Lifestyle advice and pelvic floor muscle training for women with pelvic organ prolapse

PhD Thesis

Ulla Due

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Virum, September 2015

_Ulla Due_
Scientific papers included in the PhD thesis

The thesis is based on the following papers/studies, which will be referred to by their number.

1. Due U, Brostrøm S, Lose G. Validation of the Pelvic Floor Distress Inventory-20 and the Pelvic Floor Impact Questionnaire-7 in Danish women with pelvic organ prolapse. Acta Obstet Gynecol Scand 2013;92:1041-8

2. Due U, Brostrøm S, Lose G. Lifestyle advices with or without pelvic floor muscle training for women with pelvic organ prolapse, a single-blinded randomized controlled trial (submitted for publication)

3. Due U, Brostrøm S, Lose G. The 12-month effects of structured lifestyle advice and pelvic floor muscle training for pelvic organ prolapse (manuscript)
Contents

Scientific papers included in the PhD thesis ........................................................................................................... 5
Abbreviations .......................................................................................................................................................... 8

INTRODUCTION .................................................................................................................................................. 9

BACKGROUND ..................................................................................................................................................... 10
Etiology of Pelvic organ prolapse (POP) .................................................................................................................. 10
Suspension of the pelvic organs and POP ................................................................................................................. 11
Symptoms related to POP ......................................................................................................................................... 12
Outcome measures and POP ...................................................................................................................................... 13
The pelvic floor muscles and POP ............................................................................................................................ 13
Pelvic floor muscle training and POP ....................................................................................................................... 16
Lifestyle advice and POP ........................................................................................................................................... 17

AIMS .................................................................................................................................................................... 18

MATERIALS AND METHODOLOGY .................................................................................................................... 19
Materials and methodology – study 1 ....................................................................................................................... 19
Methodological considerations – study 1 ................................................................................................................... 20
Materials ................................................................................................................................................................. 20
Study design ............................................................................................................................................................ 20
Materials and methodology - Study 2 ....................................................................................................................... 20
Materials ................................................................................................................................................................. 20
The pelvic floor muscle training program ................................................................................................................ 21
The lifestyle advice program .................................................................................................................................... 22
Subjective evaluation of POP .................................................................................................................................... 23
Objective evaluation of POP ..................................................................................................................................... 24
Methodological considerations - Study 2 ................................................................................................................... 25
Materials ................................................................................................................................................................. 25
Study design ............................................................................................................................................................ 26
Assessment of pelvic floor muscle function .......................................................................................................... 26
The pelvic floor muscle training program .............................................................................................................. 27
The lifestyle advice program .................................................................................................................................... 28
Recruitment of participants ...................................................................................................................................... 28
Materials and methodology – study 3 ....................................................................................................................... 29
Methodological consideration – study 3 ................................................................................................................... 30

STATISTICAL CONSIDERATIONS ..................................................................................................................... 30

RESULTS ............................................................................................................................................................... 32
Study 1 ........................................................................................................................................................................... 32
Study 2........................................................................................................................................32
Study 3........................................................................................................................................36

GENERAL DISCUSSION ............................................................................................................. 38
Patient reported outcome measures............................................................................................ 38
The Design of the randomized controlled trial.......................................................................... 39
Pelvic floor muscle training ......................................................................................................... 41
The lifestyle advice program.......................................................................................................... 43
Effect on objective POP ................................................................................................................ 44
The effect on sexual function ......................................................................................................... 45
The relevance of a conservative treatment program ................................................................. 45
Perspectives.................................................................................................................................. 47

FUTURE STUDIES ...................................................................................................................... 48
Danish summary .......................................................................................................................... 49
English summary......................................................................................................................... 52

REFERENCES............................................................................................................................ 55

PAPERS
DECLARATIONS OF CO-AUTHORSHIP
Abbreviations

POP: Pelvic Organ Prolapse
HRQoL: Health Related Quality of Life
POP-Q: Pelvic Organ Prolapse Quantification system
PFDI-20: Pelvic Floor Distress Inventory - short form 20
POPDI-6: Pelvic Organ Prolapse Distress Inventory 6
CRADI-8: Colorectal-Anal Distress Inventory 8
UDI-6: Urinary Distress Inventory 6
PFIQ-7: Pelvic Floor Impact Questionnaire - short form 7
UIQ-7: Urinary Impact Questionnaire 7
CRAIQ-7: Colorectal-Anal Impact Questionnaire 7
POPIQ-7: Pelvic Organ Prolapse Impact Questionnaire 7
PISQ-12: The Pelvic organ prolapse/urinary Incontinence Sexual Questionnaire 12
PGI-I: Patient Global Index of Improvement scale
NRS: Numeric Rating Scale
PFMT: Pelvic Floor Muscle Training
LG: Lifestyle advice Group
TLG: Combined pelvic floor muscle Training and Lifestyle advice Group
ITT: Intention To Treat analysis
RR: Relative Risk
IAP: Intra-abdominal pressure
Introduction

Pelvic organ prolapse (POP) as a diagnosis is based on the presence of both symptoms and signs of POP. Symptoms are defined as: “A departure from normal sensation, structure, or function, experienced by the woman in reference to the position of her pelvic organs” (Haylen 2010, page 6, column 2, line 9-114 and it may include: “vaginal bulging.. pelvic pressure, bleeding, discharge, infection.. splinting/digitation .. low backache” (Haylen 2010, page 6, column 2, line 17-324. Signs (anatomic findings) are defined as: “The descent of one or more of the anterior vaginal wall, posterior vaginal wall, the uterus (cervix), or the apex of the vagina (vaginal vault or cuff scar after hysterectomy)” (Haylen 2010, page 8, column 1, line 14-16)”4. “The presence of any such sign should correlate with relevant POP symptoms”. (Haylen 2010, page 19, column 1, line 25-26)4.

The “sign” POP has been found in 40-50% of women more than 40 years of age 5. Most of these women do not perceive their POP, and only approximately one in ten (8-11 %) women report POP related symptoms, which may lead to bother and impact on quality of life, including sexual life 6,7.

Only a few years ago treatment options for symptomatic POP were described as: “observation, pessary use, and surgery” (Jelovsek 2007, page 1027, line 10) 8. The lifetime risk for POP surgery has been found to be 12.6% 9. However surgical treatment is not always successful 10 or without complications or adverse events 11. Furthermore, the positive effect of surgical reconstruction has been found to fade in the long term 12. Many women with POP prefer conservative treatment especially if they have minor symptoms13,14. To some women with POP a supporting pessary is the solution but not all women can be fitted with a pessary15. Other conservative treatment options have therefore gained interest.

Pelvic floor muscle training (PFMT), was introduced by Arnold Kegel in 1948 for the treatment of urinary incontinence16. Nowadays, PFMT is recommended as first line of therapy for women with urinary incontinence and for fecal incontinence17 18. During the last decade PFMT has also gained interest in relation POP. A Cochrane review from 2006 found three randomized controlled trials using PFMT for POP 19-22. An update of the review in 2011 found that this number had increased to six studies23 24-26 and subsequently three more studies have been published 26-28. Five of these studies have compared an individual PFMT program with a lifestyle advice leaflet or a single lifestyle advice instruction. The studies have all found superior effect of PFMT on POP symptoms 22,25,29-31 and some have also found positive effect
on signs of POP 22,25,29. PFMT has now achieved a grade A recommendation based on level 1 evidence in the treatment of POP compared to no treatment, a short lifestyle advice instruction or a lifestyle advice leaflet 32. However, the association, between improved pelvic floor muscle (PFM) function and improvement of subjective symptoms and signs of anatomic POP remains uncertain 25. While the improvement of POP symptoms after PFMT may be related to better muscle function33, the added attention and the lifestyle advice provided with the PFMT may have a positive effect on the accompanying bladder and bowel symptoms, introducing a risk of bias. Although, it is unlikely that PFMT would be offered without lifestyle advice, a structured lifestyle advice program applied in the same manner as a PFMT program could hypothetically give the same effect as a PFMT program. The primary aim of the randomized controlled trial in this thesis was therefore to examine whether PFMT is more effective than lifestyle advice?

Background

Etiology of Pelvic organ prolapse (POP)

The development of POP is believed to be multifactorial8,34. In 1998 a theoretical model was developed to explain the multiple causes for the development of pelvic floor disorders including POP 35. This model is widely accepted and it provides a theoretical framework for the understanding of the development of POP, including the possible impact of lifestyle factors.

The factors are described as predisposing, inciting, decompensating and promoting (figure 1)35

Predisposing factors related to POP are the probable hereditary, racial and possible genetic disposition for POP causing differences in the collagen concentration of the connective tissue 7,36-38. Inciting factors most importantly include the strong connection between vaginal delivery 39-41, number of vaginal deliveries 42, increased birth weight of the child 43, more than one perineal laceration 44 and use of forceps 42,45. Surgery to the pelvis including hysterectomy has furthermore been found to increase the risk of POP and subsequent POP surgery46. A decompensating factor is the influence of ageing and the influence of female hormone deficiency described by some 47,48 and questioned by others 49,50 Promoting factors are overweight 36, heavy occupational work with many heavy lifts and low income jobs 51,52,
straining during defecation and constipation. Other factors such as chronic coughing are likely to promote the development of POP.

**Figure 1:** The multifactorial etiology in the development of POP (adapted from Bump 1998)

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**Suspension of the pelvic organs and POP**

The pelvic organs are attached to the pelvic walls through the endopelvic fascia and the attachments are functionally divided into three levels. At level I, the upper most level, the vagina is suspended by the cardinal and utero sacral ligaments and injuries at this level can result in an apical POP of the uterus, the cervix or the vaginal vault after hysterectomy. At level II the vaginal walls are attached directly to the arcus tendineus fascia pelvis, and to the superior fascia of the pelvic floor muscles (PFM). At level III, most distally, the vaginal walls are fused with the urethra, the perineal body and the pelvic floor muscles (PFM). Injuries to the vaginal walls at level II or III result in an anterior or a posterior POP.

Signs of POP can be objectively evaluated through clinical examination using the hymen as a landmark. The Pelvic Organ Quantification system (POP-Q) is a system that divides signs of POP into stages using the hymen as reference line. The POP stages are numbered from 0 to IV. A POP-Q stage of 0 indicates normal suspension of the organs, while a POP-Q stage IV indicate a total eversion of the genital tract (table 1).
Table 1: POP-Q stages adapted from the terminology report developed by the International Continence Society (ICS) and the International Urogynecological Association (IUGA), 2010

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>No prolapse is demonstrated.</td>
</tr>
<tr>
<td>Stage I</td>
<td>Most distal portion of the prolapse is more than 1 cm above the level of the hymen.</td>
</tr>
<tr>
<td>Stage II</td>
<td>Most distal portion of the prolapse is 1 cm or less proximal to or distal to the plane of the hymen.</td>
</tr>
<tr>
<td>Stage III</td>
<td>The most distal portion of the prolapse is more than 1 cm below the plane of the hymen.</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Complete eversion of the total length of the lower genital tract is demonstrated.</td>
</tr>
</tbody>
</table>

Symptoms related to POP

A cardinal symptom of POP is a perceptible or visible bulge in the vaginal opening. A vaginal bulge is the only symptom considered to be specific for POP, but mechanical symptoms are not the only symptoms related to the descending of the organs. POP is associated with a number of symptoms such as urinary incontinence, voiding difficulties, bowel problems and sexual problems. Both urinary and anal incontinence are prevalent symptoms among women with POP. Obstructive symptoms are also common either alone or concomitant with incontinence.

A study using the POP-Q to evaluate 237 consecutive patients with symptomatic POP found that while 73% reported some urinary incontinence, 50% reported difficulty with bladder emptying with 62% having a sensation of incomplete bladder emptying. Furthermore, 31% reported fecal incontinence, 67% had complaints of constipation and 52% described incomplete defecation. It seems that a worsening of symptoms and an increased number of symptoms correlate with more advanced POP. However some symptoms have been found to be inversely correlated with POP stage. Thus, women with less advanced POP have been found to have more stress urinary incontinence (SUI) while voiding difficulties and symptoms of obstructed defecation increase with in increase in the signs of anatomic POP.

POP may affect sexual life negatively because of the mechanical difficulties caused by the bulge and because of the other symptoms such as incontinence co-existing in POP.
Outcome measures and POP

According to generally accepted standardization papers: “Functional outcomes (related to POP) are best reported using valid, reliable and responsive symptom questionnaires and condition-specific HRQOL (health related quality of life) instruments (Barber 2013, page 1783, column 2, line 21-24) 70. It is recommended that signs of anatomic POP should be graded into stages using the Pelvic Organ Prolapse Quantification system (POP-Q)4,70 71 72. The POP-Q has been shown to have good intra-tester and inter-tester reliability and it is considered to be a standardized and transparent tool to document signs of POP4,71.

In the International Consultation on Incontinence (ICI) book from 2013, (page 389-391) it is described that when choosing a patient reported outcome (PRO) for clinical trials or for clinical practice: “it is important to choose a questionnaire that has been scientifically developed and validated,” (ICI 2013, page 391, column 1, line 5-7)73. The chosen PRO must furthermore fit both the target group and the purpose of measuring. The symptom score: The Pelvic Floor Distress Inventory-20 (the PFDI-20) and the matching health related quality of life score (HRQoL), the Pelvic Floor Impact Questionnaire-7 (the PFIQ-7)74 have both reached grade A recommendation as PROs for women with POP (ICI 2013, page 403, column 1, table 9) 73. A Danish-language PRO-score revealing POP related symptoms and bother exists 68.

Unfortunately it has never gained national interest and has not been implemented for clinical use. No specific PROs for women with POP have been recommended by the Danish gynecological societies (DSOG.dk (POP guideline), DUGS.dk). In order to perform the randomized controlled study included in this thesis it was therefore decided to translate the PFDI-20 and the PFIQ-7 into Danish and to validate them in Danish women with POP4.

The pelvic floor muscles and POP

The pelvic floor muscles (PFM) close the pelvic outlet most caudally. The PFM can be divided into an anterior and into a posterior part. The anterior part originating from the arcus tendinius fascia pelvis forms the pubovisceral and the puborectal muscle. Fibers of the puboviseral muscle insert into the lower part of the vaginal walls, into the perineal body and that fibers insert close to the anus, while the puborectal muscle forms a sling behind the rectum just above the external anal sphincter59. The most posterior part of the PFM, the ilieococcygeal muscles, forms a flat sheet closing the posterior part of the pelvis59, 75. The
urethra, the vagina and the anus pass through the medial opening of the PFM, the urogenital hiatus or most often called the genital hiatus.

**Figure 2:** The pelvic floor muscles seen from below showing the U-shaped muscle slings defining the genital hiatus

![Diagram of pelvic floor muscles](image)

**Figure 3:** The PFM in relaxed position (left side) and during contraction (right side)

![Diagram of pelvic floor muscles in different states](image)

*During a voluntary or an involuntary contraction of the PFM, the anterior part of the PFM shortens in an anterior direction causing closure of the genital hiatus and compression of the urethra, the vagina, and the rectum against the pubic bone. This movement also causes a slight lift of the organs*.\(^{59}\)

Weakening or damage to the striated pelvic floor muscles (PFM) is believed to play a major role in the development of POP\(^{59}\). When the PFMs are intact a constant tonic activity of the muscles will keep the genital hiatus closed offering support for the pelvic organs during rest.
reducing stress on the endopelvic fascia and the ligaments supporting the pelvic organs. During an increased intra-abdominal pressure (IAP) the PFM must automatically contract to close the genital hiatus and thereby prevent incontinence and any downward moving of the pelvic organs.

**Figure 4**: The pelvic floor during before and during an increased intra-abdominal pressure

The Illustrations show the PFM and the position of the pelvic organs during rest (A), during an increased intra-abdominal pressure (red arrows) with a pre-contraction (thick blue arrows) of the PFM offering some protection against downward movement of the pelvic organs (B) and (C) showing the descent and protrusion of the posterior vaginal wall during an increased intra-abdominal pressure when there is no pre-contraction (thin blue arrows) (adapted from xx)

Ageing has been found to reduce the number of striated muscle fibers and the nerve density in the urethra resulting in both decreased muscle strength and speed of contraction. This effect is most likely global for all striated muscles including the PFM. Adding to this, vaginal delivery has been found to cause an excessive stretch of the PFM. A three-dimensional computer model simulating vaginal delivery could demonstrate a 217% strain of the anterior and most medial part of the PFM during second stage of delivery. The same study group later demonstrated a simultaneous 35% stretch of the pudendal nerves during vaginal delivery, which exceeds the 15% considered to be the threshold for permanent injuries. The consequence of this excessive strain during vaginal delivery can be injuries on the pelvic floor (connective tissue, nerve fibers and muscles) and parous women have been found to have an increased hysteresis with a reduced stiffness of their PFM during an increased IAP. Furthermore, it has been found that vaginal delivery delays and reduces the automatic response from the PFM before an increase of the IAP indicating affection of the nerve supply. One in five women will sustain an avulsion of their PFM from the pelvic wall during
vaginal delivery and women with POP are more likely to have these avulsions of their PFM than women without POP\textsuperscript{82, 83 84}. The avulsions reduce PFM strength and cause the genital hiatus to enlarge, thereby reducing the support for the organs\textsuperscript{85, 86} increasing the risk of POP by a two- to a three-fold\textsuperscript{84 83, 84}. While deterioration because of ageing and vaginal delivery are known to affect PFM function negatively it has been suggested that the effect of age and vaginal delivery combined with predisposing and promoting factors (Figure 1) can increase the risk of pelvic floor dysfunction even further, which eventually will lead to pelvic floor disorders including POP\textsuperscript{34}. Women with POP have been shown to have impairment of their PFM function and they have been found to have reduced PFM muscle strength; endurance and resting tone\textsuperscript{87 52}. One study found that women with POP had normal muscle strength but lacked involuntary contraction of the PFM before an increased IAP\textsuperscript{88}. Two studies reported that more than one in ten women with POP or urinary incontinence were straining when attempting to perform a PFM contraction\textsuperscript{87, 89}.

**Pelvic floor muscle training and POP**

Pelvic floor muscle training has been found to improve PFM function in women with POP\textsuperscript{25, 33}. Women offered PFMT for six months achieved increased muscle thickness, a decreased genital hiatus and a more elevated bladder and rectum at rest. They furthermore had increased stiffness of their PFM reducing descent of the organs during straining. Two aspects of PFMT have been described to hypothetically improve POP\textsuperscript{90}; 1) "Conscious contractions" (the Knack) are conscious pre-contractions of the PFM in order to close the genital hiatus, to lift and stabilize the pelvic organs before and during an increased IAP\textsuperscript{91} 2)"Regular strength training" aiming to create hypertrophy to increase the cross-sectional area and thereby the stiffness of the PFM, with the purpose of lifting the organs, reducing the genital hiatus and resisting downward movement of the organs during increased IAP\textsuperscript{90}. While PFMT mainly acts on the pelvic floor muscles (PFM), it is possible that a strong PFM could potentially reduce strain on the pelvic floor\textsuperscript{34}. It has been suggested that strength training also has the ability to improve strength of the connective tissue, which could be beneficial in relation to POP\textsuperscript{34, 90}. Finally, strength training already in the early training cause an increase in number of satellite cells (stem cells) by up till 46%\textsuperscript{92}. These satellite cells are a prerequisite
for the hypertrophic reaction to strength training because of their ability to create more myonuclei in the muscle fiber.\textsuperscript{93}

**Lifestyle advice and POP**

While the overall evidence on lifestyle modifications for pelvic floor disorders is limited, clinical trials have shown some beneficial effect. Weight loss in obese women and reduction of constipation has been shown to reduce urinary incontinence\textsuperscript{94, 95}. In patients with fecal incontinence, especially the use of fiber supplements has been shown to have a positive effect on number of incontinence episodes.\textsuperscript{96}

Studies comparing women with symptomatic POP to a control group have found that women with symptomatic POP have a higher risk of being constipated and straining during defecation (odds ratio 2.1-4.0)\textsuperscript{36, 97, 98}, for being overweight (odds ratio 1.9-5.0)\textsuperscript{36, 52} and are more likely to be exposed to repetitive heavy lifting (odds ratio 2.0-9.6)\textsuperscript{36, 52}. Minimizing the effect of some of these known promoting factors for POP could therefore potentially be relevant in the treatment of POP.\textsuperscript{34, 35} Unfortunately prospective randomized controlled trials are missing. It is therefore largely unknown whether reducing any promoting factors including specific lifestyle modifications and change of habits could improve POP.\textsuperscript{36, 52, 99}

In the published studies on PFMT for POP, lifestyle advice has been used as a comparison to an active PFMT program. The lifestyle advice has been offered as a leaflet or a single instruction, with minimal contact with a health care professional. Presumably, the participants offered individual PFMT have been verbally guided in the use of different lifestyle modifications but the content of these lifestyle advice leaflets or instructions have not been described in details. Based on published studies it is therefore not possible to separate the effect of PFMT from the effect of lifestyle advice. With the multifactorial etiology of POP in mind it is possible that an educational program without PFMT, providing thorough information about lifestyle modifications could improve both subjective and objective POP.\textsuperscript{34, 35}
Aims

The aims of the included studies in this thesis were:

**Study 1**
- To translate and to validate a condition specific questionnaires for Danish women with POP

**Study 2**
- To examine the effect of a structured lifestyle advice program with or without PFMT for women with symptomatic POP stage ≥ II

**Study 3**
- To examine the 12-month effects of a structured lifestyle advice program with or without PFMT for women with symptomatic POP stage ≥ II.

Hypotheses for the randomized controlled study included in the thesis were:

**Study 2**
- PFMT in combination with a structured lifestyle advice program has better effect on symptoms, quality of life and objective POP than a structured lifestyle advice program alone
- Background variables (age, BMI, parity, work, surgery, POP-Q stage, POP position, symptoms- and HRQoL total and subscale scores) can predict effect of PFMT
- PFMT has little or no side effects.

**Study 3**
- Women receiving a combination of PFMT and structured lifestyle advices will experience better effects at a 12-month follow-up compared to women receiving a structured lifestyle advice program alone.
Materials and Methodology

Materials and methodology – study 1

Women referred to our hospital for POP evaluation were included if they were fluent in Danish and willing to participate. The women were recruited either from the hospital referral list, from the ward or contacted in the waiting room at the outpatient clinic. Furthermore, women scheduled for POP surgery were recruited in the waiting room at operating theater. As per Danish regulations, the study was reported to Danish Data Protection Agency. The primary investigator mainly recruited participants and all participants were given written information about the study. The women signed consent forms permitting access to their patient files regarding their objective POP.

In the study the Pelvic Floor Distress Inventory-20 (PFDI-20) and the Pelvic Floor Impact Questionnaire-7 (PFIQ-7) were translated and validated. The PFDI-20 has twenty items and the PFIQ-7 has 21 items. Both questionnaires are divided into three subscales; The PFDI-20 reveals POP (POPDI-6), bowel (CRADI-8) and bladder (UDI-6) symptoms and bother while the PFIQ-7 reveals impact on health related quality of life (HRQoL) related to bladder (UIQ-7), bowel (CRAIQ-7) and POP (POPIQ-7) symptoms. Single item scores, subscale and total scores can be calculated from both the PFDI-20 and PFIQ-7 with higher scores indicating more bother and impact on HRQoL.

A panel of independent translators translated the PFDI-20 and the PFIQ-7. Patient interviews were performed based on the translated versions. The interviews were followed by revisions and further pre-testings of the translated questionnaires.

The psychometric analyses included examination of construct and content validity to assure that the questionnaires were relevant for women with POP and to assure that they covered all relevant aspects of POP. Convergent validity was examined by comparing questionnaire scores with objective POP. Internal consistency of total and subscales was examined to evaluate if items in the two questionnaires were correlated relevantly with each other. Test-retest reliability was examined to confirm that the questionnaires would be stable if the condition was unchanged. Finally we examined if the questionnaire were sensitive to change and we tried to determine responsiveness of the questionnaires.
Methodological considerations - study 1

Materials
Women with POP were included because a PROM should be psychometrically evaluated on the target group to ensure validity, reliability and responsiveness\textsuperscript{101}.

Study design
We emphasized understanding and interpretability of the Danish versions of the translated questionnaires\textsuperscript{1}. It has been shown that women find vocabulary related to pelvic floor disorders difficult to comprehend\textsuperscript{104}. We therefore performed patient interviews on the Danish version of the questionnaires with the use of a probe technique as proposed by Guillem in 1993\textsuperscript{100}. This technique meant that the women were continuously asked to vocalize how they understood each item of the questionnaires. Furthermore, we used an iterative process; if an interviewee found an item difficult to understand the following interviewees would be asked how they understood the item. In some cases the interviewees were presented to different formulations of the same item and asked to explain their conception of the content. Hence, the final version of each item was based on consensus between the interviewed women and the primary investigator.

Earlier studies translating the chosen questionnaires have used classical test theory and we decided to use the same psychometrical analyses\textsuperscript{74, 101}.

Materials and methodology - Study 2

Materials
Women with symptomatic POP stage ≥ II (table 1) were included if they had at least one of three symptoms: seeing or feeling a bulge in the vaginal opening, voiding disorders or defecation problems, or feeling vaginal heaviness. Fluency in Danish language was required. Exclusion criteria were dementia, symptomatic neurological disease, including serious back problems, PFMT within the last two years, childbirth within the last year, more than one surgical treatment for POP or urinary incontinence.

The study was approved by the Danish Scientific Ethical Committee (H-4-2011-072) and by the Danish Data Protection Agency. The study was reported to Clinical.Trials.gov (NCT01612637).
Primary investigator was blinded to all outcome data throughout the whole study. The research nurse performed randomization and collected all data. A statistician not involved in the study provided computer generated random numbers and each woman drew one envelope. Each envelope contained a paper describing group allocation and a patient number. The patient number was used for the research nurse to enter data into a database. Stratification was made for age ± 60 years.

The women were randomized to the structured lifestyle advice program (LG) alone or in combination with PFMT (TLG). The six group sessions should be attended with a two-week interval between sessions within 12 weeks (Figure 5).

**Figure 5:** Timeline and headlines for each of the six group sessions in the LG and in the TLG (see table 2 for further explanation of the lifestyle advice program)

<table>
<thead>
<tr>
<th>Week number</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
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<tbody>
<tr>
<td><strong>Session number</strong></td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
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<td>5</td>
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<tr>
<td><strong>LG</strong></td>
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<td>Bladder</td>
<td>Bowel</td>
<td>Diet</td>
<td>Quality of life</td>
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<td>Intro</td>
<td>Bladder</td>
<td>Bowel</td>
<td>Diet</td>
<td>Quality of life</td>
</tr>
<tr>
<td>Individual PFMT</td>
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<td>Group PFMT</td>
<td>Group PFMT</td>
<td>Group PFMT</td>
<td>Group PFMT</td>
<td>Group PFMT</td>
</tr>
</tbody>
</table>

**LG:** Lifestyle advice Group; **TLG:** Combined pelvic floor muscle Training and Lifestyle advice Group; **PFMT:** Pelvic Floor Muscle Training

**The pelvic floor muscle training program**

The women in the combined lifestyle advice and PFMT group (TLG) received an individual assessment of their PFM function by a specialist pelvic floor physiotherapist (figure 5) before starting the group sessions. 105, 106. Women unable to perform PFMT correctly were offered
more individual sessions. During the sessions the women performed PFMT in different body positions and "Knack training".

The PFMT home training program was individually adjusted according to the results of the PFM assessment. The home training program should be performed five days a week with the use of a training dairy. The dairy was a simple two-week training dairy and the women noted in the dairy if the PFMT had caused any bother. Participants handed in their training dairies at every session, exchanging it for a new one (at the end of the session). The training program included three sets of PFM contractions with a short break between sets of max 1-2 minutes. Progression was enforced through verbal instructions by adjusting number of contractions, length of each contraction and body positions during home training. The aim was to reach 3 x 10 contractions lasting 10 seconds each and with a maximum of 10 seconds rest between each contraction. The participants were encouraged to perform “the knack” during every-day life when lifting, pushing, coughing etc.

**The lifestyle advice program**

The LG and the TLG was offered and identical lifestyle advice program. Specialized pelvic floor physiotherapists were instructed in teaching the sessions independently of the primary investigator.

The lifestyle advice program included six pre-developed power-point presentations lasting 45-60 minutes each. Each session had a different subject related to POP. The women were instructed in the anatomy of the pelvic floor and the most common symptoms related to POP were described, including possible promoting factors. This was followed by specific lifestyle advice to alleviate symptoms (table 2).

POP has been found to have a negative impact on body image and sexual life. Since these aspects can be difficult to talk about, a group session was specifically designed to encourage the women to speak openly about this. The power-point presentation for this session included relevant statements on these aspects found in the scientific literature.

The research nurse gave each of the included women a schedule for their visits and a folder describing the content of the six group sessions before commencement of the group sessions. The women were encouraged to try out any of the presented advice from the sessions that they found relevant and to share their experiences with rest of the group.
The women were given bladder and bowel diaries, and leaflets on laxatives. Handouts from the presentations were offered.

The group sessions for the LG and the TLG were held on separate days and the two groups never met. In order to make it possible for a diversity of women to participate we offered both afternoon and evening classes.

Table 2: Content of the six lectures in the structured lifestyle advice program

<table>
<thead>
<tr>
<th>Week 2 - 12</th>
<th>Content</th>
<th>Specific suggestions</th>
</tr>
</thead>
</table>
| **Introduction** | Explanation of pelvic floor anatomy and possible causes for POP. Description of anterior, posterior and apical/uterine POP | • Exercises to relieve pressure on the pelvic floor  
• Reduce heavy lifting |
| **Bladder** | Explanation of bladder anatomy Function/dysfunctions  
Urinary incontinence and voiding dysfunctions | • Normalize fluid intake and micturition  
• How to get a proper micturition technique. Double/triple voiding |
| **Bowel** | Explanation of normal bowel function including digestion  
Anal and fecal incontinence Constipation and obstructed defecation | • How to use laxatives including use of enemas  
• How to get a proper defecation technique |
| **Diet** | Explanation of official guidelines on healthy diet | • How to improve diet by increasing fibers and reducing fat  
• How to lose weight |
| **Quality of life** | Impact on quality of life including sexual life | • To talk about POP  
• How to change habits |
| **Exercising** | Description of low impact sports and reassurance of the positive effect of exercising | • Presentation of different types of low weight/impact sports |

**Subjective evaluation of POP**

The primary outcome was the Patient Global Index of Improvement scale (PGI-I) at six months follow-up. The PGI-I was also used as a secondary outcome at three- and 12-month follow-up. Secondary outcomes were the Pelvic Floor Distress Inventory - short form 20 (PFDI-20) and the Pelvic Floor Impact Questionnaire - short form 7 (PFIQ-7) to reveal symptoms and affection of quality of life related to pelvic floor disorders, respectively. Impact on sexuality was evaluated with The Pelvic organ prolapse/urinary Incontinence Sexual Questionnaire 12 (PISQ-12). The score has 12 items revealing impact on sexuality.
caused by POP, urinary incontinence and partner related problems. A total score can be calculated if there are no more than two missing response. Only single item scores were reported because of low item response rate. In the TLG the women were to note their PFMT home training in a training dairy and they were asked to describe if the PFMT gave any bother in a Numeric Rank Scale (NRS) ranging from 0 to 10. A higher number indicated more bother.

The participants filled in the symptom- and HRQoL-scores with a minimal assistance at baseline and at the three-month follow-up visit. Six-month and 12-month follow-questionnaires were sent to the women. At the six- and 12-month follow-up the women were asked to report and specify if they had received further treatment after the three-month follow-up. The questionnaires were handed or sent to the women by the research nurse who also collected all questionnaires. The primary investigator only had access to the questionnaire scores after the research nurse had entered them into a database.

**Objective evaluation of POP**

The Pelvic Organ Prolapse Quantification system (POP-Q) was used to evaluate objective POP at baseline and at the three-month follow-up. A POP-Q score of $\geq$ II was furthermore an inclusion criteria for our study. The primary outcome assessor was trained to do the POP-Q by a senior consultant urogynecologist 116. The research nurse took notes on a standardized sheet during the examination. The sheet was removed after the examination and primary investigator was blinded to the results of the baseline examination at the three-month follow-up.

The research nurse entered all results from the examination in the database. The examination was performed in the lithotomy position with the use of speculums and a measuring stick (centimeter). To standardize the examination as much as possible the women were asked to strain maximally with an open mouth for at least 6 seconds to obtain maximum descent for all points, where straining was needed 117.
**Figure 6:** The nine landmark points examined in the POP-Q assessment (Bump 1996)\(^4\)

**POP of the anterior, the middle and the posterior compartments is measured with the hymen as a reference point; POP in the anterior wall is measured with two points (Aa and Ba), POP in the posterior wall is measured with two points (Ap and Bp) and POP in the middle compartment with the C (Cervix) and the D points (posterior fornix).** Genital hiatus (Gh) is measured from the urethra to the hymen. Perineal body (pb) is the length of the perineal body form the hymen to anus. Total vaginal length (tvl) is the only point not measured during maximal straining. **POP above the hymen is indicated with a negative number. POP beyond the hymen is described with a positive number**\(^4\).

**Methodological considerations - Study 2**

**Materials**

Only women with symptomatic POP stage \(\geq II\) were included in the study because pelvic floor symptoms are more likely to be caused by POP if the objective POP is close to the hymen\(^67,119,120\). Only 6-11% of women with POP stage 0-I will describe the cardinal symptom of POP: a bulge. However, describing a bulge has been found to have a positive predictive value of 81% and a negative predictive value of 76% for POP stage II\(^64\). Furthermore the hymen is classified as point of success after surgery with the subjective sensation of not having a bulge\(^121\). POP stage I has moreover been defined as good organ support\(^70\). Finally, we wanted to include only women who would hypothetically be eligible for pessary or surgical treatment. Women with a POP stage I, are not likely to receive either.
Some studies have found that certain POP symptoms correlate with POP in a specific compartment such as bladder symptoms with anterior POP and bowel symptoms with posterior POP \(^{122,123}\) while others cannot find this association \(^{68,124}\). We therefore chose to include both women with anterior and/or posterior POP.

**Study design**

To be able to perform a randomized controlled trial we had to invent a design that could separate the effect of PFMT from the effect of lifestyle advice. We did not find studies that had used a relevant design that we could adopt for our study; one study examining the effect of a 8-week individual PFMT program for post natal women with SUI offered massage to the control group.\(^{108}\) Another study for patients with fecal incontinence gave patient education and lifestyle advice during a four-week period. If the patients had relief of symptoms they were excluded from the study and were not offered PFMT.\(^{125}\)

We did not wish to offer an irrelevant treatment for comparison and our intervention groups should be as equal as possible regarding attention from the physiotherapist to reduce risk of performance bias.\(^{126}\) To obtain this, standardization of the lifestyle advice was required. We chose to offer both study groups, six lectures comprising an identical lifestyle advice program and added group PFMT and PFMT home training to one group. The two groups were: “the Lifestyle advice Group” (LG) receiving structured lifestyle advice only and “the Combined pelvic floor muscle Training and Lifestyle advice Group (TLG)” receiving structured lifestyle advice in combination with PFMT.

We offered the interventions as group lectures for several reasons: 1) To ensure that the two groups received identical lifestyle advice through standardized lectures. 2) To ensure that both groups had the same number of lectures. 3) To ensure that interventions would be reproducible in another setting using pre-developed presentations and PFMT programs. 4) Finally, that the interventions would be financially manageable even in a setting with limited resources.

**Assessment of pelvic floor muscle function**

It has been found that women with pelvic floor disorders are more prone to be unable to contract their PFM correctly\(^{87,89}\). A recent study showed that sixty (24%) of 250 women referred to an uro-gynecology clinic could not perform a correct PFM contraction at their first
attempts. Nineteen (23%) of the 83 women who said they did PFMT regularly were unable to perform a correct PFM contraction\(^\text{127}\). All women in the TLG were offered an individual assessment of their PFM function and instruction in PFMT to assure that they could perform the PFMT program correctly. Women unable to contract their PFM correctly were offered additional individual sessions and learned to contract correctly\(^\text{2}\).

A reliability study based on the ICS standardization terminology on PFM assessment, found substantial intra-observer reliability (Weighted Kappa \(>0.60\)) for voluntary PFM contraction and relaxation, for involuntary contraction and for muscle strength and endurance. However, the study found that inter-observer reliability was disappointing and it was concluded that visual and digital assessment of PFM function was for clinical use only\(^\text{106}\). In the present study the results from the PFM examination were therefore only used to guide the women and no individual follow-up on PFM function was performed.

**The pelvic floor muscle training program**

A recent review concluded that PFMT was more efficient than no PFMT for the treatment of urinary incontinence. However it was not possible to establish which PFMT program was most efficient program. It was suggested to follow general training principles using progressive overload and specificity when prescribing PFMT \(^\text{109}\). The same principles are most likely applicable in relation to PFMT for POP. To an untrained person this requires a program using 60-65% of one Repetition Maximum (RM) (one RM = 100% effort) 3-5 times a week for 12 weeks\(^\text{128}\). Furthermore, three sets of contractions seem to be more efficient than doing one set of contractions\(^\text{129}\). The studies on PFMT for POP have described different strategies but they have all used three sets of 8-12 PFM contractions daily followed by three to 50 fast contractions. Some have described the use of maximal strength training (\(>65\%\) of 1RM)\(^\text{25,22}\) while others have not described level of effort\(^\text{30,31}\). The studies have described instruction in the use of “knack training” as part of the PFMT program \(^\text{90}\).

In our study the women were told that every contraction should be held firmly and with as much effort as possible to increase muscle strength, but with normal breathing to avoid excessive co-contraction of the abdominal muscles\(^\text{130}\). Excessive co-contraction of the abdominal muscles during a PFM contraction has been found to increase the IAP unnecessarily causing a downward movement of the organs instead of the desired lift of the organs\(^\text{130}\).
Because women with POP have been found to miss involuntary PFM contractions during increased IAP \textsuperscript{88} the "Knack training" was emphasized during the group sessions \textsuperscript{107} \textsuperscript{90}. To progress the skill learning a short catalogue with different knack exercises was developed to inspire the physiotherapists during the sessions.

We chose to offer PFMT as group training supplemented with home training. No other studies have examined individual PFMT versus group PFMT for women with POP but studies comparing group PFMT versus individual PFMT for women with SUI have found equal effect \textsuperscript{131, 132} \textsuperscript{133}. We therefore expected that group PFMT also would be applicable for women with POP.

**The lifestyle advice program**

The aim of the lifestyle advice program was to increase awareness among the women about how to reduce known promoting factors for POP\textsuperscript{35} \textsuperscript{34}. We emphasized presenting the advice in different ways to make as many participants as possible benefit from them. It has been proposed that people have different learning strategies and a number of models exist. One model, the VARK model (Visual, Aural, Reading/writing, Kinestetic) by Neil D. Fleming is widely used \textsuperscript{134}.

A variety of illustrations of the pelvic floor were used and the women were continuously offered the opportunity to ask for more explanations. It was aimed to use an understandable vocabulary, since many women do not understand the medical wordings related to pelvic floor disorders\textsuperscript{104}. The lifestyle advice program was discussed with specialist nurses and physiotherapists to assure content validity. A pretest was performed on patients with POP for relevance and understandability.

**Recruitment of participants**

Initially the participants were recruited from the hospital referral list only\textsuperscript{135}. However, the recruitment from the hospital referral list was very slow \textsuperscript{136} A recent a study found that women recruited from the public had similar symptoms as women referred by a clinician and we decided to attempt to recruit through the public\textsuperscript{136}. Advertising was conducted on Facebook \textsuperscript{TM}, posters at public places such as libraries, shopping centers and hospitals and in local new papers (Figure 7).
Figure 7: Flow-chart describing the recruitment process (adapted from\textsuperscript{2})

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{flowchart.png}
\caption{Flow-chart describing the recruitment process (adapted from\textsuperscript{2}).}
\end{figure}

Transperineal ultrasound

With the use of ultrasound\textsuperscript{137} it has become possible to visualize the PFM with a short non-invasive and reliable\textsuperscript{138}. In the RCT the primary investigator did transperineal ultrasound at baseline on all included women as it was hypothesized that thinning or avulsions of the PFM and the following enlargement of the genital hiatus would decrease the effect of PFMT\textsuperscript{139}. Because the primary investigator was blinded to group allocation all included women were examined. Transperineal ultrasound was performed during rest as 3D images and during straining as 4D films. The results from this examination were to be used as a possible explanatory factor for treatment effect after either intervention. Unfortunately it was not possible for the primary investigator to achieve adequate skills to analyze the images within the timeframe of the study. The results are therefore not reported in this thesis.

Materials and methodology – study 3

In study 3 all participants from study 2 who completed the 12-month follow-up were included. Analyses were based on 12-month scores of the PGI-I, the PFDI-20, the PFIQ-7 and
the PISQ-12\textsuperscript{74,114,115} (see materials and methodology - Study 2) The primary investigator remained blinded to all data.

Long-term treatment effects, number of women who had sought further treatment and kind of treatment were examined.

Possible associations between having sought further treatment before the 12-month follow-up and baseline data and three-month follow-up scores were evaluated: From the baseline data influence of age, BMI, parity, POP stage, position of POP, working status, referral status, and baseline symptoms- and HRQoL scores, on having sought further treatment were used in the analyses. From the three-month follow-up data results from symptoms- and HRQoL scores and results from the POP-Q assessments were used.

**Methodological consideration – study 3**

Long-term follow-up is an important measure of treatment effect. Knowledge about the long-term effect of PFMT in relation to POP is limited. Only one study so far has reported 12-month follow-up data\textsuperscript{31}. No prior studies describing causes for seeking further treatment after PFMT were identified. We therefore explored not only long-term treatment effects of either intervention but also if specific factors were associated with seeking further treatment before the 12-month follow-up.

**Statistical considerations**

In the three studies included in this thesis we used descriptive statistics to describe baseline data of our populations and we used the Chi-square/Fischers’exact test for categorical variables. Both parametric and non-parametric statistics were used for paired an unpaired analyses.

In study 1\textsuperscript{1} data were tested for normality of distribution with the Kolmogorow-Smirnov test and if data were not normally distributed non-parametric statistics was primarily used but both mean (standard deviation (SD)) and median values (range) were reported. The Cronbach’s Alpha was carried out to analyze internal item consistency and inter-item total correlation of the PFDI-20 and the PFIQ-7 subscale and total scales. Test-retest stability of the PFDI-20 and the PFIQ-7 was examined with the Intra Class Correlation coefficient (ICC). The non-parametric Spearman’s rank order correlation test was used to evaluate; the correlation between the PFDI-20 and the PFIQ-7 scores; between objective baseline POP and
questionnaire scores, and between improvement of symptoms and quality of life and response to the global score (PGI-I). Receiver Operating Characteristic (ROC) curves was made to evaluate sensitivity and specificity of the PFDI-20 and the PFIQ-7 in relation to the PGI-I. We furthermore, calculated effect-size and standardized response mean to evaluate responsiveness of the questionnaires. 

In study 2 and 3 the PFDI-20 and the PFIQ-7 total and subscale scores were analyzed with both parametric and non-parametric statistics. When both methods showed similar results only results from the parametric analyses were reported because calculated scores from the two questionnaires are normally reported as mean values (Standard Deviation). Non-parametric tests were used for the analysis of baseline data and of single item scores. A sample size calculation was performed based on the PGI-I and the PFDI-20 with 80% power at a 5% level to find a 15% difference of the PFDI-20. Based on this 45 women were required in each arm and to account for possible dropout of 20% we included 108 women (included 109). In study 2 and 3 univariable and multivariable logistic regression analyses were performed. Variables from the univariable analyses were included in the multivariable analyses if they had a p-value of 0.2 or less. Level of significance of all statistical analyses was set at a p-value of 0.05 for all statistical tests used and all p-values were reported two-sided. The analyses were performed with the SPSS, version 19.0-22.0 (SPSS Inc. Chicago, IL, USA).
Results

Study 1
One hundred and thirty-two women with POP participated in the study. Seventeen women were interviewed, mean age 68.5 years (median 70.5, range 36–84). Questionnaire responses from 115 women, mean age 63.5 years (median 65, range 30–92) were entered into a database.

After two revisions the questionnaires seemed well accepted. Response rate in the pretesting was 70%.

The PFDI-20 was found to reveal relevant POP symptoms and no floor or ceiling effect was found, while the PFIQ-7 showed ceiling effect (best score =no symptoms at baseline).

Scores of the two questionnaires correlated weakly and only single items correlated with signs of POP. The questionnaires showed good test-retest reliability but the response rate in the test-retest was only 60%.

Sensitivity to change after POP surgery was sufficient for both the PFDI-20 and the PFIQ-7, while it was not possible to accurately define the Minimal Clinical Important Difference (MCID). Only improvement of POP subscales correlated with improvement in a global scale.

Study 2

Baseline
A total of 109 women with symptomatic POP were included. Sixty-two women (57%) had POP stage II and 47 women (43%) had stage III and. Fifty-three women were allocated to the LG, 56 women to the TLG.

Table 3: Type of POP and POP stage at baseline (adapted from x)

<table>
<thead>
<tr>
<th>Type of POP</th>
<th>LG (n=53)</th>
<th>TLG (n=56)</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POP-Q stage II/III, No. (%)</td>
<td>29/24 (55/45)</td>
<td>33/23 (59 /41)</td>
<td>62/47 (57 /43)</td>
<td>0.66</td>
</tr>
<tr>
<td>Anterior POP</td>
<td>47 (89)</td>
<td>49 (88)</td>
<td>96 (88)</td>
<td>0.40</td>
</tr>
<tr>
<td>Posterior POP</td>
<td>34 (64)</td>
<td>36 (64)</td>
<td>70 (64)</td>
<td>0.10</td>
</tr>
<tr>
<td>Combined POP</td>
<td>32 (61)</td>
<td>32 (57)</td>
<td>64 (59)</td>
<td>0.73</td>
</tr>
<tr>
<td>Anterior POP ≥ 0 cm</td>
<td>38 (71)</td>
<td>40 (71)</td>
<td>78 (72)</td>
<td>0.80</td>
</tr>
<tr>
<td>Posterior POP ≥ 0 cm</td>
<td>28 (53)</td>
<td>30 (54)</td>
<td>58 (53)</td>
<td>0.79</td>
</tr>
</tbody>
</table>
The two groups were comparable in all baseline data: Median age was 60 years (range 33-79) (P=0.77), median BMI 25 (range 19-37) (P=0.46), median parity 2 (range 1-9)(P=0.07). Number of referred versus self-referred women; number of women who had received previous surgery and number of women working was similar in the two groups (table 4).

**Table 4**: Baseline characteristics in the two groups (Adapted from\textsuperscript{2})

<table>
<thead>
<tr>
<th>Variable</th>
<th>LG</th>
<th>TLG</th>
<th>Total</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery, No. (%)\textsuperscript{a}</td>
<td>7 (13)</td>
<td>9 (16)</td>
<td>16 (15)</td>
<td>0.67</td>
</tr>
<tr>
<td>Referred/self-referred, No. (%)\textsuperscript{a}</td>
<td>20/33 (38 / 62)</td>
<td>19/37 (34 / 66)</td>
<td>39/70 (36 /64)</td>
<td>0.68</td>
</tr>
<tr>
<td>Working, No. (%)\textsuperscript{a}</td>
<td>33 (62)</td>
<td>31(55)</td>
<td>64 (59)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Chi-Square tests

Symptom- and HRQoL scores including sexuality scores (data not shown) were similar in the LG and the TLG (table 5).

**Table 5**: Baseline symptom and HRQoL scores in the two groups (Adapted from\textsuperscript{2})

<table>
<thead>
<tr>
<th>Number analyzed in each group</th>
<th>LG (n=53)</th>
<th>TLG (n=56)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom and bother\textsuperscript{a}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POPDI-6</td>
<td>30.3 (19.6)</td>
<td>36.9 (24.4)</td>
<td>0.13</td>
</tr>
<tr>
<td>CRADI-8</td>
<td>24.2 (18.5)</td>
<td>24.6 (21.3)</td>
<td>0.93</td>
</tr>
<tr>
<td>UDI-6</td>
<td>32.3 (22.6)</td>
<td>29.6 (23.2)</td>
<td>0.53</td>
</tr>
<tr>
<td>PFDI-20</td>
<td>86.9 (46.3)</td>
<td>91.0 (59.4)</td>
<td>0.69</td>
</tr>
<tr>
<td>Quality of life (HRQoL)\textsuperscript{a}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UIQ-7</td>
<td>18.3 (20.6)</td>
<td>12.7 (18.3)</td>
<td>0.13</td>
</tr>
<tr>
<td>CRAIQ-7</td>
<td>8.15(16.0)</td>
<td>9.9 (18.6)</td>
<td>0.61</td>
</tr>
<tr>
<td>POPIQ-7</td>
<td>12.2(19.8)</td>
<td>14.54 (19.3)</td>
<td>0.53</td>
</tr>
<tr>
<td>PFIQ-7</td>
<td>37.7(45.2)</td>
<td>37.07 (46.9)</td>
<td>0.94</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Unpaired T-tests with scores reported as mean scores (SD)
Three-month follow-up

Eighty-nine women (82%) of the 109 included women completed three-month follow-up. Dropout was 11% in the LG and 25% in the TLG and. Dropouts were younger (P=0.004), had more affection of bowel-related HRQoL (P=0.053) and more bother related to urinary incontinence during sexual intercourse (P=0.027).

Significantly more women in the TLG reported improvement in the PGI-I compared to the LG (p=0.003). Both groups showed significant improvement of the total PFDI-20 score but only the TLG had significant improvement of the POP subscale (P=0.001). The LG only had significant improvement of the PFIQ-7 caused by improvement in the bladder subscale (UIQ-7, P=0.014).

The LG showed a mean improvement in the total PFDI-20 score of 12.4 points (SD 30.3) corresponding to a 14% overall improvement of symptoms. The TLG had a mean improvement of the PFDI-20 total score of 15.6 points (SD 29.5) corresponding to a 17% improvement. The between group difference was 3.2 (95% CL -7.9 - 14.3, P= 0.57)^2. Objective POP and the sexuality score did not improve significantly in either group. Between-group differences of symptoms or HRQoL scores were insignificant at the three-month follow-up (table 6).

Table 6: Three-month follow-up symptom and HRQoL scores in the two groups (Adapted from 2)

<table>
<thead>
<tr>
<th>Number analyzed in each group</th>
<th>LG (n=53)</th>
<th>TLG (n=56)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom and bother^a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POPDI-6</td>
<td>29.3 (17.0)</td>
<td>30.4 (22.6)</td>
<td>0.77</td>
</tr>
<tr>
<td>CRADI-8</td>
<td>19.0 (16.7)</td>
<td>20.6 (18.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>UDI-6</td>
<td>26.6 (20.7)</td>
<td>24.9 (22.1)</td>
<td>0.68</td>
</tr>
<tr>
<td>PFDI-20</td>
<td>74.9 (39.5)</td>
<td>75.9 (54.9)</td>
<td>0.91</td>
</tr>
<tr>
<td>Quality of life (HRQol)^a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UIQ-7</td>
<td>13.09 (17.1)</td>
<td>10.7 (17.0)</td>
<td>0.48</td>
</tr>
<tr>
<td>CRAIQ-7</td>
<td>5.58 (14.8)</td>
<td>10.4 (19.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>PIPIQ-7</td>
<td>9.34 (17.4)</td>
<td>12.7 (19.7)</td>
<td>0.39</td>
</tr>
<tr>
<td>PFIQ-7</td>
<td>28.02 (37.6)</td>
<td>34.0 (49.1)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

^a Unpaired T-tests with scores reported as mean scores (SD)
There were no significant associations between any baseline data and self-reported improvement in the PGI-I in the univariable and the multivariable logistic regression analyses (factors analyzed: age, BMI, parity, work, surgery, POP-Q stage, POP position, symptoms- and HRQoL total and subscale scores).

Thirty-one of the 42 women (74%) in the TLG who completed three-month follow-up handed in their training dairies. Eleven women reported a median low bother of 2 out of ten (0-5) in the NRS scores in 11% of their reported home training sessions, while reporting a bother of 0 in 89% of their home training sessions.

**Six-month follow-up**

Eighty-five women (78%) responded to the six-month follow-up. At the six-month follow-up significantly more women in the TLG reported improvement in the PGI-I ($P=0.02$). Between the LG and the TLG no significant differences were found in any of the symptom- and HRQoL scores.

In the LG 68% had sought further treatment, compared to 28% in the TLG ($P= <0.001$). (table 7). Referred women or women who previously had received POP surgery, did not seek further treatment significantly more often than self-referred women or women who had not previously received surgery$^2$.

**Table 7:** Number of women who had sought further treatment at the six-month follow-up (adapted from $^2$)

<table>
<thead>
<tr>
<th>Number analyzed in each group$^a$</th>
<th>LG (44)$^b$</th>
<th>TLG (40)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other treatment</td>
<td>30 (68%)</td>
<td>11 (28%)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>PFMT</td>
<td>24</td>
<td>3</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Pessary</td>
<td>2</td>
<td>4</td>
<td>0.30</td>
</tr>
<tr>
<td>Surgery</td>
<td>3</td>
<td>2</td>
<td>0.79</td>
</tr>
<tr>
<td>Other treatment (not described)</td>
<td>4$^c$</td>
<td>2</td>
<td>0.77</td>
</tr>
</tbody>
</table>

$^a$Chi-Square test and with Fisher’s Exact Test. $^b$One woman did not answer these questions. $^c$In the LG three women reported receiving an unspecified conservative treatment in addition to a specified treatment.
Women in both groups who had sought further treatment had significantly more POP in the anterior compartment (P = 0.03) but not significantly higher total POP-Q scores (P=0.62) nor more POP of the posterior compartment. Women seeking further treatment experienced more impact on bladder related HRQoL (UIQ-7, P= 0.05) at baseline and at three-month follow-up (UIQ-7, P= 0.04) (unpaired non-parametric tests).

**Study 3**

Eighty-three women (76%) responded to the 12-month follow-up, 43 in the LG and 40 women in the TLG. A total of 34 women had not sought further treatment, 30% (13/43) women in the LG and 52% (21/40) women in TLG, respectively (P=0.05). Compared to baseline the LG had significantly improved bladder symptoms (UDI-6, P= 0.01), while those in the TLG had significantly improved POP symptoms (POPDI-6, P=0.02) and bowel-related HRQoL (CRAIQ-7, P=0.04).3

Single item analysis showed that the LG had significant improvement of two items in the total PFDI-20 scale regarding stress urinary incontinence and “small amount leakage”. In the TLG one item about the “bulge” of the total PFDI-20 scale was significantly improved. No single item of the CRAIQ-7 was significantly improved and significance was only found in the total CRAIQ-7 score. The symptoms- or HRQoL scores did not differ significantly between the LG and the TLG (data not shown).

None of the items in the sexuality score were significantly improved between baseline and the 12-month follow-up (data not shown). Forty-nine women (59%) of the 83 respondents had sought further treatment. Thirty (70%) in the LG compared to nineteen (48%) in the TLG, respectively. Eight women, four from each group had received surgery, while 41 had received conservative treatment. Twenty-five of 30 in the LG had sought PFMT compared to five of 19 in the TLG (Figure 8).

Between women who had or had not sought further treatment no significant differences were found in any of the PFDI-20 total or subscale scores in the three-month follow-up scores (unpaired tests). In the TLG only, the women who had sought further treatment showed significantly more impact on POP related HRQoL (P= 0.03) More anterior POP (at or beyond the hymen) and more impact on bladder and POP related HRQoL was associated with seeking further treatment before the 12-month follow-up based on univariable logistic analyses of baseline data (before allocation) In the multivariable
analysis working status became significant, while the effect of POP related HRQoL disappeared.

**Figure 8:** Describing the number and kind of treatment sought before the 12-month follow-up in the two groups (Adapted from3).

**Notes:**

- One woman did not respond to these questions
- One woman who had received PFMT did not complete 12-month follow-up.
- One woman had surgery between the six and 12-month follow-up after describing "other treatment"
- Other unspecified conservative treatment.
- Two women from the LG left the study between the six- and 12-month follow-up.

Group allocation to the LG and more POP and bladder symptoms including impact on bladder and POP related HRQoL, was associated with seeking further treatment in the univariable analyses based on three-month follow-up scores. In the multivariable analysis the influence of group allocation, POP symptoms and impact on bladder and POP related HRQoL disappeared, and only more advanced anterior POP and more bladder symptoms remained significant, with more anterior POP being the strongest factor.
**General discussion**

**Patient reported outcome measures**

To be able to measure symptoms/bother and HRQoL and any effect of an intervention, it is important to have valid and reliable tools\(^{101}\). In the literature a variety of scores exist measuring symptoms and impact from pelvic floor disorders\(^6^8\). Some scores are specific for POP \(^6^8,^1^4^1\), while others cover other aspect of pelvic floor disorders that are not necessarily correlated to POP \(^1^4^2\). The PFDI-20 and the PFIQ-7 are internationally recognized\(^7^3\) and they have been translated and validated in a number of languages \(^7^4\). In study 1 we chose to translate the questionnaires in their validated short-forms \(^7^4\).

The process revealed that PFDI-20 had sufficient content validity, while the PFIQ-7 suffered from ceiling effect and missed relevant items on HRQoL. We believe that we made the best choices with the PFDI-20 and the PFIQ-7 \(^7^4\) but the PFDI-20 has some constitutional problems, which became clear to us during the translation procedure. In fifteen of the 20 items of the PFDI-20, the item had two questions in one item, saying: “Do you _usually_ have..” instead of “Do you have..?” This lack of unidimensionality caused confusion both for the translating panel and for the patients \(^1^0^1\). During the patient interviews we explored the word “usually” and we realized that the participating women interpreted this word very differently. We had to compromise using a word with the meaning: “most of the time”. We believe that this inherent problem is a weakness of the PFDI-20, which might also affect the cross-cultural validity of the scores.

We also have to account for some methodological problems in the study. The test-retest was performed in 50 women and it is recommended to have at least 100 participants completing the test-retest \(^1^4^3\). Secondly we only calculated the Intra Class Correlation coefficient (ICC). It has been found that ICC overestimates reliability while there are more exact methods to determine reliability. The 95\% limits of agreement (LoA) between the test and the retest could have been established using the Bland–Altman method\(^1^4^4\) or by calculating the Standard error of measurement (SEM)\(^1^4^3\). This would have increased the precision of the reported measurement error and thereby the smallest clinically relevant change\(^1^4^4\). It could also have strengthened the validity of the Danish versions of the PFDI-20 and the PFIQ-7 if it had been examined if improvement of symptoms and HRQoL correlated with
improvement of objective POP after surgery. Since this was not a routine procedure at the hospital, data were not available on all women and we did not perform this\textsuperscript{145}. Finally, a reference group of Danish women without pelvic floor disorders, or a group of women with pure urinary incontinence or anal incontinence could have been included, which would have strengthened interpretability and a wider usability of the translated questionnaires\textsuperscript{144}.

**The Design of the randomized controlled trial**

The aim of a randomized controlled trial (RCT) is to reduce any systematic bias that could possibly affect the outcome of an intervention. A very important factor is to avoid that bias related to the design could cause an under- or an overestimation of the true effect of an intervention. In physiotherapy studies, including studies on PFMT, “performance bias” could introduce a serious risk of bias.

According to the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011], The Cochrane Collaboration, 2011\textsuperscript{126}: “Performance bias refers to systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.” (Chapter 8.4. section 2, line 1, www.cochrane-handbook.org)\textsuperscript{126} Performance bias might have resulted in an overestimation of the effect of PFMT found in earlier studies comparing an active PFMT program with a lifestyle advice leaflet or a short instruction. The aim of our design was therefore to reduce the risk of bias related to attention. This, to minimize that any superior effect attributed to PFMT could be caused by the extra attention and information rather than by the PFMT itself.

We believe that our design was ideal to examine our hypotheses but it was not possible to blind the participants to their group allocation and this could have affected the outcome in the TLG. The women in the TLG might have felt that they received a better intervention than the LG, which may be supported by the unintended crossover with the majority of the LG seeking PFMT after completing their intervention. Interestingly, significantly more women in the TLG indicated improvement in the global scale at the three- and six month follow-up despite they had not achieved better symptom- or better HRQoL scores than women who did not indicate this improvement in both groups. A study comparing an individually tailored PFMT program with “watchful waiting” (no contact) also found that women who had received PFMT
compared to no treatment reported more improvement in a global scale despite that they had not obtained a clinically relevant improvement in their symptom- or HRQoL scores. Bias is a likely explanation for our result and as in the study by Wiegersma et al. the women in the TLG probably felt “lucky” or even felt better because of higher expectations. However, it is possible that they did experience a superior effect in areas that we did not measure, such as a sensation of improved awareness of the pelvic floor.

While we believe that our subjective outcome measures were comprehensive and suitable for women with POP other factors could have influenced the superior self-reported improvement found in the TLG. Improved body-image or the ability to be more active without getting POP symptoms could hypothetically be the cause because of the possible improvement of the support for the organs after PFMT.

It is a limitation of our study that we did not explore this finding further. We could have used a mixed methods design, combining both quantitative and qualitative approaches to learn more about our participants. While our hypotheses mainly gave reason to conduct a quantitative study, adding qualitative methods could have helped us explain why the TLG felt more improved despite of not showing superior effect in most of the symptoms- and HRQoL scores.

The choice and timing of our primary outcome might furthermore represent a weakness of our study design. We chose the Patient Global Index of Improvement scale (PGI-I) at the six-month follow-up, three months after the women had completed the interventions. The PGI-I was furthermore used as secondary outcomes at the three- and 12-month follow-up. Possibly there was recall bias at the six-month (and at the 12-month) follow-up because the women were asked to remember how they felt before entering the study (or before they had sought further treatment). This could carry a risk of over- or underestimation of the true effect of the study. By using the PGI-I scale at the six- and 12-month follow-up there was a risk of asking the women two questions in one; had she experienced positive effect of the intervention and was the effect better or worse compared to last follow-up. It might have improved validity of our results if we had described how the women felt “right now” utilizing a Visual Analog Scale (VAS) or a Numeric Rank Scale (NRS) and we suggest the use of these scores in future studies on PFMT instead.
Pelvic floor muscle training

Based on the literature PFMT could hypothetically restore some of the support for the pelvic organs and thereby improve symptoms. In our study, we could not confirm this superior effect of PFMT on POP related symptoms except for the positive response in the global scale and the significant improvement of POP symptoms at the three-month follow-up, which did not result in significantly reduced symptoms in the TLG compared to the LG. Previous studies on PFMT for POP have found significantly reduced symptoms after individual PFMT compared to lifestyle advice, but a lifestyle advice leaflet alone have also shown to improve symptoms and bother. In the study with the most intensive PFMT program, including women with POP stage I-III, “bulge symptoms” were decreased in 74% and bother was decreased in 67% of the women who had received weekly or bi-weekly PFMT for six months (18 individual sessions). In the control group, who had received a single instruction in lifestyle advice and of “the knack”, 31% reported reduced bulge symptoms and 42% reported less bother. It was not described “how much” symptoms and bother was improved and of 109 participants only 69 (63%) reported symptoms at baseline. Considering the effort of a six-month program to achieve the improvement compared to a single instruction it is most likely that the included women were very resourceful and probably not representing average women with POP.

Other studies with a less intensive but individualized PFMT program have also found positive, but less substantial effect of PFMT on symptoms compared to a lifestyle advice leaflet. The largest study published so far included women with mild to moderate symptoms and POP stage I-III. They found that significantly fewer women receiving an individual PFMT program for 16-week reported symptoms within the preceding four weeks and the women reported significantly improved HRQoL compared to women who had received a lifestyle advice leaflet. The difference in number with reduced symptoms between the study groups was 10-22% in favor of PFMT. Whether the difference was clinically relevant is debatable, but the intervention seemed more realistic and implementable.

We believe that the PFMT program used in our study was comprehensive enough to improve PFM function while still realistic for the women to accomplish. The women were thoroughly instructed and given appropriate information to understand the purpose of the PFMT program. However, it is possible that more frequent individual instructions focusing on individualized adherence strategies and the use of digital reminders could have improved
both short- and long-term effect of the PFMT program. A limitation to the study is that not all women handed in their training dairies and that we had no other possibility to measure adherence to the PFMT program. Our results give a realistic impression of what could be expected after a PFMT program for women with POP. The group design was in addition feasible in most settings within public health care service. Group supervision might also have been more motivating for some of the participants compared to individual sessions.

Although most published studies on PFMT have found significant improvement of POP symptoms after PFMT, the effect has been moderate and many women have not benefitted from PFMT. Possibly the impact of ageing on PFM function and especially the combination of ageing and injuries on the PFM caused by vaginal delivery and promoting factors are likely to reduce the potential effect of a PFMT program.

Increased muscle strength and thereby improved cross-sectional area and stiffness of the PFM can be difficult to obtain if a woman has very weak and untrained muscles. The use of biofeedback or electrical stimulation in conjunction with PFMT could possibly have increased the effect of the PFMT program but the evidence is limited and other studies using either have not been able to show substantially superior effect.

Hypothetically alternative methods could be used to enhance the effect of a strength-training program. A low intensity training program with a simultaneous partial occlusion of the blood supply for the training muscle, so called “Kaatsu” training has been found to increase muscle strength faster than ordinary strength training but with much less effort. Moreover, it has been found to increase the number of stem cells in a muscle with up till 400%. It seems difficult to make occlusion of the PFM during PFMT but a different way to use this strategy may be possible. A study found that low intensity training of the quadriceps femoris (Less than 12 RM= <50% af 1RM) with partial occlusion of the blood supply did not only increase muscle strength of the quadriceps femoris muscle. If the biceps humeri muscle was trained with low-load training and no occlusion in the same training session it also improved muscle strength of that muscle. The specific reason for this this “cross-transfer effect” could not be fully explained but it was believed to be caused by a systemic effect caused by growth hormones. Perhaps Kaatsu training could be useful for women with POP who have weak but intact pelvic floor muscles.
We did not succeed in analyzing our ultrasound images for this thesis, but it is likely that some of the participants had avulsions of their PFM, which might have affected the outcome of the PFMT program. Repair of PFM avulsions has been attempted but with little success. Perhaps in the future, the use of stem cells, especially muscle-derived stem cells could be a way to restore the missing muscle tissue in women with POP, which could thereby improve the effect of PFMT. Transplantation of fresh myofibers with their satellite cells in the urethra of pigs gave improved tonic activation after 30 days indicating innervation of the new myofibers, which could imply that it is possible to create new muscle fibers to replace missing muscle tissue.

The lifestyle advice program

From our study it seems that a comprehensive lifestyle advice program addressing known promoting factors for POP and aiming to reduce typical POP related symptoms through simple lifestyle advice, reduced most of the superior effect of a PFMT program compared to other studies. Surprisingly, only the LG had significant improvement of their HRQoL at three-month follow-up, while the TLG did not have significant improvement in any HRQoL subscales. The improvement in the LG was in the bladder- and bowel-related HRQoL and it is likely that women in the LG gained more benefit because the lifestyle advice matched their specific problems better than in the TLG.

It was emphasized to offer relevant advice and in different ways to make most women benefit from the advice. Furthermore, the participants could continuously ask for explanations if they did not understand an advice. This would not have been possible if the women had been offered a lifestyle advice leaflet only.

We did not ask the women why they decided to participate in our study, but it is likely that the LG experienced a positive short-term effect because they received information and reassurance about their condition. Probably almost all women in the LG sought PFMT because they hoped that PFMT could reduce their POP symptoms even more.

A limitation of our study is that we had to compare “a package” of lifestyle advice with or without PFMT to perform the study. Neither was the sample size large enough to stratify for either position of POP nor specific symptoms. Furthermore, the participants were not encouraged to follow the same advice and probably the women chose only to follow specific
advice relevant to their needs. Since the study was not designed to evaluate the particular effect of a specific advice it is not known if any lifestyle advice were more important than other lifestyle advice.

**Effect on objective POP**

We only included women with POP stage ≥ II, and more than 70% of our participants had a POP at or beyond the hymen. Women with POP stage 1 were excluded, because this stage rarely gives the cardinal symptom of POP: ”the bulge”64. Opposed to earlier studies that included 10-22% with POP stage III we included 43% women with POP stage III 25,30,31. None of the women participating in our study had achieved significant improvement of their objective POP at the three-month follow-up.

Except from one study showing a remarkable improvement of objective POP in women with POP stage II 29, other studies have only found reduction of objective POP in a few women after PFMT. The most intensive PFMT study found that 19% compared to 8% in the control group improved one stage but in women with POP stage III the change was similar whether they had received PFMT or not 25. In the largest study, 7.5% more of the women who had received PFMT, improved one stage compared to the group receiving a lifestyle advice leaflet only. However, the total number of women with progression or regression of their objective POP was equal whether the women had received PFMT or not 31.

The primary investigator did all the POP-Q evaluations. The POP-Q is not part of normal postgraduate education to become a specialized pelvic floor physiotherapist. The primary investigator trained with a senior consultant uro-gynecologist before the study was initiated116. It is therefore possible that the learning curve influenced the results of the POP-Q examinations. This could represent a systematic bias and it is possible that the three-month follow-up evaluations were less positive because the women were given more precise commands, were straining more correctly and the measurements were more precise71.

It has been found that signs of POP can vary after strenuous physical activity without causing more symptoms162 POP can also resolve without treatment over time 163 164. Adding to this possible natural variation, a slight measurement error could account for some of the variation found in our study and in previous studies165.

Based on our findings we believe that it is unlikely to expect a significant improvement of advanced objective POP after PFMT. Possibly a small number of very motivated women can
reduce their objective POP through a very intensive PFMT program but it requires a very resourceful patient and a very resourceful health care system\textsuperscript{25}.

**The effect on sexual function**

The women included in our study described low impact of their sexuality and almost 25\% of our participants did not fill in the sexuality score because they were not sexually active (described as not having a partner). A hypothesis could be that the women declining participation had more impact of their HRQoL and sexual function than the women accepting participation\textsuperscript{166, 167}. We do not know if the women in our study were restraining themselves from being sexually active because of their POP, and it is a limitation of our study that we did not ask them. However, we could not find significant improvement in the sexuality score at any follow-ups after either intervention. A study evaluating the effect of PFMT on sexual function found that women reported improvement of their sexual function during patient interviews but that this positive effect was not reflected in the used sexuality score\textsuperscript{168}. It is possible that if a different score than the PISQ-12 had been used, we would have achieved a more diverse picture of how the women experienced their sexuality. The PISQ-12 is very “partner related” score and “The Female Sexual Function Index” (FSFI) could have provided a broader picture of sexual function and dysfunction because it is more orientated to the woman herself\textsuperscript{169}. Finally, it is likely that we did not capture all relevant problems related to body image problems / partner related body image problems because we did not include scores on this\textsuperscript{170}.

**The relevance of a conservative treatment program**

The improvement of symptoms and HRQoL from either intervention barely reached our predefined minimally clinically important difference (MCID) of 15\% improvement at the three-month follow-up. The long-term effect of both the LG and the TLG was furthermore marginal\textsuperscript{3}. Although the overall effects were limited, some positive aspects appeared. The PFMT program caused low bother and no baseline data, including POP stage II or III could predict self-reported improvement in the short-term. Interestingly, more anterior POP and not symptoms nor impact on HRQoL was the strongest factors associated with having sought further treatment at the 12-month follow-up. This could indicate that both interventions were tolerable, that even women with advanced POP could experience some benefit from either
program, and that symptoms and impact on HRQoL alone cannot explain treatment-seeking behavior in women with POP.

Our study design was developed to minimize bias but confounding factors such as difficult recruitment may have influenced our results. Almost 90% of the women contacted from the hospital referral list declined participation and the majority of our participants were self-referred. It could be suspected that women accepting participation were more resourceful compared to the women who could not be recruited and that we recruited a selected group of women. Our results may therefore not be extrapolated to other populations of women with POP stage II-III and our findings should be interpreted with caution.

Only 10% of our participants had received surgical treatment before the 12-month follow-up. This number was comparable to the other 12-month follow-up study that only included half as many women with POP stage III. While it could be interpreted as a positive result our participants may have been a selected group, who had no prior wish for surgical treatment. It has been found that women POP accept conservative treatment or “watchful waiting” if they have less bother and less impact on their HRQoL compared to women seeking surgery and probably our participants belonged to that group.

Our findings give rise to the inevitable question if all women with POP, especially advanced POP routinely should be offered PFMT and also if the effect of a conservative treatment is worth the trouble. Are we wasting both our time and the women’s time with lifestyle advice and PFMT and is conservative treatment for a selected group of women only?

Compared to the improvement of symptoms and HRQoL found after surgery the effect of both our two interventions was low. Some might question the clinical relevance, and although in favor of PFMT the difference was negligible.

On the other hand “a bulge” is the only symptom that corrective surgery can improve and the bulge can still be objectively present even after successful surgery. Any conservative treatment can always be followed with more invasive treatment, while surgery can cause continued problems or new symptoms.

One study reported offering a preoperative PFMT program, while two studies offered PFMT postoperatively with no significant superior effect compared to no post-operative PFMT. It is therefore uncertain if PFMT could improve the long-term effect of surgery or reduce the risk of new symptoms to appear after surgery.
Perspectives

The results from our study do not give reason to change the grade A recommendations for PFMT for POP\textsuperscript{32}. However, as with PFMT for urinary incontinence it is unlikely that either lifestyle advice alone or in combination with PFMT can reduce POP related symptoms substantially\textsuperscript{173}. On the other hand as stated in a recent review article: “when choosing these conservative treatment options, patients have nothing to lose but time if they are unsuccessful” (Culligan 2012, page 860, line 37-40) \textsuperscript{174}. The interventions with or without PFMT were cheap and could easily be implemented in most settings and group education has been found to be as efficient as individual patient education\textsuperscript{175}.

We have not identified studies evaluating how Danish women seek information about “pelvic floor problems”, but a British study from 2008 found that three out of four women had sought information on the internet before attending an outpatient clinic for pelvic floor disorders\textsuperscript{176}. Danish women most likely do the same. Three recent studies, all published in 2015 have evaluated the quality of Internet based information on POP, in English-language websites\textsuperscript{177-179}. The quality was found to be poor in the vast majority of the websites. Limited information was found about conservative treatment options or about what women could expect if they did not receive any treatment for their POP. Furthermore, the information was influenced by industrial sponsored websites with a tendency to promote the effect of non-evidence based surgery methods.

Any surgical procedure implies a risk to the woman’s health and as stated in a Cochrane review on POP surgery: “The impact of pelvic organ prolapse surgery on bowel, bladder and sexual function can be unpredictable and may make symptoms worse or result in new symptoms, such as leakage of urine or problems with intercourse” (Cochrane, Maher 2013, page 3, line 2-4)\textsuperscript{180}.

Based on our findings women with POP should be told to have realistic expectations about the effect of lifestyle advice with or without PFMT but with the low risk of adverse events in mind we think that motivated women with POP should be offered lifestyle advice in combination with PFMT. Possibly information, reassurance about the condition and improvement of body awareness are the key elements in a conservative approach and future studies should address this issue in women with POP\textsuperscript{161}. 
**Future studies**

The studies included in this thesis have revealed areas that should be studied further. In study 1 we used classical test theory (CTT) to perform the psychometric analyses of the translated versions of the PFDI-20 and the PFIQ-7. We discovered that some of the assumptions for making scores of questionnaires were not fulfilled, such as normal distribution of data and item equivalence. Furthermore, we found that most of the items in the PFDI-20 lacked uni-dimensionality and that the PFIQ-7 missed relevant items. We believe that a thorough analysis using Item Response Theory (IRT) models could improve validity of the PFDI-20 and the PFIQ-7\(^{101}\).

We also realized that we miss validated body image scores for women with POP in Danish\(^{170}\). A relevant future study would be to correlate PFDI-20 and PFIQ-7 scores with body image problems in Danish women with POP\(^{110}\).

In study 2 and 3 we discovered that our studies gave rise to several more questions related to conservative treatment for POP. The questions could suggest that future studies should include both quantitative and qualitative methods addressing the following questions.

- **What makes women seek conservative treatment in spite of advanced POP?** Can other factors than symptoms- and HRQoL scores explain treatment-seeking behavior, such as health belief and personal resources?\(^{181, 182}\)
- **Could other scores than the symptom and HRQoL scores used in the present study be relevant when measuring treatment effect in Danish women with POP, such as activity, scores, body-image scores and other sexuality scores?**\(^{147, 169, 170}\)
- **Could the use of patient selected goals and composite endpoints give a better picture of treatment effect after a conservative intervention than symptom and HRQoL scores alone?**\(^{183}\)
- **What would be the optimal PFMT program?** Could alternative methods like “Kaatsu” training improve the effect of PFMT in relation to POP?\(^ {157, 158}\)
- **What specific lifestyle advice for women with POP are the most important advice; is it reduction of straining, improvement of bladder habits, weight loss or conscious reduction of heavy lifting?** Or is it something else?\(^{256}\)
Danish summary

Denne ph.d-afhandling er baseret på 3 studier som er gennemført på Herlev Hospital. Afhandlingen omhandler 3 originale artikler.


Formålet med afhandlingen var:

1. At oversætte og validere sygdomsspecifikke spørgeskemaer til kvinder med POP mhp. anvendelse af disse i studie 2 og 3
2. At undersøge effekten af et livstilsrådgivningsprogram med eller uden bækkenbundstræning til kvinder med symptomatisk POP ved en 3 og en 6 måneders opfølgning
3. At undersøge langtidseffekten af et livstilsrådgivningsprogram med eller uden bækkenbundstræning til kvinder med symptomatisk POP ved en 12 måneders opfølgning

Ad 1. I studiet oversatte og validerede vi symptomscoren: the Pelvic Floor Distress Inventory-20 (PFDI-20) og livskvalitetsscoren the Pelvic Floor Impact Questionnaire-7 (PFIQ-7) fra amerikansk til dansk. Spørgeskemaerne blev oversat af et panel og derefter afprøvet på danske kvinder med POP. Desuden blev de statistisk analyseret mhp. at vurdere deres gyldighed, reproducerbarhed og følsomhed for ændringer. Vi fandt at PFDI-20 var gyldigt og indeholdte relevante spørgsmål, mens PFIQ-7 havde loft-effekt (bedste score ved baseline), og manglede spørgsmål om livskvalitet. Begge spørgeskemaer var følsomme for ændringer, mens en mindste kliniske relevant forskel kunne ikke fastslås.
Ad 2: 109 kvinder med moderat symptomatisk POP blev ved lodtrækning allokert til én af to
grupper: En livsstilsrådgivningsgruppe (LG) og en gruppe som modtog både
livsstilsrådgivning og bækkenbundstrængning (TLG). Begge grupper modtog et identisk
livsstilsrådgivningsprogram tilbudt som gruppeundervisning 6 gange indenfor 12 uger, men
på separate dage, så grupperne aldrig mødte hinanden. Den ene af grupperne modtog
desuden bækkenbundstrængning i forbindelse med deres livsstilsrådgivningsundervisning efter
een individuel undersøgelse af deres knibefunktion.
89 (82%) kvinder gennemførte 3 måneders opfølgningen og 85 (78%) 6 måneders
opfølgningen. Ved både 3 og 6 måneders opfølgningen angav signifikant flere kvinder i TLG
forbedring på en overordnet forbedrings skala (global score). Ved 3 måneders opfølgningen
opnåede begge gruppe signifikant forbedring af deres totale symptom score, men kun TLG
opnåede signifikant forbedring af den underskala som vedrørte POP symptomer, mens LG
alene opnåede signifikant forbedring af deres livskvalitet. Ingen af grupperne opnåede
signifikant forbedring af deres objektive POP eller af deres seksualitetsscore. Effekten i begge
grupper var knap nok klinisk relevant og der var ingen forskel grupperne imellem.
Ingen baseline data dvs. alder, paritet, henvisningsstatus (henvist/selvhenvist), kropsvægt,
jobstatus, grad symptomer, påvirkning af livskvalitet eller størrelse af genital prolaps kunne
anvendes til at forudsige hvilke kvinder der ville have angive bedring af symptomer på global
scoren ved 3 måneders opfølgningen.
Ved seks måneders opfølgningen var der ingen signifikant forskel på symptomer eller
livskvalitet mellem grupperne, men 68% af LG overfor 28% i TLG havde søgt yderligere
behandling.
Ad 3: 83 kvinder (76%) gennemførte 12-måneders opfølgningen. 30% (13/43) i LG overfor
52% af (21/40) i TLG havde ikke søgt yderligere behandling. Langtidseffekten i begge grupper
var minimal og der var ingen signifikant forskel på symptomer eller livskvalitet i de to
grupper.
I alt 49 ud af de 83 kvinder havde søgt yderligere behandling før 12 måneders opfølgningen:
70% (30/43) i LG, overfor 48% (19/40) i TLG. Otte kvinder, fire i hver gruppe, havde søgt
kirurgisk behandling, mens de resterende 41 havde søgt konservativ behandling. I LG havde
25 kvinder søgt bækkenbundstrængning overfor 5 i TLG. Baseline data og 3 måneders
opfølgnings scorer blev anvendt til at undersøge om der var faktorer, som kunne forudsige
hvilke kvinder der ville have søgt yderligere behandling inden 12 måneders opfølgningen. En større grad af POP i forreste skedevæg var den stærkeste faktor i forhold til at have søgt yderligere behandling, uanset hvilken intervention kvinderne havde modtaget.

**Det konkluderes at:**

- at PFDI-20 er et anvendeligt spørgeskema til kvinder med POP, mens PFIQ-7 mangler relevante spørgsmål om livskvalitet og har lofteffekt.
- at bækkenbundstræning sammen med livsstilsrådgivning på kort sigt giver en lille yderligere bedring af oplevet effekt på en global score, men at det ikke giver færre symptomer eller bedre livskvalitet end et livsstilsrådgivningsprogram alene
- at bækkenbundstræning er forbundet med få gener
- at selvoplevet forbedring efter bækkenbundstræning ikke kan forudsiges ud fra baseline data inklusiv størrelse af objektiv genital prolaps
- at bækkenbundstræning sammen med livsstilsrådgivning ikke har bedre langtidseffekt på prolapssymptomer eller livskvalitet end et struktureret livsstilsrådgivning alene, men dog at færre kvinder som har modtaget PFMT vil have søgt yderligere behandling, ved en 12 måneders opfølgning
- at en større nedsynkning af forreste skedevæg er den stærkeste faktor associeret med at søge yderligere behandling efter deltagelse i et livsstilsrådgivningsprogram med eller uden bækkenbundstræning
**English summary**

This PhD thesis is based on three original studies. The studies were conducted at Herlev University Hospital, Copenhagen, Denmark.

One in ten women experiences symptomatic pelvic organ prolapse (POP). A decade ago, these women would most likely be offered pessary treatment or surgical treatment. It has now been shown that pelvic floor muscle training (PFMT) reduces POP symptoms better than a lifestyle advice leaflet or a single lifestyle advice instruction. No studies have examined if PFMT is more effective than a structured lifestyle advice program offered without PFMT.

The purpose of the thesis was therefore to

1. To translate and validate condition specific patient related outcome measures for women with POP to get subjective outcome measures for a randomized controlled trial.
2. To compare the effects of a structured lifestyle advice program with or without PFMT for women with moderate to advanced symptomatic POP in a three- and in a six-month follow-up
3. To evaluate long-term effects of a structured lifestyle advice program with or without PFMT for women with moderate to advanced symptomatic POP in a 12-month follow-up

**Ad 1:** In the study we translated: the Pelvic Floor Distress Inventory-20 (PFDI-20) and the quality of life score: The Pelvic Floor Impact Questionnaire-7 (PFIQ-7) form English and validated them in Danish women with POP. The two questionnaires were translated by a panel and were pre-tested in women with POP. Statistical analyses were performed to evaluate validity, reliability, sensitivity to change and responsiveness. We found that the PFDI-20 was valid and contained relevant questions related to POP, while the PFIQ-7 had ceiling effect and missed items on quality of life in women with POP. Both the PFDI-20 and the PFIQ-7 were sensitive to change, and the POP subscales were responsive to change.

**Ad 2:** A 109 women with moderate to advanced symptomatic POP were randomized to a Lifestyle advice Group (LG) or to a combined Training and Lifestyle advice Group (TLG). Both
groups received an identical structured lifestyle advice program offered as six group sessions with in 12 weeks, offered at separate days to avoid that the two groups met. One group, in addition to the lifestyle advice program, received an individual assessment of their pelvic floor muscle function and did group PFMT during the lifestyle advice sessions.

Eighty-nine women (82%) completed three-months follow-up and 85 (78%) completed the six months follow-up. At both follow-ups significantly more women in the TLG reported improvement in a global improvement scale compared to the LG. At the three-months follow-up both groups had achieved significant improvement of their total symptom score (PFDI-20), while only the TLG had significant improvement of the subscale revealing POP symptoms.

Only the LG obtained significant improvement of their quality of life (PFIQ-7). None of the two groups had significant improvement of objective POP or of their sexual function. The overall improvement of the PFDI-20 was barely clinically relevant and there were no significant differences between the groups. No baseline data including age, parity, body mass index, being referred/self-referred, job status, former surgery, degree of symptoms and impact on quality of life or size of objective POP, could act as a predictor of self-reported improvement at the three-months follow-up.

At the six-months follow-up no significant differences in symptoms or impact on quality of life were found between the two groups, but in the LG, 68% had sought further treatment compared to 28% in the TLG.

Ad 3: Eighty-three women (76%) completed 12-months follow-up. 30% (13/43) in the LG and 52% (21/40) in the TLG had not sought further treatment. Long-term effect was marginal in both groups and there were no significant differences in symptoms and quality of life between the groups.

All together 49 of the 83 women had sought further treatment, 70% (30/43) in the LG and 48% (19/40) in the TLG. Eight women, four form each group had received surgical treatment, while the remaining 41 women had sought conservative treatment. In the LG, 25 women had sought PFMT, in the TLG five women. Baseline scores and three-months follow-up scores were used to analyze possible predictors associated with having sought further treatment before the 12-months follow-up. In both groups, not being working and more advanced anterior POP at the three-months follow-up were the strongest factors associated with having sought further treatment.
Based on the three studies it is concluded that:

- The PFDI-20 is a valid and useful questionnaire for women with POP, while the PFIQ-7 shows ceiling effect and misses items related to quality of life in women with POP.
- When adding PFMT to a structured lifestyle advice program more women will report improvement in a global improvement scale and of POP symptoms, but PFMT does not result in better symptoms and quality of life scores than a structured lifestyle advice program alone.
- PFMT causes low bother.
- Self reported improvement after PFMT cannot be predicted from baseline data including size of objective POP.
- Long-term effects of adding PFMT to a structured lifestyle advice program is marginal but slightly fewer women who have received PFMT will have sought further treatment at a 12-months follow-up.
- That more advanced anterior POP is the strongest factor associated with having sought further treatment at a 12-months follow-up independent of whether the women have been offered PFMT or not.
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Validation of the Pelvic Floor Distress Inventory-20 and the Pelvic Floor Impact Questionnaire-7 in Danish women with pelvic organ prolapse

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Key words
Pelvic organ prolapse, questionnaire, validation, reliability, responsiveness

Abstract
Objective. To translate the Pelvic Floor Distress Inventory-20 (PFDI-20) and the Pelvic Floor Impact Questionnaire-7 (PFIQ-7) and to evaluate their psychometric properties in Danish women with symptomatic pelvic organ prolapse. Design and setting. Cross-sectional, university hospital setting. Sample. Women with symptomatic pelvic organ prolapse (n = 132). Methods. A panel of gynecologists performed three independent translations, which were combined and psychometrically evaluated through interviews and pretesting. Main outcome measures. Construct, content and convergent validity. Internal consistency and reliability. Sensitivity to change, responsiveness and minimal clinical important difference. Results. After two revisions PFDI-20 demonstrated good construct and content validity but PFIQ-7 showed major ceiling effect and lacked items describing affection of health-related quality of life. Convergent validity was moderate with only single items of PFDI-20 correlating with the pelvic organ prolapse quantification system (POP-Q) and only weak to moderate correlations between PFDI-20 and PFIQ-7 scores. Cronbach's alpha and inter-item-total correlation analysis were satisfactory overall. Intra-class correlation coefficient demonstrated good reliability for all but one subscale (r = 0.701–0.894 p < 0.001). Wilcoxon signed rank test showed significant sensitivity to change. Effect size and standardized response mean was good in pelvic organ prolapse subscales and correlated with the Patient Global Index of Improvement scale (PGI-I). Minimal clinical important difference could not be clearly demonstrated. Conclusion. The Danish version of PFDI-20 is valid while the PFIQ-7 has a major ceiling effect and lacks items about health-related quality of life. The subscales of PFDI-20 and PFIQ-7 demonstrate good internal consistency and reliability. Pelvic organ prolapse subscales show good responsiveness.

Abbreviations: CRADI-8, Colorectal–Anal Distress Inventory-8; CRAIQ-7, Colorectal–Anal Impact Questionnaire-7; HRQoL, health-related quality of life; ICC, intra-class correlation coefficient; PFDI-20, Pelvic Floor Distress Inventory-short form-20; PFIQ-7, Pelvic Floor Impact Questionnaire short form-7; PGI-I, Patient Global Index of Improvement scale; POPDI-6, Pelvic Organ Prolapse Distress Inventory-6; POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire-7; POP, pelvic organ prolapse; POP-Q, pelvic organ prolapse quantification system; UDI-6, Urinary Distress Inventory-6; UIQ-7, Urinary Impact Questionnaire-7.

Introduction
Pelvic organ prolapse (POP) is a prevalent condition among adult women with around 8% (1,2) of adult women having symptomatic POP. According to the recent joint standardization report by the International Urogynecological Association and the International Continence Society, POP is defined objectively as a descent of one or both vaginal walls or by a descent of the apex

Key Message
The Danish PFDI-20 and PFIQ-7 are both reliable. The PFIQ-7 has ceiling effect and lacks items regarding affection of quality of life. Subscales in both questionnaires about pelvic organ prolapse symptoms show good responsiveness after treatment for pelvic organ prolapse.
of the vagina (3). A cardinal symptom of POP is feeling or seeing a bulge in the vaginal opening but POP is a heterogeneous condition that contains a variety of symptoms (4,5). It is recommended that the presence of any objective POP should be correlated with relevant POP symptoms (3,6).

A questionnaire on POP symptoms has been developed and validated (5) in Danish but it never gained national attention. Therefore, we felt the need to introduce condition-specific questionnaires to reveal the disease-specific symptoms and impact of health-related quality of life (HRQoL), which Danish women with POP might have. We chose the Pelvic Floor Distress Inventory-20 (PFDI-20) and the Pelvic Floor Impact Questionnaire-7 (PFIQ-7) (7), which have both been thoroughly validated in their original language and later translated into several languages in both their original versions (8) and also in their short forms (9–18). The PFDI-20 has 20 items divided into three subscales revealing symptoms and bother related to POP symptoms, colorectal symptoms, and urinary/bladder symptoms, respectively [Pelvic Organ Prolapse Distress Inventory-6 (POPIQ-6), Colorectal–Anal Distress Inventory-8 (CRADI-8) and Urinary Distress Inventory-6 (UDI-6)]. The PFIQ-7 has 21 items divided into three corresponding subscales [Urinary Impact Questionnaire-7 (UIQ-7), Colorectal–Anal Impact Questionnaire-7 (CRAIQ-7), Pelvic Organ Prolapse Impact Questionnaire-7 (POPIQ-7)] measuring HRQoL related to the symptoms and bother revealed in the PFDI-20. A summary score from each subscale or a total score for each questionnaire can be calculated with a higher score indicating greater bother or affection of HRQoL. The questionnaires can be used separately but are often used in conjunction.

The questionnaires have recently been translated and validated in Swedish women with POP (12) but it has not yet been examined in Scandinavian women with POP whether objective diagnosis of POP correlates with symptoms, bother and affection of HRQoL, as indicated by the PFDI-20 and the PFIQ-7, nor if the PFDI-20 and the PFIQ-7 are responsive to change after treatment. The aim of this study was therefore to translate and to validate the PFDI-20 and the PFIQ-7 among Danish women with symptomatic POP.

**Material and methods**

Consecutive women with symptomatic POP referred to a tertiary urogynecology clinic at the Herlev University Hospital, Denmark, were recruited. Exclusion criteria were age <18 years, dementia, and an inability to understand or speak Danish. The women were recruited from waiting lists, waiting rooms, or from the ward before surgery. Only practical assistance was offered to help the women complete the questionnaires. Written consent was obtained from patients to access patient files for data on POP measurements. All letters were sent with a pre-stamped envelope enclosed. The study was approved by the Danish Data Protection Agency. The study followed the ethical standards of the Helsinki Declaration. Permission to translate the PFDI-20 and the PFIQ-7 was obtained from Dr Barber.

The translation process followed the guidelines for cross-cultural adaptation of HRQoL questionnaires as proposed by Guillemin et al. (19). A competent panel of gynecologists performed three independent translations. The translations were synthesized into the first Danish versions through consensus meetings (19). The first versions were discussed with other health professionals and a bilingual native English speaker before pretesting. A professional medical translator performed backward translations of the final versions and they were sent to Dr Barber for approval.

Construct and content validity was evaluated through discussions with health-care professionals, through patient interviews, and by examining item responses (20). The first author conducted all patient interviews and each woman signed a summary of her interview. Initially, eight women completed the questionnaires at home and brought them to their hospital visit. During the interview the women completed a new questionnaire, and were asked questions like: “How do you understand this question?” The two questionnaires were then compared (19). Subsequently nine women were interviewed after completing the questionnaires in the waiting room. Areas evaluated in all interviews were: acceptance of the questionnaires, understanding, targeting of items, and comprehension of instructions (20). Two pre-tests were performed in women with POP. In the first pre-test, 17 women recruited from the waiting room filled in the questionnaires. In the second pre-test, 27 questionnaires were sent out. Reliability of the questionnaires was assessed through a test–retest while internal consistency was examined through correlation analyses. For test–retest reliability the questionnaires were sent to 50 women with POP with an interval of 2 weeks. Internal consistency of subscales and inter item–total correlation was evaluated on all pre-tests and test–retests (n = 66).

Convergent validity was examined by comparing objective POP stage, described with the POP quantification system (POP-Q) (3) with the scores of the PFDI-20 and the PFIQ-7 and by comparing the scores of the PFDI-20 with the scores of the PFIQ-7 (20). Sensitivity to change and responsiveness, which is the ability to measure a meaningful change, were evaluated by comparing preoperative and postoperative scores (20). The minimal
clinical important difference (21), was examined by a distribution-based and an anchor-based method (21). The Patient Global Impression of Improvement scale (PGI-I) (7,22,23) served as anchor. Forty-nine women scheduled for surgery the same or the following day filled in the questionnaires. Three months after their surgery they received new questionnaires together with the PGI-I scale.

**Statistical analysis**

Descriptive statistics were used to describe response rate, item response rate and floor and ceiling effect of the questionnaires. Data were tested for normality of distribution. Baseline data were examined with the Mann-Whitney U-test. Test–retest reliability was examined with intra-class correlation coefficient (ICC). An ICC of 0.75 was considered acceptable. Internal item consistency in subscales was analyzed with the Cronbach’s alpha test with an acceptable value of 0.70. Inter-item–total correlation analysis was performed on all subscales and an acceptable value should be more than 0.2 (20,24). Correlations between POP-Q stages and the PFDI-20 and the PFIQ-7 were analyzed with Spearman’s rank order correlation test. Sensitivity to change was evaluated with the Wilcoxon signed-rank test for related samples. For estimation of distribution-based responsiveness effect size and standardized response mean (7,21) were used. An effect size or standardized response mean of 1.0 or more was considered excellent, an effect size or standardized response mean of 0.80 or higher was considered good, an effect size or standardized response mean of 0.50–0.7 was considered moderate (7). Anchor-based responsiveness was examined with Spearman’s rank order correlation (7). Receiver operating characteristic curves were used to visualize sensitivity and specificity of the PFDI-20 and the PFIQ-7. A non-discriminant test would have an area under the curve of 0.5 or less. Level of significance was set at a p-value of 0.05 for all statistical tests. All p-values are reported two-sided. All analyses were performed with SPSS version 19.0 (SPSS Inc., Chicago, IL, USA).

**Results**

In all, 132 women with POP participated in the study. Data were collected from March 2011 through December 2011. Summaries from the 17 interviewed women were kept separately; mean age 68.5 years (median 70.5, range 36–84), whereas questionnaire responses from 115 women were entered into a database; mean age 63.5 years (median 65, range 30–92). Seventy-six of 97 women (78%) gave permission to have data from their patient file examined regarding their size of POP. A POP-Q of less than II was found among 3.9%, 34, 2% had a POP-Q of II, 51, 3% had a POP-Q of III, and 10.5% had a POP-Q of IV (3).

Patient interviews demonstrated good acceptance of the questionnaires but also revealed misunderstandings or lack of understanding of some of the items of PFDI-20 and two revisions of the first Danish versions were performed. The pre-tests showed no obvious misunderstandings. Second pre-test had a response rate of 78% but two questionnaires were excluded. Adjusted response rate was 70%. Item response rate was 90% or more, which was considered satisfactory.

Response rate for the test–retest was 60% with 30 out of 50 women completing both tests. Test–retest showed good ICC for the total PFDI-20 [0.878, 95% confidence interval (CI) 0.760–0.940] and for the subscales of the PFDI-20. Total PFIQ-7 also had a good ICC (0.806, 95% CI 0.631–0.902) except for the CRAIQ-7 subscale, which had an ICC <0.75 (Table 1). Cronbach’s alpha was high in all pre-tests except for POPDI-6 (r = 0.606) (see Table 2). Corrected item total correlation was satisfactory for subscales but for total scales three items of the POPDI-6 and one item of the CRAIQ reduced correlation (Table 2).

Both health-care professionals and interviewed women indicated that the PFDI-20 had good construct validity and that content validity was satisfying overall. Two women responded that they missed an item regarding fecal soiling in the CRADI-8 subscale whereas only one woman described having symptoms that could be related to rectal prolapse. The PFDI-20 revealed that having a “bulge” in the vagina was the key symptom for all interviewed women and to 93.8% of the women participating in the study (item three, PFDI-20) and this item had most women scoring maximum bother (54.9%). Items regarding difficulty with bladder emptying, flatus incontinence, frequency for urine, and both urgency urinary incontinence and stress urinary incontinence showed the same but lower trend with 19.1–33% reporting great bother.

The patient interviews revealed low PFIQ-7 scores, indicating low affection of HRQoL. The women were asked to define when or if their POP affected their HRQoL if not as described in the PFIQ-7. One woman felt discomfort when she had to “push back the bulge” during toilet visits and one woman felt her body image affected because “she felt open.” Three women had their sexual life affected. Two women had adjusted their activities because of POP symptoms and so did not report any impact. Bicycling is a very common form of transportation in Denmark and two women missed an item describing this in the PFIQ-7.

Major ceiling effect was found in the PFIQ-7 (n = 115) and this ceiling effect was similar even among the women.
UDIQ-7, CRADIQ-7, and POPIQ-7 subscales, respectively. and 27.8% indicating no impact of their HRQoL in the scheduled for surgery (n = 49) with a total of 25.9, 52.3, and 27.8% indicating no impact of their HRQoL in the UDIQ-7, CRADIQ-7, and POPIQ-7 subscales, respectively.

No significant differences in PFDI-20 and PFIQ-7 scores could be found between women offered surgery vs. women offered conservative treatment or between younger or older women (>65 years) and no significant correlations were found between POP-Q stages and PFDI-20 or PFIQ-7 scores. Weak but significant correlations were found between descending of the anterior compartment and two items of the PFDI-20: item five (seeing or feeling a bulge) and item six (related to obstructed voiding). Item 19 was correlated with POP in the medial compartment (r = 0.247, p = 0.038) (items related to obstructed voiding). Item 19 was correlated with POP in the medial compartment (r = 0.247, p = 0.038) (items related to obstructed voiding). Overall POP-Q was weakly but significantly correlated with item three* (seeing or feeling a bulge) and item six** (need to push in the vaginal wall in relation to micturition) and item 15*** (urinary frequency) of the PFDI-20 (r = 0.271*, p = 0.018; r = 0.246**, p = 0.034; r = 0.232***, p = 0.048). Correlations between the PFDI-20 subscales and the PFIQ-7 subscales (n = 115) were significant but

### Table 1. Test–retest stability analyzed with intra-class correlation coefficient.

<table>
<thead>
<tr>
<th>Test</th>
<th>Retest</th>
<th>Intra-class correlation coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>p-value</td>
</tr>
<tr>
<td>n = 30</td>
<td>n = 29</td>
<td></td>
</tr>
<tr>
<td>PFIQ-7</td>
<td>69.3 (54.2)</td>
<td>72.2 (72.6)</td>
</tr>
<tr>
<td>UIQ-7</td>
<td>71.4</td>
<td>47.6</td>
</tr>
<tr>
<td>CRAIQ-7</td>
<td>0.0–157.1</td>
<td>0.0–281.0</td>
</tr>
<tr>
<td>POPIQ-7</td>
<td>11.3 (15.9)</td>
<td>12.9 (21.7)</td>
</tr>
<tr>
<td>POPIQ-7</td>
<td>4.8</td>
<td>0.0</td>
</tr>
<tr>
<td>PFDI-20</td>
<td>25.9 (27.8)</td>
<td>25.9 (30.3)</td>
</tr>
<tr>
<td>POPDI-6 (n = 29)</td>
<td>47.9</td>
<td>39.5</td>
</tr>
<tr>
<td>CRADI-8</td>
<td>0.0–85.7</td>
<td>0.0–100</td>
</tr>
<tr>
<td>UDI-6</td>
<td>122.5 (54.8)</td>
<td>114.4 (64.5)</td>
</tr>
<tr>
<td>UDI-6</td>
<td>123.4</td>
<td>95.3</td>
</tr>
<tr>
<td>UDI-6</td>
<td>16.7–247.9</td>
<td>12.5–231.3</td>
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<tr>
<td>UDI-6</td>
<td>46.4 (24.6)</td>
<td>43.0 (27.8)</td>
</tr>
<tr>
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<td>0.0–91.7</td>
<td>0.0–91.7</td>
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<tr>
<td>UDI-6</td>
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<td>26.3 (20.1)</td>
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<td>28.1</td>
<td>23.4</td>
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<td>0.0–75.0</td>
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<tr>
<td>UDI-6</td>
<td>46.4 (24.9)</td>
<td>47.4 (27.5)</td>
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<td>41.7</td>
<td>50.0</td>
</tr>
<tr>
<td>UDI-6</td>
<td>0.0–95.8</td>
<td>0.0–100.0</td>
</tr>
</tbody>
</table>

CI, confidence interval; CRADI-8, Colorectal–Anal Distress Inventory-8; CRAIQ-7, Colorectal–Anal Impact Questionnaire-7; PFDI-20, Pelvic Floor Distress Inventory-short form-20; PFIQ-7, Pelvic Floor Impact Questionnaire short form-7; POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire-7; SD, standard deviation; UDI-6, Urinary Distress Inventory-6; UIQ-7, Urinary Impact Questionnaire-7.

### Table 2. Cronbach’s alpha and Corrected inter-item–total correlation.

<table>
<thead>
<tr>
<th>(n = 66)</th>
<th>Cronbach’s alpha</th>
<th>Corrected item–total correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFIQ-7</td>
<td>0.874</td>
<td>r = 0.112–0.715</td>
</tr>
<tr>
<td>UIQ-7</td>
<td>0.833</td>
<td>r = 0.411–0.678</td>
</tr>
<tr>
<td>CRAIQ-7</td>
<td>0.864</td>
<td>r = 0.550–0.729</td>
</tr>
<tr>
<td>POPIQ-7</td>
<td>0.913</td>
<td>r = 0.634–0.805</td>
</tr>
<tr>
<td>PFDI-20</td>
<td>0.804</td>
<td>r = 0.102–0.582</td>
</tr>
<tr>
<td>POPDI-6</td>
<td>0.606</td>
<td>r = 0.283–0.403</td>
</tr>
<tr>
<td>CRADI-8</td>
<td>0.782</td>
<td>r = 0.357–0.665</td>
</tr>
<tr>
<td>UDI-6</td>
<td>0.721</td>
<td>r = 0.298–0.609</td>
</tr>
</tbody>
</table>
moderate. Only the POPDI-6 score correlated with all three PFIQ-7 subscales (Table 3).

Forty-nine women agreed to participate and 43 women filled in the questionnaires after surgery (88% response rate). All subscales demonstrated significant sensitivity to change (Table 4). Only the POPDI-6 and the POPIQ-7 subscales resulted in excellent and good responsiveness and significant correlations with the PGI-I (Table 4). No women responded that their condition had become worse and the two groups with the lowest PGI-I scores did not differ significantly. Therefore the minimal clinical important difference could not be based on these figures. A significant difference was found between women reporting that they were “a little better” vs. women reporting that they were “much better” and an alternative cut-off value between these two groups was chosen (Table 4). With this value we found a minimal clinical important difference for the total score of the PFDI-20 of 53.1 points (17.7% improvement), and a minimal clinical important difference for the PFIQ-7 of 46.6 points (15.5% improvement) (Table 5). We also found a large area under the curve for total scores of PFDI-20 and for total PFIQ-7 and all subscales except for the CRADI-8 but only the POP subscales had significant values (Table 4).

Discussion

We chose an extensive procedure for the translation of the questionnaires the PFDI-20 and the PFIQ-7 and we found that that the process was beneficial; especially the interviews revealed problems with the Danish translations that might not have been detected otherwise and it gave a broader picture of the affection of HRQoL than was captured with the PFIQ-7. There is no reference standard for translating and validating HRQoL questionnaires, but it is suggested that a multistep procedure is used to ensure quality and that each step is well documented (25), which we believe our study is a good example of.

In general we found good construct and content validity of the PFDI-20 whereas the PFIQ-7 showed lack of items regarding affection of HRQoL and a major ceiling effect also among women scheduled for surgery. Most of the published studies on translation and validation of the PFDI-20 and the PFIQ-7 do not report evaluating the ceiling or floor effect (7,9,11,13–15). A recent Swedish study by Teleman et al. (12) reported no ceiling or floor effect of either the PFDI-20 or the PFIQ-7 while a newly published Chinese study reported a ceiling effect of the PFIQ-7 (16). The difference between Danish and Swedish results was unexpected because culture and the translations of the PFDI-20 and the PFIQ-7 are similar. We also looked at women waiting for surgery alone as in the Swedish study but that did not change our results. We

| Table 3. | Spearman’s rank correlations between PFDI-20 and PFIQ-7. |
| n = 115 | | |
| POPDI-6 | UIQ-7 | CRAIQ-7 | POPIQ-7 | PFIQ-7 |
| 0.359 | 0.273 | 0.408 | 0.441 |
| 0.358 | 0.641 | – | 0.427 |
| 0.697 | – | 0.316 | 0.507 |
| 0.631 | 0.364 | 0.210 | 0.508 |

Only significant correlations between subscales or between total scores of the PFDI-20 and the PFIQ-7 are shown. CRADI-8, Colorectal–Anus Distress Inventory-8; CRAIQ-7, Colorectal–Anus Impact Questionnaire-7; PFDI-20, Pelvic Floor Distress Inventory-short form-20; PFIQ-7, Pelvic Floor Impact Questionnaire short form-7; POPDI-6, Pelvic Organ Prolapse Distress Inventory-6; POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire-7; SD, standard deviation; UDI-6, Urinary Distress Inventory-6; UIQ-7, Urinary Impact Questionnaire-7.

| Table 4. | Results from analyses of sensitivity to change and responsiveness. |
| n = 43 | | |
| POPDI-6 | Mean preoperative scores (SD) | Mean postoperative scores (SD) | Mean change (SD) | Wilcoxon signed rank test (p-value) | Standardized response mean | Effect size | Spearman’s rho (p-value) | ROC curve (p-value) |
| 44.7 (24.1) | 9.9 (13.5) | 34.8 (22.9) | <0.001 | 1.5 | 1.4 | –0.326 (0.033) | 0.942 (0.012)* |
| 20.1 (20.6) | 12.5 (16.1) | 8.8 (16.2) | 0.002 | 0.5 | 0.4 | – | 0.467 (0.849)* |
| 37.8 (28.3) | 18.7 (23.2) | 19.1 (26.0) | <0.001 | 0.7 | 0.7 | – | 0.813 (0.074)* |
| 21.4 (26.5) | 7.1 (14.1) | 13.6 (25.2) | 0.002 | 0.5 | 0.5 | – | 0.797 (0.086)* |
| 11.0 (15.7) | 4.6 (10.7) | 6.3 (13.8) | 0.014 | 0.5 | 0.4 | – | 0.789 (0.099)* |
| 26.3 (26.9) | 3.8 (8.9) | 22.3 (27.3) | <0.001 | 0.8 | 0.8 | –0.507 (0.001) | 0.856 (0.043)* |
| 104.6 (60.7) | 40.4 (46.1) | 61.8 (49.7) | <0.001 | 1.2 | 1.0 | –0.344 (0.024) | 0.825 (0.063)* |
| 56.7 (59.1) | 15.0 (30.7) | 41.9 (53.4) | <0.001 | 0.8 | 0.7 | –0.477 (0.001) | 0.900 (0.022)* |

CRADI-8, Colorectal–Anus Distress Inventory-8; CRAIQ-7, Colorectal–Anus Impact Questionnaire-7; PFDI-20, Pelvic Floor Distress Inventory-short form-20; PFIQ-7, Pelvic floor impact questionnaire short form-7; PGI-I, Patient Global Index of Improvement scale; POPDI-6, Pelvic Organ Prolapse Distress Inventory-6; POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire-7; ROC, receiver operating characteristic; SD, standard deviation; UDI-6, Urinary Distress Inventory-6; UIQ-7, Urinary Impact Questionnaire-7.

*ROC curves were calculated between a score of “a little better” and “much better.” See Table 5 for the differences in scores.
therefore have no explanation for this but our results indicate that the PFIQ-7 does not reveal all relevant aspects or the true impact of HRQoL among Danish women with POP. We suggest, as in the study by Chan et al. (16), that the PFIQ-7 is always used in conjunction with the PFDI-20 or together with another HRQoL instrument (26).

Unlike other studies that have also correlated POP-Q stages with PFDI-20 and PFIQ-7 scores (8,10,13,15) we could not find significant correlations between POP stages and questionnaire scores but only weak correlations between single items and POP stages. Our results might have appeared different if we had been able to separate women with a grade II POP in women having a POP above, at the hymen or below the hymen. The majority of our participants had a grade III prolapse or more (61.8%) indicating that their prolapse was at least 2 cm below the hymen and yet we only found significant correlations with single items and POP-Q scores. Our result is in concordance with other studies that have also, although using different questionnaires, found that POP-Q stages do not necessarily correlate with degree of symptoms except in specific areas, such as bulging (1,5).

We find our result intriguing and think that it strengthens the recommendation that objective POP should always be correlated with subjective symptoms before any treatment is offered (3,6).

Cronbach’s alpha and corrected total item correlation demonstrated reasonable homogeneity for all subscales whereas some items decreased homogeneity for total scales. Deleting items could increase internal consistency of the total scales but with the heterogeneous nature of POP we believe that this would instead decrease the content validity of the subscales (20).

Like other published studies on the PFDI-20 and the PFIQ-7 we found an overall good stability of the questionnaires but response rate for the test–retest was only 60%. This could weaken our conclusion. We consider this low response rate a coincidence because we otherwise obtained good response rates.

All subscales of the PFDI-20 and the PFIQ-7 were sensitive to change but only the POP-subscales demonstrated excellent responsiveness. We believe that our results indicate that the PFDI-20 and the PFIQ-7 are in a sense generic questionnaires for pelvic floor disorders and it should be accepted that women with POP would have the largest changes in the POP subscales (27). Based on our findings it is informative to evaluate subscale scores and single-item scores in the PFDI-20 and in the PFIQ-7 although calculating total scores seems less relevant. We could not demonstrate the minimal clinical important difference but with an alternative cut-off value our results became similar to previous findings (7). A larger sample size might have improved our results.

<table>
<thead>
<tr>
<th>Table 5. Changes in scores of subscales and total scores in relation to determination of MCID.</th>
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<tbody>
<tr>
<td>Change in score</td>
</tr>
<tr>
<td>POPD-6</td>
</tr>
<tr>
<td>n = 43 PGI-I</td>
</tr>
<tr>
<td>Very much better</td>
</tr>
<tr>
<td>Much better</td>
</tr>
<tr>
<td>A little better</td>
</tr>
<tr>
<td>No change</td>
</tr>
</tbody>
</table>

CRADI-8, Colorectal–Anal Distress Inventory-8; CRAIQ-7, Colorectal–Anal Impact Questionnaire-7; PFDI-20, MCID, minimal clinically important difference; Pelvic Floor Distress Inventory-short form-20; PFIQ-7, Pelvic Floor Impact Questionnaire short form-7; PGI-I, Patient Global Index of Improvement scale; POPD-6, Pelvic Organ Prolapse Distress Inventory-6; POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire-7; SD, standard deviation; UDI-6, Urinary Distress Inventory-6; UIQ-7, Urinary Impact Questionnaire-7.

We conclude that the PFDI-20 is a reliable and valid instrument to use in Danish women with POP. Both the PFDI-20 and the PFIQ-7 are well accepted in their validated Danish versions and the POP subscales show good responsiveness (see Danish versions in Figures S1 and S2). The PFIQ-7 shows a major ceiling effect in all subscales and it is uncertain whether PFIQ-7 captures all relevant aspects related to HRQoL among Danish women with POP.

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References


Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. PFDI-20 Danish version 2012.
Table S2. PFIQ-7 Danish version 2012.
Lifestyle Advice with or without Pelvic Floor Muscle Training for Pelvic Organ Prolapse, a randomized controlled trial

Authors

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**Each authors contribution to the manuscript**

U Due: Protocol/project development, Data Collection, Data analyses, Manuscript writing manuscript editing

G Lose: Protocol/project development, data analyses, manuscript editing

S Brostrøm: Protocol/project development, data analyses, manuscript editing

Abstract 249 words, Main text 3478 words
Objective:

To evaluate the effect of adding pelvic floor muscle training to a structured lifestyle advice program.

Methods

Single-blinded randomized trial of women with symptomatic pelvic organ prolapse (POP) stage ≥ II. Participants were randomized to a structured lifestyle advice program with or without pelvic floor muscle training. Both groups received similar lifestyle advices in six separate group sessions. The ‘combined group’ performed group pelvic floor muscle training after an individual assessment. Primary outcome was a global improvement scale at six-month follow-up. Secondary outcomes were the global scale and objective POP at three-month follow-up, symptoms and quality of life including sexuality, at three and six-month follow-up. A clinically relevant change of symptoms was defined as ≥15%.

Results

We included 109 women. Eighty-nine women (82%) completed three months follow-up, 85 (78 %) completed six-month follow-up. At both follow-ups significantly more women in the combined group reported improvement in the global scale. At three-month follow-up only the combined group had significant improvement of POP symptoms while only the lifestyle advice group had significant improvement of quality of life. Change of objective POP and sexuality was non-significant. The symptom score improved 17% in the combined group and 14% in the lifestyle advice group (P= 0.57). Significantly more women in the lifestyle advice group had sought further treatment at six-month follow-up.

Conclusion
Adding pelvic floor muscle training to a structured lifestyle advice program gave superior effect in a global scale and of POP symptoms. Overall effect of either intervention barely reached clinical relevance.

**Key words**: Conservative treatment, lifestyle advice, pelvic floor muscle training, pelvic organ prolapse

**Brief summary**

Adding pelvic floor muscle training to a structured lifestyle advice program for pelvic organ prolapse affects global improvement but not symptoms and quality of life.
Abbreviations

POP: Pelvic Organ Prolapse

HRQoL: Health Related Quality of Life

POP-Q: Pelvic Organ Prolapse Quantification system

PFDI-20: Pelvic Floor Distress Inventory - short form 20

POPD-6: Pelvic Organ Prolapse Distress Inventory 6

CRADI-8: Colorectal-Anal Distress Inventory 8

UDI-6: Urinary Distress Inventory 6

PFIQ-7: Pelvic Floor Impact Questionnaire - short form 7

UIQ-7: Urinary Impact Questionnaire 7

CRAIQ-7: Colorectal-Anal Impact Questionnaire 7

POPIQ-7: Pelvic Organ Prolapse Impact Questionnaire 7

PISQ-12: The Pelvic organ prolapse/urinary Incontinence Sexual Questionnaire 12

PGI-I: Patient Global Index of Improvement scale

NRS: Numeric Rating Scale

PFMT: Pelvic Floor Muscle Training

LG: Lifestyle advice Group

TLG: Combined pelvic floor muscle Training and Lifestyle advice Group
95 ITT: Intention To Treat analysis

96 RR: Relative Risk
Introduction

Symptomatic pelvic organ prolapse (POP) is prevalent and has been found in 2.9-11.4% of adult women [1, 2]. POP commonly becomes symptomatic when the prolapse reaches at or beyond the hymen (hymenal remnant) in the vaginal opening [3, 4], which corresponds to stage II or greater [5, 6]. Women with POP stage II or greater often feel or see a bulge in the vaginal opening and they typically have concurrent bladder, bowel and/or sexual symptoms [7, 8]. Although lifetime risk of surgical intervention for POP has been found to be 12.6% [9] spontaneous regression of POP is possible [10] and especially elderly women will prefer conservative treatment [11, 12].

Studies have shown that individual pelvic floor muscle training (PFMT) can reduce POP symptoms compared to offering lifestyle advice as a leaflet with or without a single instruction [13-17]. A recent well-powered study [13] found a significant improvement of POP symptoms but could not confirm previous findings demonstrating significant improvement of objective POP after PFMT [14-17]. The study offering the most intensive individual PFMT program found increased pelvic floor muscle strength and a higher cranial position of the pelvic organs after PFMT but could not find significant correlations between these findings and improvement of subjective nor objective POP [16].

Based on the existing evidence, PFMT seems to have a positive effect on POP symptoms while the effect on objective POP seems limited. Thus, the subjective improvement could hypothetically be caused by the attention from health care professionals and the lifestyle advice offered with PFMT and the true impact of PFMT might be questionable.
The primary objective of this study was to examine whether PFMT offered in combination with a structured lifestyle advice program would have better effect on a global improvement scale than a structured lifestyle advice program alone in women with symptomatic POP stage ≥ II.

**Materials and Methods**

This study was a single-blinded randomized controlled trial. The study included women aged ≥18 years with a Pelvic Organ Prolapse Quantification system (POP-Q) of ≥ II and at least one of three symptoms; seeing or feeling a bulge in the vaginal opening, voiding dysfunctions or defecation problems, or feeling vaginal heaviness. Fluency of Danish language was required.

Exclusion criteria were: Dementia, symptomatic neurological disease, including serious back problems, PFMT within the last two years, childbirth within the last year, more than one surgical treatment for POP or urinary incontinence. Women with POP stage I, were excluded since they are less likely to have symptoms correlated with POP [3] and they are less likely to be offered pessary treatment or surgical treatment.

Women recruited were examined and scored with the POP-Q by the primary investigator. Women who fulfilled the inclusion criteria had a standard gynecological examination performed by a gynecologist to exclude differential diagnoses. Postmenopausal women with signs of vaginal atrophy were routinely offered vaginal estrogen.

After inclusion, baseline questionnaires were administered. The women completed questionnaires without help but were offered assistance from the research nurse.
A research nurse administered randomization envelopes. A statistician not involved in the study provided computer generated random numbers with stratification for age groups ≥ 60 years. Participants drew one closed envelope each. The primary investigator remained blinded throughout the study.

All participants received six group sessions within twelve weeks. Only participants from the combined PFMT and lifestyle advice group (TLG) received an appointment with a specialized pelvic floor physical therapist for a visual and a digital assessment of their pelvic floor muscle function and an individual instruction in PFMT before starting the group sessions to assure that they could perform the PFMT program correctly. Women unable to contract their pelvic floor muscles correctly were offered more individual sessions before starting the group training.

The lifestyle advice group (LG) was not given any information about PFMT during their sessions. The TLG and the LG group sessions were held on separate days and the two groups never met.

At the three-month follow-up the primary investigator repeated the POP-Q examination, remaining blinded to all data. All women completed questionnaires again including the PGI-I.

At six-month follow-up, three months after last group session, the questionnaires including the PGI-I was sent to the women and they were asked if they had sought further treatment.

The study took place at Herlev University Hospital, Copenhagen, Denmark. Participants were recruited by the primary investigator from hospital waiting list and from the
outpatient clinic, through websites, local newspapers, and through posters at public places (fig 1).

Comprehensive written study information was provided and all women signed an informed consent before entering the study.

The study was approved by the Danish Scientific Ethical Committee (H-4-2011-072) and by the Danish Data Protection Agency. The study was reported to Clinical.Trials.gov (NCT01612637). Data are reported in accordance with the CONSORT statement.

Outcome measures:

Primary outcome was the Patient Global Index of Improvement scale (PGI-I) [18, 19] at six-month follow-up, three months after last group session. Secondary outcomes were the Pelvic Organ Prolapse Quantification system (POP-Q) [6] performed at baseline and at three-month follow up; The PGI-I at three-month follow up; the Pelvic Floor Distress Inventory-short form 20 (PFDI-20); the Pelvic Floor Impact Questionnaire-short form 7 (PFIQ-7) [20] and the Pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12) completed at baseline and at three- and six-month follow-up [21]. Women receiving PFMT reported bother from PFMT in their training diaries using a Numeric Rank Scale (NRS) ranging from 0 to 10. A higher number indicated more bother.

The PFDI-20 contains twenty items divided into three subscales revealing bladder (UDI-6), bowel (CRADI-8), and prolapse (POPDI-6) symptoms as well as bother. Each item can be scored on a scale from 0 to 4. A higher score indicates greater bother. The PFIQ-7 reveals health-related quality of life (HRQoL) related to pelvic floor disorders. The scale has twenty-one items divided into three subscales revealing affection of HRQoL related to bladder...
(UIQ-7), bowel (CRAIQ-7) and POP (POPIQ-7) symptoms. Each item is scored from 0 to 3 with a higher score indicating a greater affection of HRQoL. Total and subscale scores can be calculated from PFDI-20 and PFIQ-7. Subscale scores reach from 0-100 and total scores from 0-300 where higher scores indicate increased symptoms, bother and HRQoL affection.

The PISQ-12 has twelve items on sexual problems in relation to pelvic floor disorders. Each item is scored from 0 to 4 with a lower score indicating more impact. Only single item scores were analyzed in this study.

Interventions

Lifestyle advice sessions

Both groups received an identical lifestyle advice program. The primary investigator developed six power point teaching modules lasting 45-60 minutes each. Specialized pelvic floor physical therapists were instructed in teaching the group sessions and carried out the group sessions independent of the primary investigator. The subjects for the six group sessions were based on known promoting factors for POP, such as straining, constipation, overweight and heavy lifting[22]. The following subjects were presented: Introduction to POP and how to reduce pressure on the pelvic floor; bladder function and POP; bowel function and POP, and how to improve micturition and defecation technique; diet, weight loss and POP; quality of life and POP, and the impact of POP on body image and sexuality; sports and POP, and how to increase level of activity without increasing pressure on the pelvic floor. The women were offered handouts during the sessions, bladder and bowel dairies and encouraged to try out any lifestyle advice that they found relevant for their specific POP related symptoms.
Combined therapy and lifestyle advice sessions

Along with the lifestyle advice sessions the TLG performed group PFMT with focus on conscious pre-contractions before an increased intra-abdominal pressure (“knack training”) [23, 24]. The home training was based on generally accepted training principles and it was to be performed five days a week [25]. Each participant had an individually adjusted home training program comprising of three sets of up till ten sustained (10 seconds) pelvic floor muscle contractions. The women were instructed in contracting with as much effort as possible while maintaining normal respiration. The physical therapists teaching the TLG had access to the results of the initial pelvic floor muscle function assessment of the women in the TLG. The home training program was verbally adjusted during the group PFMT, when a woman expressed ease with her program. Progression of the home training program included increasing effort and number of contractions, length of each contraction and increasing load on the pelvic floor varying body positions. The women were additionally taught to do knack training during their everyday activities. The TLG filled in a training dairy and reported bother related to the home training in the NRS.

Statistics

Descriptive statistics were used to describe baseline data. Both parametric and non-parametric statistics were used to analyze questionnaire scores and POP-Q scores. Since analyses showed similar results we only reported results from the parametric analyses to be comparable with other studies. Non-parametric statistics was used for single item analyses. Categorical data were analyzed with Chi-square test and a relative risk (RR) was calculated for improvement of the PGI-I. Three- and six-month follow-up analyses were done by intention-to-treat (ITT) with last-observation-carried-forward (LOCF). Univariable
and multivariable forward logistic regression analyses (P value of ≤0.20, ≥80% data completeness) were performed to find possible baseline predictors of improvement (dichotomized) at three-month follow-up. Level of significance was set at a P-value of .05 for all statistical tests. All P values were reported two-sided. All analyses were performed with SPSS version 22.0 (SPSS Inc., Chicago, IL. USA).

**Sample size**

Sample size was based on the PGI-I and the PFDI-20 aiming to find a minimal clinical relevant difference defined as a change greater than or equal to 15% [20]. With a power of 80% at a 5% significance level we needed to include 45 women in each arm. To compensate for possible dropouts we recruited 54 women in each arm.

**Results**

**Baseline**

Between October 2012 and December 2013, 109 women were included and randomized. Sixty-two women (57%) had stage II and 47 women (43%) had stage III POP. Of the 109 women, 96 (88%) had had prolapse of the anterior compartment, 70 (64%) had prolapse of the posterior compartment, while 64 (59%) had prolapse of more than one compartment. None had isolated prolapse of the middle compartment. Anterior and posterior POP at or beyond the hymen was found in 78 (72%) and in 58 (53%) women respectively (table 1). Thirty-nine women (36%) were recruited from hospital referral lists or from the outpatient clinic. Seventy women (64%) were self-referred (fig. 1). Women recruited from referral lists
or from the outpatient clinic had a higher POP-Q score (P= 0.037), but were otherwise comparable to self-referred women.

Fifty-three women (49%) were randomized to the LG and 56 to the TLG (51%). At baseline the two groups were comparable in all scores and they reported moderate symptoms and bother in the PFDI-20 with no significant group differences (table 2).

In the TLG two women required three individual sessions to learn to perform PFMT correctly. They both learned to contract their pelvic floor muscles correctly.

Single items analysis of the baseline questionnaire revealed that 87 (80%) reported seeing or feeling a bulge, 77 (71%) had pelvic heaviness, 66 (61%) experienced urinary frequency and 63 (58%) had fecal urgency. Fifty-eight women (53%) reported incomplete bladder emptying and/or incomplete bowel movement, 57 (53%) reported urinary urgency, while 54 (51%) had flatus incontinence.

The PFIQ-7 scores indicated low impact of HRQoL (table 2) and 33%, 57%, 44% scored no affection of their HRQoL in the UIQ-7, the CRAIQ-7, and in the POPIQ-7 at baseline, respectively. In the total baseline PFIQ-7 score 18% indicated no HRQoL affection.

PISQ-12 item response rate ranged from 92 (84 %) to 72 (66 %). Non-responders indicated lack of partner or no active sexual life. The women reported moderate to low impact on sexual function (Data not shown).
Three-month follow-up

Eighty-nine women completed the study (82%), (Fig 1). Fourteen women (25%) in the TLG and six women (11%) in the LG left the study before the three-month follow-up. These women were younger (P = 0.004), had more affection of bowel related HRQoL (P = 0.053) and reported more bother related to urinary incontinence during sexual intercourse (P = 0.027).

Both the LG and the TLG attended median five group sessions (0-6).

Nine women (16%) in the TLG compared to one woman (2%) in the LG reported being ‘much better’ or ‘very much better’ on the PGI-I, resulting in a RR of 8.5 (CI 95%: 1.1-66.0, P = 0.017) of being very improved if in the TLG. Overall, twenty-nine women (51%) in the TLG compared to eleven women (21%) in the LG reported improvement, giving a RR of 2.5 (CI 95%: 1.4-4.5, P = 0.001 (table 3). The regression analyses showed no significant associations between self-reported improvement in the PGI-I and any baseline data including the PFDI-20 and the PFIQ-7 total and subscale scores or POP stage (Data not shown).

No significant differences in the PFDI-20 total or subscale scores could be found between groups (table 2). Both groups had significant improvement of the bladder and bowel subscales but only the TLG had significant improvement of the POP subscale (POPDI-6, P = 0.001) (table 4). The TLG had a mean improvement of the PFDI-20 total score of 15.6 points (SD 29.5) corresponding to a 17% improvement and the LG improved mean 12.4 points (SD 30.3) corresponding to a 14% improvement. The between group difference was 3.2 (95% CL -7.9 - 14.3, P = 0.57).
Single-item analyses of the PFDI-20 revealed that only the TLG had significant improvement of pelvic heaviness (P=0.032), of feeling or seeing a bulge (P=0.009), urinary frequency (P=0.039) and small amount leakage (P=0.027). Only the LG reported significant reduction of straining in relation to bowel movements (P=0.015). Both groups had significant improvement concerning flatus incontinence and voiding difficulties.

No significant between-group differences were found in the PFIQ-7 total or subscales scores at three-month follow-up (table 2). Only the LG had significant improvement of the PFIQ-7 total score caused by improvement in the bladder subscale (table 4).

None of the women obtained significant improvement in the PISQ-12 (Data not shown).

POP-Q stage did not improve significantly in either two groups (table 4).

No significant between-group differences could be found between referred versus self-referred women in any three-month follow-up scores.

Thirty-one women of the 42 women completing the TLG handed in their training dairies (74%). Eleven women reported bother in relation to PFMT. Bother was low with a median NRS of 2 (0-5) in 85 (11%) of 805 times of reported training.

**Six-month follow-up**

Eighty-five women (78%) returned the questionnaires. Significantly more women in the TLG reported improvement in the PGI-I (P=0.003) (table 3). Thirty women (68%) in the LG compared to 11 women (28%) in the TLG had sought further treatment (P=<0.001).

Twenty-four women in the LG compared to three women in the TLG had sought PFMT (P<0.001). Two women in the LG and 4 women in the TLG had received a pessary treatment...
(P=0.30). Three women in the LG and 2 women in the TLG had received surgery (P=0.79).

Four women in the LG and two women in the TLG had received a non-specified conservative treatment (P=0.77), three women in the LG together with a specified treatment.

Between-group analyses showed no significant differences in any PFDI-20 scores while the LG had lower bother in the bowel subscale of the PFIQ-7 (CRAIQ-7, P=0.037) (table 2).

Women who had sought further treatment had significantly greater POP stage in the anterior compartment (P= 0.029), more affection of bladder related HRQoL (UIQ-7, P= 0.046) at baseline and at three-month follow-up (UIQ-7, P= 0.037). Five women had subsequent POP surgery and besides more anterior POP (P= 0.017) they reported more prolapse symptoms (POPDI-6, P= 0.008) and more affection of POP related HRQoL (POPIQ-7, P= 0.019) at three-month follow-up. No significant difference in further treatment was found between referred and self-referred women or between women with or without previous POP surgery.

Discussion

When offered a combined program of lifestyle advice and PFMT significantly more women considered them selves improved in the global scale at both three- and six-month follow-up. They also showed significant improvement of POP symptoms in the paired tests.

However, this improvement was not reflected in additional reduction of symptoms, better HRQoL, reduction of sexual problems or improvement of POP-Q scores.

Compared to the earlier studies on PFMT and lifestyle advice our results do not convincingly favor PFMT. The major difference between these studies and our study was
the design. We used an identical lifestyle advice program in both groups with the same number of sessions and the same attention except for the PFMT as opposed to comparing a PFMT program with a lifestyle advice leaflet or a single instruction[13-17]. A second important difference was that our proportion of patients with stage III was twice as big as other studies, and that we excluded women with stage I POP[13-17]. Physiologically there is a large difference between stage I and stage III POP and this might have influenced the overall effect found in our study.

We chose to offer our intervention as group sessions to ensure that the women received an identical lifestyle advice program except from the PFMT and the TLG were only offered one individual assessment of pelvic floor muscle function followed by six group-training sessions. The number of sessions and the home training program was comparable to most other studies [14, 15, 17], however, adjustments of home training programs could only be through verbal instructions and possibly the PFMT was not individualized enough to produce a pronounced effect. Furthermore the large drop out in the TLG, particularly amongst the younger women, might have been influenced our results negatively.

Only 11% of the women contacted from the hospital referral lists accepted recruitment to our study. This could represent a selection bias but while women referred by a clinician had more advanced POP they had same moderate level of POP symptoms as self-referred women. Furthermore, we found that our participants were comparable to women with pelvic floor disorders referred to a tertiary center [26] and they had higher PFDI-20 scores than women with stage I-II POP recruited from general practice [27]. We did though find low baseline PFIQ-7 scores implying low impact of HRQoL. This could be a sign of ceiling effect of PFIQ-7, defined as more than 15% scoring no impact on their HRQoL [28]. The
PFIQ-7 might overlook important aspects of POP-related HRQoL [26, 29] but perhaps women accepting participation in our study had lower impact on their HRQoL than women declining.

The indications for POP surgery are relative, and many women prefer conservative treatment [11, 12]. When PFMT was compared with “watchful waiting”, 57% receiving PFMT considered themselves improved compared to 13% in the watchful waiting group despite questionable improvement of symptoms [27]. We found that women receiving the combined treatment were 2.5 to 8.5 times more likely to consider themselves improved in spite not presenting with significantly less symptoms or better HRQoL scores than the LG except for a significant improvement of POP symptoms in the paired test. This makes us suspect that the positive effect found in the global scale might partly be explained by placebo and since the majority of the LG sought PFMT after completing the intervention it is likely that women with POP expect to receive PFMT in a conservative treatment program[13].

A recent Dutch validation of the PFDI-20 and the PFIQ-7 found that a clinically relevant improvement of the PFDI-20 should exceed 22.9 points to account for possible measurement errors and that only a change of 16.3 points could be trusted as a true improvement [26]. We found a reduction in the PFDI-20 of 15.6 points (17%) in the TLG and of 12.4 points (14%) in the LG at the three-month follow-up. The difference between the groups was only 3.1 point (95% CL -8.22-14.43). A limitation of our study was that our sample size calculation might have been too optimistic since both groups reached our predefined smallest relevant change of 15%. Furthermore, we barely accomplished to
achieve the required number of women at three-month follow-up and we cannot exclude that a larger sample would have given a different result [20, 29].

Based on our findings we cannot make strong recommendations about the use of PFMT in women with POP stage II-III. But if a woman wishes for a conservative approach, or if surgery is not an option, our study supports a small positive effect of lifestyle advices alone, or in combination with PFMT.

In conclusion, adding PFMT to a structured lifestyle advice program gave more perceived improvement in a global scale and of POP symptoms but did not reduce symptoms or improve health-related quality of life more than lifestyle advices alone. Thus, the treatment effect of either interventions was low and of questionable clinical relevance.
Acknowledgments

We wish to thank the physical therapists Dorthe Svarre Petersen, Katrin Jacobæus, Therese Simonsen, Annette Sørensen and Marie Thorsager for their help with the two interventions; Tobias Wirenfeldt Clausen, statistician at the Department of Hematology, Herlev Hospital for his help with the statistical analyses; research nurse Berit Sejersen Larsen, Department of Gynecology and Obstetrics, Herlev Hospital for her tremendous work with the randomization and follow-up of the included women; The Department of Physical therapy, Herlev Hospital for letting us use all the facilities.


Figure 1: Consolidated Standards of Reporting Trials (CONSORT) flow diagram describing the trial process.

Abbreviations: GP, General Practitioner; POP, Pelvic Organ Prolapse;

*Analysis was performed as Intention to Treat with baseline scores carried forward.

*bThree-month follow-up scores were carried forward in women who had sought further treatment.
Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lifestyle advices</th>
<th>Lifestyle advices + PFMT</th>
<th>Total</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of women randomized</td>
<td>53</td>
<td>56</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>Age, years&lt;sup&gt;a&lt;/sup&gt;</td>
<td>58 (34-79)</td>
<td>60 (33-79)</td>
<td>60 (33-79)</td>
<td>0.77</td>
</tr>
<tr>
<td>BMI&lt;sup&gt;a&lt;/sup&gt;, kg/m&lt;sup&gt;2&lt;/sup&gt;</td>
<td>25 (20-36)</td>
<td>24 (19-37)</td>
<td>25 (19-37)</td>
<td>0.46</td>
</tr>
<tr>
<td>Surgery, No. (%)</td>
<td>7 (13)</td>
<td>9 (16)</td>
<td>16 (15)</td>
<td>0.67</td>
</tr>
<tr>
<td>Referred/self-referred, No. (%)</td>
<td>20/33 (38 / 62)</td>
<td>19/37 (34 / 66)</td>
<td>39/70 (36 /64)</td>
<td>0.68</td>
</tr>
<tr>
<td>Parity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 (1-4)</td>
<td>2 (1-9)</td>
<td>2 (1-9)</td>
<td>0.07</td>
</tr>
<tr>
<td>Working, No. (%)</td>
<td>33 (62)</td>
<td>31(55)</td>
<td>64 (59)</td>
<td>0.60</td>
</tr>
<tr>
<td><strong>Objective POP at baseline, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POP-Q stage II/III, No. (%)</td>
<td>29/24 (55/45)</td>
<td>33/23 (59/41)</td>
<td>62/47 (57/43)</td>
<td>0.66</td>
</tr>
<tr>
<td>Anterior POP</td>
<td>47 (89)</td>
<td>49 (88)</td>
<td>96 (88)</td>
<td>0.40</td>
</tr>
<tr>
<td>Posterior POP</td>
<td>34 (64)</td>
<td>36 (64)</td>
<td>70 (64)</td>
<td>0.10</td>
</tr>
<tr>
<td>Combined POP</td>
<td>32 (61)</td>
<td>32 (57)</td>
<td>64 (59)</td>
<td>0.73</td>
</tr>
<tr>
<td>Anterior POP ≥ 0 cm</td>
<td>38 (71)</td>
<td>40 (71)</td>
<td>78 (72)</td>
<td>0.80</td>
</tr>
<tr>
<td>Posterior POP ≥ 0 cm</td>
<td>28 (53)</td>
<td>30 (54)</td>
<td>58 (53)</td>
<td>0.79</td>
</tr>
</tbody>
</table>
Abbreviations: BMI: Body Mass Index; POP: pelvic Organ Prolapse; POP-Q, Pelvic Organ Prolapse Quantification system; “Data are reported as median values with minimum and maximum values in brackets.
Table 2: Between-group differences in Symptom and quality of life scores at baseline, at three- and at six-month follow-up

<table>
<thead>
<tr>
<th>No. of women analyzed</th>
<th>LG (53)</th>
<th>TLG (56)</th>
<th>P</th>
<th>LG (53)</th>
<th>TLG (56)</th>
<th>P</th>
<th>LG (45)</th>
<th>TLG (40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom and bother</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POPDI-6</td>
<td>30.3 (19.6)</td>
<td>37.2 (24.4)</td>
<td>0.11</td>
<td>29.3 (17.0)</td>
<td>30.6 (23.0)</td>
<td>0.74</td>
<td>27.3 (15.4)</td>
<td>27.5 (21.3)</td>
<td>0.96</td>
</tr>
<tr>
<td>CRADI-8</td>
<td>24.2 (18.5)</td>
<td>24.6 (21.3)</td>
<td>0.93</td>
<td>19.0 (16.7)</td>
<td>20.5 (18.0)</td>
<td>0.65</td>
<td>17.0 (13.6)</td>
<td>21.7 (19.6)</td>
<td>0.20</td>
</tr>
<tr>
<td>UDI-6</td>
<td>32.3 (22.6)</td>
<td>29.6 (23.2)</td>
<td>0.53</td>
<td>26.4 (21.0)</td>
<td>24.7 (22.0)</td>
<td>0.68</td>
<td>20.4 (17.5)</td>
<td>23.4 (20.9)</td>
<td>0.47</td>
</tr>
<tr>
<td>PFDI-20</td>
<td>87.0 (46.3)</td>
<td>91.3 (59.7)</td>
<td>0.67</td>
<td>74.6 (39.5)</td>
<td>75.7 (55.2)</td>
<td>0.90</td>
<td>64.7 (32.7)</td>
<td>72.6 (51.8)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Quality of life
<table>
<thead>
<tr>
<th>Abbreviations: LG, Lifestyle advice Group; TLG, Combined pelvic floor muscle Training and Lifestyle advice Group; POPDI-6, Pelvic Organ Prolapse Distress Inventory – 6; CRADI-8, Colorectal-Anal Distress Inventory – 8; UDI-6, Urinary Distress Inventory – 6; PFDI-20, Pelvic Floor Distress Inventory - short form 20; UIQ-7, Urinary Impact Questionnaire 7; CRAIQ-7, Colorectal-Anal Impact Questionnaire 7; POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire 7; PFIQ-7: Pelvic Floor Impact Questionnaire - short form 7;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CRAIQ-7</strong></td>
</tr>
<tr>
<td><strong>POPIQ-7</strong></td>
</tr>
<tr>
<td><strong>PFIQ-7</strong></td>
</tr>
<tr>
<td>aNumber in each group analyzed  bBaseline scores carried forward in women that left the study before three months follow-up  cThree months scores carried forward in women that had sought other treatment  dData were analyzed with the unpaired samples t-test and values are presented as mean values with standard deviation in brackets(SD</td>
</tr>
</tbody>
</table>
Table 3: Distribution and between-group differences in the global score at three- and six-month follow up

<table>
<thead>
<tr>
<th>PGI-I (No.)</th>
<th>Three-month follow-up&lt;sup&gt;b&lt;/sup&gt; (109)</th>
<th></th>
<th>Six month follow-up&lt;sup&gt;c&lt;/sup&gt; (85)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LG (53)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>TLG (56)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>P Value 0.003</td>
<td>LG (44)&lt;sup&gt;a,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very much</td>
<td>0 (0 %)</td>
<td>3 (5 %)</td>
<td></td>
<td>0 (0 %)</td>
</tr>
<tr>
<td>Much better</td>
<td>1 (2 %)</td>
<td>6 (11 %)</td>
<td></td>
<td>3 (6 %)</td>
</tr>
<tr>
<td>Little better</td>
<td>10 (19 %)</td>
<td>20 (36 %)</td>
<td></td>
<td>6 (14 %)</td>
</tr>
<tr>
<td>No change</td>
<td>36 (68 %)</td>
<td>21 (37 %)</td>
<td></td>
<td>29 (66 %)</td>
</tr>
<tr>
<td>Little worse</td>
<td>6 (11 %)</td>
<td>6 (11 %)</td>
<td></td>
<td>6 (14 %)</td>
</tr>
<tr>
<td>Much worse</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
<td></td>
<td>0 (0 %)</td>
</tr>
</tbody>
</table>

Abbreviations: PGI-I: Patient Global Index of Improvement scale; LG, Lifestyle advice Group; TLG; Combined pelvic floor muscle Training and Lifestyle advice Group; <sup>a</sup>Number analyzed in each group. Analyses were performed with the Mann-Whitney test

<sup>b</sup>Dropouts before three months follow-up set as “no change”. <sup>c</sup>Three months scores carried forward in women that had sought further treatment  <sup>d</sup>One woman did not answer these questions.
Table 4: Paired test between baseline scores and 3 months follow up

<table>
<thead>
<tr>
<th>Variables</th>
<th>LG (53)$^a$</th>
<th>TLG (56)$^a$</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Three-month follow-up</td>
<td>P</td>
<td>Baseline</td>
<td>Three-month follow-up</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Symptom and bother$^b$</td>
<td></td>
<td></td>
<td>Value</td>
<td>Value</td>
<td>Value</td>
<td>Value</td>
<td>Value</td>
</tr>
<tr>
<td>POPDI-6</td>
<td>30.3 (19.6)</td>
<td>29.3 (17.0)</td>
<td>0.56</td>
<td>37.2 (24.6)</td>
<td>30.6 (23.0)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>CRADI-8</td>
<td>24.2 (18.5)</td>
<td>19.0 (16.7)</td>
<td>0.011</td>
<td>24.6 (21.3)</td>
<td>20.5 (18.0)</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>UDI-6</td>
<td>32.4 (22.6)</td>
<td>26.4 (21.0)</td>
<td>0.002</td>
<td>29.6 (23.2)</td>
<td>24.6 (22.0)</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>PFDI-20</td>
<td>87.0 (46.3)</td>
<td>74.6 (39.5)</td>
<td>0.004</td>
<td>91.3 (59.7)</td>
<td>75.7 (55.2)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Quality of life$^b$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UIQ-7</td>
<td>18.3 (20.6)</td>
<td>13.1 (17.1)</td>
<td>0.014</td>
<td>12.9 (18.4)</td>
<td>11.5 (17.9)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>CRAIQ-7</td>
<td>8.15 (16.0)</td>
<td>5.6 (14.8)</td>
<td>0.073</td>
<td>10.1 (18.7)</td>
<td>10.2 (18.5)</td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td>POPIQ-7</td>
<td>11.9 (19.8)</td>
<td>9.5 (17.6)</td>
<td>0.12</td>
<td>13.1 (18.2)</td>
<td>12.0 (18.9)</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>PFIQ-7</td>
<td>37.9 (45.6)</td>
<td>28.3 (38.5)</td>
<td>0.011</td>
<td>36.1 (47.5)</td>
<td>33.8 (48.0)</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>POP-Q$^b$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POP-Q total score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>+2.5 (0.5)</td>
<td>+2.4 (0.5)</td>
<td>0.21</td>
<td>+2.4 (0.5)</td>
<td>+2.3 (0.5)</td>
<td>0.10</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: LG, Lifestyle advice Group; TLG, Combined pelvic floor muscle Training and lifestyle advice Group; POP-Q: Pelvic Organ Prolapse Quantification system; Abbreviations: LG, Lifestyle advice Group; TLG, Combined pelvic floor muscle Training and Lifestyle advice Group;

POPDI-6, Pelvic Organ Prolapse Distress Inventory – 6; CRADI-8, Colorectal-Anal Distress Inventory – 8; UDI-6, Urinary Distress Inventory – 6; PFDI-20, Pelvic Floor Distress Inventory - short form 20; UIQ-7, Urinary Impact Questionnaire 7; CRAIQ-7, Colorectal-Anal Impact Questionnaire 7; POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire 7; PFIQ-7: Pelvic Floor Impact Questionnaire - short form 7;

<sup>a</sup>Baseline scores carried forward in women who left the study before the three-month follow-up.  <sup>b</sup>All analyses were performed with the paired-samples t-test.  <sup>c</sup>Based on the POP-Q system where POP is described in millimeters with positive numbers indicating POP beyond hymen and negative numbers indicating POP above hymen.
Title: The 12-month effects of structured lifestyle advice and pelvic floor muscle training for pelvic organ prolapse

Authors

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The study was approved by the Danish Scientific Ethical Committee (H-4-2011-072) August 24th 2011
Each authors contribution to the manuscript

U Due: Protocol/project development, Data Collection, Data analyses, Manuscript writing manuscript editing

G Lose: Protocol/project development, data analyses, manuscript editing

S Brostrøm: Protocol/project development, data analyses, manuscript editing

Abstract 325 words, Main text 2806 words
Abbreviations

POP: Pelvic Organ Prolapse

HRQoL: Health Related Quality of Life

POP-Q: Pelvic Organ Prolapse Quantification system

PFDI-20: Pelvic Floor Distress Inventory - short form 20

POPDI-6: Pelvic Organ Prolapse Distress Inventory 6

CRADI-8: Colorectal-Anal Distress Inventory 8

UDI-6: Urinary Distress Inventory 6

PFIQ-7: Pelvic Floor Impact Questionnaire - short form 7

UIQ-7: Urinary Impact Questionnaire 7

CRAIQ-7: Colorectal-Anal Impact Questionnaire 7

POPIQ-7: Pelvic Organ Prolapse Impact Questionnaire 7

PISQ-12: The Pelvic organ prolapse/urinary Incontinence Sexual Questionnaire 12

PGI-I: Patient Global Index of Improvement scale

PFMT: Pelvic Floor Muscle Training

LG: Lifestyle advice Group

TLG: Combined pelvic floor muscle Training and Lifestyle advice Group
**Objective**

To conduct a 12-month follow-up to evaluate the effects of adding pelvic floor muscle training (PFMT) to a lifestyle advice program in women with symptomatic pelvic organ prolapse (POP) stage II-III.

**Study design**

This study was a 12-month follow-up of a randomized controlled trial comparing a structured lifestyle advice program alone (the LG) or in combination with PFMT (the TLG). The two programs had been offered as six separate group sessions during a twelve-week period. We evaluated the treatment effects of the interventions based on symptom- and quality of life (HRQoL) scores. Furthermore, we examined the number of women who had sought further treatment and reasons for doing so, in the two groups.

**Results**

Data were available from 83 (76 %) of the 109 originally included women.

All together 34 (41%) of the 83 women had not sought further treatment, 30% (13/43) in the LG and 52% (21/40) in the TLG, respectively (P=0.05).

At the 12-month follow-up the women in the LG had significantly improved bladder symptoms (paired test, P=0.01) compared to baseline. Those in the TLG had significantly improved POP symptoms (paired test, P=0.02) and bowel-related HRQoL score (paired test, P=0.04)

No significant between-group differences (LG versus TLG) were found in any of the symptom- and HRQoL scores (unpaired tests).
All together 49 women (59%) had sought further treatment, 70% (30/43) in the LG and 48% (19/40) in the TLG, respectively.

Twenty-six women (of 30) in the LG, and 15 (of 19) in the TLG had sought conservative treatment. Eight women, four from each group had received surgery.

For both groups, more severe anterior prolapse and more bladder symptoms were significantly associated with having sought further treatment in the multivariate logistic regression analyses of post-intervention scores.

**Conclusion**

At the 12-month follow-up, marginally more women with POP stage II-III offered a structured lifestyle advice program without PFMT had sought further treatment. The effect of adding PFMT to a structured lifestyle advice program was limited.

**Key words:** pelvic organ prolapse, lifestyle advices, pelvic floor muscle training, conservative treatment, long-term follow-up

**Condensation:**

Adding pelvic floor muscle training to a lifestyle advice program is marginally more efficient than a structured lifestyle advice program alone

**Short title:** 12-month follow-up after structured lifestyle advice and pelvic floor muscle training for pelvic organ prolapse
**Introduction**

The effect of lifestyle advice either alone or in combination with Pelvic Floor Muscle Training (PFMT) for pelvic organ prolapse (POP) remains controversial and long term data are sparse.\(^1\)\(^3\)\(^4\)\(^5\)\(^6\)\(^7\)

It has been reported that women with symptomatic POP stage I-III offered individual PFMT compared to a lifestyle advice leaflet had significantly reduced symptoms and were less likely to have received further treatment at a 12-month follow-up.\(^5\) The same authors recently reported a continuous positive effect of PFMT in a 24 months follow-up (IUGA 2015). However, no studies have examined the 12-month effect of PFMT when compared to another active intervention and there is a lack of data about the long-term effects of offering a structured lifestyle advice program with or without PFMT in women with POP stage II-III.

In a recent single-blinded randomized controlled trial,\(^8\) we found that adding PFMT to a structured lifestyle advice program for women with POP stage II-III had a statistically significant greater effect as measured on a global improvement scale. However, the clinically relevant improvement in POP specific symptom and HRQoL scores was marginal and similar at three- and six-month follow-up for both groups.

The aim of the present 12-month follow-up study was therefore to evaluate the long term effects of adding PFMT to a structured lifestyle advice program in women with symptomatic POP stage II-III and to explore factors possibly related to seeking further treatment.

**Materials and methods**

This study was a follow-up study after a single-blinded randomized controlled trial, which has previously been described in detail and will be briefly described in the following.\(^8\)
The 109 participating women were randomly assigned to receive either a structured lifestyle advice program alone (LG) (n=53) or a combined program with PFMT and structured lifestyle advice (TLG) (n=56).

Recruited participants were women aged 18 years or older and with a POP-Q of ≥ II and at least one of three symptoms; seeing or feeling a bulge in the vaginal opening, voiding dysfunctions or defecation problems, or feeling vaginal heaviness. Women with POP stage I were not included because they are often asymptomatic.9,10

Women with one or more of the following criteria were excluded: Dementia, symptomatic neurological disease, including serious back problems, PFMT within the last two years, childbirth within the last year, more than one surgical treatment for POP or urinary incontinence.

Participants received six group sessions with an identical lifestyle advice program within twelve weeks, because it is assumed that lifestyle modifications could have a beneficial effect on pelvic floor disorders.7,11,12 The lifestyle advice program contained information about POP and had specific suggestions on how to improve bladder and bowel function, how to adhere to healthy diet with more fiber and less fat and how to increase activity level without increasing load on the pelvic floor. The TLG were initially examined by a specialized pelvic floor physiotherapist and individually instructed in PFMT before starting the group sessions. The TLG lifestyle advice sessions included group PFMT and the participants did home training five days a week based on an individually adjusted program based on generally accepted training principles13,14. The LG were not given information about PFMT and the TLG and the LG sessions were held on separate days.

Recruited women were examined by the primary investigator and scored with the POP-Q at baseline and at the three-month follow-up.15
All included women completed the same questionnaires at baseline, three, six and twelve months after inclusion. A global scale was added at the three-, six- and the 12-month follow-up. At the three-month follow-up, the primary investigator repeated the POP-Q examination, remaining blinded to baseline POP-Q scores. At the six- and the 12-month follow-up, the women were asked if they had received further treatment after completing the interventions.

The primary investigator remained blinded throughout the study. A research nurse administered randomization envelopes. Randomization was stratified for age groups ≥ 60 years.

The study took place at Herlev University Hospital, Copenhagen, Denmark. Participants were recruited by the primary investigator from the hospital referral list and outpatient clinic, as well as through websites, local newspapers, and posters at public places. Comprehensive written study information was provided and all women signed an informed consent before entering the study. The study was approved by the Danish Scientific Ethical Committee (H-4-2011-072) and by the Danish Data Protection Agency. The study was reported to ClinicalTrials.gov (NCT01612637).

**Outcome measures**

Global sense of improvement was scored with the Patient Global Index of Improvement scale (PGI-I)\textsuperscript{16, 17}. Symptoms were evaluated with the Pelvic Floor Distress Inventory-short form 20 (PFDI-20); and quality of life (HRQoL) with the Pelvic Floor Impact Questionnaire-short form 7 (PFIQ-7)\textsuperscript{18}. The PFDI-20 contains twenty items divided into three subscales revealing bladder (UDI-6), bowel (CRADI-8), and prolapse (POPDI-6) symptoms and bother. A score from each item can be obtained on a scale from 0 to 4 with a higher score indicating greater bother. Quality of life was evaluated with the PFIQ-7. The PFIQ-7 has twenty-one items divided into three subscales of seven questions each asking about impact on HRQoL related to bladder (UIQ-7), bowel (CRAIQ-7) and POP (POPIQ-7) symptoms. Every item can be scored from 0 to 3 with a higher score indicating more impact on
HRQoL. For both the PFDI-20 and the PFIQ-7 it is possible to calculate both total and subscale scores. Subscale scores range from 0-100 and total scores from 0-300. Higher scores indicate more symptoms, more bother and greater impact on HRQoL. Impact on sexuality was examined with the Pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12)\textsuperscript{19}. The PISQ-12 has twelve items concerning sexual problems. Each item is scored from 0 to 4 with a lower score indicating more impact on sexual life.

We compared the 12-month treatment effects and compared number of women in the two intervention groups who had received further treatment. We used baseline variables (before randomization) including age, parity, BMI, work, surgery, referral status, symptom scores, HRQoL scores, and POP stage and three-month follow-up scores (immediately after completing the interventions) to search for possible explanatory factors related to seeking further treatment. We dichotomized POP scores for the anterior and posterior POP compartment as; POP at or below the hymen or POP above the hymen, as it has been shown that POP is likely to give symptoms when it reaches the hymen\textsuperscript{9,10}.

**Statistics**

Data analyses were performed as per protocol analyses. Descriptive statistics were used to describe baseline and follow-up data. PFDI-20 and PFIQ-7 total and subscale scores were analyzed with both parametric and non-parametric statistics. Since results from both methods were similar, we reported data from the parametric tests in order to be comparable with other studies using the same scores. Non-parametric statistics was used for single item analyses. Categorical data were analyzed with the Chi-square test. Logistic regression analyses were performed to find possible explanatory factors related to seeking further treatment before the 12-month follow-up: Univariable logistic regression analyses were performed in variables with ≥80% data completeness.
and variables were included in the forward multivariable logistic regression if a P value of ≤0.20 was achieved. Level of significance was set at a P-value of .05 for all statistical tests. All P values were reported two-sided. All analyses were performed with SPSS version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

Of the 109 women originally included, data were available from 83 (76%) women at the 12-month follow-up. Forty-three women (81%) from the LG and 40 women (71%) from the TLG responded to the 12-month follow-up questionnaires (Fig 1).

All together 34 women had not sought further treatment, 13 (30%) of the 43 women in the LG and 21 (52%) of the 40 women in the TLG, respectively (P= 0.05).

At the 12-month follow-up the 13 women in the LG showed significant improvement in the bladder symptom score compared to baseline (UDI-6, P=0.01) (Table 1). Single item analyses showed that the women had significantly reduced symptoms in two items; stress urinary incontinence (P=0.04) and small amount urinary leakage (P=0.04) (Data not shown). No significant improvements were found in any of the PFIQ-7 subscales.

In the TLG the 21 women showed significantly improved POP symptoms (POPDI-6, P= 0.02) and bowel-related HRQoL (CRAIQ-7, P= 0.04) compared to baseline (Table 1). Single item analyses showed that the TLG had significantly reduced symptoms related to a single item: “bulge in vagina” (P=0.005). No single item in the bowel-related HRQoL subscale (CRAIQ-7) was significantly improved and the improvement was only found in the total CRAIQ-7 subscale (P=0.04) (data not shown).
At the 12-month follow-up (Table 2) no significant between-group differences were found between the LG and the TLG in the global score (P = 1.0) or in any symptom or HRQoL scores (unpaired tests, table 2).

All together 49 women had sought further treatment, 30 (70%) of 43 in the LG and 19 (48%) of the 40 in the TLG, respectively (P = 0.05).

In the LG, all but one of the 30 women had sought further treatment before the six-month follow-up. Twenty-six women had received conservative treatment mainly as PFMT and four had received surgery (Fig. 1).

In the TLG, 19 women (48%) had sought further treatment, 11 before the six-month follow-up and another eight women between the six- and the 12-month follow-up. Fifteen women had received conservative treatment and four had received surgery (Fig 1).

In the PISQ-12 scores no significant differences could be found between the LG and the TLG at the 12-month follow-up or between women who had received further treatment or not (data not shown).

When comparing women who later sought further treatment with women who did not, there were no significant differences in the post-intervention symptom scores at the three-month follow-up in either group (data not shown). For women in the LG who had sought further treatment there was no difference in HRQoL scores compared to women in the LG group having sought further treatment. Conversely, women in the TLG who had sought further treatment did show statistically significant greater impact of their POP-related quality of life (P = 0.03) as compared to women who did not.
The eight women, four from each group, who had received surgery, were older (P= 0.03) and had reported more impact on their bladder-related HRQoL at both baseline (P= 0.05) and at the three-month follow-up (P= 0.02). Otherwise they were not different from women who did not seek surgery (unpaired tests, data not shown).

Having an anterior POP at or beyond the hymen or having greater baseline scores in POP- and in bladder-related HRQoL in both groups significantly increased the risk of having sought further treatment before the 12-month follow-up in the univariable logistic regression analyses. “Not working” also became a significant factor in the multivariable analysis of baseline data (Table 3).

Group allocation to the LG, more POP and bladder symptoms, more impact on POP and bladder-related quality of life and anterior prolapse at or beyond the hymen significantly increased the risk of having sought further treatment in the univariable analyses of the three-month follow-up scores. However, in the multivariable analysis, only more anterior POP (BaHy: OR: 5.886, 95% CI 1.659-20.878, P=0.006) and more bladder symptoms (UDI-6, OR: 1.046, 95% CI 1.013-1.080, P=0.006) remained significant (Table 3).

Discussion

In this 12-month follow-up study we could not demonstrate superior long-term effect of adding PFMT to a structured lifestyle advice program.

We found that a structured lifestyle advice program alone improved symptoms of stress urinary incontinence and “small amount” leakage. Adding PFMT to the lifestyle advice program improved “bulge” symptoms and bowel-related HRQoL. It is likely that the LG had a continued positive effect on voiding behavior, while the alone TLG sustained relief from a better support for their POP. On the other hand the all over long-term treatment effects, while statistically significant, where of limited magnitude, and neither group had improvements in the majority of the symptom- and HRQoL
scores. Furthermore, no significant between-group differences were found between the LG and the TLG in any of the symptom and HRQoL scores.

Our study is original compared with previously published studies on PFMT for POP in offering an identical number of group sessions of lifestyle advice program for women in both the intervention and control group. The group design was chosen to minimize the possible risk of performance bias that could arise if one group received substantially more attention than the other. The only difference between the study groups was that the TLG had an individual assessment and instruction in PFMT and they did group PFMT during their group sessions, while the LG did not receive any information about PFMT. In the present study we furthermore did not include women with POP stage I.

More women in the LG than in the TLG had received further treatment before the 12-month follow-up with a risk difference of 22% (P = 0.05). This is comparable to the other study reporting 12-month follow-up data, except that the number was 70% in the LG and 48% in the TLG compared to 50% of the women who had received a lifestyle advice leaflet and 24% of the women who had received PFMT in the other study5. The higher number of women seeking further treatment could be explained by the exclusion of women with POP stage I. Our participants had moderate POP symptoms, which could be demonstrated with the use of widely recognized symptoms- and HRQoL scores 20-22. Unfortunately, earlier studies on PFMT have applied less generally used symptoms scores, which makes it difficult to compare the degree of symptoms with other studies on PFMT.

Interestingly, all but one of the 30 women in the LG who had sought further treatment had done it before the six-month follow-up. Surprisingly they did not have more symptoms or more impact on their HRQoL than women who did not seek further treatment, in the LG. Furthermore the majority
had sought PFMT. Contrary to this, more women in the TLG waited until after the six-month follow-up before seeking further treatment and those who did seek further treatment had more impact on their POP-related HRQoL. This difference in behavior between the two study groups was unexpected but could be explained by bias induced by the study design. Similar to the study by Hagen et al.\textsuperscript{5}, the majority of the LG had sought PFMT, and they probably did this because they had not received it initially and because information about PFMT is easily available.

Studies have shown that an important reason for women with POP to seek treatment is negative impact of their body image and decreased quality of life including sexual problems\textsuperscript{23,24}. At baseline, our participants reported moderate symptoms\textsuperscript{21,22} and they had advanced objective POP\textsuperscript{10} but limited impact on HRQoL on sexuality. Due to the more severe objective POP and the moderate symptoms we expected a higher percentage to have received surgery compared to the other 12-month follow-up study\textsuperscript{5}. Surprisingly this was not the case and as similar to the other study it was approximately 10\%\textsuperscript{5}. One study found that almost two-thirds with POP preferred a non-surgical treatment and impact on sexual function was a driver for seeking surgery\textsuperscript{25}. Furthermore, it has been shown that women with POP worry more about the risk of complications from surgery than women with urinary incontinence\textsuperscript{26}. The participants might therefore have been a selected resourceful group, who despite of advanced POP were highly motivated for conservative treatment. It is also possible that the interventions made some women not to choose surgery. A longer follow-up could have confirmed this finding.

In the univariable logistic regression analyses of the three-month follow-up scores, we found that group allocation to the LG was a significant factor associated with seeking further treatment. When we adjusted for more anterior POP at or beyond the hymen and more bladder symptoms the group effect disappeared. More anterior POP remained the strongest factor with a five times increased
odds ratio for seeking further treatment, while bladder symptoms explained less than five percent of the association. It is puzzling and surprising that having more objective POP was a much stronger predictor of seeking further treatment than any of the POP related symptoms. This could be due to an investigator-induced perception of illness severity caused by the objective ‘confirmation’ of the woman’s symptoms at the baseline examination.

The strength of our study was that we had a 76% response rate compared to the 66% in the other 12-month follow-up study. A limitation of our study was the large dropout, especially in the TLG before the three-month follow-up. Furthermore, because of our small sample-size the number of women in the different subgroups was small and our results should be interpreted with caution.

Based on the findings from our study women with POP should be advised to have realistic expectations about the long-term effect of conservative program with or without PFMT.
Acknowledgments

We wish to thank the physical therapists Dorthe Svarre Petersen, Katrin Jacobæus, Therese Simonsen, Annette Sørensen and Marie Thorsager for teaching the group sessions and performing the pelvic floor muscle function assessments; Tobias Wirenfeldt Clausen, statistician at the Department of Hematology, Herlev Hospital for his guidance with the statistical analyses; research nurse Berit Sejersen Larsen, Department of Gynecology and Obstetrics, Herlev Hospital for her tremendous work with the randomization and the many follow-ups of the included women; The, Department of occupational and physical therapy, Herlev Hospital for the support and use all the facilities.
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Figure 1. Flow-chart describing the follow-up of the included women

Abbreviations: PFMT, Pelvic Floor Muscle Training

*One woman did not respond to these questions.  
One woman who had received PFMT did not complete 12-month follow-up;  
One more woman had surgery between the six and 12-month follow-up after describing “other treatment;”  
Other conservative treatment but not described and three women in the LG described this together with a described treatment.  
Two women from the LG left the study between the six and 12-month follow-up.
Table 1: Mean difference in symptom- and HRQoL scores from baseline to the 12-month follow-up

<table>
<thead>
<tr>
<th></th>
<th>LG</th>
<th></th>
<th></th>
<th>TLG</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No further treatment (n = 13)</td>
<td></td>
<td></td>
<td>No further treatment (n = 21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
<td>12 month</td>
<td>Mean diff (SD)</td>
<td>P value</td>
<td>Baseline</td>
<td>12-month</td>
<td>Mean diff (SD)</td>
</tr>
<tr>
<td>POPDI-6</td>
<td>27.9 (14.1)</td>
<td>22.4 (14.0)</td>
<td>5.4 (9.7)</td>
<td>0.07</td>
<td>33.7 (21.6)</td>
<td>26.0 (16.8)</td>
<td>7.7 (14.5)</td>
</tr>
<tr>
<td>CRAD-8</td>
<td>20.0 (15.4)</td>
<td>14.9 (14.8)</td>
<td>5.1 (11.9)</td>
<td>0.15</td>
<td>24.1 (20.5)</td>
<td>18.6 (18.2)</td>
<td>5.5 (12.8)</td>
</tr>
<tr>
<td>UDI-6</td>
<td>23.7 (14.2)</td>
<td>9.9 (13.5)</td>
<td>13.8 (17.0)</td>
<td>0.01</td>
<td>24.0 (14.7)</td>
<td>22.4 (21.4)</td>
<td>1.6 (1.5)</td>
</tr>
<tr>
<td>PFDI-20</td>
<td>71.6 (34.8)</td>
<td>47.3 (34.4)</td>
<td>24.3 (29.)</td>
<td>0.01</td>
<td>81.8 (47.4)</td>
<td>67.0 (43.1)</td>
<td>14.8 (26.2)</td>
</tr>
<tr>
<td>UIQ-7</td>
<td>9.9 (14.6)</td>
<td>4.3 (7.1)</td>
<td>5.6 (15.3)</td>
<td>0.22</td>
<td>7.9 (10.5)</td>
<td>8.4 (14.0)</td>
<td>-0.5 (7.8)</td>
</tr>
<tr>
<td>CRAIQ-7</td>
<td>2.9 (4.6)</td>
<td>4.0 (7.5)</td>
<td>-1.1 (7.6)</td>
<td>0.61</td>
<td>7.0 (12.5)</td>
<td>2.9 (5.2)</td>
<td>4.1 (8.5)</td>
</tr>
<tr>
<td>POPIQ-7</td>
<td>4.4 (5.7)</td>
<td>5.2 (7.4)</td>
<td>-0.7 (7.5)</td>
<td>0.73</td>
<td>9.1 (10.7)</td>
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<td>3.2 (10.7)</td>
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<td>PFIQ-7</td>
<td>17.2 (16.7)</td>
<td>13.6 (17.5)</td>
<td>2.6 (22.8)</td>
<td>0.57</td>
<td>24.0 (24.0)</td>
<td>17.2 (22.2)</td>
<td>6.8 (16.9)</td>
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### Table 2: Between-group differences in PFDI-20 and PFIQ-7 scores at 12-month follow-up in the women who did not seek further treatment after the three-month follow-up

<table>
<thead>
<tr>
<th></th>
<th>LG (n=13)</th>
<th>TLG (n=21)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POPDI-6</td>
<td>22.4 (14.0)</td>
<td>26.0 (16.8)</td>
<td>0.53</td>
</tr>
<tr>
<td>CRADI-8</td>
<td>14.9 (14.8)</td>
<td>18.6 (18.2)</td>
<td>0.54</td>
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<tr>
<td>UDI-6</td>
<td>9.9 (13.5)</td>
<td>22.4 (21.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>PFDI-20</td>
<td>47.3 (34.4)</td>
<td>67.0 (43.0)</td>
<td>0.17</td>
</tr>
<tr>
<td>UIQ-7</td>
<td>4.3 (7.1)</td>
<td>8.4 (13.9)</td>
<td>0.35</td>
</tr>
<tr>
<td>CRAIQ-7</td>
<td>4.0 (7.5)</td>
<td>2.9 (5.3)</td>
<td>0.63</td>
</tr>
<tr>
<td>POPIQ-7</td>
<td>5.2 (7.4)</td>
<td>5.9 (8.8)</td>
<td>0.79</td>
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<tr>
<td>PFIQ-7</td>
<td>13.6 (17.5)</td>
<td>17.2 (22.2)</td>
<td>0.62</td>
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</tbody>
</table>

**Abbreviations:** LG, Lifestyle advice Group, TLG, Combined pelvic floor muscle Training and Lifestyle advice Group, POPDI-6, Pelvic Organ Prolapse Distress Inventory – 6, CRADI-8, Colorectal-Anal Distress Inventory – 8, UDI-6, Urinary Distress Inventory – 6, PFDI-20, Pelvic Floor Distress Inventory - short form 20, UIQ-7, Urinary Impact Questionnaire 7, CRAIQ-7, Colorectal-Anal Impact Questionnaire 7, POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire 7, PFIQ-7, Pelvic Floor Impact Questionnaire - short form

*All scores are reported as mean scores with standard deviations in brackets (SD)*
Table 3: Logistic regression analyses of factors possibly related to seeking further treatment between the three- and the 12-months follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable OR (95% CI)</th>
<th>P value</th>
<th>Multivariable OR (95% CI)</th>
<th>P value</th>
<th>Variable</th>
<th>Univariable OR (95% CI)</th>
<th>P value</th>
<th>Multivariable OR (95% CI)</th>
<th>P value</th>
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<td>Age</td>
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<td></td>
<td></td>
<td>Group allocation</td>
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<td>.031</td>
<td>2.610 (1.972-7.009)</td>
<td>0.057</td>
</tr>
<tr>
<td>surgery</td>
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<td></td>
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<tr>
<td>Referred/ self-referred</td>
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<tr>
<td>Job</td>
<td>0.067</td>
<td></td>
<td>2.943 (1.014-8.447)</td>
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<tr>
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<tr>
<td>POP-Q</td>
<td>0.464</td>
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<td>POP-Qd</td>
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<tr>
<td>BaHy\textsuperscript{b}</td>
<td>3.417 (1.238-9.432)</td>
<td>0.018\textsuperscript{a}</td>
<td>5.290 (1.571-17.817)</td>
<td>0.007</td>
<td>BaHy\textsuperscript{d}</td>
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<td>BpHy\textsuperscript{d}</td>
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<td>1.003-1.059)</td>
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<tr>
<td>CRADI-8</td>
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<td>CRADI-8\textsuperscript{d}</td>
<td>0.800</td>
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<td>1.027</td>
<td>1.000-1.055)</td>
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<td>1.036</td>
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<td>UIQ-7\textsuperscript{d}</td>
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<td>0.033\textsuperscript{\wedge}</td>
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<td>1.002-1.067)</td>
<td>0.037\textsuperscript{a}</td>
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<td>POPIQ-7\textsuperscript{d}</td>
<td>1.050 (1.003-1.098)</td>
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</table>

Abbreviations: LG, Lifestyle advice Group, TLG, Combined pelvic floor muscle Training and Lifestyle advice Group, POPDI-6, Pelvic Organ Prolapse Distress Inventory – 6, CRADI-8, Colorectal-Anal Distress Inventory – 8, UDI-6, Urinary Distress Inventory – 6, PFDI-20, Pelvic Floor Distress Inventory - short form 20, UIQ-7, Urinary Impact Questionnaire 7, CRAIQ-7, Colorectal-Anal Impact Questionnaire 7, POPIQ-7, Pelvic Organ Prolapse Impact Questionnaire 7, PFIQ-7, Pelvic Floor Impact Questionnaire - short form, BaHy; Anterior POP above or at or beyond the hymen, BpHy; Posterior POP above or at or beyond the hymen

\textsuperscript{a}Variables with a P value of ≤0.20 from the univariable analyses were included in the multiple variable analysis

\textsuperscript{b}Anterior or posterior POP at or beyond the hymen compared to POP above the hymen

\textsuperscript{c}Women still working were less likely to seek further treatment

\textsuperscript{d}Three-month follow-up scores
## DECLARATION OF CO-AUTHORSHIP

### Information on PhD student:

<table>
<thead>
<tr>
<th>Name of PhD student</th>
<th>Ulla Due</th>
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</thead>
<tbody>
<tr>
<td>E-mail</td>
<td><a href="mailto:ulla.due@regionh.dk">ulla.due@regionh.dk</a></td>
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<tr>
<td>Date of birth</td>
<td>140664</td>
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<tr>
<td>Work place</td>
<td>Herlev Hospital</td>
</tr>
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<td>Principal supervisor</td>
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</table>

### Title of PhD thesis:

Lifestyle advice and pelvic floor muscle training for women with pelvic organ prolapse

### This declaration concerns the following article:

Validation of the Pelvic Floor Distress Inventory-20 and the Pelvic Floor Impact Questionnaire-7 in Danish women with Pelvic organ prolapse

### The PhD student's contribution to the article:

<table>
<thead>
<tr>
<th>(A, B, C)</th>
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<tbody>
<tr>
<td>1. Formulation/identification of the scientific problem that from theoretical questions need to be clarified. This includes a condensation of the problem to specific scientific questions that is judged to be answerable by experiments</td>
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*Benchmark scale of the PhD student's contribution to the article*

| A. refers to: | Has contributed to the co-operation | 0-33 % |
| B. refers to: | Has contributed considerably to the co-operation | 34-66 % |
| C. refers to: | Has predominantly executed the work independently | 67-100 % |

### Signature of the co-authors:

<table>
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<th>Date</th>
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<td>27/4/15</td>
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# DECLARATION OF CO-AUTHORSHIP

**Information on PhD student:**
- **Name of PhD student:** Ulla Due
- **E-mail:** ulla.due@regionh.dk
- **Date of birth:** 140654
- **Work place:** Herlev Hospital
- **Principal supervisor:** Gunnar Lose

**Title of PhD thesis:**
Lifestyle advice and pelvic floor muscle training for women with pelvic organ prolapse

**This declaration concerns the following article:**
Lifestyle Advice with or without Pelvic Floor Muscle Training for Pelvic Organ Prolapse, a randomized controlled trial

**The PhD student’s contribution to the article:**

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## Title of PhD thesis:

Lifestyle advice and pelvic floor muscle training for women with pelvic organ prolapse

## This declaration concerns the following article:

The 12-month effects of structured lifestyle advice and pelvic floor muscle training for pelvic organ prolapse

## The PhD student's contribution to the article:

(please use the scale (A,B,C) below as benchmark* )

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