal of sexual medicine. 2014;11(3):776-785.

232.   Reissing ED, Binik YM, Khalife S, Cohen D, Amsel R. Vaginal spasm, pain, and behavior: an empirical investigation of the diagnosis of vaginismus. Arch Sex Behav. 2004;33(1):5-17.

233.   Næss I, Bø K. Pelvic floor muscle function in women with provoked vestibulodynia and asymptomatic controls. International urogynecology journal. 2015;26(10):1467–1473.

234.   Hoffman BL, Schorge JO, Schaffer JI, Halvorson LM, Bradshaw KD, Cunningham FG. Williams Gynecology. 2 ed. Texas: McGraw-Hill Medical; 2012.

235.   Both S, Laan E. Simultaneous measurement of pelvic floor muscle activity and vaginal blood flow: a pilot study. The journal of sexual medicine. 2007;4(3):690-701.

236.   Frawley H. Pelvic floor pain and the overactive pelvic floor. In: Bø K BB, Mørkved S, van Kampen M, editor. Evidence based physical therapy for the pelvic floor Bridging science and clinical practice. 2. Philadelphia: Churchill Livingstone Elsevier; 2015. p. 333-253.

237.   Falkert A, Willmann A, Endress E, Meint P, Seelbach-Gobel B. Three-dimensional ultrasound of pelvic floor: is there a correlation with delivery mode and persisting pelvic floor disorders 18-24 months after first delivery? Ultrasound Obstet Gynecol. 2013;41(2):204-209.

238.   Elenskaia K, Thakar R, Sultan AH, Scheer I, Onwude J. Effect of childbirth on pelvic organ support and quality of life: a longitudinal cohort study. International urogynecology journal. 2013;24:927-937.

239.   McDonald EA, Gartland D, Small R, Brown JS. Frequency, severity and persistance of postnatal dyspareunia to 18 months post partum: A cohort study. Midwifery. 2016;34:15-20.

240.   McDonald EA, Gartland D, Small R, Brown JS. Dyspareunia and childbirth: a prospective study. BJOG : an international journal of obstetrics and gynaecology. 2015;122:672-679.

241.   De Souza A, Dwyer PL, Charity M, Thomas E, Ferreira CHJ, Schierlitz L. The effects of mode delivery on postpartum sexual function: a prospective study. BJOG : an international journal of obstetrics and gynaecology. 2015.

242.   Durnea CM, Khashan AS, Kenny LC, Tabirca SS, O'Reilly BA. The role of prepregnancy pelvic floor dysfunction in postnatal pelvic morbidity in primiparous women. International urogynecology journal. 2014;25:1363–1374.

.

243.   Yeniel AO, Petri E. Pregnancy, childbirth, and sexual function: perceptions and facts. International urogynecology journal. 2014;25(1):5-14.

244.   van Delft K, Sultan A, Thakar R, Schwertner-Tiepelmann N, Kluivers K. The relationship between postpartum levator ani muscle avulsion and signs and symptoms of pelvic

floor dysfunction. BJOG : an international journal of obstetrics and gynaecology. 2014;121:1164-1171.

245.   Thibault-Gagnon S, Yusuf S, Langer S, Wong V, Shek KL, Martin A, et al. Do women notice the impact of childbirth-related levator trauma on pelvic floor and sexual function? Results of an observational ultrasound study. International urogynecology journal. 2014;25:1389–1398.

246.   Laterza RM, Schrutka L, Umek W, Albrich S, Koelbl H. Pelvic floor dysfunction after levator trauma 1-year postpartum: a prospective case-control study. International urogynecology journal. 2014.

247.   Cyr M-P, Kruger J, Wong V, al. e. Pelvic floor morphometry and function in women with and without puborectalis avulsion in the early postpartum period. AJOG. 2017;216(274):e1-8.

248.   Roos AM, Sultan AH, Thakar R. Sexual problems in the gynecology clinic: are we making a mountain out of a molehill? International urogynecology journal. 2012;23(2):145-152.

249.   Laterza RM, Schrutka L, Umek W, Albrich S, Koelbl H. Pelvic floor dysfunction after levator trauma 1-year postpartum: a prospective case-control study. Int Urogyn J 2015;26:41-47.

250.   Guzman Rojas R, Wong V, Shek KL, Dietz HP. Impact of levator trauma on pelvic floor muscle function. International urogynecology journal. 2014;25:375-380.

251.   Van Delft K, Shobeiri A, Sultan AH, Thakar R. Haematomas may masquerade as levator ani muscle defects. Int Urogyn J. 2012;23:S237.

252.   Brækken IH, Majida M, Engh ME, Bø K. Can pelvic floor muscle training reverse pelvic organ prolapse and reduce prolapse symptoms? An assessor-blinded, randomized, controlled trial. American journal of obstetrics and gynecology. 2010;203(2):170 e171-177.

253.   Bland JM, Altman DG. Absence of evidence is not evidence of absence. BMJ. 1995;311:485.

254.   Neels H, De Wachter S, Wyndaele JJ, Wyndaele M, Vermandel A. Does pelvic floor muscle contraction early after delivery cause perineal pain in postpartum women? European Journal of Obstetrics & Gynecology and Reproductive Biology. 2017;208:1-5.

255.   Næss I, Bø K. Can a pelvic floor muscle contraction reduce vaginal resting pressure and resting EMG activity? . Abstract International Continence Society, Barcelona. 2013.

256.   Bazi T, Takahashi S, Ismail S, Bø K, Ruiz-Zapata AM, Duckett J, et al. Prevention of pelvic floor disorders: international urogynecological association research and development committee opinion. International urogynecology journal. 2016.

257.   Herbert RD, Bø K. Analysis of quality of interventions in systematic reviews. BMJ. 2005;331:507–509.

258.   Ferreira CHJ, Dwyer PL, Davidson M, De Souza A, J.A. U, Frawley HC. Does pelvic floor muscle training improve female sexual function? A systematic review. International urogynecology journal. 2015.

259.   Tennfjord MK, Ellström Engh M, Bø K. Role of physical therapy in the treatment of female sexual dysfunction. In: Costantini E, Villari D, Filocamo M, eds., editors. Female sexual function and dysfunction: Springer, Cham; 2017.