Effects of pelvic floor muscle training in pregnancy on pelvic floor muscle strength, urinary- and anal incontinence:

A randomized controlled trial in overweight and obese women

Lisa Torsdatter Markussen

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Advisor: Trine Tegdan Moholdt

NTNU

Faculty of Medicine and Health Sciences

Institute of Medical Imaging and Circulation

Abstract

Background and Aim: Reduction of pelvic floor muscle (PFM) strength is a natural consequence of pregnancy and (vaginal) labor. Urinary and anal incontinence (UI and AI) during and after pregnancy are a commonly reported condition during this period. Overweight and obese women have a higher risk of UI and AI than normal weight women. Pregnancy or postpartum incontinence can become a persistent and bothersome condition for years after the first delivery. The primary aim of this study was to assess if providing a general supervised exercise intervention, including intensive pelvic floor muscle training (PFMT), to previously sedentary overweight and obese pregnant women could affect PFM strength. Secondary aim was to investigate if PFMT could prevent or treat UI and AI in this population group.

Methods: Previously sedentary pregnant women with self-reported pre-pregnancy body mass index (BMI, weight in kg/height in m^2) of ≥ 28 were allocated by 1:1 randomizarion into either a supervised exercise training program including intensive PFMT or standard maternity care. Seventy women (36 in exercise group and 34 in control group) were included for analysis in this sub-study. Assessments of PFM strength were performed by gynecological examinaton and measured with the Modified Oxford Grading System. Symptoms and prevalence of UI and AI were collected by questionnaires at baseline (gestational week 12-18), late pregnancy (gestational week 34-37) and three months postpartum.

Results: No statistically significant differences were observed between the groups PFM strength, prevalence of UI or AI on any of the assessment points. Both groups had no change from baseline strength in either late pregacy or three months postpartum. Prevalences of UI at baseline for the whole study population was 42,8%, in late pregnancy; 52,2% and 3 months postpartum 39,1%. The most commonly reported type of UI vas stress urinary incontinence (SUI). Prevalence of AI at baseline for the whole study population was 41,7%, in late pregnancy 30,2% and 3 months postpartum 35%. The PFMT intervention reduced UI severity in late pregnancy.

Conclsion: Providing a supervised exercise intervention with focus on intensive PFMT to previously sedentary overweight and obese pregnant women did not affect PFM strength or prevalence of UI and AI in late pregnancy or postpartum, when compared with standard materal care.

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Abbreviations

ACOG – American College of Obstetricians and Gynecologists

AI – Anal Incontinence

ANCOVA – Analysis of Covariance

BMI - Body Mass Index

CI – Confidence Interval

ETIP – Exercise Training In Pregnancy

FI – Fecal Incontinence

ICS – International Continence Society

MUI – Mixed Urinary Incontinence

N – Number of participants

OR – Odds Ratio

P – P-value/probability value

PFM – Pelvic Floor Muscles

PFMT – Pelvic Floor Muscle Training

RCT – Randomized Controlled Trial

SD – Standard Deviation

SUI – Stress Urinary Incontinence

UI – Urinary Incontinence

UUI – Urgency Urinary Incontinence

WHO – World Health Organization

Introduction

Overweight and obesity is a threat to public health, with reports of increasing prevalence world-wide[1]. Overweight is defined by the World Health Organization (WHO) as a body mass index (BMI, as weight in kg/height in metres squared) above 25 kg/m², and obesity is defined as a BMI >30 kg/m². Obesity is further classified into three sub-classes, class I (30-34.9 kg/m²), class II (35-39.9 kg/m²), and class III (40 kg/m² or higher)[2]. The increasing prevalence of obesity is affecting the female population to a higher degree than age-matched male population[3]. Women in child-bearing age are no exception, the 2011-2012 National Health and Nutrition Examination Survey (NHANES) reported 32% of all US women were obese in this age group (20-39 years old)[4]. The 2014 birth statistics of Norway reported 33% of pregnant women to have BMI ≥ 25[5]. This proportion was also valid for Australia in 2006[6]. Obese expecting mothers have, per definition, a pregnancy with an increased risk for several possibly serious complications for both mother and child[7-9].

Incontinence is a common condition during pregnancy and in the postpartum period for women of all weight classes. Even if this condition is not life-threatening or physically harmful, it is associated with shame and lowered quality of life[10, 11]. Urinary incontinence (UI) is defined by the International Continence Society (ICS) to be involuntary loss of urine, and anal incontinence (AI) is defined as involuntary loss of flatus or feces[12]. The strain and stretching of the pelvic floor muscles (PFM), the weight of the growing fetus and changes in the tissues surrounding the uterus, and hormonal changes in pregnancy[13-15] are all factors that contribute to developing incontinence during pregnancy. However, overweight and obese women have a higher prevalence of UI and AI in pregnancy and postpartum compared to normal weight women[16-20], as the increased bodyweight (and especially belly weight[21]) is in itself a strong contributing factor to the development of incontinence[13, 18, 20, 22, 23].

Widely varying time points for measurement, as well as no consistency between tools to assess incontinence, makes it difficult to state a precise prevalence of incontinence. Parity affects the prevalence rates, as multiparous women report UI to a higher degree than primiparous[14]. Various reports present prevalence rates from 27%[16] to 68%[18] mid- to late pregnancy, and between 6,9% to 45% within the first 6 months postpartum[16, 17, 24-27]. AI during pregnancy

and postpartum is less investigated, and has a lower prevalence than UI. Depending on type of AI, the prevalence ranges from 3,1% to 25,5%[28-31].

Physical Activity and Pregnancy

The Norwegian Directorate of Health recommends everyone, including the pregnant population, weekly 150 minutes (or 2,5 hours) moderate physical activity[32]. This is similar to the current recommendations from the American College of Obstetricians and Gynecologists (ACOG), which recommend at least 20-30 minutes moderate physical activity or exercise on most or all days of the week[33]. In addition, strength exercises with a focus on the pelvic, back and abdominal muscles, but also the body in general, are recommended during pregnancy. The general recommendation for a strength exercise program is to include around eight exercises for the larger muscle groups with three sets of 8 to 12 repetitions. Very heavy resistance training should be avoided in pregnancy to prevent contractions of the uterus[34]. It is also recommended to limit exercises in the supine position after gestational week 16, as the weight of the uterus and fetus may compress the vena cava and decrease the blood flow returning to the heart[33]. Women who were previously sedentary are recommended to start slow and increase the amount of activity to eventually reach the recommended amount[33, 34]. ACOG[33] recommends individual evaluation of sedentary women and women who might have obstetric or medical complications before starting an exercise program, and make individual adjustments if needed (Ibid). Physical activity or exercise maintains (or increases), the physical fitness level, and may be helpful for common pregnancy ailments like tiredness, anxiety or depression, edema and stress[34]. Physically active pregnant women tend to turn into active mothers[34], and for the overweight and obese female population this is an important factor for their future health. In a summary of current knowledge on exercise and its effects on the fetus, labor and birth by an IOC expert group[35], a high level of evidence was found that exercise during pregnancy reduces the risk of giving birth to an infant large for gestational age.

Pregnancy is sometimes referred to as a golden opportunity or a "teachable moment"[36] to adopt a more active and healthy lifestyle, and health practitioners are encouraged to advice about healthy choices to their pregnant clients[33]. Being pregnant and overweight or obese is rarely a

contraindication for being physically active[33], and this population should be encouraged to increase their activity level, for benefit both to themselves and their fetus. There are very few restrictions as to what type of activity a pregnant woman can do. However, activities with increased risk of falling and/or injuries to the abdomen (for example contact sports and horseback riding) and scuba diving should be avoided[34, 37]. Paying attention to the changes in the pregnant body (such as change in balance and increased flexibility in the joints) and acting accordingly is recommended[34]. There are a few absolute contraindications to aerobic exercise. These are significant heart disease, restrictive lung disease, risk of premature labor, expecting twins (or more) with risk for premature labor, persistent bleeding, incompetent cervix, placenta previa (after 26th gestational week), ruptured membranes, preeclampsia and severe anemia. Some conditions are also seen as more relative contraindications, such as (but not exclusively) extreme morbid obesity, extreme underweight, poorly controlled hypertension, hyperthyroidism and diabetes mellitus type 1, and intrauterine growth restrictions[33]. Exercise during a normal, uncomplicated pregnancy is beneficial when current recommendations are followed[34] and regular physical activity during pregnancy has no significant effect on gestational age at birth or preterm deliveries[33, 38], the duration of labor or prolonged second stage of labor[35, 38].

Incontinence

UI has several sub-classifications, but the following three are most reported in the literature; Stress urinary incontinence (SUI), incontinence related to urgency (UUI), and mixed reason incontinence (MUI). SUI is involuntary loss of urine when sneezing, coughing, laughing or during physical activity and (sudden) strenuous movements that increase the intra-abdominal pressure, straining the pelvic floor and urethra and thereby causing the leakage. UUI is involuntary loss of urine associated with an urgency to void. MUI is involuntary loss of urine due to both of the prior mentioned reasons[12]. SUI is the most common form of incontinence developed during pregnancy[23]. Anal incontinence is the involuntary loss of feces or flatus, and is often sub-divided into either fecal incontinence with loss of either liquid or solid stool, or incontinence of flatus[12].

A number of risk factors have been established for UI, including pregnancy and vaginal delivery[16-18, 22, 39, 40], being overweight or obese (defined by high BMI) both during and prior to pregnancy[16-18, 22, 39, 41, 42], high gestational weight gain [41] and smoking[17, 43, 44]. Having had UI in previous pregnancies, or having had UI before getting pregnant, increases the risk of having UI during a pregnancy and postpartum. In a study of postpartum women considered to have high risk of UI, investigators found that regardless of group allocation (exercise or control), if the woman was incontinent prior to the pregnancy, the incontinence rate increased significantly (with an odds ratio of 2,53)[24]. The presence of UI in the postpartum period has been found to be strongly correlated with being incontinent prior to delivery[16, 17, 44]. Furthermore, delivering an infant with high birth weight ($\geq$ 4000 g) has been identified as a significant risk factor for any UI in the EPINCONT study, a part of the HUNT 2-study[42], however, others have found no such relation[16]. Since children of obese mothers tend to be large for gestational age[45], together with the knowledge that the increased BMI is a contributing factor for the development of UI, these women have a multiplied risk of UI either during or after their pregnancies. The risk factors for AI are less investigated than for UI, but obstetric trauma such as anal sphincter ruptures, is one of the major causes of AI in women[28].

Urinary Incontinence

UI has a complex etiology, with many factors contributing to the problem, and it is not entirely known why some women get UI, while up to two thirds (depending on which prevalence report is read) stay continent throughout their pregnancies. The literature often focuses on two main theories about the causation of pregnancy-related incontinence. One of these theories says that UI is due to hormonal changes. The hormonal changes during pregnancy is a complex picture that changes throughout the course of pregnancy, and these hormone changes affect the female body in a great number of ways. This topic is still in its early stages, and is not yet fully understood, and research is still on-going both in animal studies and on humans. What we do know, is that the predominately female steroid hormones estrogen and progesterone levels increase during prengnancy[46]. Progesterone, which is a dominant pregnancy hormone from early on in the pregnancy has a relaxing effect on smooth muscle fibers, which is found in the urethra and the detrusor muscle (bladder)[46], may cause incontinence symptoms which exercise can not directly

prevent. Associations between rising steroid hormone levels and SUI was not present in a cohort study of gestational hormone effects on SUI[47], and the authors found this discovery a contradiction to the known effects of progesterone. The pregnancy hormone relaxin causes collagen in the connective tissue to become lax and decrease in function[46, 48]. The levels of relaxin changes during pregnancy, with an increase during the first trimester with a peak around 14 weeks of gestation and a subsequent decrease to about half the level of the peak around 24 weeks of gestation.. Observations of these changing relaxin levels and their correlation to SUI throughout pregnancy show that women with more stable (between gestational weeks 24-28)[49] and higher levels[47] of relaxin report no SUI. Which is, in fact, yet another contradiction to the known functions of the hormone, and further research is ongoing. However, in summary, what we do know is that these hormonal changes affect the pelvic floor and surrounding tissues to facilitate childbirth, but also relaxes the continence mechanism by loosening the ligaments supporting the urethra, bladder and vaginal wall and in effect activates the urination reflex prematurely[15, 48]. The second theory is that UI is caused by the anatomical changes and the mechanical pressure that a pregnancy entails[15, 50]. A literature review by Sangsawang[13] indicated that development of SUI during pregnancy was related to weaker pelvic floor muscles. Indeed, some studies investigating PFM strength and incontinence have found that women with a stronger pelvic floor were more continent[51, 52]. Continent women also had significantly thicker superficial PFM both during relaxation and muscle contraction, measured by perineal ultrasound[52]. Hilde and colleagues [53] investigated the PFM strength in nulliparous pregnant women with SUI and observed that the pelvic floor of the incontinent pregnant women was weaker than that of continent pregnant women in early pregnancy. Sangsawang[13] identified three underlying mechanisms that weaken the pelvic floor and lead to incontinence and pelvic floor dysfunction; An increased intra-abdominal pressure, impaired blood flow, and increased pressure to the PFM, the urethra and the bladder. Taken together, this will result in impaired oxygen flow to the tissue, and thereby impaired function of the continence mechanism. Pre-pregnant high BMI, high gestational weight gain and the growing uterus and fetus all cause these effects. All risk factors identified by Sangsawang[13] (smoking, age, constipation, pre-pregnancy SUI and gestational diabetes mellitus) could individually cause these effects by different mechanisms, and women could have several of the risk factors present, presenting a multiplied risk of getting SUI[13]. It becomes apparent that overweight and obese pregnant women have

multiple factors that could lead to incontinence, and we need to pay extra attention to prevent this problem in this population.

Anal Incontinence

Incontinence of stool (fecal incontinence) has been found present after both cesarean deliveries and vaginal deliveries, and frequently in women with a clinically recognized anal sphincter damage after vaginal delivery[31, 54]. Parous women with complete obstetric anal sphincter tears had twice the risk of AI, compared to parous women without such tears (relative risk=2,00)[54]. Risk factors associated with FI are macrosomia, median episiotomy, anal sphincter tears, UI prior to pregnancy[28], occipitoposterior presentation of the baby (abnormal position of the head during labor)[55]and delivery with need for assistance by forceps[56]. Higher maternal age have also been associated with an increased risk of AI by some[56], but not by others[28]. The risk factors associated with incontinence of flatus are similar to those of fecal incontinence[28]. One study found that it was more common for women who had a median episiotomy to experience FI than women with first and second degree lacerations after vaginal delivery[28]. In a long-term study 6-11 years after the first delivery, AI was associated with a weak pelvic floor[57]. Even longer-term follow-up about 22 years after birth, of women who suffered complete anal sphincter tears during labor found significantly higher incidence of fecal incontinence in these women, compared to a matched control group without sphincter tears[54].

A multivariate analysis of any postpartum AI showed that delivery by forceps significantly increased the risk, and forceps that needed episiotomy increased the risk of AI to 39% for women giving birth vaginally for the first time [28]. However, the authors found no association between maternal age, BMI, parity or epidural anesthesia.

The Pelvic Floor Anatomy and Physiology

The pelvic floor is built up of several striated skeletal muscles in two layers, the urogenital diaphragm and the pelvic diaphragm. It extends from the sacrum and coccyx to the pubis and ischium[46] (Figure 1). The muscles have different muscle fiber directions and sphincter functions, creating a structural supporting floor that creates an inward lift and luminal narrowing of the anus, vagina and urethra. A voluntary contraction of the optimally functioning pelvic floor muscles not only creates a closure of the urethra enough to cut off a stream of urine, but also stabilizes the pelvic organs and makes the pelvic floor more resistant to downward pressure. The continence mechanism includes the PFM, the sphincteric closure mechanisms of the striated and smooth muscle fibers of the urethra and the bladder support system (anterior vagina, endopelvic fascia, arcus tendineus fasciae pelvis and pelvic bone)[51].
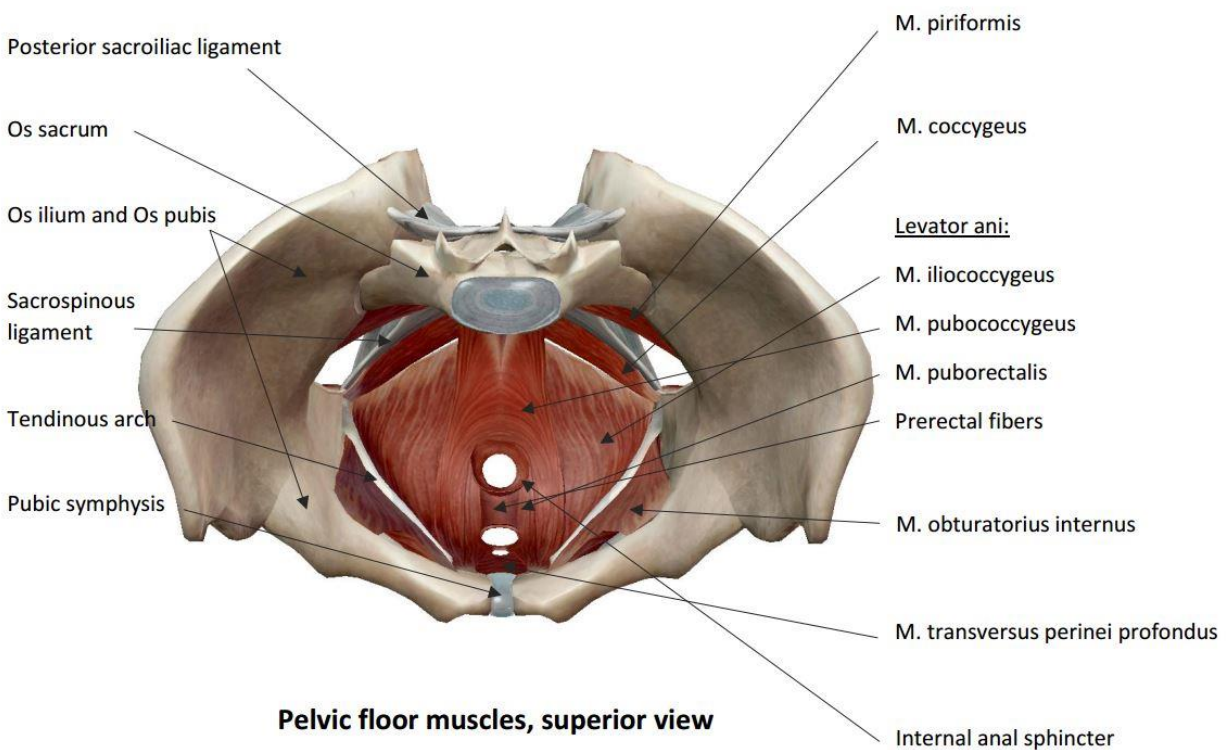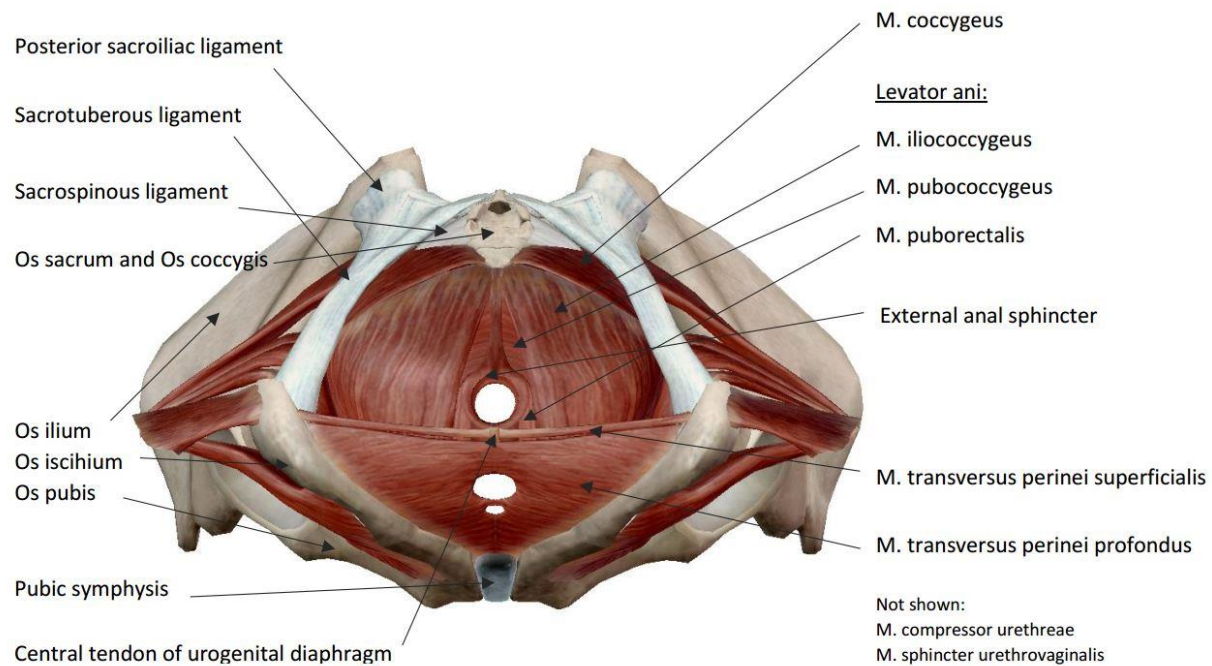
Figure 1. The pelvic floor anatomy. Image courtesy of Visible Body

Pelvic floor muscles, inferior view

Figure 2. The pelvic floor anatomy. Image courtesy of Visible Body

A correct voluntary contraction of the PFM is described as an inward movement or visually confirmed lift of the perineum while pressure around the pelvic openings is registered by either electromyography (EMG), manometry or palpation[58]. Manometry (or perineometry) is an objective tool for measuring the vaginal squeeze pressure. A manometer consists of a balloon catheter with a sensor attached by a (latex) tube to an electronic device which measures the level of displacement of water in centimeters as the catheter is squeezed. However, a manometer is not able to measure whether the movement is correctly performed, only that there is a pressure change[59]. An EMG vaginal/anal probe is a small cone-shaped device with electrodes on its surface that measures the muscle contraction by electronically detecting the neuronal activity during a muscle contraction[60]. This method of measurement is also, like manometry, not able to discern a faulty from a correct pelvic floor muscle contraction. Additionally, the (surface) EMG probe does not distinguish the signal from one muscle to another, and will signal muscle contraction from the surrounding muscles also[51, 60]. Both methods can be applied when measuring a maximum voluntary contraction (MVC) of the PFM held during some seconds, and also the PFM endurance, where the MVC is held, up to 10 seconds. The contraction is timed until

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the strength of the vaginal squeeze falters and weaken[61]. Both manometry and EMG produce reliable objective measurements, with a high level of both inter- and intra-rater reproducibility[59, 62].

Palpation is a subjective measurement method of vaginal squeeze strength and endurance. Such measurement is undertaken by inserting one or two fingers 4 to 6 cm inside the vagina, measuring circumferentially, the subjective level of strength[60, 61].The strength is graded by grading scales, most commonly the Modified Oxford Grading Scale[61]. Palpation is the only method to assess the correct performance of the contraction, but the validity of this method is discussed. When performed by an experienced practitioner, the palpation method to measure the PFM strength and endurance has shown a good intra-rater reliability[61] as well as showing a strong and significant correlation with manometry results[63, 64], but have a lower inter-rater reliability when compared to measurement with manometry[59].

Prevention and Treatment of Incontinence

Pelvic floor muscle training (PFMT), as further discussed below, is recommended as prevention of UI and PFMT has status as level 1, grade A evidence for the effectiveness of treatment and should be the first line of treatment[65, 66] for women with mild to moderate complaints of incontinence before exploring pharmacological, invasive or other treatments[51, 67]. Pharmacological treatments include (but are not limited to) anticholinergic and antimuscarinic drugs to suppress the detrusor to contract the bladder, and injections of botulinum toxin to the detrusor muscle. Surgery procedures, like the pubovaginal sling or injection of bulking agents to the surrounding tissue of the urethra helps by stabilizing the bladder neck[68, 69]. Other treatments include "bladder training", behavioral therapy or lifestyle changes, wearing of vaginal plug, and removable transvaginal, transanal and peripheral nerve stimulators[68, 69]. For AI, the conservative treatments include dietary and lifestyle changes, wearing an anal plug, and pharmacological treatments to manage diarrhea or constipation[70]. Sphincteroplasty and injection of bulking agents are common surgical treatments for persistent AI when other treatments prove ineffective[71]. These treatments will not be further discussed in this thesis.

Pelvic Floor Muscle Training (PFMT)

In 1990, Bø and colleagues[72] set out a course of approach to PFMT which was termed "intensive". This approach emphasizes the importance of MVCs to improve the strength of the pelvic floor and gain the best results for the patients in treating UI. After an intervention comparing intensive PFMT plus home-based PFMT, with home-based PFMT only, the intensive and supervised approach showed a clear advantage in terms of increased PFM strength and UI cure rates. Both groups were taught individually the correct performance of a PFM contraction, and the exercises were the same in both groups, but the intensive PFMT group met weekly with an instructor who encouraged and instructed in performing the PFMT exercises with MVC or close to MVC[72]. According to the recommendations on intensive PFMT, daily performing three sets of 8-12 repetitions of sub-maximum, or as close to MVC as possible, and holding the contraction 6-8 seconds, and if necessary, begin the exercise routine with fewer contractions if you are a novice[72, 73].

The theoretical background for this approach is based on current knowledge in muscle physiology, and the general recommendations about strength and hypertrophy training of skeletal muscles[51, 74]. Resistance training changes the muscular morphology, i.e. increased motor unit recruitment and an improved neuromuscular function, increased cross-sectional area of the muscle fiber and increase strength of connective tissue surrounding the muscle and enhanced tensile strength[51, 74, 75]. According to the American College of Sports Medicine[74], there is strong evidence that the number of repetitions (8-12) and sets (three) maximizes the muscular strength and hypertrophy, and affects all the aforementioned effects of muscle morphology, in untrained and intermediate level individuals. For large muscle groups the intensity (or MVC) is measured in a percentage of the maximal load for one repetition maximum[74]. To my knowledge, measuring one repetition maximum for the PFM is either very difficult or impossible due to the anatomy of the muscle group and its location, as the PFM is not attached across any joints and forms a stabilizing "hammock" inside the pelvis. The high frequency of the exercise is supported by the rationale that high intensity high frequency exercise with short sessions allow for periods of recovery and reduced fatigue[74]. When the PFM are strong, only maintenance of the strength is necessary. And according to Mørkved and Bø[73] very few have studied the long-

term maintenance training effect for the PFM, and indicate that twice weekly PFMT sessions is sufficient once the strength in the PFM is adequate.

The intent of the intensive PFMT protocol is to achieve larger strength and muscle volume, and increased control of the PFM. Ideally to a level where the pelvic floor responses automatically to events causing increase of abdominal pressure due to the greater "stiffness" in the pelvic floor, and to help bring the levator plate to an elevated and more functional position in the pelvis, granting a better support of the pelvic organs [51]. Additionally, the conscious contraction of the PFM in anticipation of any event that causes leakage (a cough for example), or the "knack", is a behavioral change aspect to the PFMT, which will affect the pelvic floor stiffness and prevent urethral descent[76] and, in effect, SUI in these situations[51, 65, 77]. The "knack" has been added to the exercise protocol in some interventions[20, 24, 78], to be performed as often as needed and remembered, aiming to teach automated behavior patterns that lessen the SUI symptom burden, but its effects are rarely analyzed alone[65].

Dumoulin and colleagues[77] aimed to review the literature to conclude about the optimal exercise in treatment of SUI for women. In their search, only 8 RCTs (with 370 participating women) were identified, with a large variance in the training interventions. The authors concluded that PFMT was better in treating SUI than no training or placebo drug therapy. The women in the interventions groups (pooled data from all 8 studies) were 17 times more likely to partly or totally get cured from SUI than control group-participants, regardless of type of training program they were introduced to[77]. In several RCTs reviewed by Mørkved and Bø[73], an intensive training protocol gave both statistically significant and clinically relevant results on improvement of PFM strength and UI symptoms, and this approach to PFMT interventions was the authors recommendation. This is also one of the conclusions from a Cochrane review[40], saying that the dose of exercise combined with increased health practitioner contact (as opposed to the standard care) was beneficial as a primary or secondary prevention of incontinence. Very few reports of adverse effects after PFMT exist, and the side effects of PFMT are considered mild (pain or uncomfortable feeling during exercise and of psychological/social nature)[65]. The addition of bio-feedback or electrostimulation to a PFMT protocol has shown promising results, and could further improve or make the progress more efficient[65, 79], although all studies do not agree with this[80]. Vaginal cones and low intensity PFM contractions give significantly less

result in treating or preventing UI[81, 82]. The MVC or intensive training approach to PFMT has been shown to be superior to other methods to training the pelvic floor. The use of bio-feedback, electrostimulation and vaginal weight cones is beyond the scope of this thesis.

As we have learned above, there is a number of RCTs that have shown that PFMT is effective for preventing UI or as treatment for UI when performed correctly[20, 24, 29, 79-81, 83-87]. There are also a number of alternative approaches to exercise of the PFM for treatment of incontinence that are more or less investigated with RCTs. Approaches like pilates, yoga, deep abdominal muscle exercises for the transversus abdominis, breathing exercises and the "paula method" (the theory that all sphincter muscles are connected and will co-contract) all have insufficient evidence of effectiveness, according to Bø and Herbert[88]. However, the Cochrane Continence Group is currently undertaking a systematic review on the effectiveness of yoga to treat incontinence in women[89], and position on this topic might need to change.

Many studies experience problems with adherence to the prescribed PFMT protocol, or drop-out of participants[73]. Indeed, adherence to exercise interventions are important, as there is a clear dose-response to all exercise. The PFM is no different than the larger skeletal muscles in this effect. Reilly and colleagues[20] analyzed the correlation between the effectiveness of the PFMT protocol, and the participants' adherence to the protocol. They found that adherence to the PFMT protocol for 28 days or more was enough to show a significant dose-response causal relationship to the exercise in terms of cure-rate of UI. Women exercising PFMT for 28 days or more had less likelihood of having postpartum stress incontinence (18%), compared with both the control group (33%) and those in the intervention group who did less than 28 days of training[20]. Similar conclusions were drawn by Mørkved and Bø[90], who found a clear dose-response to exercise, as the participants (from both intervention and control groups pooled together) who had done PFMT 3 times or more weekly had significantly stronger PFM compared to participants who had done less than 3 times PFMT weekly.

The education part prior to training is important in order to prevent incorrect performance of the contraction. As these exercises are of a more "personal nature", it needs a personal motivation to perform. If done incorrectly (straining or using different muscles) the exercise could lead to no improvement or worsening of symptoms. One study reported that 4% of the women could not do a correct PFM contraction at baseline, even after thorough instruction[26]. Bø and colleagues[72]

reported that 31% of their participants contracted the PFM incorrectly at baseline. This proportion dropped to 7,7% after 6 months of training. Furthermore, in a cross-sectional study of 666 women 6-11 years after delivery, the investigators found 2% of their participants unable to perform a voluntary PFM contraction[57]. Compliance to a PFMT program is higher when the patient receives regular individual instruction and guidance, rather than information pamphlets[86, 87]. Additionally, supervised PFMT, with frequent consultations or classes is more effective than home exercise[65]. Based on the above findings, it seems beneficial for correct performance of the PFMT to have individual instruction from an experienced physiotherapist or gynecologist.

PFMT Interventions

There are a few different ways to look at the results of a PFMT intervention, depending on the aim of the intervention. Following is a detailed look at the most commonly found aims of PFMT interventions: to study the effects of the intervention on PFM strength, to prevent incontinence during pregnancy and/or the postpartum period, to treat incontinence during pregnancy and/or the postpartum period, and finally, a mixed approach of either preventing or treating incontinence by including women both with ad without symptoms of incontinence. The effectiveness of PFMT in prevention and treatment of AI is less investigated, and is presented by itself.

Intervention and Pelvic Floor Muscle Strength

As with all strength training, muscle fibers in PFM will increase in cross-sectional diameter via hypertrophy by strength exercise. In addition, the training strengthens the connective tissue and neural adaptations become more effective by recruiting more active motor neurons. This increase in muscle power and muscle tone may lead to a higher resting position of the PFM in the pelvis (especially in the untrained, damaged or dysfunctional pelvic floor), and hence restore a more optimal function and reflex activity to the continence mechanism[51].

A quite recent cross-sectional study compared the PFM strength of primigravidae, all three trimesters represented, with non-pregnant nulliparous women, to assess what effects pregnancy itself has on the PFM strength. The nulliparous control group was significantly stronger than all

women in all trimesters. The women in first and second trimester was significantly stronger than the women in the third trimester[91]. This is in line with earlier findings from Resende and colleagues[92] who also observed lower PFM strength in women in the third trimester compared to the non-pregnant control women. Long term effects on the PFM after giving birth have been studied, and a significantly reduced PFM strength was seen 6-11 years after first vaginal labor, compared with women delivered by cesarean section. The strength was further reduced by having had instrumental deliveries[57]. Baessler and Schuessler[93] concluded in their review that regardless of measurement method used, the PFM strength decreases after normal vaginal delivery of a child, this is in agreement with Sigurdardottir and colleagues'[94] findings. Furthermore, the PFM endurance is significantly reduced after first vaginal birth, both normal and with instrumental assistance, in nulliparous women[94]. A non-randomized controlled study aimed specifically at investigating the effects of PFMT during pregnancy, had the intervention group practice an intensive PFMT program (in line with Bø et al[82]). They found an increase in PFM strength in both the intervention and control group after the intervention ended in late pregnancy. However, the increase in the intervention group was significantly larger than the increase in the control group, measured by digital palpation and perineometry[95].

Hilde and colleagues[96] investigated women with and without major levator ani defects 6 weeks postpartum. Such defects to this muscle is due to damage to the perineum during vaginal delivery. They found that women with major defects to the levator ani muscle had 47% lower PFM strength and endurance compared to those without such defects. A very small proportion of the participants (4%) was unable to contract the pelvic floor, even after thorough instruction, and this was not restricted only to the women with the levator ani muscle defects[96]. As most of the participants with or without levator ani defects could contract the PFM correctly relatively shortly after giving birth, the authors suggest that undamaged muscle fibers can compensate for the loss of function in the injured parts of the muscle[96].

Several interventions are aimed at preventing or treating UI, AI or pelvic organ prolapse by use of PFMT in one form or another. Study populations vary, from non-pregnant to pregnant or in the postpartum, and among different age groups. Regardless, these studies possess valuable information as to how PFMT can improve the PFM function and strength. In a study of non-pregnant women with urodynamically proven SUI (mean age 50 years), PFM strength increased

significantly when PFMT was taught on the individual level, compared to PFMT taught in a group setting (no untreated control group was included). Both interventions lasted 12 weeks with 2 weekly sessions. The individual exercise group increased the mean PFM strength by 2 grades on the Modified Oxford Grading System scale, whereas women in the group setting showed an increase of one grade (p=0,0001)[84]. Women with pelvic organ prolapse also increased significantly in PFM strength and endurance (and symptom burden) after following an intensive 14-weeks PFMT program, when compared with an untreated control group. Both groups received individual instruction on how to perform PFM contraction correctly at inclusion in order to collect data, but the control group was not given instruction on exercise protocols and was not in contact until the end of the study[97]. This finding was confirmed by Brækken and colleagues[98], who also aimed mainly at treating middle-aged women with pelvic organ prolapse, showing a significant effect on PFM strength and endurance[98]. Additionally, 3D/4D ultrasound of the pelvic floor and pelvic organs showed a significantly greater elevation of the bladder and rectum in the exercise group, and this had a significant positive correlation to the increased PFM strength.

A RCT by Hilde and colleagues[26] had the aim of both treatment and prevention of UI (of the same postpartum study population as a previously mentioned study, with participants with and without major levator ani muscle defects[96]). Starting 6 weeks postpartum, their exercise group did an intensive PFMT program, using the same exercise protocol as the previously mentioned study by Brækken and colleagues[98], for 16 weeks. As with the previous study, both groups increased in PFM strength and endurance, but with no significant difference between the intervention and control group. Stratified analyses to control for levator ani muscle defects, gave the same non-significant conclusion[26]. These are in contradiction to findings by Mørkved and Bø[86]. In their postpartum intervention of 99 matched pairs of mothers, which had the same aim as Hilde and colleagues[26], to prevent and treat UI after labor. Eight weeks of intensive PFMT with physiotherapist-led group exercise resulted in significant increase of PFM strength, compared to the control group. The control group had also increased significantly in PFM strength at post-test compared to pretest values, but the intervention groups strength increased significantly more[86]. The same participants were contacted for a one-year follow-up[90]. More than half of the former PFMT group had continued with the exercise, and the whole group had further significantly increased in strength since the intervention ended[90]. Dumoulin and

colleagues[99] undertook a tree-armed RCT aimed to treat persistent postpartum UI in parous but currently non-pregnant young women. They requested their control group to not exercise the pelvic floor. Surprisingly, they found no significant difference in the change of PFM strength or explosive strength (measured by dynamometer in Newton/second) between any of their groups after 8 weeks of either PFMT, PFMT with abdominal exercise, or no PFMT exercise at all. However, the number of participants in each group was low, limiting the statistical power of the study[99]. Sampselle and colleagues[100] found that the intervention group, that received individualized intensive PFMT programs, showed a non-significant tendency of stronger PFM than the control group 6 weeks postpartum. Unfortunately, this study was also underpowered for analysis on PFM strength, as a wide range was observed. Similarily, findings by Meyer and colleagues[80] also failed to see any difference in strength between the groups after a 6 weeks biofeedback PFMT-intervention two months postpartum.

In summary, several studies find both confirming and opposing results of a PFMT intervention and its effects on PFM strength. I interpret this to be due to differences in methods of measurement, as no direct comparison can be drawn if methods differ, and differences in exercise dose and intensity. Additionally, the populations studied are not identical, they have different ethnologic heritage and dissimilar medical history or cause for the PFM weakness.

Prevention of Incontinence During Pregnancy and the Postpartum Period

The theoretical rationale behind why PFMT will prevent or treat UI, is that trained muscles are less prone to injury, and might be easier to "bounce back" after injury as the motor patterns and the cognitive learning of muscle contraction has already been learned. The greater strength and increased neuronal pathways in the trained PFM serve as a buffer for injury and muscle function maintain the urethral closure pressure and prevent leakage[40].

Conclusions on the preventive effect of PFMT by the latest Cochrane review on PFMT interventions during or after pregnancy[101], was that beginning an exercise routine for the pelvic floor during pregnancy protects against postpartum incontinence for many women. Participants in prenatal PFMT interventions were about 50% less likely to develop UI in the first 6 weeks postpartum, and 29% less likely to report UI 3-6 months postpartum compared to the

control group[101]. Sampselle and colleagues[100] found significant difference in UI symptoms with women in the intervention group reporting less UI at 36th gestational week, 6 weeks and 6 months postpartum. Similar results were seen by Mørkved and colleagues[29] who observed significantly fewer leakage episodes in gestational week 36 and 3 months postpartum in the intervention group. Recent results from a RCT including 63 pregnant women by Sangsawang and Sangsawang[102], are in agreement with this, the PFMT group had significantly less participants with SUI at 38th gestational week after a 6 week intervention. Furthermore, the 9 participants in the intervention group who reported SUI, experienced significantly smaller volume of leakage, and the leakage was less severe and less frequent than what was seen among the women with SUI in the control group[102]. The intervention was bi-weekly visits and training in groups supervised by a midwife, and home exercises. Their PFMT protocol was to perform close to MVC held for 10 seconds and 10 rapid contractions, 40 times minimum 5 days weekly, in supine, sitting, standing positions.

Reilly and colleagues[20] included pregnant women who were about halfway into their pregnancies, who had increased bladder-neck mobility during Valsalva maneuver. Increased bladder neck mobility may be a marker for developing SUI. Their intervention group participated in monthly supervised intensive PFMT supervised by a physiotherapist, and repetitions of PFMT individually 2 times daily. Additionally, the women were instructed to perform "the knack". The intervention group had significantly less SUI three months postpartum than the control group, but no differences was seen in bladder-neck mobility or PFM strength[20].

I have not found any RCTs that solely aims to prevent pregnancy and postpartum AI, or that aims to prevent pregnancy and postpartum UI and AI.

Intervention to Treat UI

Regarding treatment of UI during pregnancy or in the postpartum period, conclusion of the above Cochrane review was that regardless of time of implementation of the training program, the women in the PFMT groups (pooled data from 6 studies) were less likely to report any UI postpartum, and this effect was seen up until 1 year postpartum[101].

Dinc and colleagues[103] included 80 incontinent pregnant women between gestational week 20 and 34, and offered the intervention group intensive PFMT in three stages, with both quick and continuous hold PFM contractions, with increasing amount of sets (2-3 daily), repetitions (10-15 daily) and seconds to hold the contraction (3-10 seconds). Number of incontinence daily episodes, i.e. the number of incontinent women (per authors definitions) in the PFMT group decreased significantly compared to the decrease in the control group both in late pregnancy (36th to 38th week) and in 6th to 8th weeks postpartum (43% vs 71% in late pregnancy and 17% vs. 38% postpartum in the intervention and control group, respectively)[103]. Group aerobic fitness classes with focus on PFMT during pregnancy has been found to be ineffective. Bø and Haakstad[104] randomized 105 sedentary women in the first half of their pregnancy either to attend (preferably at least twice weekly) a general fitness class for 12 weeks, or to a control group receiving standard maternal care only. There were no differences with regards to self-reported UI or AI between the groups at the end of the intervention, and no difference at 6 to 8 weeks postpartum.

Dumoulin and colleagues[99], who included postnatal women with persistent UI three months postpartum, with episodes at least once per week, asked their control group specifically to not practice PFMT until the 8 weeks trial period had ended. There were two parallel exercise interventions in this study. The PFMT group met a physiotherapist individually once every week during the intervention span and performed PFMT with electrostimulation and biofeedback. The second intervention group did the same PFMT protocol and in addition, a training program focusing on the deep abdominal muscles (transversus abdominis). Both intervention groups were asked to perform PFMT home exercise 5 days weekly. The two intervention groups improved significantly from baseline, with over 70% of the participants defined as cured from UI (pad test) in both groups. The control group did not improve[99]. Similar results were seen by Wilson and Herbison[105], allocating postpartum women to an intervention group (n=117), receiving one out of three different PFMT protocols (PFMT alone, vaginal weight cones alone, and PFMT plus vaginal weight cones), or inactive standard postpartum care control group (n=113). Half of the participants in the intervention group got continent, significantly more than in the control group (24% continent) at the end of the study.

Mixed PFMT Intervention to Prevent and Treat Incontinence

Some studies include both continent and incontinent women, and the intervention has a mixed prevention and treatment approach. The current Cochrane review concluded that prenatal mixed prevention and treatment interventions reduce the prevalence of UI in late pregnancy, and in studies that have had an adequate exercise dose, the effect was found to last through to 6 months postpartum[40]. Chiarelli and Cockburn[24] included 676 women who were at higher risk for developing UI postpartum. The participants had either given birth to a large for gestational age baby (≥ 4000g) and/or had forceps or ventouse delivery. Special efforts were made to increase the compliance through the use of "the health believe model" and various motivational tools. Significantly more participants in the intervention group performed PFMT 3 times or more weekly. The PFMT were performed three times daily, each contraction was held for 3-6 seconds. Amount and intensity of contractions was not mentioned, as the intervention was individually tailored. Additionally, it included "the knack" and co-contraction of the transversus abdominus muscle. The UI at 3 months postpartum in the intervention group was 31,8% compared to the 38,4% in the control group, significantly less (adjusted OR=0,65, p=0,01). The intervention group performed significantly more PFMT during the three months, compared to the control group, and the authors credit this to the behavioral model component in the intervention. No urodynamic and clinical PFM assessment were performed[24]. Stafne and colleagues[87] found a significant preventive effect in their PFMT intervention group; significantly more women who had been continent at inclusion (around 20th gestational week) remained continent after 12 weeks of supervised PFMT and general exercise classes and home-based PFMT, compared to the control group receiving standard maternity care only. Furthermore, among the women who were incontinent at inclusion, significantly less UI of any kind was observed in the intervention group, hence showing a treatment effect[87].

Interventions to Prevent or Treat AI

A recent RCT that aimed to treat or reduce postpartum AI[106], used the intensive PFMT intervention by Mørkved and Bø[73], with emphasis on close to maximum PFM contractions. The participants were encouraged to perform PFMT daily for 6 months. A significant and clinically relevant reduction in St. Mark's score (which is one of the two measures of

incontinence used in this thesis, described in detail below in the methods-section) was seen in the intervention group[106]. The women were included in this study approximately 1 year postpartum, and therefore it is unlikely that results were due to normal rate of restitution after giving birth. On the other hand, no difference in mean anal sphincter strength was seen between the group after the intervention[106].

Similarly, Stafne and colleagues[87] found that multiparous women in their intensive PFMT intervention group reported significantly less AI after the intervention compared to the multiparous women in the control group (3% vs. 8% p=0,03). A trend of lower prevalence of AI was found in the PFMT group, however this was not significant[87]. In contrast, Wilson and Herbison[105] found no differences in prevalence of AI a year postpartum between their groups in a PFMT intervention that started 3 months postpartum. This intervention group was either one of three alternatives: PFMT, vaginal weight cones, or PFMT and vaginal weight cones. The PFMT group met with a physiotherapist at 4 occasions from inclusion till 12 months postpartum, and the protocol consisted of many PFM contractions (up to 100) daily. Contradicting to these findings, another study with similar exercise protocol, found significantly reduced numbers of FI in the intervention group after low-intensity PFMT (80-100 PFM contractions daily), compared to the control group (4,4% vs 10,5%, p=0,012) at 12 months postpartum[107]. At long-term follow-up of these participants[107], the significant difference in rate of FI was lost after 6 years.

Interventions Without Evidence for Effect on Incontinence

A few studies have found PFMT to have negligible or no effect in preventing or treating UI both in late pregnancy and postpartum[108-110]. Mason and colleagues[109] found no significant effects of PFMT on late pregnancy and postpartum SUI. Their exercise group performed more PFMT than the control group, and performed high intensity training with MVCs as recommended by earlier studies which did find an effect of PFMT[29, 72]. However, Mason and colleagues [109] had only one physical meeting/trainings session monthly for four months, compared with weekly supervised sessions for 12 weeks intervention showing significant results[72]. Sleep and Grant[110] also reported a similar prevalence (about 22%) of UI in both of their groups 3 months postpartum. This study is from 1987, and the exercise program was very different to what is recommended today. The intervention group was mostly left to themselves after hospital

discharge, with a training diary with new approaches weekly to exercising the PFM, some of which have been recommended against in later time[69, 73] (practice by cutting off urine stream). Returning to our century, a Dutch RCT[108] found no difference in UI prevalence or severity of UI between intervention and control group. Over half of the participants were still incontinent at 6 and 12 months postpartum. Only incontinent pregnant women were included in this study. The intervention group were given individual training sessions (bi-weekly for a total of 4 times during pregnancy). However, the training program is not described in terms of which exercises were performed and how (repetitions, duration and intensity etc), and was highly individualised, making it difficult to make comparisons with studies that found effects of PFMT.

Long-term studies have shown that after taking part in a PFMT intervention, the effects of training are evened out so the initial differences between groups are less prominent in longer time-span follow-up(6-12 years)[111]. However, the intensive PFMT has been suggested to still have effect about a year postpartum[90]. This finding is supported by Boyle and colleagues[40] where PFMT used as treatment for UI, was still effective at 12 months postpartum no matter if the treatment began ante- or postnatally. The systematic Cochrane review saw this as the most significant conclusion of their review [40]. In contrast, Sampselle and colleagues[100] did not find any between-group difference in UI symptoms between the groups 12 months postpartum.

Subgroup analyses of the effects of PFMT on groups with a high BMI are rare. An Egyptian RCT allocated obese non-pregnant women with SUI to either deep abdominal muscle training or PFMT for 12 weeks. The results showed significant within-group increase in vaginal squeeze pressure and urethral leak-point pressure (a way of diagnosing SUI) in the group exercising the deep abdominal muscles and not in the PFMT group. However, there was no significant between-group difference after the intervention, and the authors suggested that the contraction of the transversus abdominis and obliquus internus muscles also activates the pelvic floor[112]. In this study, however, the approach to PFMT was different to that of the intensive PMFT protocol described above, as they had a constant monitoring (both with manometry and palpation) of the pelvic floor on all training sessions, with a total of 45 contractions held 10 seconds each. To the best of my knowledge, there is no previous PFMT interventions including only obese pregnant women, but some of the previous studies have done subgroup analyses for different BMI strata.

Reilly and colleagues[20] presented a subgroup analysis showing that the likelihood of being continent postpartum was significantly higher for the women with a lower BMI. It is only a slight difference in BMI for the continent and incontinent (BMI=24,1 vs. 25,4, p=0,042), so the clinical significance for this finding is questionable. As stated above, Wesnes and colleagues[18] found high BMI to be a risk factor for UI during pregnancy, with an increased prevalence of any UI in the strata of women with a BMI above 25 kg/m², with increasing numbers correlating with increasing BMI. Findings from NHANES are in agreement, with increased BMI associated with pelvic floor disorders, including UI and AI[19]. This association is also recommended for further study by Diez-Itza and colleagues[23]. Approximately 30% of the participants in an Australian postpartum intervention were classified as obese, and analysis of this subgroup was pooled together with the overweight women in the study. The overweight and obese had a non-significant, but increased risk of developing UI 3 months postpartum (adjusted OR= 1,23, p=0,269)[24]. These results were, however, not explored further for possible causes for this, even though over 30% (238 women) of their participants were BMI ≥25 kg/m².

Urinary and anal incontinence is a wide-spread problem which is associated with shame, hygienic or social problems and a lowered quality of life for years following the delivery[11]. Incontinence is a more common problem for obese women(ref), but very few studies have been undertaken in addressing this population. Prevention and treatment of incontinence with PFMT has, as we have seen above, proven effective[73, 83, 101], and has had very few reports of adverse effects[73] for normal-weight pregnant or postpartum women (or in a study population with a mixed weight class). But little is known about if and how PFMT works in preventing or treating incontinence in overweight and obese pregnant women.

My hypothesis was that overweight and obese pregnant women allocated to a training intervention with a specific focus on pelvic floor muscles, would have stronger pelvic floor muscles in late pregnancy and postpartum, compared to a control group receiving standard maternal care only. Secondary, I hypothesized that the stronger pelvic floor musculature would result in a lower prevalence of incontinence.

Method

Design

This is a sub-study of "Exercise Training in Pregnancy" (ETIP)[113] . ETIP was a single centre, randomized controlled trial with two parallel groups, with allocation ratio 1:1. The groups were one intervention group that was offered supervised exercise training during pregnancy at the St. Olav's Hospital in Trondheim, Norway. The other group was a control group, receiving the standard maternity care only. The ETIP trial was undertaken at the Norwegian University of Science and Technology (NTNU) and the university hospital, St. Olav's Hospital. Recruitment of participants started in September 2010 and ended in March 2015, with the last data collection in September 2015. The trial was approved by the Regional Committee for Medical and Health Research Ethics (REK midt 2010/1522), and registered in ClinicalTrials.gov (NCT01243554). All procedures in the ETIP trial were consistent with ethical standards of research and the Declaration of Helsinki.

Participants and Recruitment

Women with self-reported pre-pregnancy BMI of 28 kg/m^2 or more were invited to participate in the study by letter sent along with the invitation for the routine anatomical screening ultrasound (which is done around gestational week 18) at the hospital. Google advertisements, distribution of information sheets about the trial at St. Olav's hospital and information sent to all general practitioners in Trondheim were also used for recruitment.

Participants were eligible for ETIP if they were over 18 years, with a singleton pregnancy confirmed by ultrasound at 11-14 gestational weeks, previously sedentary, and without risk factors (apart from high BMI) for complications during pregnancy or preterm delivery. Participants also had to be able to participate in testing and exercise training at St. Olav's Hospital. Exclusion criteria were having a high risk for preterm labor, disease that could limit participation, and habitual exercise (twice or more weekly) in the period before inclusion. All participants received written information about the trial, a standard information pamphlet from the Norwegian Health Directory[114], and signed informed consent on behalf of themselves and

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their offspring before participation and randomization. All women received infant food worth 500 NOK at the postpartum visit.

Interventions

Intervention Group

Women in the intervention group were invited to come for organized, supervised exercise training at St. Olav's Hospital three times per week from inclusion to delivery. The exercise was supervised by physiotherapists, and was offered both during daytime and afternoons, in small groups when possible, or individual sessions. The program was designed in accordance to the guidelines from the American College of Obstetrics and Gynecology[115] and recommendations from the Norwegian Health Directory[34]. The exercise training consisted of warm-up for 10 minutes, followed by endurance training as walking or running on a treadmill for 25 minutes; with a moderate intensity of up to 80% maximal capacity using the Borg scale for rate of perceived exertion (where a rating of 12-15 corresponds to 80 % of maximal capacity)[116]. The endurance was followed by strength exercises, stabilization exercises of the pelvic and back muscles and PFM exercises. The strength exercises were squats, diagonal lift on all fours, push-ups, the "plank", and oblique abdominal crunch. The PFM exercises consisted of three sets of 10 repetitions of 6-8 seconds duration, with maximum contraction, followed by three to five quick contractions immediately after the sustained hold repetitions. There was a one-minute break between sets. The sets were possible to perform in three different positions; standing, kneeling on all fours and sitting (Figure 3). Positions were individually chosen based on personal preference, need for variation and also progression of skill or improved strength. The women were instructed to "pull up and hold the pelvic floor, hold, hold, hold! Release slowly." They were also recommended to do home-based exercise of 45 minutes at least once per week, and to keep an exercise diary individually. The home exercises were the same as the supervised program at the hospital. They were encouraged to undertake PFM exercises at home daily in addition to the hospital-based program. The intervention ended at delivery. All participants in the intervention group were offered one half-hour session of motivational interviewing at the beginning of the training period.

Positions for PFMT

a) Sitting with straight back

b) kneeling on all fours

c) standing, keeping glutes relaxed

Figure 3. Illustration of PFM exercises.

Control Group

Women in the control group received the standard prenatal follow-ups by midwife and/or general practitioner. In Norway, the prenatal maternity care is free, and consists of 8 routine prenatal visits, and a routine ultrasound at week 18. They were not told to restrain from exercise or physical activity or PFMT.

Both groups received a standardized pamphlet containing general advice when pregnant, in which there is advice about nutrition and physical activity (including PFMT) in pregnancy.

Assessments and Outcomes

Assessments were done at inclusion/baseline (12-18th gestational weeks), in late pregnancy (34-37th gestational weeks) and three months postpartum.

Primary Outcome

The primary outcome measures in this sub-study was change in PFM strength between time of inclusion and late pregnancy, and between inclusion and 3 months postpartum, which was assessed by clinical examination performed by a gynecologist. The gynecologist assessed PFM strength and PFM contraction by use of the Modified Oxford Grading System[61]. With the participant in supine position with bent hips and knees, an observation of the perineal lift during PFM contraction was followed by digital palpation to evaluate if the contraction technique was correct. After instruction, if needed, the grade of the contraction was set by Modified Oxford Grading System, where grades are "no contraction", "flicker", "weak", "moderate", "good" and "strong". During the clinical exam, the women got instruction on a correct PFM contraction, after a first attempt without instruction. Only PFM contractions producing a visible inwards movement of the perineum was approved as correct. Co-contraction of surrounding muscles (abdomen and glutes) was discouraged. Collection of data by manometry of vaginal squeeze pressure (MVC and endurance) with was performed. Due to technical difficulties with the apparatus, the data was considered unreliable and has not been included in the analysis. The same gynecologist undertook all the tests. Self-reported frequency of home-based PFMT was collected by questionnaire on baseline, late pregnancy and three months postpartum. Additionally, the number of daily PFM contractions was asked in the three months postpartum questionnaire.

Secondary Outcomes

Secondary outcomes were self-reported prevalence of UI and/or AI. Two validated questionnaires for self-assessment of UI symptoms (Severity index)[117] and AI symptoms (St. Mark's score)[118] were answered by both groups prior to all clinical examinations.

The severity index (UI) consists of two questions, "how often do you experience urine leakage?" and "how much urine do you lose each time?". The frequency question has four levels plus an option for "never", ranging from "less than once per month", to "every day and/or night", which were coded 1-4 and never=0. The question about leakage amount has three levels, "droplets", "small splashes" and "more", plus an option for never. These alternatives were coded 1-3, and "never" being 0. The index is then created by multiplying the values from these two questions,

and further classified into the following classes: 1–2=slight, 3–6=moderate, 8–9=severe, 12=very severe.

Women answering "yes" to one or more of the following questions were considered to have SUI: "Do you have loss of urine now during:" "cough, laughter or sneezing?", "Physical activity"or "sudden movement, lifting". The women were considered to have UUI with a positive answer to the question "sudden urge, problems reaching the toilet on time". MUI was defined if there was positive answer in both categories.

The St. Mark's score questionnaire was used to assess the severity of self-reported anal incontinence. Answers to questions about leakage of solid or liquid stool, gas and if the incontinence caused alterations in lifestyle had five answer options about frequency, and were coded as 0 (=never) to 4 (=daily). Two questions ("do you need to wear protection or plug?" and "do you take constipating medications?") had options of yes and no, coded to no=0 and yes=2. The last question in the scoring system ("lack the ability to defer from defecation for 15 minutes?") also had a yes/no option, but "yes" is coded to 4. All these questions values were added up, and the sum gave a score on severity of AI. Minimum score is 0 =perfect continence, and maximum score 24= totally incontinent.

Sample Size/Power

The power calculation for the ETIP trial was based on the primary outcome measure; maternal weight gain from inclusion to delivery. It was assumed that a 6 kg mean difference between groups to have clinical relevance, according to findings from earlier research[119, 120]. Setting a 5 % level of significance, and a standard deviation of 10, and a power of 0.90 gave a target study population of 59 in each group. An estimated dropout-rate of 15 % made the goal to include 150 women in the study. No power calculation was made for this sub study.

Randomization and Allocation

The women were randomized 1:1 to either exercise or control group after the baseline assessments by a computer based randomization system developed and administered by another department of NTNU (unit for applied clinical research).

Blinding

The clinical tests were done by a gynecologist blinded for group allocation. The remaining data collection and exercise training in the ETIP trial were done by Kirsti Krohn Garnæs and Trine Moholdt. These were not blinded to group allocation. During the last period of the data collection I observed some of the women coming in for assessments and was blinded for group allocation of these participants.

Statistical Methods

In this secondary analysis, I only performed analysis on participants that had measurements of the PFM strength undertaken by the gynecologist. Exclusions from analysis were made by filtering out participants having no data in neither of the assessments of Modified Oxford Grading System. Furthermore, the analysis of the main and secondary outcome was made with including only participants who had at least two time points of measure, with one of them being the baseline measurement. Due to variations of which one of the post-tests (late pregnancy or 3 months postpartum) that was missing for some individuals, a separate baseline value for Modified Oxford Grading System is presented together with each of the analyses for comparison.

To determine if the data was normally distributed, I inspected histograms, Q-Q plots and tested for normality with Shaphiro Wilks test. Some data, including main outcome (change in PFM strength) and St. Mark's score on all test points were found to not be normally distributed. The baseline severity index data was also not normally distributed, and on closer inspection, one outlier was identified. Experimental removal of this outlier gave the data a normal distribution. This outlier also did not fit the requirements for further analyses, as this participant had only met for the baseline the strength measurements. I removed this outlier from the analyses. The data from the St. Mark's score presented a severe positive skew. I log10-transformed these to see if it

could get them more normally distributed, but the data was still not within the requirement of normality. Hence, these log-transformations were discarded. The self-reported number of daily PFM contractions in home-based PFMT was also not normally distributed.

Between-group differences in categorical data were analyzed with Pearson's chi square test and Fisher's exact test to compare the groups. When some of the data had expected count in the cells less than 5 in more than 20% of the cells, I used the non-parametric Mann-Whitney U test for independent samples to analyze if differences between groups existed on data that had many answer categories (Modified Oxford Grading System, parity, BMI classes, education, type of UI and AI). For continuous baseline data (BMI, weight, height, age), and for all test points' Severity Index I used a two-sample t-test for difference between groups. Results are displayed with mean and standard deviation. Number of participants (n=) and percentages are displayed for categorical data.

For the analysis of the primary outcome, change in PFM strength, as the measured strength at baseline deducted from the measurements at late pregnancy and 3 months postpartum, were analyzed with Mann Whitney U test, as the data was not normally distributed. A within-group analysis on change of strength between all test points were analyzed with Wilcoxon signed ranks test. Self-reported weekly frequency of home-based PFMT was dichotomized to ≥3 times weekly, and < 3 times weekly, and analyzed with Fisher's Exact test. Number of daily PFM contractions (at 3 months postpartum, home exercise) were not normally distributed and was analyzed with Mann Whitney U test to compare groups.

The secondary outcome, urinary incontinence measured with severity index[117] at late pregnancy and at 3 months postpartum, were analyzed separately with analysis of co-variance (ANCOVA). These two test scores were set as dependent variables, group allocation was the independent variable (fixed factor), and the baseline score for severity index was set as a covariate. Type of UI are presented with prevalence (number of individuals (n) and percentages) at the three different time points, and analyzed for differences between groups with independent samples Mann-Whitney U test.

Anal incontinence, measured with St. Mark's score[118], presented a severe positive skew and not meeting the first assumption for ANCOVA (normal distribution across each category of the fixed factor). Thus, Mann-Whitney U test was used to analyze for differences in St. Mark's score

between groups at all test points. Type of AI are presented with prevalence (n and percentages) at the three different time points, and analyzed for differences between groups with independent samples Mann-Whitney U test. These results are presented with median and range. All data analysis was performed with SPSS version 24.0. Level of significance was set to 95%, with p-values under 0,05 seen as significant. All tests were two-sided.

Results

After a slow recruitment process, the goal of 150 participants in the ETIP trial was not achieved. At the end, 91 women were recruited and randomized to intervention and control groups. Some were lost to follow-up, and some did not participate in the gynecological examinations. More details about exclusions and their reasons (if known) are presented in the flow diagram, Figure 4.
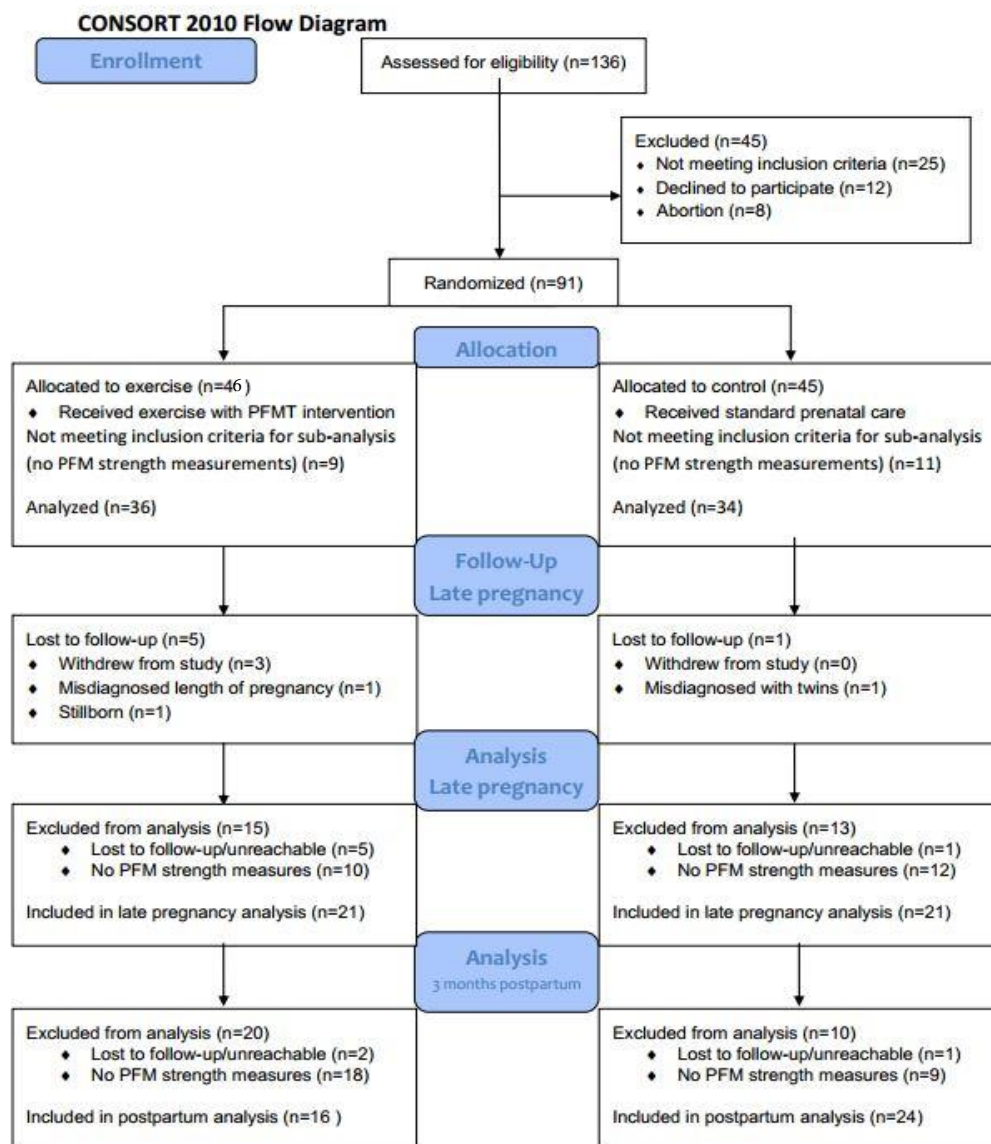

Figure 4. CONSORT 2010 Flow Diagram

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Some women declined the gynecological examination and this is the main reason for missing data on PFM strength, resulting in the lowered number of participants in this sub-study. In some cases, practicalities (for example conflicting time schedules for the gynecologist and the participants testing time) was the reason for missing data of PFM strength. The participating women were between 22 and 43 years old, and had a BMI ranging from 28 to 46 kg/m² at inclusion. Over half were nulliparous, and about a third were expecting their second child. There were no significant differences between the groups at baseline for age, weight, height, education, smoking, parity and BMI classification (Table 1).

Table 1. Baseline characteristics according to groups. Numbers are average and standard deviation (SD) if not otherwise noted.

	N analyzed	Exercise group N=36	N analyzed	Control group N=34	P-value
		Mean ± SD		Mean ± SD	
Age, years	36	31,06 ± 3,46	34	31,5 ± 4,7	0,653
Height, cm	36	167,93 ± 6,37	34	168,15 ± 6,097	0,882
Weight at inclusion, kg	36	96,34 ± 13,86	34	99,185 ± 13,508	0,388
BMI at inclusion	36	34,09 ± 3,99	34	35,018 ± 4,3016	0,354
Severity index	17	1,942 ± 1,74895	15	2,333 ± 1,83874	0,541
St. Marks score, median (range)	34	0 (7)	31	1 (12)	0,249
		n= (%)		**n= (%)**	
BMI classification Overweight BMI 25.0-29.9 Obese 1, BMI 30.0-34.9 Obese 2, BMI 35.0-39.9 Obese 3, BMI ≥40,0	35	2 (5,6) 21 (58,3) 10 (27,8) 3 (8,3)	32	3 (8,8) 15 (44,1) 12 (35,3) 4 (11,8)	0,499
Education	35		33		0,265

Vocational High school		8 (22,2)		5 (14,7)	
High school		4 (11,1)		4 (11,1)	
University degree ≤4 years		11 (30,6)		9 (26,5)	
University degree ≥4 years		12 (36,1)		13 (38,2)	
Other		0		2 (5,9)	
Smokers	34	4 (11,8)	34	5 (14,7)	
Parity	36		34		0,240
0		21 (58,30)		16 (47,10)	
1		13 (36,10)		13 (38,20)	
2		2 (5,60)		4 (11,80)	
3 or more		0		1 (2,90)	
PFM strength, Modified Oxford Grading System	36		31		0,803
No contraction		1 (2,8)		0 (0)	
Flicker		2 (5,6)		0 (0)	
Weak		5 (13,9)		3 (9,7)	
Moderate		8 (22,2)		15 (48,4)	
Good		13 (36,1)		8 (25,8)	
Strong		7 (19,4)		5 (16,1)	
Prevalence of UI	36		34		1
Has UI, any form		15 (41,7)		15 (44,1)	
Type of UI	36		34		0,672
No UI		21 (58,3)		19 (55,9)	
SUI		14 (38,9)		12 (35,3)	
UUI		1 (2,8)		0	
MUI		0		3 (8,8)	
Severity index, categorized	17		15		0,418
None		4 (23,5)		3 (20)	
Slight		8 (41,7)		5 (33,3)	
Moderate		5 (29,4)		7 (46,7)	
Severe		0		0	
Very severe		0		0	
Prevalence of AI	34		33		0,327

Has AI, any form		12 (35,3)		16 (48,5)	
Type of AI	34		33		0,673
No AI		22 (64,7)		17 (51,5)	
FI, solid stool		0		0	
FI, liquid stool		0		0	
Flatus*		10 (29,4)*		12 (36,4)*	

N = number of participants analyzed for each outcome variable. BMI= body mass index (kg/m²), PFM= pelvic floor muscles, UI= urinary incontinence, SUI=stress urinary incontinence, UUI=urgency urinary incontinence, MUI= mixed urinary incontinence, Severity Index=score from 0-12; high score means high severity of UI. AI= anal incontinence, FI= fecal incontinence. St. Marks score=score from 0-24; high score means high severity of AI. *2 (exercise group) and 4 (control group) participants experienced both AI of stool and flatus (data not shown), percentage not adding up to 100%.

Primary outcome: Change in PFM Strength

Baseline values for PFM strength were not significantly different between the groups (Table 1). Late pregnancy and postpartum strength measurements are shown in detail in Table 2 and 3. I observed no within-group differences with regards to change in median strength from baseline to late pregnancy (change in median grade=0, Z= -0,733, p=0,464 in the exercise group. Change in median grade=0, Z=0,000, p=1.0 in the control group), nor from baseline to 3 months postpartum (change in median grade=0, Z= -1,357, p=0,175 in the exercise group, change in median grade=0, Z= -0,832, p=0,405 in the control group), as presented in Figures 5 and 6. These changes were also not different between groups at late pregnancy (p=0,362, Table 2), and 3 months postpartum (p = 0,439, Table 3). All women performed the PFM contraction correctly after instruction at baseline and late pregnancy. At 3 months postpartum, one woman in the exercise group (6,3%) and one woman in the control group (4,8%) either strained or used other muscles in co-contraction of the PFM, also after instruction.

Home-based PFMT three or more times per week was reported by only five women in the exercise group and seven women in the control group at baseline. Six and nine women (exercise and control group, respectively) reported that they never performed any PFMT at home at baseline. At late pregnancy, 70% (n=14) in the exercise group and 52% (n=12) of the women in the control group reported home-based PFMT ≥3 times per week. Three months postpartum the reports of home-based PFMT ≥3 times per week were n=9 (50%) in the exercise group and n=9 (41%) in the control group. Median number of PFM contractions daily three months postpartum was 20 (min-max 0-80) in the exercise group, and 12,5 (min-max 3-60) for the control group. None of these distributions were significantly different. PFM strength at all three assessments stratified to home exercise of PFMT (instead of allocated intervention groups) is illustrated in Figure 7.
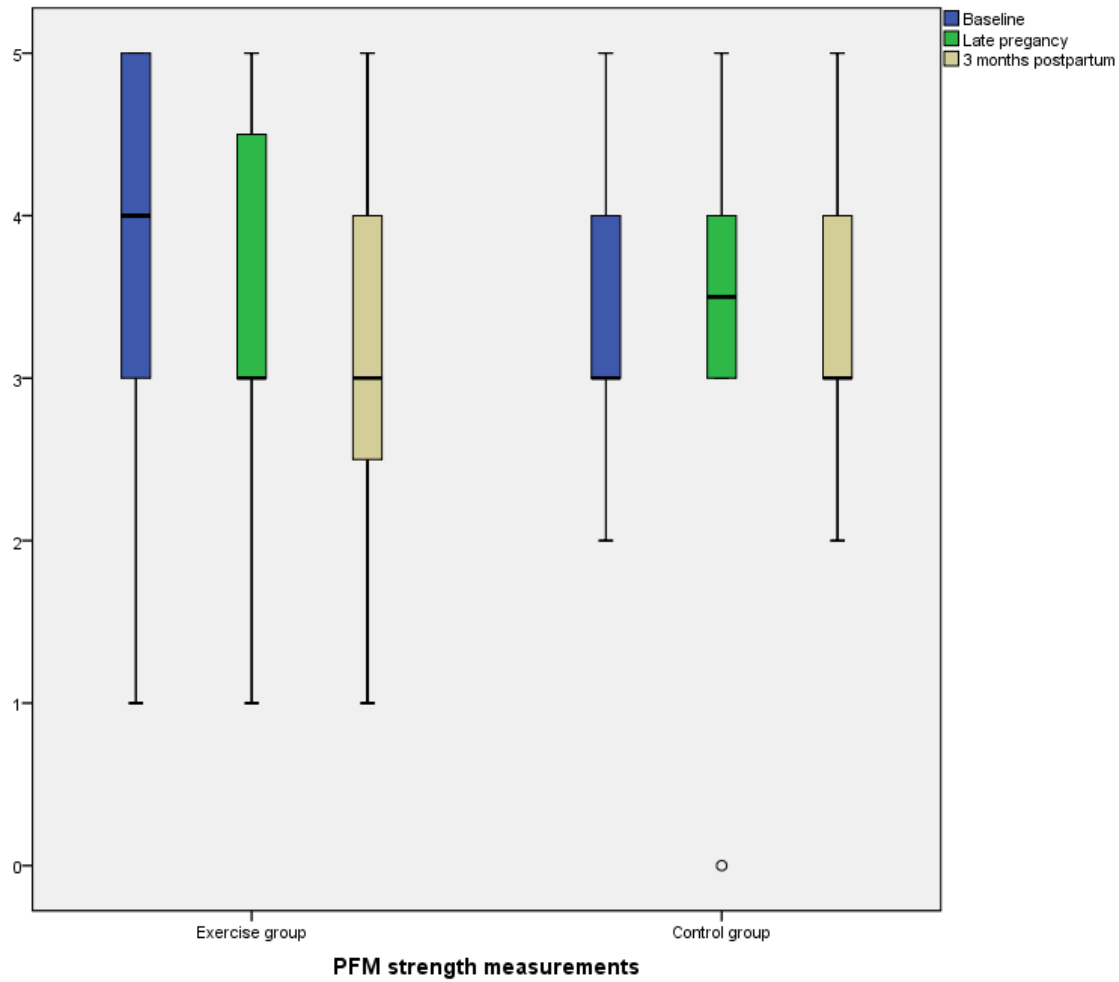
Figure 5. Modified Oxford Grading System measurements at baseline, late pregnancy and 3 months postpartum. For some boxes, the median markers coincide with the first quartile, and therefore appears "missing".
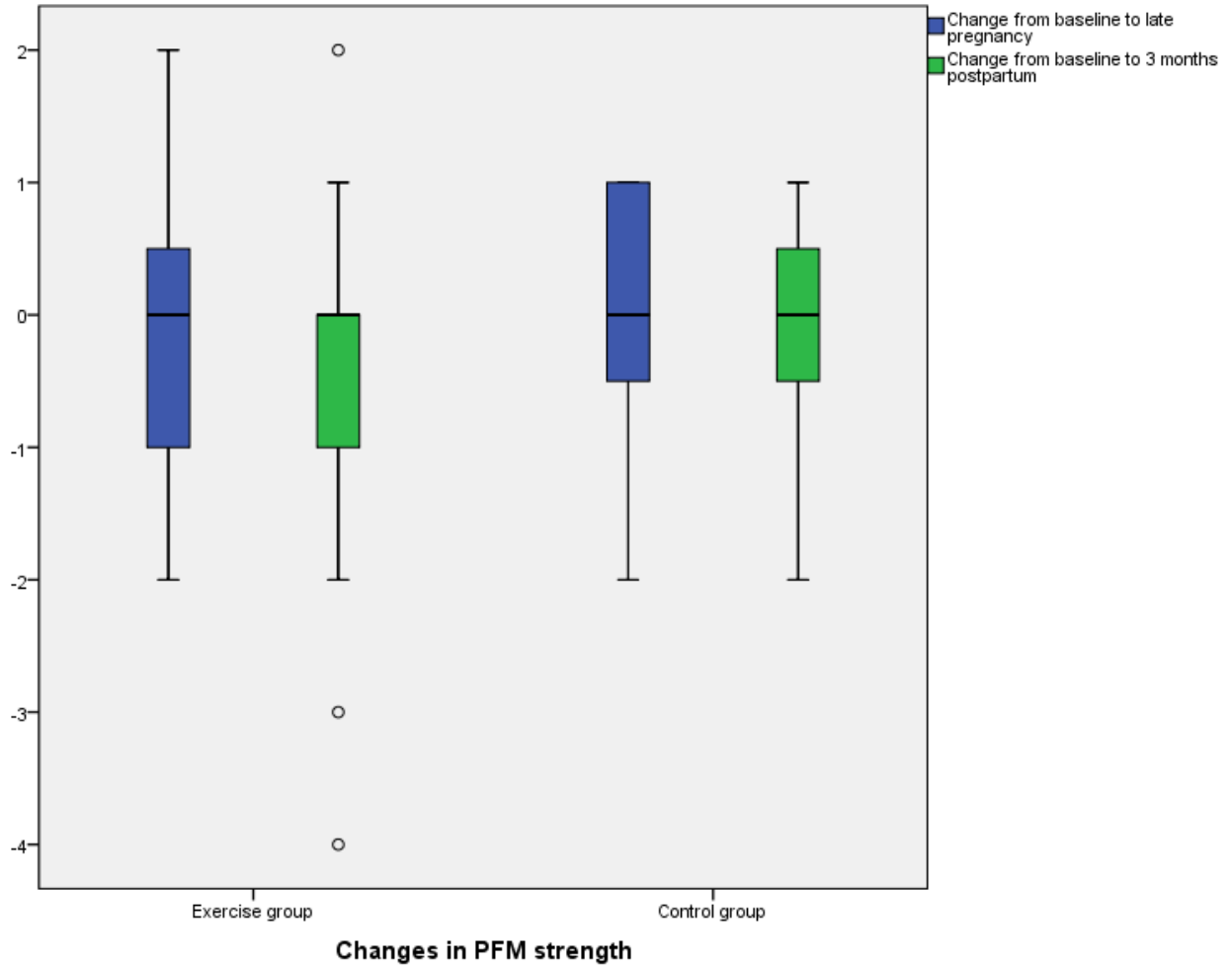
Figure 6. Change in Modified Oxford Grading System measurements from baseline to late pregnancy and from baseline to 3 months postpartum. For some boxes, the median markers coincide with the third quartile, and therefore appears "missing".
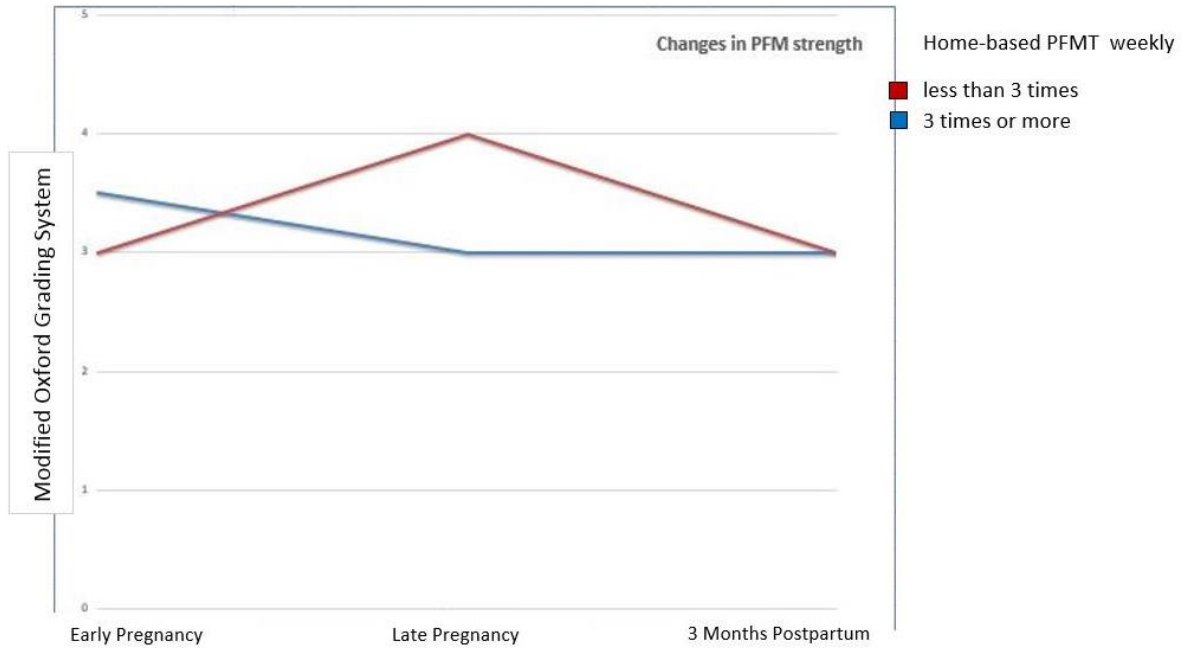
Figure 7. Median PFM strength development, from baseline to 3 months postpartum, grouped by frequency of home-based PFMT.

Table 2. PFM strength at baseline and late pregnancy, Modified Oxford Grading System and analysis of between-group change in strength from baseline. (Showing baseline values only for participants that have Modified Oxford Grading System measurements at both the baseline and the late pregnancy examination).

	Baseline		Late pregnancy	
	Exercise group **N=21**	**Control group** **N=19**	**Exercise group** **N=21**	**Control group** **N=19**
	N (%)	N (%)	N (%)	N (%)
No contraction	0 (0)	0 (0)	0 (0)	1 (4,8)
Flicker	1 (4,8)	0 (0)	1 (4,8)	0 (0)
Weak	2 (9,5)	2 (10,5)	1 (4,8)	0 (0)
Moderate	7 (33,3)	10 (52,6)	11 (52,4)	9 (42,9)
Good	5 (23,8)	3 (15,8)	4 (19)	6 (31,6)
Strong	6 (28,6)	4 (21,1)	4 (19)	3 (14,3)

Change of PFM strength from baseline to late pregnancy				
		Exercise group	**Control group**	
		Median (min-max)	Median (min-max)	p-value
		0 (-2 to 2)	0 (-2 to 1)	0,405

N = Number of participants. PFM= pelvic floor muscles. Missing: baseline n=30, late pregnancy n=28. Statistics: Mann-Whitney U. Change in PFM strength: 0= no change

Table 3. PFM strength at baseline and 3 months postpartum, Modified Oxford Grading System and analysis of between-group change from baseline. (showing baseline values only for participants that have Modified Oxford Grading System measurements on 3 months postpartum examination)

	Baseline		3 months postpartum	
	Exercise group N=16	Control group N=21	Exercise group N=16	Control group N=21
	N (%)	N (%)	N (%)	N (%)
No contraction	0 (0)	0 (0)	0 (0)	0 (0)
Flicker	1 (6,3)	0 (0)	1 (6,3)	0 (0)
Weak	1 (6,3)	2 (9,5)	3 (18,8)	3 (12,5)
Moderate	5 (31,3)	11 (52,4)	7 (43,8)	9 (42,9)
Good	4 (25)	4 (19)	3 (18,8)	8 (21,6)
Strong	5 (31,3)	4 (19)	2 (12,5	1 (4,2)

Change of PFM strength from baseline to 3 months postpartum

	Exercise group	Control group	
	Median (min-max)	Median (min-max)	p-value
	0 (-4 to 2)	0 (-2 to 1)	0,439

N = Number of participants. PFM= pelvic floor muscles. Missing: baseline n=31, 3 months postpartum n=28
Statistics: Mann-Whitney U. Change in PFM strength: 0= no change

Secondary Outcome: Incontinence

No significant difference between the groups was observed for any UI or AI or type of UI and AI at baseline (Table 1). SUI was the most commonly reported form of UI in both groups, with a total prevalence of 37% of all participants across both groups. Incontinence of flatus was the most reported type of AI, with a prevalence of 42% in total at baseline. This persisted all the way through to the postpartum test in both groups, and there was no difference between type of UI and AI between the groups (Table 4). The reports of any UI increased from baseline in both groups at late pregnancy, to a total prevalence of 52% in the whole study population, and decreased to 39% at 3 months postpartum. Prevalence of any AI decreased in both groups from

baseline to late pregnancy (34%) and increased slightly at 3 months postpartum (37%). No significant difference was observed of the prevalence between the groups on any UI and AI at any of the assessment times (Table 4).

The mean severity index scores were not significantly different between groups at late pregnancy and three months postpartum (Table 5). However, the late pregnancy index score adjusted for baseline had a significant between-group difference (p=0,020), with lower adjusted mean scores in the exercise group. There was no significant between-group difference in the adjusted mean of the severity index at 3 months postpartum (Table 6). The St. Mark's scores were similar across the groups, at both late pregnancy and three months postpartum, with no significant difference between the groups on any of the assessment times (Table 7).

Table 4. Prevalence and type of incontinence at late pregnancy and 3 months postpartum

	Late pregnancy				3 months postpartum			
	N analyzed	**Exercise group**	**N analyzed**	**Control group**	**N analyzed**	**Exercise group**	**N analyzed**	**Control group**
Prevalence of UI	22		24		22		24	
Has UI, any form		13 (59,1)		11 (45,8)		11 (50)		7 (29,2)
p-value				0,394				0,227
Type of UI	22		24		22		24	
No UI		9 (40,9)		13 (54,2)		11 (50)		17 (70,8)
SUI		12 (54,5)		11 (45,8)		9 (40,9)		6 (25)
UUI		1 (4,5)		0 (0)		1 (4,5)		1 (4,2)
MUI		0 (0)		0 (0)		1 (4,5)		0 (0)
p-value				0,309				0,145
Prevalence of AI	20		23		18		22	
Has AI, any form		5 (25)		8 (34,8)		6 (33,3)		8 (36,4)
p-value				0,526				1,0
Type of AI	20		23		18		22	
No AI		15 (75)		15 (65,2)		12 (66,7)		14 (63,6)
FI, solid stool		0		0		0		0
FI, liquid stool		0		0		0		0
Flatus*		4 (20)		7 (30,4)		6 (33,3)		5 (22,7)
p-value				0,524				0,697

N = Number of participants. UI= urinary incontinence, SUI= stress urinary incontinence, UUI=urgency urinary incontinence, MUI=mixed urinary incontinence, AI=anal incontinence, FI=fecal incontinence *1 (in both groups) participant at late pregnancy, 0 (exercise group) and 3 (control group) participants postpartum experienced both AI of stool and flatus (data not shown), percentage not adding up to 100%. Statistics: Mann-Whitney U.

Table 5. Severity index at late pregnancy and 3 months postpartum

Late pregnancy			3 months postpartum		
Exercise group N=11	**Control group N=9**	**P-value**	**Exercise group N=7**	**Control group N=7**	**P-value**
Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
2,8182 ± 2,04050	4,444 ± 1,81046	0,079	3,0 ± 1,0	2,1429 ± 1,95180	0,321

N = Number of participants. Missing/low n: Analyses possible only on participants reporting any form of UI. Statistics: independent samples t-test

Table 6. Analysis of severity index in late pregnancy and 3 months postpartum, means adjusted for baseline values.

Late pregnancy	**Adjusted mean**	**95% CI**	**P-value**
Exercise group	2,369	1,252 to 3,486	0,020
Control group	4,508	3,211 to 5,805	
3 months postpartum			
Exercise group	2,333	0,143 to 4,524	0,868
Control group	2,583	0,099 to 5,068	

CI=confidence interval. Statistics: ANCOVA

Table 7. St. Marks score at late pregnancy and 3 months postpartum

Late pregnancy			3 months postpartum		
Exercise group N=19	**Control group N=22**	**P-value**	**Exercise group N=18**	**Control group N=22**	**P-value**
Median (range)	Median (range)		Median (range)	Median (range)	
0 (3)	0,5 (13)	0,128	0 (4)	0 (15)	0,249

N = Number of participants. AI=anal incontinence. St. Marks score=score from 0-24; high score means high severity of AI. Statistics: Mann-Whitney U.

Discussion

The main finding in this thesis was that there was no difference in PFM strength between an exercise group participating in supervised classes with general exercise and intensive PFMT plus home-based PFMT, and a control group with standard maternal care only, at either late pregnancy (gestational weeks 34-37) or at 3 months postpartum. The exercise group had a lower score for UI severity at late pregnancy, compared to the control group. Apart from this finding, there were no significant difference between the groups in prevalence of UI or AI, type of incontinence or severity of AI at any of the assessment points. There was no difference between the groups on severity of UI at baseline or at 3 months postpartum.

Very few published studies have as primary aim to measure changes in PFM strength after an exercise intervention during pregnancy. Fewer yet have found no effect of the intervenion. The majority of the litterature I have read has regarded changes of PFM strength as a secondary outcomeand previous studieshave pirmarily aimed at prevention or treatment of UI, AI or other pelvic floor disorders. I have looked at primary and secondary aims when comparing published results to the current study. The results in the current sudy, that showed no effect of PFMT in change of PFM strength are in line with the findings of some previous studies However, both of these studies had postpartum interventions and thereby differed from the ETIP trial where the intervention was during pregnancy. The length of the interventions were vastly different. Dumoulin and colleagues[99] aimed to treat persistent postpartum UI and the 8 weeks of intervention was commenced postpartum, whereas in the current study, intervention took place during pregnancy and lasted 16-25 weeks (depending on which gestational week the women were enrolled). Meyer and colleagues[80] followed their participants during pregnancy, assessed PFM strength and other measures before commencing a 6-week intervention postpartum. In addition, both of the above- mentioned studies incorporated biofeedback and electrostimulation into their PFMT protocol. In the Canadian study[99] participants in the active intervention groups were encouraged to undertake PFMT at home[99], but its unclear if the participants in the Swiss study[80] were. These interventions are in stark contrast to the ETIP intervention, where the exercise group was encouraged to carry out both supervised and home-based PFMT frequently, with high contraction intensity, without the aid of intravaginal devices. Common for this sub-

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study of the ETIP trial and both of the studies discussed above, is that the number of participants were relatively low, with 107 participants enrolled in the Swiss study[80], 64 participants in the Canadian study[99], and 70 participants in the ETIP trial. Furthermore, the current results are based on data collected from a larger study, unlike the two above studies, which were primarily designed for their purpose. All three studies were likely underpowered for the analyses performed on PFM strength, UI and AI. The total number of participants in the ETIP trial was calculated based on the main outcome of the study, which was gestational weight gain, and no power calculation for this sub-study has been undertaken. The observed effect size of the PFM strength changes was minimal (0 to -0,04). Mechanical and hormonal influence negatively affects the PFM during pregnancy, causing the pelvic floor to become weaker throughout the course of the pregnancy[91, 92]. Unless, as we can see from de Oliveira and colleagues[95] results, an intervention counteract this loss of strength. It should be possible to strengthen the pelvic floor by PFMT during pregnancy. Indeed, nulliparous pregnant women who started with intensive PFMT intervention in the 20th gestational week, increased PFM strength significantly by 47% (measured with manometry) after 12 weeks[95].

Despite of no difference in the change of PFM strength, Dumoulin and colleagues[99] saw a significant decrease in both objective and subjective remission of UI in both of the intervention groups compared with the control after the 8 weeks intervention. This was also observed by Meyer and colleagues[80], who found significant reduction in incidence of SUI among the intervention group at 10 months postpartum. Two older studies by Sampselle and colleagues[100] and Wilson and Herbison[105] support these findings.

In regards to the effect of PFMT and prevalence of UI, study findings are equivocal. A RCT aiming to see if general group aerobic exercise with focus on PFMT could prevent or treat UI, found no differences in self-reported UI or AI during pregnancy or postpartum between the group exercise and the control group[104]. This study was similar to the current study, as it was a sub-study of a larger trial with another primary outcome, had no power calculations for the prevalence of incontinence. This study used the same PFMT protocol as the ETIP trial, but did no assessments of PFM strength or confirmed a correct performance of the PFM contraction. Another RCT reporting no effect of PFMT[26], saw no reduction in self-reported UI, or any difference in UI prevalence between the exercise and control groups. In addition to this, they

found no differences between the groups' PFM strength after the intervention, confirming the results in the current study. Hilde and colleagues[26] also used the same PFMT protocol as the current study for 16 weeks, but started the intervention postpartum.

The results of this sub-study of the ETIP trial stand in contrast to the previous study by Stafne and colleagues[87], which had many similarities to the ETIP trial. They found significantly lower prevalence of UI in their exercise group after the end of their intervention at gestational week 32 to 36 (42% with UI in the exercise group vs. 53% in the control group, OR=0,6, p=0,004, adjusted for baseline). Mørkved and colleagues[29] observed even lower prevalences in gestational week 36 (32% in the exercise group vs 48% in the control group, p=0,007). Both of the above studies had a lower prevalence of UI in late pregnancy compared to the ETIP trial. Three months postpartum the prevalence of UI in the study by Mørkved and colleagues[29] was 20% in the exercise group and 32% in the control group (p<0,05). The same research group had also years earlier found similar significant differences in UI at four months postpartum, after a eight week postpartum intervention[86]. These two results are in contrast to the non-significant finding in the present study of 50% and 29% (exercise group vs control group) of the participants reporting any UI three months postpartum.

The ETIP control group was showing a nonsignificant trend of less UI at the late pregnancy and postpartum assessments than the exercise group. However, among the participants with UI, the control group experienced a significantly higher severity of UI compared to the exercise group in late pregnancy. This can potentially suggest that the intervention had some degree of treatment effect. However, the adjusted means were in the lower end of the Severity Index, combined with the result of somewhat higher prevalence of UI in the exercise group, makes it questionable if this difference in severity has any clinical relevance. The study by Stafne and colleagues[87] could show that the intervention had worked as treatment for UI. They performed a stratified analysis based on if the women were incontinent at inclusion. This showed that significantly fewer women in the exercise group were incontinent after the intervention, compared to the control group (71% intervention group vs 85% control group, p=0,002). In the current study, stratified analysis of continence/incontinence at baseline was not conducted and no comparisons and conclusions can be drawn to this respect. The intervention protocol in both previous studies from Trondheim[29, 87] was similar to the ETIP trials intervention, with both supervised training sessions of general

exercise with special focus on PFMT and home-based PFMT, with the same amount of sets, repetitions and duration of PFM contractions. What made the two Norwegian studies[26, 29] different to the ETIP trial was that more women were included (Hilde et al[26], n=855, and Mørkved et al[29], n=301), and in Hilde and colleagues[26] study only the women included in the exercise group had pelvic floor education, i.e. the correct PFM contraction was individually confirmed by palpation, and thurough instructions about the PFM anatomy and function. In contrast, in the ETIP trial, all women were invited to undergo three examinations of PFM strength and function. Some participants did not agree to this examination, and some could not be performed due to practical causes (schedules and availability of gynecologist etc).

The reason for the differences in findings between the ETIP study and the studies mentioned above is probably not only due to the PFM assessments. Indeed, all participants underwent similar PFM assessments as in the current study also in the study by Mørkved and colleagues[29], and they observed significantly reduced rate of UI and increased PFM strength (in 36th gestational week and 3 months postpartum) in the intervention group compared to the control. One important factor that is likely to explain some of the difference in findings , is the adherence to protocol. Strength training has a clear dose-response relationship[74] and in Mørkved and colleagues[29] study, 81% of the participants in the exercise group adhered to protocol (daily performing 2 sets of 8-12 PFM contractions plus >6 supervised training sessions). Compared to this, the participants in the ETIP exercise group had the best adherence to protocol at late pregnancy, where 70% performed home-based PFMT ≥3 times per week. Additionally, when comparing performance of PFMT in the Mørkved[29] participants and the current studys participants at baseline, both studies had similar proportions of participants exercising undertaking PFMT regularly at baseline (29% in Mørved et al[29] and 26% in the current study).average of 27% for all participants both studies). In an earlier study undertaken by the same resarch team with the same PFMT protocol[86], a high level of weekly PFMT was observed in both groups. More participants in the control group were performing sufficient amount of home-based PFMT than the intervention group, but only the intervention group had significant increase in PFM strength. As the exercise group were encouraged to and supervised in intensive PFMT weekly, the authors concluded from that in order to be effective, PFMT needs to be performed with an intensive effort[86].

In contrast to Mørkved and colleagues[86], no significant results were found in the current study for the change in PFM strength through the whole study, and only some weak trends were observed. Over the time span from baseline to late pregnancy, the exercise group decreased more than the control group both in strength in terms of number of grades decreased, as well as number of participants who decreased one grade or more. But the changes in PFM strength from early pregnancy to late pregnancy and postpartum showed a large variation within the exercise group, as also a few participants had increased by one or two grades. The change in strength from baseline to postpartum was showing a tendency of higher strength loss in the exercise group, and most participants in the control group had no change in strength on any of the test points compared to the previous one, and was in that way a more stable group compared to the exercise group with regards of PFM strength. These observations can be compared to a recent cross-sectional study from Brazil, investigating the PFM strength in pregnant women in all three trimesters[91]. One of the instruments used was Modified Oxford Grading System, the same instrument as in this sub-study of ETIP. The inclusion and baseline PFM strength measurements in the ETIP trial was between gestational weeks 12 to 18, and late pregnancy measurements in gestational weeks 34-37. This makes the current study measurements comparable to the strength measures performed by Palmezoni and colleagues[91] on women in their second and third trimester. Compared to the Brazilian women, who were weaker and measured on average "weak" (=grade 2) on the Oxford scale at 2nd and 3rd trimesters, both the intervention group and the control group in the ETIP trial were within the "moderate" (=grade 3) grade at late pregnancy, and had also come closer to term than the women in the Palmezoni and colleagues study[91]. In comparison, Resende and colleagues[92] found similar results to Palmezoni and colleagues [91] on 3rd trimester women, also scoring on average the grade "weak", showing significantly lower PFM strength than non-pregnant nulliparas using both palpation and EMG measurements[92].

The prevalence of AI in the whole population of the ETIP trial was showing a trend of decrease from baseline (42%) to late pregnancy (34%), with a small increase three months postpartum (37%). Almost all of the cases of AI was incontinence of flatus, with just a few cases of incontinence of liquid or solid stool. There was observed no difference in the rates of AI at any of the assessment points. This is supported by some studies[80, 87], but not by others[87, 106, 107]. Stafne and colleagues[87] found no between-group difference of prevalence of AI in the whole study population, but significantly less AI among multiparous women in the exercise group in

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stratified analyses. The former is similar when compared to the current study. Supporting these findings, Meyer and colleagues[80] also saw no significant difference of AI incidence during their study. On the contrary, Glazener and colleagues[107] found a significant reduction of AI prevalence in the intervention group 12 months postpartum, compared to the control group. Confirming these findings, Johannessen and colleagues[106] also saw significant reduction of AI severity after a postpartum PFMT intervention. Despite of similar results, the two latter studies had very different PFMT protocol. The intervention by Glazener and colleagues[107] included up to 100 daily PFM contraction without any emphasis on the strength or force of the contraction and quite dissimilar from the intensive PFMT approach previously proven effective against UI, used by Johannessen and colleagues in their study[106].

Research is also ongoing in preventive and therapeutic measures against pelvic floor dysfunction in other than exercise intervention. Since vaginal delivery causes neuromuscular, muscular and connective tissue damage in the birth canal and the pelvic floor[93], some evidence point to that delivery by elective cesarean section (i.e. performed before an attempt of normal vaginal delivery) seems protective against anatomical and physiological changes caused by this damage. Elective cesarean section has been associated with a stronger pelvic floor and lower rates of incontinence in the postpartum period [57, 121-123]. Some studies find only a weak assocoation of reduced risk of incontinence[56]. Jundt and colleagues[50] observed that women who had delivered by cesarean section had less changes in the bladder necks position and mobility compared with vaginal (and in particular vaginal instrumental) deliveries. However, to make cesarean section the common clinical practice in order to lower the risks of PFM damage, is not adviceable due to the numerous associated adverse outcomes for both mother and infant in delivery by this method (trombosis, exessive bleeding, infection etc)[124]. No benefit was found for the use of cesarean section to prevent postpartum AI in a systematic review of 21 studies including 31,698 women[125]. Another often used intervention to reduce or help cure UI in obese women is weight loss (non pregnant), and it has proven effective[126, 127]. However this approach is not valid for pregnant women or to breastfeeding women due to possible harm to the babys development either in utero or through the release of fatty tissue-stored toxins to the breast

milk. Pre- and postnatal exercise with PFMT on the other hand, is safe and without any adverse side effects.

Prevalence of incontinence

The prevalence of all UI in the whole study population of ETIP was high, but somewhat lower than prevalences reported among the overweight and obese population in the Norwegian Mother and Child Cohort (MoBa cohort) study from 2007[18]. In the current study, the total population prevalence of any UI was 52% at late pregnancy, compared to the MoBa cohort which reported 66% of any UI for women with BMI ≥30. These observations are similar to observations of prevalence in a Turkish cross-sectional study, where 57% of the women with BMI ≥30 experienced UI[14]. One of the above studies was basing its calculations on both recalled data and only specifying the prevalence as "during pregnancy" [18], so the comparison to the ETIP trial might be somewhat inaccurate. Compared to RCTs with PFMT interventions, which specify the gestational weeks for the either self-reported or physically measured (for example with pad test) data on UI, comparing the ETIP prevalence to these is more accurate. Reports of early pregnancy (gestational weeks 12-24) prevalences in RCTs vary from 21%[104] to 53%[85], the prevalence at inclusion to the ETIP come in the higher end, with 43% of all the women across both groups experiencing any UI. Without exception, all prevalence reports on subclassifications of UI during pregnancy and in the postpartum period is SUI [14, 18, 22, 87], in line with the findings from this study.

Adherence and contamination

The control group in this sub-study was a group of relatively active women. Published analyses on the whole study population in the ETIP trial show that, at late pregnancy, 61% of the intervention group and 66% of the control group (p=0,73) was physically active daily for at least 30 minutes[128]. Detailed analyses on their answers to questions about home-based exercise show that they were also quite active in terms of PFMT, both groups had equally performed PFMT at home three or more times at weekly basis (n=14/70% in the exercise group vs

n=12/52% in the control group) in late pregnancy. Both groups also increased the home-based PFMT frequency between early and late pregnancy, as just five and seven participants in the intervention and control group, respectively, were performing home-based PFMT three or more days weekly at inclusion to the study. Such an active control group makes analyses difficult, as it is obscuring the possible effects of the exercise intervention. This type of threat to validity is termed contamination; when the control group is taking it on themselves to start an exercise program. Contamination in exercise RCTs is said to be just as devastating to the results, as low adherence to protocol in the exercise group[129]. In the current study, all participants got instruction on an individual level on how to perform an approved PFM contraction and MVC PFM contraction at three separate occasions during the length of the study, regardless of group allocation. This was necessary to get comparable data of PFM strength between the groups, but in so doing, the control group would (in theory) have gotten access to all the information needed to successfully exercise the PFM by themselves at home. Even if the gynecologist who performed all the PFM assessments was blinded to group allocation, the participants themselves were fully aware of which group they belonged to. Blinding participants for group allocation in exercise studies is virtually impossible, and the control group might "try harder" simply because they were in the control group, otherwise known as the "avis effect"[130]. This effect is a threat to internal validity. Dumoulin and colleagues [99] made arrangements with their control group that they would not exercise the PFM, and receive only relaxing massage during the intervention period. They offered them treatment after the project ended. With this they managed to control the PFM exercise behaviour of the control group, plus it was a relatively short intervention length (8 weeks) so the control group participants was perhaps more readily compliant because of this. Another project spent extra effort on trying to increase the exercise groups adherence through the use of different tools and printed material that was developed based on the behavioral change theory called the health belief model[24]. They could report significant adherence; 83% of the exercise group performed home-based PFMT ≥3 times weekly, which is relatively high, since the women in this study were mainly left to themselves after initial instructions at baseline.

There are many factors which are impossible to control in a study of community dwelling population, such as advice given to the participants by others. According to the Norwegian Directorate of Health[124], standard prenatal care in Norway should contain information about PFMT and its value to maternal health and well-being. However, the midwives and general

practitioners who administer the prenatal care have many topics of importance, and limited time. Thus, it will vary between different practioners to what degree PFMT is discussed at prenatal visits, based on personal interest of the client and knowledge among the health practitioners. It is also very high likelihood that the women in the control group got information about PFMT from online pregnancy communities.

Generalizability

The current study was a mixed approach of both preventing and treating incontinence. Because the main aim of the ETIP trial was to investigate the effects of regular exercise training in pregnancy on gestationalmaternal weight gain[131], both continent and incontinent pregnant women were included. What makes the currentresults different from trials showing effective cure or prevention of UI with the intensive approach to PFMT[20, 29, 72, 82, 86, 87], was low adherence, low number of participants, exclusively overweight or obese study population and an active control group. Additionally, some of the studies showing significant effects were performed on either non-pregnant or non-postpartum and somewhat older women[72, 82] than in the ETIP trial. The population of women giving birth in Sør Trøndelag county is quite representative of the whole country in regards of age, parity and BMI when compared to the Norwegian medical birth registry[5]. About 6-7% of all births in Norway happens in Sør Trøndelag county, and approximately 15% of all children are born to mothers being overweight or obese prior to pregnancy both in the Trondheim region and nationally[5]. The participants in the current sub-study represent approximately 2% of all births in St. Olav's hospital (calculated based on average number of births from 2011 to 2015). In all likelihood, as volunteers to an exercise trial, participants in the ETIP trial were well informed and interested in healthy living habits and exercise, and its possible benefits to the child and maternal health. The current study population is not representative in terms of PFMT, as all participants were on average more actively performing PFMT than 384 women participating in the Norwegian STORK cohort [132]. Only 17% of the STORK participants performed PFMT once or more weekly in the third trimester. Compared to the ETIP participants, the STORK participants were normal-weight, lower prevalence of UI (24%) and mostly of higher education, but belonged to same age group and of similar parity as the ETIP participants.

Strengths and limitations

Strengths in the present study was that this was a RCT, which is considered the "gold standard" in clinical research[133], as the groups are selected randomly among the participants. Randomization protects the trial against selection bias affecting the results[130]. When both groups are considered equal based on background data and current status when starting the intervention, any post-test differences between the groups is considered a result of the intervention given to one of the groups[133]. The use of validated indexes for self-report of UI and AI was also a strength of the study. Blinding of the outcome analyst, and the use of an experienced gynecologist that was blinded for group allocation were also strengths of the study, as blinded assessors will have no possibility to influence the participants positively or negatively. Additionally, the use of an exercise protocol based on current recommendations of exercise during pregnancy[115] and strength training principles[74], which has proven effective in both prevention and treatment of UI and AI [29, 72, 86]

Limitations to the study was that no analysis could be performed on the collected manometry data due to the technical irregularities creating unreliable measurement results. Moreover, the goal of including the estimated 150 participants to the main ETIP trial could not be met, possibly making it underpowered. This increases the risk of making a type II error: not discovering any effect of the intervention where there migh be one. Another limitation to the study was the rate of drop-outs and/or not available gynecology exam data for varying assessment points (due to either unwillingnes to undergo examination or scheduling practicalities) for some participants. Additionally, adherence to protocol in the exercise group combined with the contamination of the control group made it hard to analyse what the effects of the PFMT intervention were. Further limitations is that the analysis of the postpartum severity index was performed on data with borderline normal distribution, but I decided to continue with parametric analyses because ANCOVA is robust towards data that does not meet the normality assumption[134]. Another limitation in the statistical analyses was that no stratified analysis was performed based on continence status at baseline or prior to pregnancy.

Methodological Considerations

The use of a subjective scale as Modified Oxford Grading System, can be problematic. Most modern studies that measure PFM strength and endurance use manometry or dynamometer, to get objective and reliable results which is not dependable upon the operator. However, the digital palpation measurement of strength, quantified with the Modified Oxford Grading System or with other subjective scales (like the Ortiz scale, which is not vastly different from the Modified Oxford Grading System), has shown sufficient agreement with measurements performed with manometry both in nulliparous and parous women[63] and during pregnancy[95] when all measurements are performed by the same therapist. The Modified Oxford Grading System has also been found to agree well with surface EMG measurements of strength during pregnancy[92] and dynamometric tests of vaginal squeeze pressure in both continent and incontinent women[135]. Inter-rater concordance of measurements on the Modified Oxford Grading System has shown both great correlations[61], and "fair" correlations[59]. The authors of the latter study does not support the use of this scale if more than one person is assessing the participants. The measurements with manometry has shown to have a very good intra-rater reliability[62] and inter-rater reliability[59] in several positions and both within- and between-session. This makes the manometer a good tool for use in larger or multi-center studies where more personnell carry out the measurements. In ETIP, it was collected manometry data, but the equipment was faulty and gave unpredictable results, not agreeing with the gynechologists experienced subjective measurements. It is ill-advised to analyse unreliable data, so the manometry measurements were not used in this analysis. Based on the above discussion of methodology, and as it was one single gynecologist assessing all the women in this sub-study, we deem these PFM strength measurements with digital palpation as valid and reliable data.

Implications for future research

Methods to increase adherence to PFMT is needed in the overweight and obese pregnant population. Additionally, methods to reduce the contamination of the control group needs to be researched further, as information about exercise and lifestyle for various life situations is readily available for anyone online and other public channels. Furthermore, a deeper ivestigation into the muscle physiology and trainability of the PFM should be conducted. Some PFMT studies during pregnancy exists with pre- and post-intervention measurements of muscle cross sectional diameter measured with ultrasound. Most PFMT studies investigates its effects on various symptoms of pelvic floor dysfunction on normal weight women. Investigations on the obese pregnant population and PFM trainability are neccesary. Interventions during pregnancy and its effects specifically on PFM function, strength and endurance changes are needed. Moreover, furhter development of methodology for accurate testing of PFM strength should be conducted.

Conclusion

This sub-study of the ETIP trial found no effect on PFM strenght, UI or AI in overweight and obese women randomised to a supervised exercise intervention, including PFMT, during pregnancy. This study found a high prevalence of UI and AI, higher than most prevalences previously reported in late pregnancy and three months postpartum. Low adherence and high degree of contamination affected the results of the study.

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