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## Pelvic floor muscle training is effective in treatment of female stress urinary incontinence, but how does it work?

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**Abstract** To date several randomized controlled trials (RCT) have shown that pelvic floor muscle (PFM) training is effective in the treatment of female stress (SUI) and mixed urinary incontinence and, therefore, it is recommended as a first-line therapy. While the effectiveness of treatment is established, there are different theoretical rationales for why PFM training is effective. The aims of this article are to discuss the theories behind why PFM training is effective in treating SUI and to discuss each theory in the framework of new knowledge of functional anatomy and examples of results from RCTs. There are three proposed theories to explain the effectiveness of PFM training for SUI: 1) women learn to consciously pre-contract the PFMs before and during increases in abdominal pressure (such as coughing, physical activity) to prevent leakage; 2) strength training builds up long-lasting muscle volume and thus provides structural support; and 3) abdominal muscle training indirectly strengthens the PFM. The first can be placed in a behavioral construct, while the two latter both have the aim of changing neuromuscular function and morphology, thus making the PFM contraction automatic. To date there are RCTs and basic anatomy studies to support the first two concepts only.

**Keywords** Anatomy · Exercise · Pelvic floor muscles · Stress urinary incontinence · Training

### Introduction

Kegel is credited with introducing pelvic floor muscle (PFM) training as an effective therapy for urinary incontinence in women [1]. However, Chang notes that

PFM exercises have been an important part of exercise programs within Chinese Taoism for more than 6,000 years [2], and pelvic floor “tensing” has been used to treat and prevent urinary and fecal incontinence at least since the 1920s within the British physical therapy profession [3].

Kegel [4] reported that 84% of his patients with urinary incontinence were cured after doing PFM exercises. While his studies were uncontrolled and lacked rigorous outcome measures, several randomized controlled trials (RCT) and systematic reviews have confirmed that PFM training is an effective treatment for stress (SUI) and mixed urinary incontinence. PFM training is now recommended as first-line treatment [5, 6, 7]. Cure and improvement rates in RCTs that include both stress and mixed incontinence vary between 56 and 70% [6, 7]. There seems to be a rather strong belief in the literature that PFM training improves, but does not abolish, the condition [5]. However, it has been documented in some RCTs that 44–69% of SUI women are cured, defined as  $\leq 2$  g of leakage on pad tests, after PFM training [8, 9, 10, 11].

The PFM are comprised of a three-layer muscular plate expanding from the pubic symphysis along the sidewalls of the ileum towards the coccyx (Fig. 1). The different muscles have different fiber directions, and if each muscle could contract in isolation, they would all have different functions. However, the only known voluntary function of the PFM is a mass contraction best described as an inward lift and squeeze around the urethra, vagina and rectum [12]. Because of its location inside the pelvis, the PFM is the only muscle group in the body capable of giving structural support for the pelvic organs (urethra, vagina and rectum) (Fig. 2). The stress continence system includes not only the PFM, but also the sphincteric closure mechanism consisting of urethral striated muscle, urethral smooth muscle and vascular elements and the remainder of the bladder support system consisting of the anterior vagina, endopelvic fascia, arcus tendineus fasciae pelvis, and bony pelvis [13].

A conscious, voluntary PFM contraction causes a squeeze and inward lift of the PFM, with resultant

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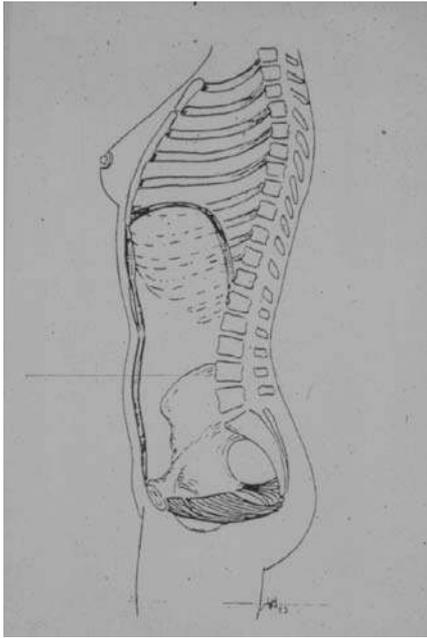
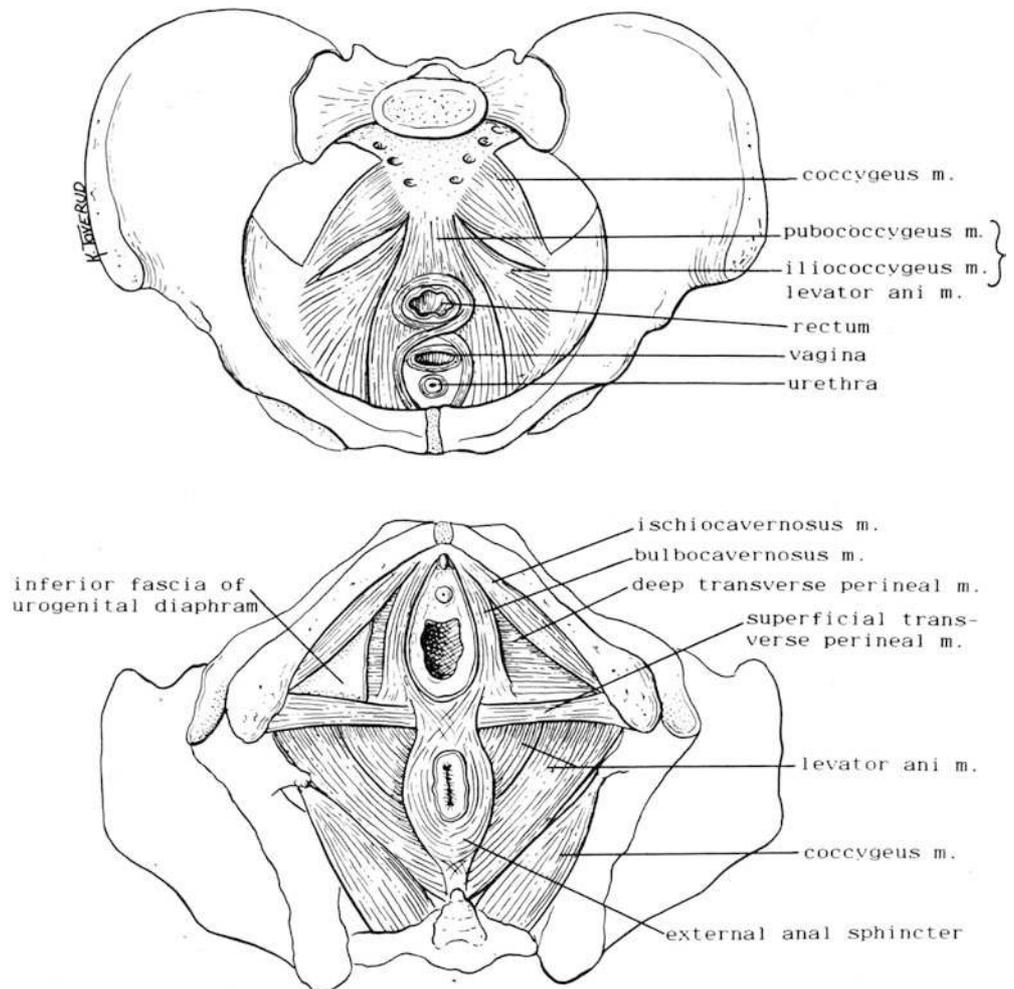


Fig. 1 The pelvic floor muscles [67]

urethral closure, stabilization, and resistance to downward movement. In healthy volunteers, contractions of other large muscle groups such as the gluteals, hip adductors and abdominals result in a simultaneous contraction (termed “co-contraction”) of the PFM [14, 15, 16, 17, 18]. However, unlike the PFM, these other muscle groups are not in an anatomical position to act as a structural support to prevent bladder neck and urethral descent. Further, contracting muscle groups other than the PFM can not increase urethral pressure by a direct squeeze around the urethral lumen.

Case control studies demonstrate a significant difference in PFM function, strength and structural support (as measured by vaginal squeeze pressure, EMG, ultrasound and MRI) in continent and incontinent women. Hahn et al. [19] and Mørkved et al. [20] found greater PFM strength in continent women than women with urodynamic SUI. Gunnarson and Mattiasson [21] showed that continent women had better muscle function than incontinent ones. Both Bernstein et al. [22] and Mørkved et al. [20] reported significantly greater PFM thickness in continent women compared to those with SUI.

Fig. 2 The pelvic floor muscles are located inside the pelvis and forms a structural support for internal organs [68]



Using perineal ultrasound, Miller et al. [23] demonstrated that in a group of older parous incontinent women (mean age 66.67 years, SD 3.9) at rest, the median position of the vesical neck was significantly more dorso-caudal, than its position in younger continent nulliparous women (mean age 24.8 years, SD 7.0). Peschers et al. [24] showed that the bladder neck was significantly lower at rest in women after vaginal delivery than in those who had elective cesarean delivery or in nulligravid controls. They concluded that vaginal delivery altered vesical neck descent during valsalva, as well as the ability of the PFM to elevate the urethra in some women. Their study corresponded with previous results reported by Small and Wynne [25].

Muscle stiffness is an indicator of muscle's ability to resist force. To explore the concept of PFM stiffness, Howard et al. [26] measured vesical neck mobility using perineal ultrasound in nulliparous continent, primiparous continent and primiparous stress incontinent women. They simultaneously recorded abdominal pressure by means of an intravaginal micro transducer catheter. Pelvic floor stiffness was calculated by dividing the pressure exerted during a particular effort by the urethral descent during that effort. Nulliparas displayed greater pelvic floor stiffness during a cough than either continent or incontinent primiparas. For each 15-cm H<sub>2</sub>O increase in abdominal pressure, a healthy pelvic floor is expected to stretch downward only 1 mm [13, 26]. These studies indicate that healthy PFM may occupy an optimal anatomical position inside the pelvis for the PFM in which the muscles are able to function automatically.

Although the effect of training the PFM to treat SUI is logical based on an understanding of functional anatomy, exercise protocols vary and seem to be based on different assumptions of how PFM training affects continence. The purpose of this article is to describe the different theories about why PFM training is effective, determine whether these rationales are supported by data from RCTs, and discuss the theories and training principles in light of functional anatomy. The basis for this discussion is RCTs included in the Cochrane systematic review "Pelvic floor muscle training for female urinary incontinence" [7]. While this Cochrane review presented combined results from studies including stress, urge and mixed incontinence, only studies reporting results in women with SUI are included in this article. The pathogenesis for urge and stress urinary incontinence may differ, and these two forms of urinary incontinence may need different treatment approaches. Therefore, this discussion will be limited to consideration of stress incontinence alone. In addition to the Cochrane review, newer RCTs and articles on theories of PFM efficacy found on computerized searches on Medline and Sport from 2000–2002 and hand searches of English language physical therapy journals during the same period were included.

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### **Theory 1: conscious PFM pre-contraction during physical stress (often termed "counterbracing" or "the Knack")**

Mantle [3] discusses a common technique termed "counterbracing" which is taught by physical therapists to prevent leakage during increases in abdominal pressure. The patient is taught to contract the PFM just ahead of physical stressors, and to hold the contraction throughout the stress, with the rationale being that the urethra and bladder base is thus prevented from descending. In addition, the PFM contraction squeezes around the urethra and increases the urethral pressure [27, 28, 29]. In Cochrane review studies of SUI alone, four of 34 RCTs reported that strength training was combined with counterbracing. In only one study was counterbracing the sole intervention [7].

In 1996 Miller et al. [30] named this voluntary counterbracing-type contraction the "Knack". In a single-blind RCT, subjects were taught to contract before and during a cough. No additional strength training regimen was performed. A paper towel test was used at baseline and after 1 week of performing the maneuver at home. The results showed that the "Knack" performed during a medium and deep cough reduced urinary leakage by 98.2 and 73.3%, respectively. Cure rate in "real life" was not reported.

Research on basic and functional anatomy supports the "Knack" as an effective maneuver to prevent leakage. Peschers et al. [31] evaluated ten nulliparous women by perineal ultrasound and EMG during coughing with and without a voluntary PFM contraction. Bladder neck descent was significantly less when women were asked to contract the PFM before cough (4.7 mm (SD 2.9) than when coughing without such contraction (8.1 mm (SD 2.9)). The authors concluded that the PFM voluntary contraction stabilizes the vesical neck during increases in abdominal pressure. Miller et al. [23] used perineal ultrasound to compare eleven young, continent nulliparous women with eleven older, incontinent parous women when subjects coughed with and without voluntary PFM contraction. Vesical neck mobility was significantly reduced from median 5.4 to 2.9 mm when voluntary contraction was performed.

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### **Commentary**

There is only one published RCT showing the effect of the "Knack" [30]. Neither bladder volume nor coughing force was standardized, and the assessors were not blinded. The measurement was made during cough only, and not during more complex and demanding activities. However, it is reasonable to assume that the results would be the same in other single-task activities where increases in abdominal pressure occur such as lifting, sneezing, jumping and sit-ups. The results of performing "the Knack" are

impressive and may help women who are able to correctly perform an effective PFM contraction.

An important question is how strong this voluntary contraction needs to be to prevent leakage. Bump et al. [27] demonstrated that 49% of women were not able to contract the PFM in a way that increased the urethral closure pressure. This may have been due to a weak contraction. Alternately, the PFM may have been too stretched, or located in a position too low to allow an effective contraction to occur. If the muscles are not strong enough or localized in a suboptimal position, simply telling women to contract may not be enough to cure or even improve their condition [24, 26].

On the other hand, if the PFM are in position, performing an effective “Knack” may be sufficient for some women to be “cured” or vastly improved. Sedentary women may only leak when coughing and sneezing. By learning this behavioral concept they may be able to stay dry or to significantly reduce their leakage. However, women who want to be physically active either for fitness or competitive sport are frequently exposed to much higher and more repetitive increases in abdominal pressures than those occurring during a single cough. The prevalence of SUI in young, nulliparous elite athletes is high [32, 33]. However, most athletes do not leak, despite the fact that the vertical ground forces occurring during provocative events like landing from a double back summersault are up to 14 times the body weight [34]. It can therefore be postulated that leakage may be due to individual and inherited differences in anatomical position of the pelvic floor, connective tissue composition, distribution of slow and fast twitch fibers, and cross-sectional area of the PFM. Further injuries to the pelvic floor during pregnancy and vaginal birth such as stretch and ruptures of muscle fibers, peripheral nerves, and connective tissue in ligaments and fascias may later add to genetic factors.

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## Theory 2: strength training

Kegel originally described PFM training as physiological training or “tightening up” the pelvic floor, and women were asked to contract the PFM 500 times per day to strengthen the muscles [35]. Modern exercise science provides an excellent foundation for understanding PFM training in the context of strength training.

Muscle strength is defined as the “maximum force which can be exerted against an immovable object (static or isometric strength), the heaviest weight which can be lifted or lowered (dynamic strength), or the maximum torque which can be developed against a pre-set rate limiting device (isokinetic strength) [36]. Muscle strength is strongly correlated to the cross-sectional area of the muscle (muscle volume) and neural factors such as the total number of activated motor units and frequency of excitation [37]. Other determinants of muscle strength include joint angle and lever arm, the relationship between length and tension, the relationship between force and velocity (force decreases as speed increases in concentric

contractions), and the metabolic component (rate of which myosin split ATP) [36]. As in other skeletal muscles, these components affect an individual’s PFM strength.

The aim of a strength training regimen in regular skeletal muscles is to change muscle morphology by increasing the cross-sectional area, improve neuromuscular function by increasing the number of activated motor neurons and their frequency of excitation, and to improve muscle “tone” [37]. Connective tissue is abundant within and around all skeletal muscles including the epimysium, perimysium, and endomysium. These connective tissue sheaths provide the tensile strength and viscoelastic properties (“stiffness”) of muscle and provide support for the loading of muscle [38]. There is evidence that physical activity and strength training can increase connective tissue mass, and that intensity of training and load bearing are major factors for effective training [38, 39, 40]. For effective muscle strengthening in skeletal muscles in adults, exercise physiologists recommend three sets of 8–12 slow velocity close to maximum contractions 2–4 days a week [41]. Maximal effect may not be achieved for 5 months [42]. The PFM are regular skeletal muscles and, therefore, recommendations for effective PFM training should be no different from that of other skeletal muscles.

The theoretical rationale for intensive strength training (exercise) of the PFM is that strength training may build up the structural support of the pelvis by elevating the levator plate to a permanent higher location inside the pelvis and by enhancing hypertrophy and stiffness of the PFM and connective tissue. This would facilitate a more effective automatic motor unit firing (neural adaptation), preventing descent during increase in abdominal pressure.

In the above-mentioned Cochrane review, 29 of the 34 RCTs on PFM training for female SUI used a protocol that focused solely on regular (that is, not high dose) strength training over time [7]. Only a few studies have differentiated between cure and improvement rates. However, cure rates, defined as  $\leq 2$  g of leakage on different pad tests, have been shown in RCTs [8, 9, 10, 11].

Just as with pharmaceutical therapy, there is a dose-response relationship in all forms of exercise training [43, 44]. The term “exercise dosage” includes the type of exercise, frequency, intensity, and duration of the training period [44, 45]. All of these factors, in addition to adherence to the training protocol, affect the final outcome. Intensity is defined as a certain percentage of maximum performance. For strength training, this is defined as percentage of one maximum contraction termed “one repetition maximum” (1 RM). In the RCTs evaluating the effect of PFM training on SUI, the number of contractions per day varied from 36 to 360, maximum length of the holding period (squeeze) varied between 4 s and 30–40 s, and the duration of the training period varied between 4 weeks and 6 months [7]. Unfortunately, the training protocols are often poorly described, but most do employ regular strength training and not simply pre-contraction during stressful activities

(the “Knack”) [7]. In most protocols the women are taught how to contract the PFM and then left alone to actually perform the training by themselves [7]. However, in some RCTs health care providers supervised the strength training in various ways.

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### Commentary

Because of the heterogeneity of patients, outcome measures, and training protocols, comparison between studies is difficult, and no conclusion can be drawn as to which PFM training protocol is the most effective to treat SUI [7]. Several RCTs have shown an increase in PFM strength after training [8, 11, 46]. However, only Bernstein et al. measured PFM volume before and after training [47]. In this uncontrolled study a significant increase in muscle volume after training was shown by ultrasound. Due to the lack of a control group, more research is needed to provide conclusive evidence that muscle hypertrophies after PFM training. None of the strength training studies to date have evaluated the effect of PFM training on PFM tone or connective tissue stiffness, position of the muscles within the pelvic cavity, their cross-sectional area or neurophysiologic function. Therefore, we cannot conclude whether such changes did occur.

PFM strength training programs have proven effective in preventing leakage during prolonged provocative physical activities such as running and jumping, during which participants were not instructed to contract the PFM voluntarily during exercise [8, 11, 46]. It seems unlikely, in fact, that one could continuously contract the PFM voluntarily during prolonged exercise, and thus one could postulate that morphological changes have occurred.

At this time, there have been two studies presented that compared the “Knack” with additional strength training programs [48, 49]. Miller et al. [48] showed in an uncontrolled study that urine loss was reduced significantly from 38% after 1 week, to 74% after 1 month of practicing the “Knack”. A further significant reduction to 82% was shown after adding 3 months of PFM strength training ( $p = 0.005$ ). In contradiction to this, Hay-Smith et al. [49] did not find any difference between women who had been randomized either to 5 months of the “Knack” or to a combination of the “Knack” and strength training. However, the strength training regimen used in the latter study had previously been shown to be significantly less effective than a more intensive training program. The training dosage may therefore not have been optimal [46].

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### Theory 3: indirect training of the PFM via abdominal muscle training

Sapsford [50] suggests that the PFM can be trained indirectly by training the transversus abdominis (TrA) muscle. This is based on an understanding that the PFM

are part of the abdominal capsule surrounding the abdominal and pelvic organs. The structures included in this capsule (often referred to as the “pelvic core”) are the lumbar vertebrae and deeper layers of the multifidus muscle, the diaphragm, the TrA and the PFM [50, 51].

Several studies have shown that different abdominal muscles co-contract during PFM contraction [14, 15, 16, 16, 18]. In addition, some studies have shown that there is a co-contraction of the PFM during different abdominal muscle contractions in healthy volunteers. Bø and Stien [15], using concentric needle EMG, found that there was a co-contraction of the PFM during contractions of the rectus abdominis in continent women. Sapsford and Hodges [52] found that PFM surface electromyography (EMG) increased with TrA contractions in six healthy females, and this was supported by a study of four continent women by Neumann and Gill [18]. In continent women, Sapsford et al. [53] found that a strong isometric abdominal contraction termed “hal- lowing,” in which the TrA and internal obliques are forcefully contracted, increased the urethral pressure as much as a maximal PFM contraction. Based on these findings, Sapsford [50] recommends that incontinence training should begin by training the TrA, rather than the PFM specifically.

To date there are no RCTs comparing the effect of indirect training of the PFM via TrA on stress incontinence with either untreated control, conscious pre-contraction of the PFM or strength-training groups. Dumolin et al. [54] compared PFM training with PFM training + TrA training, and did not find any further benefit of adding TrA training to the protocol.

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### Commentary

The recent recommendation to train the PFM indirectly through training the TrA muscles is based on results from small experimental studies with only continent subjects [18, 52]. These studies found some co-contraction of the PFM during different abdominal muscle contractions. Due to the few studies and the small sample sizes in each study, caution should be taken to generalize these findings to either continent or, particularly, incontinent women. Lack of co-contraction or inadequate timing of the co-contraction may be the crucial factor causing urinary leakage in women with SUI. Neumann and Gill [18] stated in their study that such co-activation of the PFM during abdominal muscle contraction should not be extrapolated to parous or symptomatic women. In support of the latter statement, an ultrasound study demonstrated that contracting of the TrA depressed (rather than elevated) the levator plate in 30% of healthy physical therapists [55]. Significant research is needed before this technique can be applied to women with damaged pelvic floors.

In addition, all the above mentioned studies, except one [15], used surface electrodes to measure PFM activity during different abdominal muscle contractions.

Surface EMG of the PFM has been criticized because of the possible influence of cross-talk from other muscles [56]. Hence, such studies must be interpreted with caution. Some argue, in support of TrA training, that contracting the TrA has been shown to increase urethral pressure [53]. However, contractions of the TrA increase abdominal pressure [51] and increases in abdominal pressure increase urethral pressure. The TrA itself has no direct anatomical connection to the urethra and can therefore not increase urethral pressure by direct contraction. In the above-mentioned study the researchers ensured that there was an inward movement of the perineum during contraction of TrA. Such a co-contraction has not been established in a wider population. Thus, data is currently too scant to support the contention that the increase in urethral pressure during TrA contraction is due to co-contraction of the PFM [55].

Danneels et al. [57] compared nonspecific low-load stabilization training of the back extensor muscles with stabilization training + specific strength training of the same muscles and found that only training that included specific strength training of the target muscle groups increased the cross-sectional area of the muscles. They concluded that intensive resistance training of the targeted muscle group is necessary to restore the size of the muscles in patients with atrophy. Hence, training the PFM indirectly via TrA does not seem to have any support in the general exercise science literature.

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## General Discussion

Antonovsky [58] suggested that to understand pathophysiology and illness, we need to study healthy subjects. It is unlikely that continent young athletes or nulliparous women in general think much about or have ever learned about contracting the PFM, or that they consciously contract the PFM during increases in abdominal pressure. In addition, it does not seem to be possible to contract the PFM continuously and actively during most activities of daily living. Women would not be able to participate in popular female fitness activities such as tennis, dancing, aerobics or jogging if they needed to contract the PFM continuously before each step or move to prevent leakage. Therefore, the optimal outcome of a PFM training program is to reach the automatic (unconscious) co-contraction level present in continent women.

An important question is whether PFM rehabilitation programs first need to focus on the pre-contraction during physical stressors in order to eventually obtain an automatic PFM co-contraction during increases in abdominal pressure. Some authors suggest that this is one way to build automatic function [3]. On the other hand, it has long been known that there are differences in reflex responses in trained and untrained individuals. In a study measuring EMG activity in the quadriceps muscle, untrained subjects responded with a period of inhibition when jumping down to the floor from a height

of 110 cm, whereas a trained jumper responded with a period of facilitation during the eccentric phase in the knee extensors [59]. It has been assumed that the degree of reflex potentiation is correlated with the degree of motor unit activation achieved by voluntary effort. Indeed, enhanced motor unit synchronization has been shown in weightlifters and others who perform maximum strength training regimens [59]. Hence, one could postulate that building up muscle strength and changing muscle morphology (via permanent elevation of the levator plate into a higher location inside the pelvis, increasing muscle volume, strengthening connective tissue in the muscles, strengthening bony connections, and more effectively recruiting motor neurons) may lift and “tighten” the structural base made up by the pelvic floor, thus making an automatic co-contraction possible. When a correct PFM contraction is learned, and the structural base is built up, combinations of the TrA and the PFM may be one way to increase progression and enhance automatic function.

Based on studies in the general strength training literature, intensity seems to be the most important factor in developing muscle volume and strength. Very few close to maximum contractions is used by power and Olympic lifters to optimize strength and power in skeletal muscles [41]. In a recent meta-analysis to determine the dose response for strength development in skeletal muscles in general, it was concluded that there seems to be a different response based on the training status of the participants [60]. Training with an intensity of 60% of one repetition maximum (1 RM) seems to be sufficient in untrained individuals, whereas 80% is required in those who are trained. Untrained individuals need to train 3 days per week, whereas 2 days seem to be sufficient for trained subjects. Four sets elicited maximal gains in both untrained and trained individuals [60]. Similarly, several studies have concluded that higher dosage of PFM training is more effective in treating SUI [46, 61, 62].

Several research groups have looked into the long-term effect of PFM training for SUI [7]. However, as concluded by Hay-Smith et al. [7], follow-up data have been difficult to interpret. Some studies followed up only on one of the comparisons groups, reported results for the whole cohort rather than by group allocation, or had difficulty tracing an adequate proportion of the original sample. In addition, there are only few studies that included clinical assessment. However, in a study that followed women who completed a supervised PFM training program 5 years later, 70% were still exercising at least once a week and 70% had no leakage on coughing [63]. Cammu et al. [64] showed that only two patients (8%) of those being successfully treated after a PFM training program had undergone surgery 10 years later. Interestingly, although initially during the supervised PFM training women had performed both PFM strength training and pre-contraction of the PFM equally frequently, pre-contraction seemed to be more popular in the long term.

The belief that PFM training must be done throughout life to sustain results has been used as an argument against the method. Many health professionals argue that women are not motivated to start PFM training because they believe they need to train intensively for the rest of their life. However, in fact strength training changes PFM morphology and position, the muscles may start to act automatically during rises in abdominal pressure in the same way as they seem to do in continent women [65], and this pre or co-contraction may be sufficient to maintain strength. In addition, exercise science studies have shown that much less effort is needed to maintain than to build muscle strength [66]. Intensity of the contraction seems to be the most important factor both in building up and maintaining muscle strength, and a frequency of training of two times per week is sufficient to maintain strength [66, 41].

In contrast to the need for a strong maximum contraction to build up muscle strength, the automatic co-contraction needed for everyday life once a structural base is built up may require less strength than timing [50, 65]. Compared with a strong voluntary contraction, this co-contraction is barely perceived, and may be due to the PFM being located in an optimal anatomical location. However, some women need stronger support than others, e.g. weight lifters, gymnasts and others performing heavy lifting, strenuous work, and high-impact activities. Again, if the structural support is optimally located inside the pelvis and the connective tissue is strong, only a little downward movement will occur during a rise in abdominal pressure: the PFM is “stiff” and the urethra and bladder base is kept in place [26].

## Conclusion

Basic research and RCTs support the theoretical rationales for conscious pre-contraction of the PFM before and during stressful situations and strength training regimens to treat SUI. At this time, there is little support for indirect training of the TrA, and this should therefore not be recommended. To optimize the effect of PFM training, women with SUI should be taught both to pre-contrast before rises in abdominal pressure and to strength train their PFM. Most likely the two systems have a common base in the pelvic floor acting as a structural base, stabilizing the bladder and urethra during increases in abdominal pressure. To be able to produce an effective voluntary or automatic contraction during increases in abdominal pressure, the PFM most likely need to be situated at a specific location inside the pelvis.

Optimally, women would reach a level where the PFM contractions act automatically whenever needed. Future studies are needed to assess whether PFM strength training can lift a sagging, stretched and weak pelvic floor into a more optimal position where it can counteract the rise in abdominal pressure. In order to achieve such measurable effects, most likely a high-dosage strength-training program is needed. To date no

studies have evaluated structural changes, proprioception changes, or changes in speed of an automatic PFM contraction after training. Such studies are warranted, and in the future, EMG, ultrasound and MRI studies may improve our understanding of how PFM training can cure SUI. A careful study of the mechanism of PFM training will allow us to tailor training programs to the individual woman in the future, and thus enable more women to benefit from this therapy. Until then, the current evidence-based recommendations outlined above should be followed.

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