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The research reported in this issue of the journal was commissioned by the HTA programme as project number 06/41/02. The contractual start date was in July 2007. The draft report began editorial review in March 2009 and was accepted for publication in October 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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# Abstract

## Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence

M Imamura,[1,2] P Abrams,[3] C Bain,[4] B Buckley,[5] L Cardozo,[6] J Cody,[7] J Cook,[1] S Eustice,[8] C Glazener,[1,7] A Grant,[9] J Hay-Smith,[7,10] J Hislop,[1] D Jenkinson,[1] M Kilonzo,[11] G Nabi,[2] J N'Dow,[2,7] R Pickard,[12] L Ternent,[1,11] S Wallace,[7] J Wardle,[13] S Zhu[1] and L Vale[1,11]*

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**Objectives:** To assess the clinical effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence (SUI) through systematic review and economic modelling.
**Data sources:** The Cochrane Incontinence Group Specialised Register, electronic databases and the websites of relevant professional organisations and manufacturers, and the following databases: CINAHL, EMBASE, BIOSIS, Science Citation Index and Social Science Citation Index, Current Controlled Trials, ClinicalTrials.gov and the UKCRN Portfolio Database.
**Study selection:** The study comprised three distinct elements. (1) A survey of 188 women with SUI to identify outcomes of importance to them (activities of daily living; sex, hygiene and lifestyle issues; emotional health; and the availability of services). (2) A systematic review and meta-analysis of non-surgical treatments for SUI to find out which are most effective by comparing results of trials (direct pairwise comparisons) and by modelling results (mixed-treatment comparisons – MTCs). A total of 88 randomised controlled trials (RCTs) and quasi-RCTs reporting data from 9721 women were identified, considering five generic interventions [pelvic floor muscle training (PFMT), electrical stimulation (ES), vaginal cones (VCs), bladder training (BT) and serotonin–noradrenaline reuptake inhibitor (SNRI) medications], in many variations and combinations. Data were available for 37 interventions and 68 treatment comparisons by direct pairwise assessment. Mixed-treatment comparison models compared 14 interventions, using data from 55 trials (6608 women). (3) Economic modelling, using a Markov model, to find out which combinations of treatments (treatment pathways) are most cost-effective for SUI.
**Data extraction:** Titles and abstracts identified were assessed by one reviewer and full-text copies of all potentially relevant reports independently assessed by two reviewers. Any disagreements were resolved by consensus or arbitration by a third person.
**Results:** Direct pairwise comparison and MTC analysis showed that the treatments were more effective than no treatment. Delivering PFMT in a more intense fashion, either through extra sessions or with

biofeedback (BF), appeared to be the most effective treatment [PFMT extra sessions vs no treatment (NT) odds ratio (OR) 10.7, 95% credible interval (CrI) 5.03 to 26.2; PFMT + BF vs NT OR 12.3, 95% CrI 5.35 to 32.7]. Only when success was measured in terms of improvement was there evidence that basic PFMT was better than no treatment (PFMT basic vs NT OR 4.47, 95% CrI 2.03 to 11.9). Analysis of cost-effectiveness showed that for *cure rates*, the strategy using lifestyle changes and PFMT with extra sessions followed by tension-free vaginal tape (TVT) (lifestyle advice–PFMT extra sessions–TVT) had a probability of greater than 70% of being considered cost-effective for all threshold values for willingness to pay for a QALY up to £50,000. For *improvement rates*, lifestyle advice–PFMT extra sessions–TVT had a probability of greater than 50% of being considered cost-effective when society's willingness to pay for an additional QALY was more than £10,000. The results were most sensitive to changes in the long-term performance of PFMT and also in the relative effectiveness of basic PFMT and PFMT with extra sessions.

**Limitations:** Although a large number of studies were identified, few data were available for most comparisons and long-term data were sparse. Challenges for evidence synthesis were the lack of consensus on the most appropriate method for assessing incontinence and intervention protocols that were complex and varied considerably across studies.

**Conclusions:** More intensive forms of PFMT appear worthwhile, but further research is required to define an optimal form of more intensive therapy that is feasible and efficient for the NHS to provide, along with further definitive evidence from large, well-designed studies.

# Contents

# List of abbreviations

| | |
|---|---|
| BF | biofeedback |
| b.i.d. | twice daily |
| BT | bladder training |
| CI | confidence interval |
| CrI | credible interval |
| DO | detrusor overactivity |
| EMG | electromyography |
| ES | electrical stimulation |
| GP | general practitioner |
| GSI | genuine stress incontinence |
| HRQoL | health-related quality of life |
| HTA | Health Technology Assessment |
| ICER | incremental cost-effectiveness ratio |
| ICIQ-UI SF | International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form |
| IDO | idiopathic detrusor overactivity |
| IEF | incontinence episode frequency |
| IFT | interferential therapy |
| I-QoL | Urinary Incontinence Quality of Life Scale |
| LS | lifestyle advice |
| MTC | mixed-treatment comparison |
| MUI | mixed urinary incontinence |
| NA | not applicable |
| NHS | National Health Service |
| NICE | National Institute for Health and Clinical Excellence |
| NR | not reported |
| NS | not statistically significant |
| NT | no treatment |
| OR | odds ratio |
| PFMT | pelvic floor muscle training |
| PFMT basic | PFMT, delivered with up to two sessions or contacts with a health-care professional per month |
| PFMT extra sessions | PFMT, delivered with more than two sessions or contacts with a health-care professional per month |
| PGI | Patient Generated Index |
| QALY | quality-adjusted life-year |
| q.d. | once daily |
| RCT | randomised controlled trial |
| SD | standard deviation |
| SIGN | Scottish Intercollegiate Guidelines Network |
| SMD | standardised mean difference |
| SNRI | serotonin–noradrenaline reuptake inhibitor |
| SUI | stress urinary incontinence |
| TVT | tension-free vaginal tape |
| TVT-O | tension-free transobturator vaginal tape |
| USI | urodynamic stress incontinence |
| UUI | urgency urinary incontinence |
| VC | vaginal cone |
| VPFMC | voluntary pelvic floor muscle contraction |

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

# Executive summary

## Description of proposed service

The treatment options for stress urinary incontinence (SUI) can be classified as non-surgical and surgical. Lifestyle changes, such as weight loss, smoking cessation, etc. may reduce the risk of leakage but all need continued adherence. Non-surgical interventions, such as pelvic floor muscle training (PFMT), biofeedback (BF), electrical stimulation (ES), bladder training (BT), vaginal cones (VCs), etc., may also require long-term adherence to the taught programmes in order to produce continued benefit. However, these interventions have few adverse events compared with surgical treatment. Alternatively, the leakage can be contained using absorbent pads, an indwelling urinary catheter or, very rarely, urinary diversion.

## Epidemiology and background

Stress urinary incontinence is the involuntary leakage of urine associated with effort or exertion, or on sneezing or coughing. Some women may also have symptoms of urge incontinence (a sudden compelling desire to pass urine, which is difficult to defer). Estimates of prevalence suggest that over 30% of women aged ≥ 40 years have SUI. The annual incidence increases with age (aged > 65 years, annual incidence rates ≈ 9%).

## Objective

This study aimed to assess the clinical effectiveness and cost-effectiveness of non-surgical treatments for women with SUI.

## Methods

The work comprised three distinct elements: (1) a survey of women with SUI to identify outcomes of importance to them [using a Patient Generated Index (PGI)]; (2) a systematic review and a meta-analysis of non-surgical treatments for SUI to find out which are most effective [this was done in two ways, by comparing results of trials (direct pairwise comparisons) and by modelling results (mixed-treatment comparisons, MTCs)]; and (3) economic modelling of non-surgical and surgical treatments for SUI to find out which combinations of treatments (treatment pathways) are most cost-effective.

The survey identified areas of importance to women who suffer from SUI, using a PGI. A total of 188 women were invited to take part.

Literature searching included the Cochrane Incontinence Group Specialised Register (last searched March 2008), electronic databases (1980 to March 2008) and the websites of relevant professional organisations and manufacturers. Randomised controlled trials (RCTs) and quasi-RCTs (alternate allocation) were eligible. Random effects models were used to derive summary estimates with 95% confidence intervals (CIs) or credible intervals (CrIs) of the odds ratio (OR) for dichotomous variables and standardised mean difference (SMD) for continuous variables (direct pairwise comparison only).

To compare the cost-effectiveness of the treatment pathways, a Markov model was used. The model was developed using data from the review of effectiveness and data on resource use systematically identified as being relevant to the UK National Health Service (NHS). The model estimated cost and quality-adjusted life-years (QALYs) for a 40-year time horizon. Discounting at 3.5% was performed, as was deterministic and probabilistic sensitivity analysis.

## Results

### Survey

Overall, 38 different areas were reported by respondents on the PGI. These areas were divided into four themes: activities of daily living; sex, hygiene and lifestyle issues; emotional health; and the availability services.

### Number and risk of bias in studies included in the systematic review

A total of 88 trials reporting data from 9721 women were identified, considering five generic interventions [PFMT, ES, VCs, BT and serotonin–noradrenaline reuptake inhibitors (SNRI) medications], in many variations and combinations. PFMT data were split into PFMT basic (fewer than two sessions of training per month) and PFMT with extra sessions (more than two sessions per month). Data were available for 37 interventions and 68 treatment comparisons by direct pairwise assessment. Mixed-treatment comparison models compared 14 interventions, using data from 55 trials (6608 women). Included studies were generally small and had short follow-up periods. Fourteen studies (16%) reported both adequate random allocation sequence generation and concealment.

### Summary of clinical effectiveness

The direct pairwise comparison analysis and the MTC analysis showed that the treatments were, on average, more effective than no treatment. Delivering PFMT in a more intense fashion, either through extra sessions (more than two per month) or with BF, appears to be the most effective treatment [PFMT extra sessions vs NT odds ratio (OR) 10.7, 95% CrI 5.03 to 26.2; PFMT + BF vs NT OR 12.3, 95% CrI 5.35 to 32.7]. Only when success was measured in terms of improvement was there evidence that PFMT basic was better than no treatment (PFMT basic vs NT OR 4.47, 95% CrI 2.03 to 11.9). Adverse events were uncommon except for SNRI medication.

### Costs

The perspective adopted for the analysis is that of the UK NHS. The total costs for each intervention over a 3-monthly period (the cycle length of the Markov model) were lifestyle changes £27, PFMT basic £189, PFMT with extra sessions £351, drug therapy £164, tension-free vaginal tape (TVT) £1135, colposuspension £1396 and containment products £39.

Using cure rates, a strategy of lifestyle changes and PFMT with extra sessions followed by TVT was the least costly (£1644) and the most effective (16.20 QALYs). The strategy that had lifestyle changes followed by TVT (LS–TVT) was the most costly (£1973).

Using improvement rates, the strategy LS–PFMT basic–PFMT extra sessions–TVT was the least costly (£1795). The strategy LS–TVT was the most costly (£2425).

### Quality-adjusted life-years

Using cure rates, the strategy that used lifestyle changes and PFMT basic, followed by PFMT with extra sessions, followed by SNRI and then TVT (LS–PFMT basic–PFMT extra sessions–SNRI–TVT), was the least effective (15.89 QALYs).

Using improvement rates, the strategy LS–PFMT extra sessions–TVT was the most effective (16.37 QALYs). The strategy LS–TVT was the least effective (16.2 QALYs) (and, as noted above, the most costly).

### Cost-effectiveness

For cure rates, the strategy using lifestyle changes and PFMT with extra sessions followed by TVT (LS–PFMT extra sessions–TVT) had a probability of greater than 70% of being considered cost-effective for all threshold values for willingness to pay for a QALY of up to £50,000.

For improvement rates, LS–PFMT extra sessions–TVT had a probability of greater than 50% of being considered cost-effective when society's willingness to pay for an additional QALY was more than £10,000.

### Sensitivity analysis

The results were most sensitive to changes in the long-term performance of PFMT and also in the relative effectiveness of PFMT basic and PFMT with extra sessions. The results were not sensitive to plausible changes in the structure of the model (use of containment products instead of using an active treatment, introduction of vaginal cones and ES into treatment strategies). The results were also insensitive to plausible changes in the age of women, time horizon, discount rates, quality-of-life estimates, and mortality from surgery.

## Limitations of the calculations

Few data were available for most comparisons and a pragmatic decision was made to include women with urgency urinary incontinence (UUI) symptoms, but only if the proportion of women

with UUI was less than 50% of the study sample. The definitions of outcomes differed between studies and the interventions were varied in terms of the precise nature of the exercise as well as the duration of therapy.

All of these results need to be considered cautiously as very few data were available for interventions. The 95% central CrIs for these interventions are very wide and indicate that we know very little about their relative effectiveness. There were few long-term data for any of the therapies. These data are important determinants of cost-effectiveness, yet little is known about how quickly symptoms might return.

## Other important issues regarding implications

There may not be sufficient trained therapists to provide the potentially more effective and cost-effective intensive non-surgical treatments. For the use of these therapies to increase, staff would need to be recruited, trained and retained.

Within all of the analyses, the preferences of women for the process of care have not been considered. Women are likely to have preferences about who provides the care, where the care is provided, and what risks and costs they face themselves.

The value of the non-surgical treatments depends upon its ability to maintain women's long-term adherence to therapy. How this might be achieved in practice will involve a complex interplay of factors, including who provides the therapy, how it is provided, for how long, the preferences of women, and so on. These issues could not be fully explored in this study because of the limited evidence base.

## Implications for practice

Non-surgical treatments for SUI in women are effective and could potentially be cost-effective, but a judgement is required as to whether the benefits are worth the cost.

There is clear evidence that PFMT plus BF and PFMT with extra sessions was effective. Several other treatments (PFMT plus BT and BF; PFMT plus BF and VCs or ES) are promising, but there is insufficient evidence to recommend their routine use.

There is no evidence that PFMT basic is any better than no treatment in terms of cure, although it does improve symptoms compared with no treatment.

The cost-effectiveness of the non-surgical treatments is dependent upon whether their short-term effectiveness is sustained.

## Recommendations for further research

Conclusions are based on data from a limited number of small trials.

More intensive forms of PFMT appear worthwhile, but research is required to define an optimal form of more intensive therapy that is feasible and efficient for the NHS to provide.

Further definitive evidence from large, well-designed studies is required in order to provide a definitive answer.

Any further research on long-term outcomes, benefit assessment or costs should be incorporated into an updated economic evaluation, as and when it becomes available.

If an effective and efficient follow-up regimen can be developed, then the incentives/disincentives faced by NHS providers may need to be reconsidered to aid its implementation.

# Chapter 1
# Background

## Description of underlying health problem

### Continence mechanisms in health

Efficient mechanisms have evolved to ensure reliable urine storage and complete bladder emptying at socially convenient times. Mechanisms that prevent urine leakage involve the bladder, the urethra and the pelvic floor muscles, together with their controlling nerve pathways. The bladder is a highly compliant organ, allowing the storage of increasing quantities of urine without rise in pressure, a property underpinned by passive stretch and active relaxation of its smooth muscle (detrusor). Active central nervous control mechanisms in the pons and cerebrum inhibit detrusor contraction despite increasing sensation of bladder fullness until micturition is appropriate. Urethral mechanisms promoting continence are less well understood, but are thought to involve tonic contraction of smooth muscle in the urethral wall, together with a tight seal formed by the urethral lining (mucosa) and the highly vascular submucosal layer. Contraction of the pelvic floor striated muscles acts as an additional guarding mechanism, compressing the urethra and preventing leakage during actions that raise intra-abdominal pressure.

These features maintain continence during the storage phase of the micturition cycle by ensuring that bladder pressure is always lower than urethral closure pressure. Incontinence is therefore likely to result from deficiency of urethral closure mechanisms and/or involuntary detrusor activity, aggravated by factors that chronically increase intra-abdominal pressure. In general, maximal urethral closure pressure is higher in men and therefore incontinence is far more prevalent amongst women, who are the target population for this review.[1]

### Definition of urinary incontinence

The symptom of urinary incontinence is defined as the involuntary leakage of urine,[2,3] and this can be subcategorised qualitatively according to the patient's description (*Box 1*).

This symptom categorisation[2,3] is based on a detailed history and provides a useful basis for discussion of the problem with the patient, identification of patient-centred treatment goals and initiation of treatment pathways.

When the patient first reports the problem to a clinician it is usual for the clinician to define possible causative factors and commonly associated problems by further questioning, physical examination and performance of simple tests. The severity of incontinence and the degree of bother it causes the individual can be estimated by appropriate direct questioning, including pad usage, or can be quantified more objectively using validated symptom scores[4] or bladder diaries.

Further categorisation of incontinence according to the underlying functional or anatomical cause requires simultaneous measurement of bladder and rectal pressure, together with observation of urine loss during bladder filling. This invasive clinical test, filling cystometry, requires catheterisation of the bladder and is therefore generally performed only when more accurate categorisation is required, for example prior to surgical treatment in women with MUI. This test will differentiate urodynamic stress incontinence (USI) due to bladder outlet weakness from detrusor overactivity (DO) incontinence due to involuntary contraction of the bladder muscle (*Box 2*).

***BOX 1*** *Symptom categories of urinary incontinence*

***Stress urinary incontinence (SUI)***
Involuntary leakage of urine associated with effort or exertion, or on sneezing or coughing

***Urgency urinary incontinence (UUI)***
Involuntary leakage of urine accompanied, or immediately preceded, by urgency, which is a sudden compelling desire to pass urine that is difficult to defer

***Mixed urinary incontinence (MUI)***
When complaints of both SUI and UUI coexist

***BOX 2*** *Urodynamic diagnostic categorisation of urinary incontinence*

***Urodynamic stress incontinence (USI)***
Involuntary leakage of urine during increased abdominal pressure in the *absence* of a detrusor contraction

***Detrusor overactivity (DO) incontinence***
Leakage of urine due to an involuntary detrusor contraction

***BOX 3*** *Variables used as primary outcome measures in trials of treatment of stress urinary incontinence*

***Patient defined***
Self-report of outcome or change in symptom score

***Quantified***
Change in reported episodes on bladder diaries
Weight of urine loss during exercise pad tests

***Clinician defined***
Direct observation of urine loss
Cystometric diagnosis

***Quality of life defined***
Change in generic ratings, such as EQ-5D
Change in condition-specific ratings, such as King's Health Questionnaire

The test may be accompanied by radiographic visualisation of the bladder outlet to qualitatively subcategorise USI according to the degree of descent of the bladder neck on coughing (hypermobility) or loss of the sealing mechanism of the urethra (intrinsic sphincter deficiency). The diagnostic and prognostic usefulness of this additional imaging, together with related indices such as abdominal leak point pressure, is uncertain and currently not recommended for routine use by the International Continence Society.[2]

Most people complaining of the symptom of SUI will have USI, which is demonstrable on cystometry, and this can be aggravated by conditions that chronically raise abdominal pressure, such as obesity and chronic obstructive pulmonary disease. In approximately 10–20% of cases, however, the symptom of SUI can result from DO provoked by coughing, for example, or from loss of bladder compliance due to fibrosis or neurological disease (low bladder compliance). It should therefore be noted that the symptom of stress incontinence does not always relate to weakness of the bladder outlet or urethral closure mechanism.

Practical definition of incontinence for outcome purposes requires a variable that can be measured before and after treatment. This presents a particular problem for evidence synthesis, as there is a lack of consensus on the most appropriate method, with a variety of variables being used to define improvement or cure (*Box 3*). It is also recognised that these variables may not capture outcomes of prime importance to individual women suffering SUI.

# Epidemiology and natural history

## Prevalence

Prevalence estimates vary depending on population sampled, definition of incontinence, severity threshold and survey methodology.[5] A recent longitudinal study from one county in the UK surveyed a random sample of over 15,000 community-dwelling individuals aged ≥ 40 years and found prevalences of 34% in women and 14% in men.[6] These data were in line with prevalence rates among adults living in the UK, summarised from previous studies, showing a mean (range) of 40% (2–69%) for women and 10% (2–25%) for men.[7] These ranges were consistent with findings from other developed countries, which documented rates of 10–72% for women and 3–20% for men.[7]

The EPINCONT study surveyed over 34,000 community-dwelling Norwegian women and found that the prevalence of urinary incontinence increased during young adult life, reached a broad peak between the ages of 45 and 55 years, and then showed a further steady increase in the elderly (*Figure 1*).[8–12] This study also found that about one-quarter of women with incontinence rated it as severe, a proportion in line with previous reports.[13]

This study also provided differential prevalence rates for symptoms of stress, urge and mixed incontinence.[10] Overall, SUI was the most common type, experienced by 50% of incontinent women, whereas 11% reported urgency incontinence alone and 36% reported mixed symptoms (*Figure 1*). The pattern does vary, however, according to age group, with SUI alone being most frequently reported in women who are younger than 50–55 years, after which urgency incontinence is reported most often, either alone or in combination, possibly reflecting

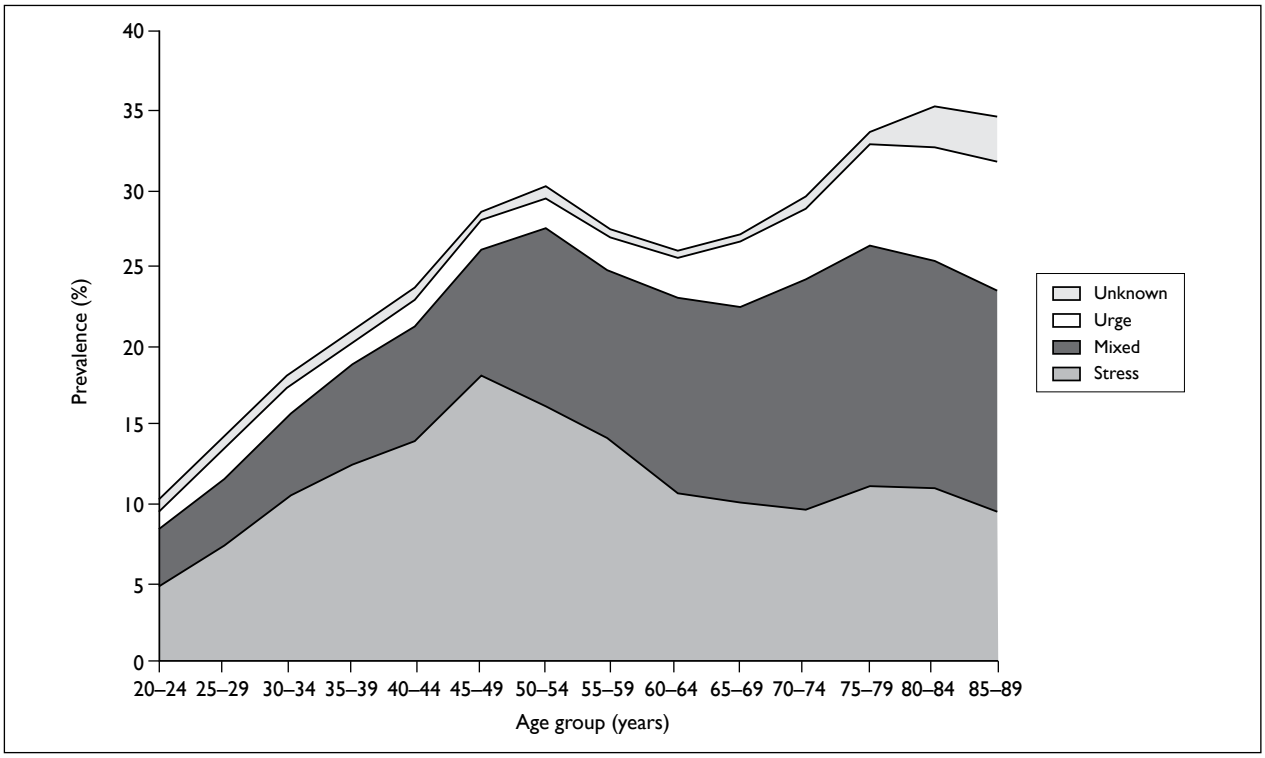



***FIGURE 1*** *Prevalence of female urinary incontinence by age group and symptomatic type of incontinence. Compiled from data in Hannestad and colleagues (2000).*[8]

menopausal status.[12] This pattern was also found in a large cross-sectional European study using validated questionnaires, for which SUI was most often reported by women under 60 years old.[11] Overall prevalence rates for urinary incontinence amongst older women who are living in supported accommodation are usually much higher, reaching 40–50%.[14]

This high community prevalence does not tend to lead to equivalent rates of consultation with a clinician. Studies estimate that only 15% of the women identified as suffering from SUI in cross-sectional surveys have consulted a health professional about the problem.[15,16] The reasons for this are unclear but may relate to social class, mild symptoms, lack of bother, embarrassment, disinclination towards treatment options and perceived lack of effective treatment.[17]

## Natural history

In comparison with the many cross-sectional prevalence surveys, fewer longitudinal studies have examined the incidence and remission of urinary incontinence symptoms. One study followed a large cohort of community-dwelling middle-aged women (mean age 46 years) for 2 years and documented an average annual incidence of new incontinence of 9%.[18] The incidence increased with age, with the majority reporting mild, non-disabling leakage (*Figure 2*). Subanalysis of type of incontinence showed an annual incidence of frequent or severe stress incontinence of about 2% (*Figure 3*). This study also documented a 7% annual remission rate among those women reporting urinary incontinence at baseline. Similar results were found from a cohort of older, postmenopausal women (mean age 64 years), followed for 2 years, and a further large cohort study of women aged > 65 years, with rates of annual incidence for SUI of 9% and 9.5%, respectively, and annual remission rates of 7% and 8%, respectively.[19,20]

A number of studies have reported questionnaire follow-up of numerically smaller cohorts of younger women (mean age 26–30 years) before and after their first vaginal delivery and reported the annual incidence of new urinary incontinence to be 5%, 1% and 4% over periods of 4, 10 and 12 years, respectively.[21–23]

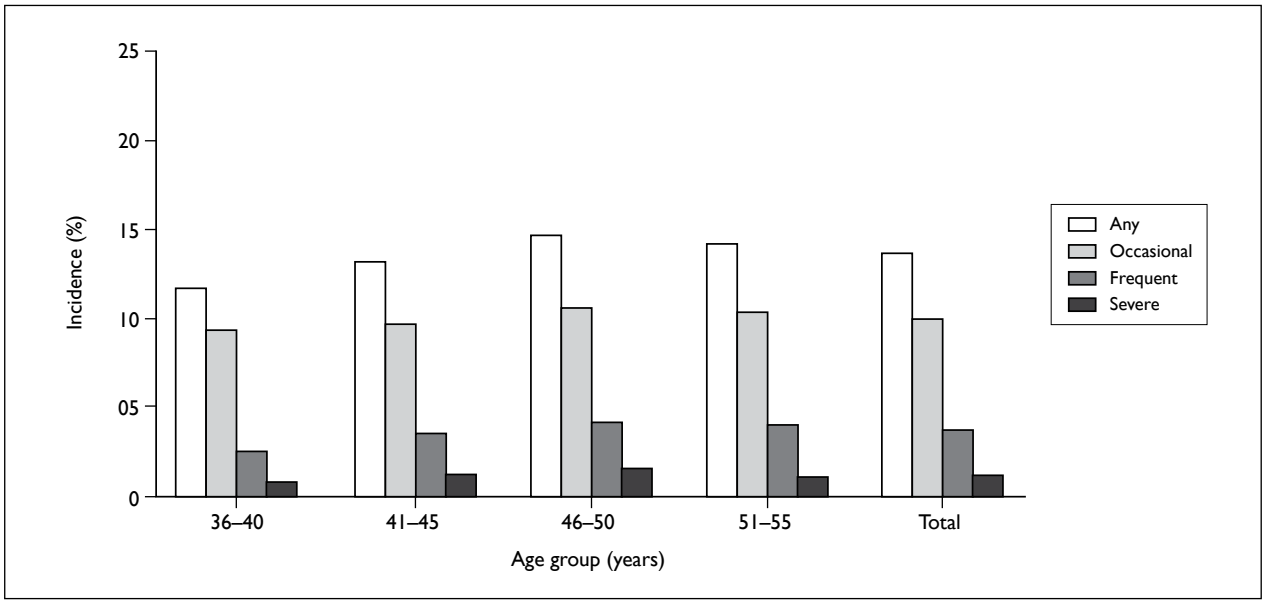



***FIGURE 2*** *Two-year incidence of urinary incontinence by severity. Based on a cohort of 33,952 American women. Any incontinence defined as leaking at least once per month; occasional incontinence defined as leaking one to three times per month; frequent incontinence defined as leaking at least once per week; severe incontinence defined as frequent leaking of quantities at least enough to wet the underwear. Adapted from Townsend and colleagues (2007).*[18]

## Factors associated with SUI

The main risk factors for female SUI are pregnancy, vaginal delivery, increasing parity, increasing age, obesity and postmenopausal status.[24–26] In older women, particularly those requiring social care, age-related changes to the lower urinary tract (such as reduced bladder capacity) and comorbidity in other organ systems (such as cardiac or cognitive impairment treated with drugs such as diuretics) can precipitate or worsen incontinence. Consideration of these multiple factors, together with the increasing preponderance of mixed urgency and stress incontinence symptoms, makes effective management of the problem in the elderly more difficult.[14]

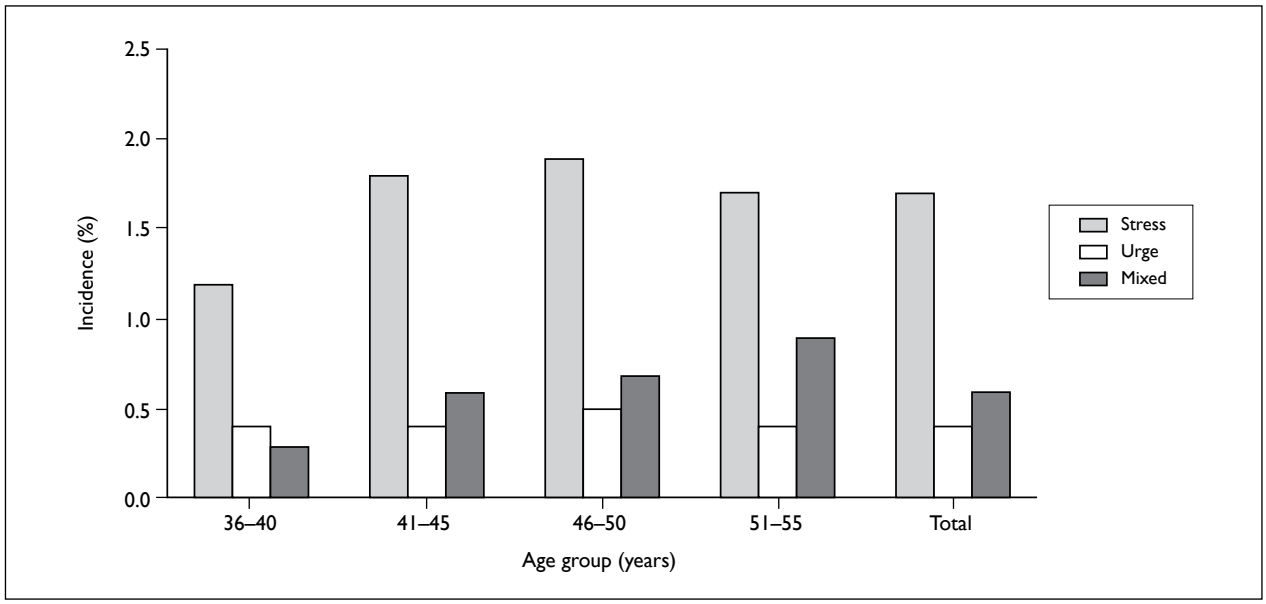



***FIGURE 3*** *Two-year incidence of frequent (at least once weekly) urinary incontinence by incontinence type. Cases of incident frequent incontinence; missing data on incontinence type symptoms are excluded from these calculations. Adapted from Townsend and colleagues (2007).*[18]

#### *Postpartum SUI*

Childbearing is the main predisposing factor that is specific for SUI, although the exact mechanism of pelvic floor injury that contributes to the development of outlet weakness during pregnancy and vaginal delivery is unclear.[26,27] Longitudinal studies have reported that two-thirds of women with SUI during their first pregnancy continue to have symptoms at a follow up of 15 years. Having antenatal SUI doubles this risk.[28] Immediately after childbirth women may expect to have higher levels of incontinence, which can often resolve spontaneously over the first 6 months. As this natural resolution might confound the effect of any intervention, data from trials in women in the immediate postpartum period were not included in the main body of the systematic review or in the cost-effectiveness analysis (results are reported in Appendix 20).

#### *Other risk factors*

In a large population-based cross-sectional study of premenopausal women, high body mass index (BMI > 30), diabetes mellitus and previous urinary incontinence surgery were identified as significant risk factors for severe SUI.[29] A history of gynaecological surgery for prolapse increased the risk of developing stress leakage over twofold, and hysterectomy and other gynaecological procedures also doubled the risk.[30,31]

## Significance in terms of ill health

### Effect on well-being

Embarrassment associated with urinary incontinence may cause withdrawal from social situations and reduce quality of life.[32] Women with a severe or frequent problem find the leakage distressing and socially disabling. They may avoid going away from home, using public transport and sexual activity.[33] SUI does not generally lead to deterioration in physical health but can be associated with depression and other psychological morbidity.[33] The problem may also lead to withdrawal from regular physical activities, potentially harming general health.[34]

### Extent of problem in the UK

Assuming an overall prevalence for SUI of 15% among women aged over 20 years, it can be estimated that there are 3.3 million sufferers in the UK.[35]

### Cost to society

The high prevalence of urinary incontinence results in a high overall cost of treatment and containment. Precise cost is difficult to define but a recent study suggested an estimated figure for combined health care, personal and societal expenditure of £248 per person per year in the UK, which would equate to a total annual cost of £818M for SUI.[36] A further estimate, assuming that SUI accounts for 50% of cases, suggested a health care cost to the UK National Health Service (NHS) of £117M per year.[37]

## Description of interventions

The treatment options for SUI can be classified as non-surgical and surgical. Lifestyle changes, such as weight loss, smoking cessation, control of chronic obstructive pulmonary disease, timed voiding and oral fluid management, may reduce risk of leakage but all need continued adherence to the required adjustments in order to maintain response. Specific non-surgical interventions, such as pelvic floor muscle training and biofeedback (BF), also require long-term adherence to the taught programmes in order to produce continued benefit. However, these interventions have few or no adverse events. Surgical treatment, on the other hand, may have a higher rate of benefit but has a greater risk of complications.[38] Alternatively, the leakage can be contained using absorbent pads, an indwelling urinary catheter or, very rarely, urinary diversion.

The choice of treatment depends on patient preference and professional advice and will take into account factors, such as symptom severity, degree of interference with lifestyle, presence of related problems and degree of comorbidity. The importance of patient preference as the primary consideration in selecting a particular treatment for SUI was underlined by the findings of a recent survey which reported that most preferred less invasive treatment and management options.[39] From a health service perspective it is important to balance short- and long-term efficacy against potential adverse events and costs.

### Existing guidelines

Epidemiological studies consistently demonstrate that proportionally few women who experience urinary leakage approach clinicians for advice and treatment.[15,16] It is likely that most women first seek advice from family, friends and the media and, for individually varying reasons, decide to manage

the problem themselves. Those who present their problem to health-care professionals tend to have more severe symptoms, which cause interference to their social activities and they are therefore generally seeking active treatment. Most countries, such as the UK, have attempted to standardise the assessment and initial management of women with incontinence by publication of consensus documents and guidelines.[40–44] Despite this, uniformity of care remains lacking and will depend on individual clinician opinion and local service provision.

## Current UK NHS care pathway

In the UK, the first port of call is likely to be the general practitioner (GP – primary care physician). An initial assessment will document the severity of the problem and the degree to which it bothers the women, and make sure that there are no more immediate health-threatening problems. Lifestyle advice, such as smoking cessation and weight loss, to modify risk factors may be offered. It is then possible that conservative therapy, in terms of bladder training (BT) or pelvic floor education and therapy, will be suggested, with referral to a practice nurse, physiotherapist or continence nurse specialist. Alternatively, or if these approaches subsequently fail, the woman will be offered referral to secondary care, to a urologist, urogynaecologist or gynaecologist, depending on local service arrangements. Such referrals will mostly result in further investigation, further conservative treatment including the use of drugs and eventually the offer of surgery to those with predominant SUI.

### *Lifestyle changes*

Symptomatic SUI may be improved or cured by changing lifestyle factors. This can be achieved by interventions, such as weight loss, fluid restriction, reduction of caffeine or alcohol intake, limiting heavy activity, stopping smoking and treatment of constipation (*Table 1*). The effect of weight loss has been most intensively studied, with evidence summarised in a recent systematic review.[45] Successful weight-loss programmes require intensive therapy, involving diet, exercise and behavioural modification over a prolonged period.

**Setting**

In the context of a consultation in primary care, the possible benefit of lifestyle modifications, such as weight loss, would be discussed and reinforced by a patient information leaflet, together with the offer of further therapeutic help. Intensive weight-loss programmes are not widely available at present but are most likely to be community based.

**Personnel involved**

Weight loss or smoking cessation therapy is most likely to be effective if it is supervised, preferably on a weekly basis, by a therapist who has undergone recognised training and obtained appropriate qualifications. Such programmes are frequently run as group sessions.

**Costs**

The cost of lifestyle changes will vary according to the intensity of the intervention. It might range from simple provision of information at a primary care consultation with a specialist nurse (£13.95)[46] to the taking of active steps to lose weight. For example, a 6-month supervised group weight-reduction programme with the leading commercial provider in the UK, WeightWatchers®, would currently cost £152,[47] with possible additional costs to the individual related to dietary changes and exercise programme.

### *Pelvic floor muscle training*

Recommendations for the standardisation of these treatments have been published by the UK Chartered Society of Physiotherapists.[40]

**Basic pelvic floor muscle training (PFMT basic)**

Popularised by Arnold Kegel,[48] basic pelvic floor muscle training (PFMT) is generally the first-line non-surgical management for SUI. The principle behind this intervention is to condition and strengthen the striated pelvic floor muscles in order to improve the urethral sphincter closure mechanism during provocative activity (such as coughing) that raises intra-abdominal pressure. There is a variety of regimens to provide PFMT to women. The simplest involves education about pelvic floor structure and function, together with demonstration, using digital vaginal examination by the therapist or woman herself, of a correct and effective pelvic floor muscle contraction. A regular exercise programme schedule is then agreed between the woman and her therapist, with intermittent checks of progress and benefit over a 3- to 4-month period. The schedule suggested by Kegel was five contractions performed every waking hour,[49] whereas that recommended by recent guidelines is a sequence of eight contractions three times daily.[43] A summary of current recommendations is given in *Box 4*.

***TABLE 1*** *Lifestyle changes as treatment for stress urinary incontinence*

| Lifestyle change | Methods | Evidence of effectiveness for SUI[a] |
|---|---|---|
| Weight loss | Diet<br>Exercise<br>Behavioural modification | Level 1a |
| Adjustment of fluid intake | Reduced volume<br>Avoidance of caffeine<br>Avoidance of carbonated drinks | Level 2b |
| Smoking cessation | Behavioural modification<br>Nicotine replacement | Level 4 |
| Exercise modification | Avoidance of provocative exercise | Level 4 |
| Regularisation of bowel habit | Interventions to prevent constipation and straining to defecate | Level 4 |

a Graded according to Oxford Centre for Evidence Based Medicine (2009). Available at www.cebm.net/index.aspx?o=1025.

## Augmented PFMT

### *Plus biofeedback (PFMT plus BF)*

The addition of BF as a teaching and performance-enhancing device, in the form of vaginal pressure recording using a perineometer or electromyographic demonstration of muscle activity, can be helpful to visually demonstrate to the patient when they are performing a correct pelvic contraction and to quantify improvement. This feedback should encourage and motivate perseverance with a regular exercise programme. Digital BF is the practice of assessing pelvic muscle strength by vaginal examination, with verbal feedback concerning correctness and strength of the contraction. Once benefit is established and the woman is discharged from the therapist's care, a continued exercise programme is encouraged. Biofeedback may also be used as a training device or as an aid to pelvic floor muscle exercising. Women use a pressure perineometer to monitor strength and endurance of a series of pelvic floor muscle contractions over a period of time, typically 20–30 minutes, at weekly or monthly intervals.

### *Plus vaginal cones*

As an adjunct to standard pelvic floor training programmes, women can be instructed to retain graded cone-shaped weights [vaginal cones (VCs)] within the vagina to improve pelvic floor muscle strength. Starting with the lightest weight, women are advised to hold a cone in their vagina and prevent it from slipping out, while standing, moving around or coughing. It is suggested that the use of cones improves compliance with the

***BOX 4*** *Current recommendations for conduct of pelvic floor muscle training programme[a]*

- Pelvic floor muscle awareness is taught
- The pelvic floor is assessed and exercised in functional positions
- The use of anticipatory pelvic floor muscle contraction immediately prior to an activity that causes urine leakage ('The Knack') is taught
- A programme of pelvic floor muscle exercises is tailored to individual patients and includes exercises for both fast- and slow-twitch muscle fibres
- Pelvic floor muscle exercises are performed several times a day until the muscle fatigues
- Pelvic floor muscle exercises are practised for 15–20 weeks
- Patients are initially seen weekly, but account may need to be taken of their circumstances and/or the available resources
- Pelvic floor muscle exercises are continued on a maintenance programme

a Recommendation from Laycock and colleagues (2001).[40]

exercise schedule, individualises the exercise regimen, gives BF and improves knowledge of the functional anatomy of the vagina and pelvic floor. Cones may also be used as a standalone treatment at home for women who do not wish to, or cannot, access a health professional.[50]

***Plus electrical stimulation***

A further possible adjunct to PFMT is electrical stimulation (ES). This causes the pelvic floor muscles to contract, either directly or indirectly, by excitation of the motor efferent fibres of the pudendal nerve. The electrodes can be placed on the perineal skin, within the vagina or within the anus. The vaginal route is recommended with set stimulation parameters (*Box 5*). It is thought that ES may be particularly useful for women who are unable to contract their pelvic floor muscles voluntarily, or to help build up muscle strength prior to a supervised PFMT programme. The reported advantages of this intervention include high patient acceptability, little or no discomfort and home-managed delivery of the treatment.[51]

**Setting**

These interventions are organised through a primary care continence or physiotherapy service, which may be located in a primary health care centre or local hospital department. The patient will typically attend weekly or fortnightly sessions over a 3- to 4-month period, depending on compliance and improvement. They will be instructed to continue the exercise programme at home, during daily activity between visits to the therapist, and to continue the programme themselves, lifelong, after discharge from the therapist's care.

**Personnel involved**

These treatments will be typically supervised by a chartered physiotherapist who has undergone education to degree level and has undertaken a recognised professional training programme leading to the relevant professional registration. In some cases sessions may be delegated to trainees or assistants under supervision. Alternatively, the treatment will be administered by a continence nurse specialist who has undergone training in the provision of pelvic floor exercise programmes and has achieved appropriate competencies signified by additional qualifications.

**Costs**

Based on Personal and Social Services Research Unit (PSSRU) figures, the average cost for a consultation with a physiotherapist is approximately £13.[46] Additional costs for PFMT programmes would include overheads and consumables for basic intervention (£4), and additional equipment for BF (£35) and ES (£11). VCs are not provided by the UK NHS, and women would have to purchase them commercially at a cost of £20.[52] The total cost of all these interventions is determined by the number of sessions the women receive. For basic PFMT, the average cost for a 3-month cycle of treatment is £189, for BF it is £224 and for ES it is £398. These costs are similar if the programme is provided by a continence nurse specialist.[43]

***BOX 5*** *Suggested parameters for intravaginal electrical stimulation of the pelvic floor as treatment for stress urinary incontinence*[a]

- Frequency: 35 Hz
- Pulse width: 250 microseconds (0.25 milliseconds)
- Current type: biphasic rectangular
- Intensity: maximum tolerated
- Duty cycle: 5 seconds on/10 seconds off. Very weak muscles: 5 seconds on/15 seconds off
- Treatment daily/twice daily (home treatment)
- Treatment time: 5 minutes initially, gradually increasing to 20 minutes

a Recommendation from Laycock and colleagues (2001).[40]

***Bladder training***

Bladder training to regain control of micturition is more predominantly used for UUI or those women with mixed symptoms. Typical programmes involve a gradually progressive voiding schedule to delay micturition, together with distraction and relaxation techniques to suppress urgency. This would generally involve an initial assessment consultation and subsequent visits or telephone follow-up over a period of 8–12 weeks. Bladder diaries are often used as additional BF and outcome tools.[53]

**Setting**

The initial assessment would take place in a primary health care centre, with follow-up visits in the health centre, patient's home or by telephone as appropriate.

**Personnel involved**

This type of therapy is generally supervised in primary care by a designated member of the

district nursing team with expertise in continence promotion or by a continence nurse specialist.

**Costs**

UK NHS reference costs for district nursing contacts (CN301AF) average £31 (range £26–40), while continence nurse specialist contacts (CN204AF) are costed at between £48 and £114. This would give an approximate total cost, assuming fortnightly visits for 12 weeks, of £180–540.[54]

### *Pharmacotherapy*

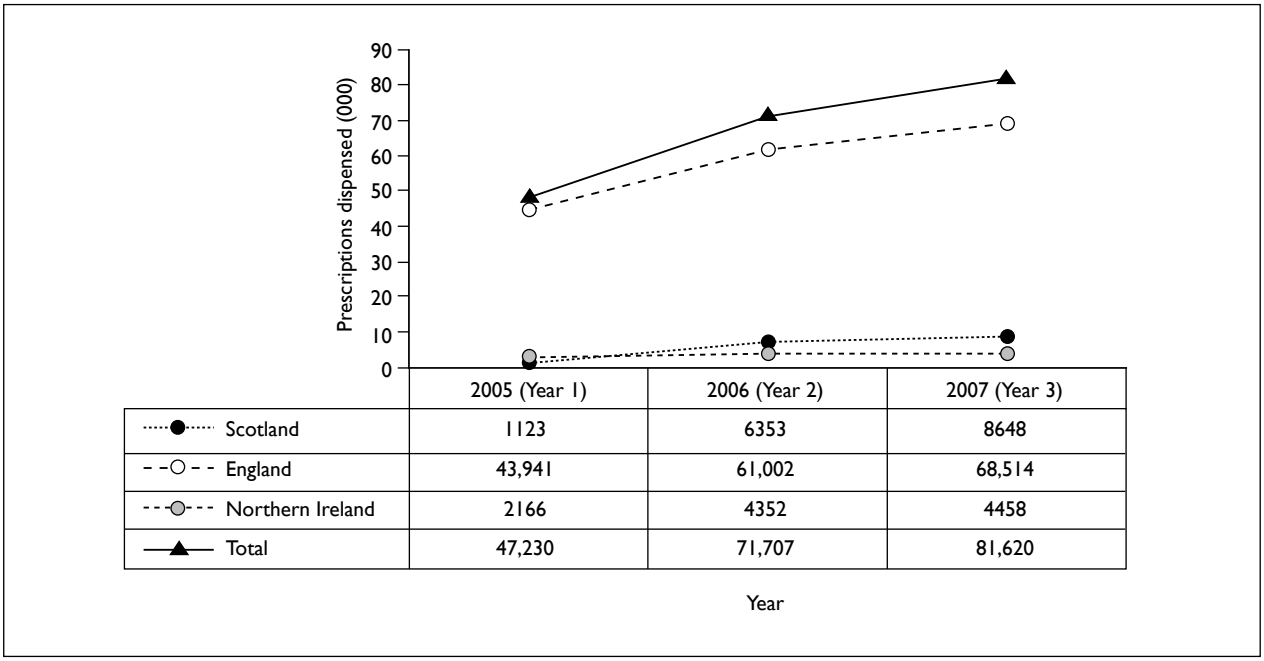
**Serotonin–noradrenaline reuptake inhibitor**

Experimental studies in animals suggest that noradrenaline and serotonin (5-hydroxytryptamine) act on efferent neurons in the sacral spinal cord (Onuf's nucleus) to encourage contraction of the periurethral striated muscle of the urethral sphincter and relaxation of the bladder wall muscle (detrusor muscle), thereby promoting urine storage and continence. Duloxetine hydrochloride, a balanced serotonin–noradrenaline reuptake inhibitor (SNRI), was tested as an antidepressant but found to have an effect on reducing stress incontinence in women. It is now licensed as a continence-promoting drug in women with SUI.[55] Although it has been shown to improve symptoms of SUI, the usefulness of duloxetine is limited by side effects, particularly nausea, which result in up to 20% of women being unable to tolerate the drug.[56] There is some evidence to suggest that this drug may be more useful as an adjunct to other conservative therapies, such as PFMT.[57] Despite poor tolerability and modest efficacy, the prescribing of this drug appears to be increasing in the UK (*Figure 4*). Further details on the current use of SNRI's were obtained from a survey of members of the Association of Continence Advisors (ACA). The ACA provided a copy of their e-mail distribution list and members were surveyed during January and February 2009. Out of approximately 650 ACA members on the distribution list, 86 responded (a 13.2% response rate). Of these, 57 provided details of their SUI caseload, of which 15/57 (26.3%) advisors reported that they had patients using duloxetine for the treatment of SUI. The number being treated was 92 out of a caseload of 1234 patients (7.5%); the majority of these, however, came from the caseloads of two respondents.

The drug is generally prescribed in divided doses, totalling 40–80 mg per day, and the response is assessed over a 12-week period. The relatively high risk of side effects requires initial close monitoring by the specialist or GP.

### *Setting*

The poor tolerability profile of this drug has resulted in it mainly being prescribed by specialists through hospital clinics.




| | 2005 (Year 1) | 2006 (Year 2) | 2007 (Year 3) |
|---|---|---|---|
| Scotland | 1123 | 6353 | 8648 |
| England | 43,941 | 61,002 | 68,514 |
| Northern Ireland | 2166 | 4352 | 4458 |
| Total | 47,230 | 71,707 | 81,620 |

***FIGURE 4*** *Serotonin–noradrenaline reuptake inhibitor prescriptions for stress urinary incontinence. UK NHS prescribing data obtained from NHS information centre.*[58]

### *Personnel*

The drug is predominantly initiated by hospital specialists for women with SUI, who are unsuitable for surgery or do not wish to undergo surgery.

### *Costs*

The cost of a 56 × 40-mg tablet pack of duloxetine is £30.80.[59] This equates to an average annual cost per patient, for drugs alone, of £402. If two visits to the GP are included the total annual cost rises to £474.

## Estrogen

Estrogens are thought to affect female continence through several modes of action, including maintenance of pelvic floor musculature and enhancement of urethra mucosal sealing. It was therefore considered that therapeutic estrogen supplementation in postmenopausal women would be beneficial delivered either locally or systemically. Overall, there is a high level of evidence that oral estrogen replacement therapy appears to increase incontinence symptoms amongst postmenopausal women,[60–62] and its use for this indication is therefore not recommended. Recent appraisal of evidence for topical vaginal estrogen therapy suggests that it may benefit women with incontinence but not to any consistent degree,[63] and it is currently only recommended for women with overactive bladder symptoms that are associated with mucosal atrophy.[43] The opinion from the expert group for the current review was in agreement with this guidance and so oral or topical estrogen were not included as a treatment option for SUI.

## Adrenergic agonists

Despite a theoretical and experimental expectation that alpha-adrenergic drugs should improve urethral and bladder neck smooth muscle activity, no consistent clinical benefit was found in women with stress incontinence.[63,64] These drugs are neither licensed for this treatment indication nor recommended by current guidance,[43] and were considered to be very rarely used in practice by our expert group. On this basis, the use of adrenergic agonists as a treatment option for SUI was not considered further.

### *Mechanical devices*

Consideration of the underlying urodynamic changes that result in SUI has continued to encourage the design and testing of intraurethral or intravaginal mechanical devices to prevent leakage. The mechanism of action of intravaginal devices is either by compression of the urethra against the inferior margin of the pubis or adjunctive bladder neck support with tampons such as Contrelle™.[65] Intraurethral devices, such as NEAT Expandable Tip Continence Device™,[66] and FemSoft™,[67] plug the urethral lumen. The clinical effectiveness of these devices in comparison with no treatment or other conservative methods of managing stress incontinence was the subject of a recent systematic review.[68] This review included six trials with a total of 286 participants. The mechanical devices used were five intravaginal devices and five intraurethral devices. The included trials either compared a mechanical device with no treatment or with an alternative device. There were no published data comparing devices with other non-surgical interventions for the treatment of SUI. The published data were unsuited to meta-analysis and the individual trials had small sample sizes and poor methodology ratings. The review therefore concluded that there was insufficient evidence to estimate the effect of mechanical devices for the treatment of women with SUI. In summary, although these devices are conceptually attractive, they do not appear to be widely used at present.[49] Some further information was obtained from the previously described survey of ACA members. The respondents had a total caseload of 1187 women. A total of 80 women were using mechanical devices, although 35 (43.8%) of these came from the caseload of a single respondent. The vast majority of devices used were vaginal devices, used by 78/80 women (97.5%). The most popular of these was pessaries, used by 77.5% (62/80) of the women. The Contrelle Activeguard was used by 7/80 (8.8%) women, tampons by 4/80 (5%) women, the Incostress device by 2/80 (2.5%) women, and vaginal sponges by 3/80 (3.8%) women. The only non-vaginal device used was an anal plug used by 2/80 (2.5%) women.

## Setting and personnel

These devices require a preliminary assessment by a trained health-care professional, who will also instruct the patient on their use. However, this could occur in primary or secondary care settings.

## Costs

The Contrelle device costs £50 and can be reused, whereas the FemSoft urethral insert costs £1.50 and has to be changed for a new device after urination.

### *Electromagnetic stimulation*

Experimental studies have shown that electromagnetic stimulation of the S3 and S4

sacral nerves increases maximum urethral closing pressure by 34% compared with baseline.[69] However, few randomised controlled trials (RCTs) have reported on the cure or improvement of SUI using electromagnetic stimulation compared with placebo,[69,70] and the intervention is not in current clinical use. It will not be considered further in this review.

### *Periurethral injectable bulking agents*

Stress urinary incontinence can be treated by periurethral injections of agents that bulk the urethral wall to encourage sealing during urine storage and hence improve continence. Conceptually, they occupy a 'grey' area between truly non-surgical treatments and operations. We chose to define periurethral injection therapy as surgical treatment, as this is carried out by surgically qualified clinicians, in an operating room environment, with the standard precautions and care process that this entails. This treatment modality will not therefore be included in treatment pathways, but a summary of a recently updated Cochrane review of the subject is included here for completeness.[71] This review looked at the effects of periurethral or transurethral injection therapy for the treatment of women with urinary incontinence. It identified 12 relevant trials, including 1318 participants in total, and examined eight types of injectable material (*Box 6*) along with one dummy injection (saline).

***BOX 6*** *Types of implants used for periurethral bulking*[a]

***Currently available***

Macroplastique™ – silicon particles

Durasphere™ – carbon particles

Contigen™ – glutaraldehyde cross-linked bovine collagen

Coaptite™ – calcium hydroxylappatite

Uryx™ – ethylene vinyl alcohol copolymer

Permacol™ – porcine dermal collagen

***Experimental use***

Silicon microballoons

Dextran copolymer

Alginate gels

Autologous chondrocytes

Autologous myoblasts

***Discontinued***

Autologous fat

Polytef™ – polytetrafluoroethylene

Zuidex™ – dextranomer/hyaluronic acid copolymer

a Full details available from Keegan and colleagues (2007).[71]

One study comparing periurethral injection to dummy treatment with saline was terminated due to safety concerns, although early results had not indicated any significant difference in treatment effect prior to this.[72] There were no relevant studies comparing periurethral injection to conservative management of urinary incontinence. However, in two studies comparing periurethral injection with surgery, surgery was reported to result in significantly greater improvement as measured by clinical observation. Comparisons between different types of agents used for periurethral injection suggested a variety of new agents to be as effective as collagen, and porcine dermal implant as effective as silicone, although confidence intervals (CIs) were wide and longer-term data were required. In general, approximately 50% of patients were satisfied in the short term (less than 1 year) after injection therapy. The review concluded that methodologically robust trials were needed, particularly with longer follow-up data and when using non-surgical treatments, such as PFMT, as comparators. Currently, the lack of useful high-quality evidence makes it difficult to draw conclusions regarding the place of periurethral injection therapy in the care pathway for women with SUI and it will not be used in the care pathways described in this review.

### Surgery for SUI

Since the introduction of the first surgical procedure, anterior colporrhaphy with plication of the urethra by Kelly and Dumm in 1911,[73] the number of different surgical procedures used to treat stress incontinence has grown to about 100. They are covered by six published Cochrane reviews (*Box 7*).

The development of a novel theory of causation of SUI by Petros and Ulmsten[79] has clarified the rationale for different surgeries. Older abdominal techniques, such as Burch colposuspension and pubovaginal sling insertion, aim to reduce mobility of the bladder neck and proximal urethra by providing fixation to the pubis. Newer techniques popularised by Ulmsten aim to increase support

***BOX 7*** *Current surgical procedures to treat stress urinary incontinence*

***Procedures covered by published Cochrane reviews***

Open Burch retropubic colposuspension – Lapitan and colleagues (2005)[38]

Laparoscopic colposuspension – Dean and colleagues (2006)[74]

Suburethral slings – Bezerra and colleagues (2005)[75]

Anterior colporrhaphy – Glazener and Cooper (2001)[76]

Needle urethral suspension – Glazener and Cooper (2004)[77]

Tension-free transvaginal tape (TVT) – Ogah and colleagues[78]

Tension-free transobturator vaginal tape (TVT-O) – Ogah and colleagues[78]

to the mid-urethra, typically using a synthetic tape introduced through the vagina and fixed either suprapubically or in the obturator fossa without tension.[80,81] These latter two procedures – TVT and TVT-O – are currently the most popular surgical techniques for treatment of SUI in women, having the advantages of a vaginal approach, minimally invasive insertion and a favourable adverse event profile.[82] The procedures involve blind passage of a length of monofilament macroporous polypropylene tape to provide a 'hammock' for the mid-urethra. The tape is positioned without tension using specially designed curved needles through suprapubic (TVT) or medial groin (TVT-O) incisions, and an incision in the anterior vaginal wall beneath the mid-urethra. The procedure can be performed under local anaesthetic and sedation or, more usually, a general or regional anaesthetic, and can be accomplished within a 24-hour hospital stay. The TVT variant also requires cystoscopy to detect and correct bladder perforation. Burch colposuspension or pubovaginal sling insertion, on the other hand, are open surgical procedures requiring a formal suprapubic incision. They require a general anaesthetic and a 2- to 3-day hospital stay. The main risk of all such procedures is transient (10%) or permanent (1%) voiding difficulty requiring intermittent self-catheterisation. Surgical success rates after 1–5 years of follow-up vary between 51% and 87% for Burch colposuspension/pubovaginal sling and between 63% and 85% for TVT/TVT-O, according to definition of cure/improvement and length of follow-up.[80]

**Setting**
All procedures require an appropriately equipped hospital or clinic environment for safe surgical conduct. This will include a preoperative area, a fully equipped operating room and facilities for postoperative recovery. The newer minimally invasive procedures, such as TVT and TVT-O, can be carried out in an ambulatory care unit that is designed for stays of up to 24 hours.

**Personnel**
The procedures require staff for preoperative preparation, a surgical team including an anaesthetist and appropriately trained surgeon, and postoperative recovery staff. Staff and facilities to monitor residual urine and teach intermittent self-catheterisation when required are also needed.

**Cost**
UK National Health service reference costs[54] for TVT and TVT-O, classified as 'lower genital tract minor procedures without complications', are, on average (interquartile range), £1135 (£741–1357) for inpatient treatment (mean stay of 2 days) and £629 (£456–828) for day-case treatment. Colposuspension classified as an 'open bladder neck procedure in women' has an average (interquartile range) cost of £1396 (£1011–2013) for inpatient treatment (mean stay of 2 days).[54]

## Criteria for treatment

Women with incontinence who choose to seek clinician advice generally have more severe symptoms that are bothersome and therefore desire treatment to improve their continence and lessen the impact on their day-to-day life. It is the clinician's responsibility to gather evidence of the severity, type and degree of bother suffered by the individual in order to suggest the most appropriate first-line treatment options for the patient to consider. Selection of the initial treatment is then negotiated according to patient choice, clinician opinion and local availability. Subsequent consultations will decide on the need for further trials of treatment if the initial outcome is unsatisfactory. This assessment requires the exclusion, by examination and simple testing, of complicating factors, such as relevant neurological dysfunction, impaired voiding, infection and pelvic

organ prolapse. Those with modifiable lifestyle factors, such as high body mass index and smoking, should be encouraged and helped to address these either before, or concurrent with, more active treatment. The selection for active treatment then depends on the individual's desire and motivation, the presence of comorbidity and local service availability.

For women with a predominant symptom of SUI, education about their pelvic floor anatomy and function, and supervised training to improve pelvic floor muscle function, are the most used first-line treatments in the UK. This may sometimes be augmented by transvaginal ES or BF techniques, including use of VCs. To benefit from these therapies, women require sufficient mobility, motivation and the ability to attend frequent therapy sessions. Following a trial of PFMT, the next step is likely to be referral to a specialist for consideration of surgery.

Most high-level evidence for the effectiveness of each of these treatments is based on randomised trials with set inclusion and exclusion criteria. It is uncertain how the results of these trials and meta-analysis of multiple trials relate to individual patients, particularly those who would not meet the inclusion criteria (*Table 2*).

***TABLE 2*** *Summarised inclusion and exclusion criteria for interventions for stress urinary incontinence from studies included in relevant Cochrane reviews*

| Treatment | Inclusion criteria | Exclusion criteria |
|---|---|---|
| PFMT[83] | SUI<br>USI<br>More than two episodes of incontinence per week<br>18–75 years | Urinary tract infection<br>Incomplete voiding<br>Neurological disorders<br>Cognitive impairment |
| BT[53] | Age >35<br>Urgency or MUI<br>DO (urodynamic diagnosis) | Previous surgery for incontinence<br>Neurological disease<br>Urinary tract infection<br>Predominant stress incontinence<br>Diabetes mellitus<br>Inability to reach toilet unaided |
| Duloxetine[56] | Age 30–80 years<br>SUI<br>USI | Pregnancy<br>Breastfeeding<br>Urinary tract infection<br>Arrhythmias or liver disease<br>Advanced pelvic organ prolapse<br>Continence surgery within 1 year<br>Prior hip fracture or replacement<br>Prior formal PFMT |
| Surgery[38,74–77] | SUI<br>USI | Age <21 years<br>Age >65 years<br>Non-ambulatory<br>Pregnancy<br>Current cancer treatment<br>Systemic disease affecting bladder function<br>Urethral diverticulum<br>Recent pelvic surgery<br>Grade III incontinence<br>DO<br>Urinary tract infection<br>Severe medical disease |

## Containment options

Methods for containment of urinary incontinence do not constitute a means of treatment and are therefore not included in the systematic review. It is acknowledged, however, that pads are widely used by women in all phases of management of their incontinence problem and that methods for urinary diversion form the 'last resort' for women with severe incontinence who cannot be treated, or have failed repeated attempts at curative treatment, typically following multiple surgical procedures. As such, the use of containment products is included in the economic evaluation as they form part of the care that a woman might receive over her lifetime.

### Absorbent pads

The most commonly used method of incontinence management is absorbent pads. The total expenditure on such products is large and, although not altering the underlying condition, it can be a satisfactory option for women with minimal or predictable leakage, or for those who are unsuited to treatments or have failed to benefit from treatment. The products range from thin panty-liners to large nappy (diaper)-type pads.

Despite their widespread use, little research has been conducted concerning patient satisfaction or effectiveness, although recent evidence summarised in a Cochrane review does suggest that specifically designed pant insert pads are superior to those designed for menstrual loss.[84,85] Containment-using pads was also the subject of a previous UK Health Technology Assessment (HTA) monograph.[86]

### Urinary diversion

Some women with severe intractable incontinence that has not responded to corrective methods of management may choose to undergo urinary diversion. The simplest method is transurethral or suprapubic insertion of an indwelling catheter, with continuous drainage into a collection bag. Summarised evidence regarding types of catheter and policies for their use has previously been published.[87,88] Generally, indwelling catheters are unsuited for women with long life expectancy, who are often better served with a formal surgical urinary diversion procedure. This can be performed using an ileal conduit or continent diversion. The techniques, benefits and adverse events have been described in a Cochrane review.[89]

# Chapter 2
# Aims and objectives

The aim of this study was to estimate the effectiveness and cost-effectiveness of non-surgical treatment for women with SUI.

The objectives are to:

- develop a series of management pathways that describe potential sequence of non-surgical and surgical treatments for SUI
- determine the clinical effectiveness of the different individual treatments for SUI
- determine the safety in terms of the magnitude of any risks or side effects of treatments for SUI
- estimate the cost-effectiveness of the alternative management pathways
- identify areas for future research.

The remainder of the report is structured as follows:

- Chapter 3 describes the definition of the decision problems and the patient treatment pathway.
- Chapter 4 presents the results of a survey performed on women with SUI to identify the outcomes of importance to them.
- Chapter 5 describes the methods used for reviewing clinical effectiveness and provides information on the inclusion and exclusion criteria, search methods for identification of studies, data collection and analysis.
- Chapter 6 describes the studies included in the systematic review of clinical effectiveness.
- Chapter 7 assesses the clinical effectiveness of the major treatments using direct pair-wise (head-to-head) comparisons.
- Chapter 8 assesses the clinical effectiveness of the treatment using a mixed-treatment comparison (MTC) model.
- Chapter 9 assesses the cost-effectiveness using an economic model; this chapter describes the basics of the modelling approach and the key assumptions underpinning the estimates of cost-effectiveness results.
- Chapter 10 discusses the results of the study.
- Chapter 11 is the conclusion, which highlights the implications of the findings for the NHS, women and research.

# Chapter 3
# Definition of the decision problem

The impact of SUI on individual women with the condition, their families and carers, and on the NHS, as a whole, is huge.[43] There are many potential methods for treating SUI which might be used alone or as part of a management strategy. However, while there is some evidence of the relative effectiveness of individual treatments, there is a lack of evidence on how the various interventions might be combined into management strategies. We therefore sought to identify plausible treatment strategies comprising sequences of non-surgical and surgical interventions. The clinical pathways were based on advice from the health-care professionals and patient group representatives who were involved in the study on what interventions patients could receive and the sequencing of the interventions. Even though the focus of this study is on non-surgical treatments, surgery is considered, as it may form part of a treatment strategy. For example, it may be a viable alternative for some women seeking treatment for SUI. For other women, surgery may be resorted to if a non-surgical intervention fails to satisfactorily resolve symptoms.

The Agency for Healthcare Research and Quality (AHRQ)[90] and the third International Consultation on Incontinence[91] have published a comprehensive literature review and consensus opinion of treatment guidelines for therapeutic interventions for SUI (the AHRQ has declared its guidelines obsolete). It is generally accepted that there is no 'perfect' therapy for all patients with SUI. Many factors should be considered when determining the optimal therapy for SUI in women. These include the aetiology and type of SUI, bladder capacity, renal function, sexual function, severity of the leakage and degree of bother to the patient, the presence of associated conditions – such as vaginal prolapse – or concurrent abdominal or pelvic pathology requiring surgical correction, prior abdominal and/or pelvic surgery, and, finally, willingness to accept the costs, risks, morbidity and success (or failure) rates associated with each intervention.

For most women with SUI it is sensible to discuss first the most reversible, simplest, least invasive and least expensive service-provider interventions, such as lifestyle changes and PFMT. The clinical consensus appears to be that the initial treatments for SUI involve a variety of non-surgical interventions, including lifestyle modification, PFMT with or without BF, and other accessory teaching aids, such as electronic devices and VCs. Further strategies can be formulated, which would consist of sequences of non-surgical and surgical interventions. These strategies will take into account the mechanism by which the treatment works and will also place limits on the number of retreatments allowed, based on current concepts of the use and effectiveness of the different procedures. More invasive or expensive interventions, such as surgery, are pursued if the clinician and patient decide that the current therapy is either ineffective or otherwise undesirable.

The importance of patient preference as the primary consideration in selecting a particular treatment for SUI was underlined by the findings of a recent survey which reported that most women preferred less invasive options.[92,93] From a health service perspective it is important to balance short- and long-term effectiveness against the potential adverse events and costs. Compared with surgical treatments, non-surgical treatments, such as lifestyle changes and physical therapies (such as PFMT), are associated with limited side effects and do not preclude future changes in management. Hence, non-surgical procedures have been considered to be the choice of primary treatments for SUI.[43] In developing the care pathways we have categorised treatments as being either non-surgical or surgical procedures and then considered how these treatments might be combined into management strategies for women presenting with SUI. While it is true that the specific treatment strategy adopted will vary from woman to woman, broad exemplars of specific strategies can be defined. In the following sections, descriptions of possible management strategies of women with SUI are presented, which vary in terms of the type and sequences of treatments that might be offered.

## Descriptions of the patient treatment pathways

*Figure 5* describes the treatment pathways that are compared within the economic model reported in Chapter 9. Potentially there are a very large number of alternative pathways that might be considered, and the pathways selected were derived following discussion with the health-care professionals and patient representatives involved in this study. They represent plausible care pathways that women might follow and might also be used to infer the value of other potential pathways not otherwise considered.

### Patient treatment pathway 1

Patient treatment pathway 1, in *Figure 5*, details one plausible strategy of care for a woman presenting with SUI. The first line of treatment that women presenting with SUI are offered is lifestyle modification. Lifestyle modification may involve a combination of one or more elements. These are dietary factors, reduction of caffeine intake, fluid intake, smoking, weight, physical exercise, alcohol consumption and limiting heavy activity (it may be possible that there are several ways lifestyle modifications can be performed so that they can be considered as different treatments, therefore allowing someone to get more than one lifestyle modification treatment). There are three states that could arise after treatment: 'continent', 'incontinent' or 'dead' (from natural causes). The continent state includes women who report that they are completely cured and those that feel that their condition has improved to the extent that they require no further treatment at the present time. Women could remain continent and hence require no further treatment, but some of them may experience a return or worsening of symptoms of SUI at some point in the future and then require further treatment. The women who report that they are not cured are said to be in the incontinent state. These women could either require or not require further treatment. The women who require further treatment get the next treatment option in the pathway they are following. In the first care pathway, all of the women who need further treatment are offered the second line of treatment: physical therapy. There are different forms of physical therapies that women can receive. These include PFMT alone or in combination with an adjunct, such as BF, ES or VCs. Based on the number of sessions women receive, PFMT can be classed as 'basic', when a patient has a maximum of two sessions per month, or 'PFMT with extra sessions', when the patient receives more than two sessions per month. This pathway offers only basic PFMT without any adjunct. Women who are not cured and do not receive any further treatment may use containment products, such as pads, to manage symptoms.

If women are not cured after PFMT they progress to the third line of treatment, which is surgery. Those who are not cured and need further treatment are offered a second surgical procedure. If the second surgical procedure does not work then women use containment products until they die. It is appreciated that women may also use containment products even when they are receiving other possible interventions. *Figure 6* provides a detailed description of pathway 1. Similar figures could have been developed for all of the other pathways.

### Patient treatment pathway 2

The treatment pathway option 2 is similar to that depicted in option 1. The only difference is that PFMT with extra sessions is offered as an additional non-surgical treatment between basic PFMT and surgery.

### Patient treatment pathway 3

Pathway 3 extends pathway 2 by adding a drug therapy (an SNRI) between PFMT with extra sessions and surgery.

### Patient treatment pathway 4

The treatment pathway 4 is substantially the same as pathway 1. The difference is that women receive PFMT with extra sessions straight away, instead of PFMT basic.

### Patient treatment pathway 5

Pathway 5 extends pathway 4 by adding SNRI therapy between PFMT extra sessions and surgery.

### Patient treatment pathway 6

In this pathway women would, as in all other pathways, initially receive the relevant advice or treatment aimed at modifying lifestyle. If they experienced a recurrence, had insufficient improvement or no improvement, they would proceed straight to surgery. Such a strategy might be appropriate for some subgroups of women. Alternatively, it may be popular with some women because it gives the prospect of relatively rapid relief from symptoms.

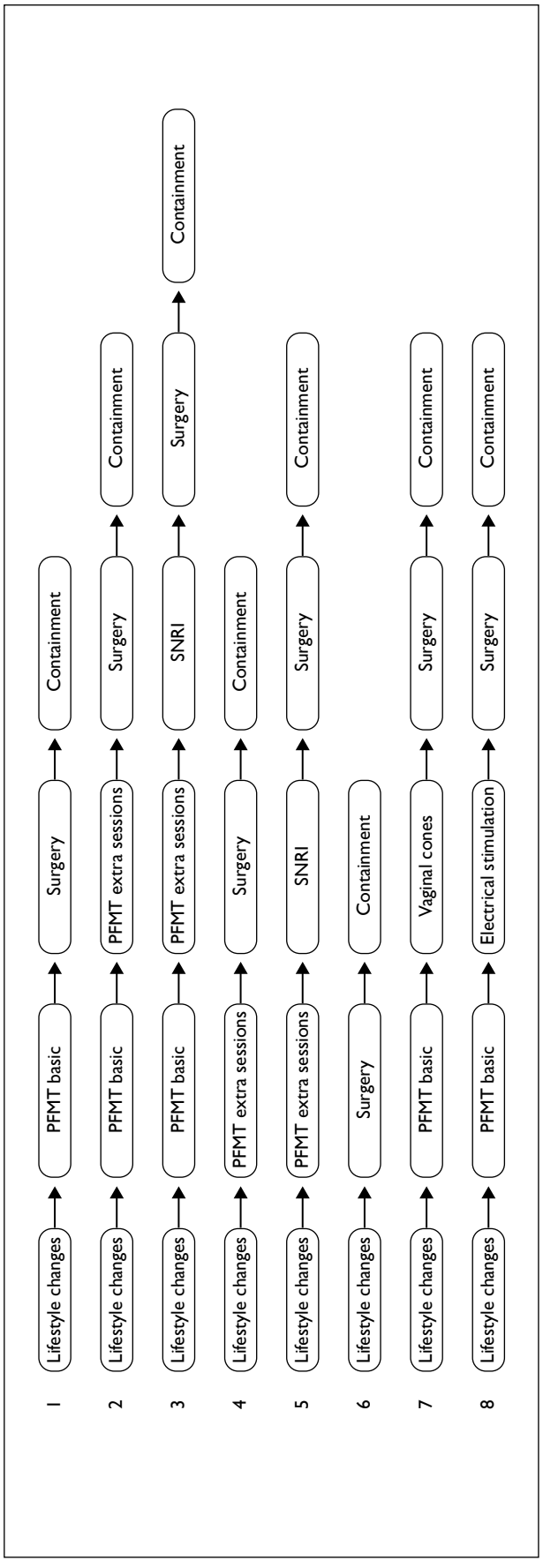



***FIGURE 5*** *Description of patient care pathways*

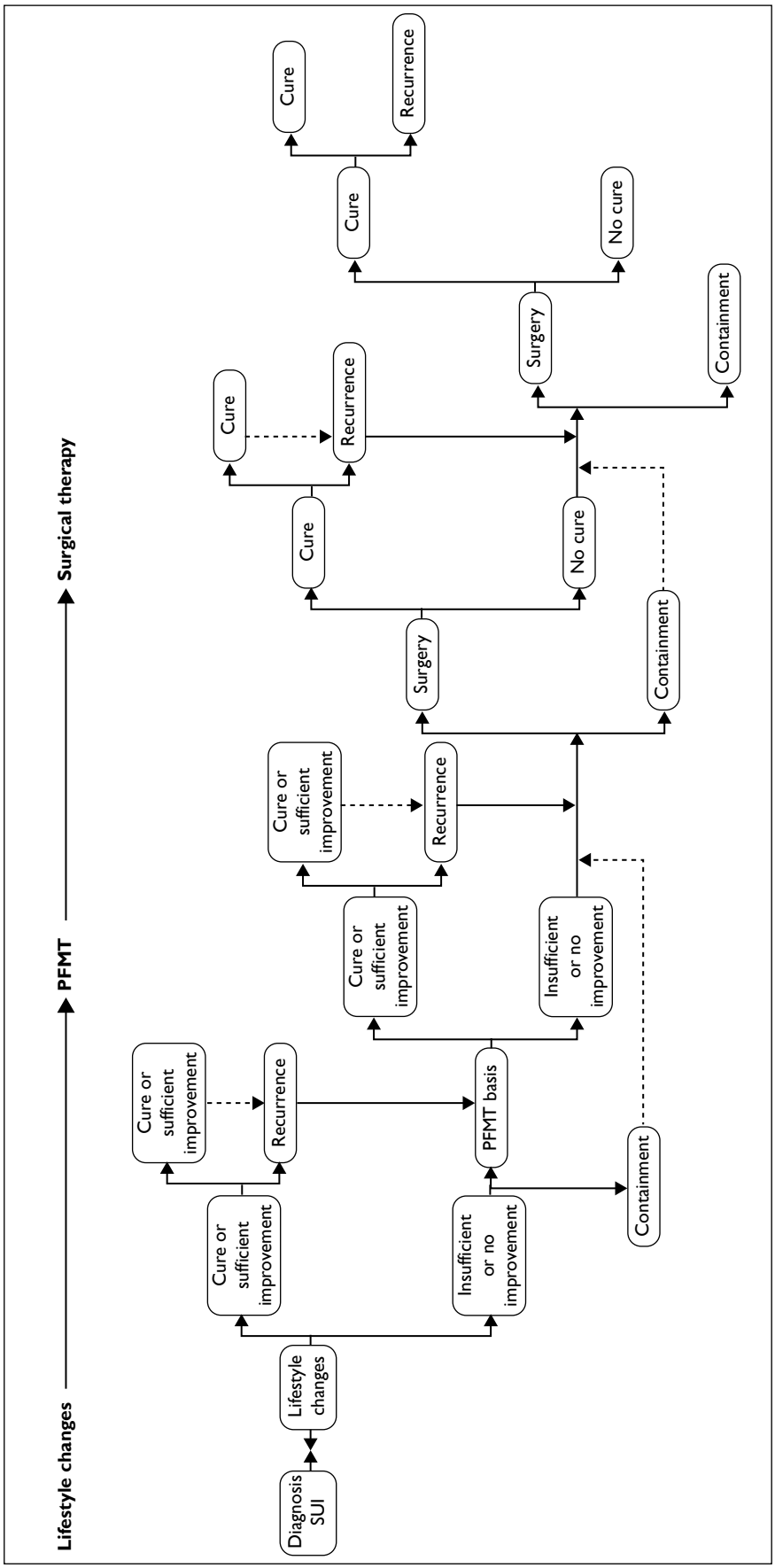



***FIGURE 6*** *Description of alternative treatment strategies (note: women may choose not to seek further treatment at any point).*

## Patient treatment pathway 7

This treatment pathway is similar to pathway 1 but with VCs as a treatment option between basic PFMT and surgery.

## Patient treatment pathway 8

This treatment pathway is similar to pathway 1 but with ES as a treatment option between basic PFMT and surgery.

These patient care pathways will be used in the study to inform the economic model reported in Chapter 9. These pathways will also assist in identifying outcomes of interest for the systematic review of effectiveness and identify the data required to populate the model. The key outcome of these pathways is that any need for further treatment is heavily influenced by whether the prior treatment has resulted in sufficient resolution of symptoms.

# Chapter 4

# Identification of outcomes of importance to women with stress urinary incontinence

## Introduction

It has been recognised for many years that the embarrassment associated with urinary incontinence may cause withdrawal from social situations and reduce quality of life.[32] Many women with SUI show symptoms of depression and introverted behaviour, together with dysfunctional interpersonal relationships.[33] Furthermore, SUI may lead to withdrawal from regular physical activities and hence impair women's general health.[34] One of the problems with the assessment of incontinence is that outcome measures frequently used in primary research may not perfectly map on to outcomes of importance to women. For example, the commonly reported outcome measure in clinical trials is 'cure', which is the satisfactory resolution (or near resolution) of symptoms. Using this definition usually means the patient self-report of the absence of incontinence. However, the ideal measure of how women are after treatment should reflect the ability to lead a normal social life, which may be compatible with improvements in the level of continence.

Given that much of the available literature focuses on clinical outcomes, which, as a result, may have limited relevance to the lives of women with SUI, the aim of this survey was to provide evidence on outcomes of importance to women.

The purpose of this work was to prospectively survey women with SUI to provide information on outcomes of importance to them; a secondary aim was to identify additional outcomes that ought to be collected in future primary studies and hence to define relevant outcomes for systematic reviews of the literature.

## Methods

In order to identify the areas of importance to women who suffer from SUI, a questionnaire was designed. A Patient Generated Index (PGI)[94] was used to allow respondents to state and evaluate the areas of their life affected by SUI. In addition to the PGI, the questionnaire included the King's Health Questionnaire,[95] the EQ-5D, and questions relating to socioeconomic and demographic information. The rationale for choosing the PGI was that as it is an individualised instrument – it would provide information on the specific concerns of women with SUI. In addition, these outcomes could then be compared with generic measures, such as the King's Health Questionnaire and the EQ-5D.

### The questionnaire

The PGI is an individualised patient-reported health instrument that allows the respondent to select, weight and rate the importance of a particular health outcome.[96] The PGI was designed with the aim of producing a valid measure of outcome that reflected areas of importance to patients' lives.[94] The PGI involves the respondent deciding what factors are important to her. Examples of the types of factors that may be important are included to provide guidance. The aim of the PGI is therefore to capture the diverse range of concerns or priorities of respondents. Using the PGI, respondents can vary the weight they attach to these concerns or priorities, which provides researchers with an insight into each respondent's viewpoint. An overall score for the PGI for each respondent can then be calculated by multiplying the rating for each health area by the proportion of points allocated to that particular area.

The PGI is completed in three stages. In the first stage, respondents are asked to identify up to five areas of their life that are affected by their SUI. Respondents are given a list of outcomes to act as prompts to help them think about which areas of their life might be affected by their condition. Respondents can then choose from these options or provide their own examples. In addition to the five boxes, there is a sixth box that enables respondents to rate all other areas of their life affected by their SUI. Examples of the factors to include as prompts on the PGI were drawn from three sources. The first of these was the King's Health Questionnaire,[95]

which was used to generate a list of outcomes under the broad headings of: 'role limitations', 'physical limitations', 'social limitations' and 'personal relationships and emotions'. These outcomes were supplemented from Cochrane reviews of non-surgical treatments.[56,75,83,97] Finally, a general literature search was also conducted, although this did not provide further additions to the 17 different outcomes identified from the King's Health Questionnaire and the Cochrane reviews. These outcomes were then narrowed down to broad categories of those considered most relevant by members of the project team. These were 'work', 'household tasks', 'social activities', 'feeling depressed/anxious', 'personal hygiene' and 'affecting sleep'. In addition to the methods used to generate the prompt list, further qualitative work could have been conducted. This could have included a focus group of women with SUI to further refine the areas to include in the prompt list. This is an area that could be considered in future use of the PGI.

In stage two of the PGI, respondents were asked to score each area listed in stage one of the PGI on a scale ranging from 0 to 6. The score given in stage two was intended to reflect how the individual was affected by their SUI in the past month. A score of 0 would signify that the effect on their life was as bad as it could possibly be and a score of 6 would correspond to an effect that was as good as it could possibly be.

Finally, in stage three, respondents were asked to 'spend' 10 points to indicate the relative importance of each of the areas mentioned in stage one. Respondents were requested to spend more points on areas that were the most important to them.

As noted above, in addition to the PGI, the questionnaire also contained the King's Health Questionnaire and the EQ-5D. The King's Health Questionnaire is a condition specific questionnaire that aims to assess the impact of urinary incontinence on an individual's quality of life. It contains questions set in nine domains relating to: general health perception, incontinence impact, role limitations, physical limitations, social limitations, personal relationships, emotions, sleep and energy, and severity. With the exception of the final part of the questionnaire (severity measures) scores can be calculated for each domain (0–100). The higher the score the worse off an individual feels they are and the lower they perceive their quality of life to be.

The EQ-5D is a standardised instrument used to measure quality of life. The EQ-5D is applicable to a wide range of health conditions and treatments and it provides a simple descriptive profile and a single index value for health status.[98] The EQ-5D has five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) that can be converted into a utility score.

## Sample

The Bladder and Bowel Foundation (formerly 'InContact' and the 'Continence Foundation') is a national charity that provides information and support to people with bladder and bowel problems, representing the interests of people with continence problems with the aim of ensuring they have access to the latest information and services available.[99] In 2006 a survey conducted by InContact was completed by 755 people affected by bladder and bowel problems.[100] Of these, 188 women with SUI gave consent for future contact about relevant research and formed the sample for the current study. In July 2007 these women were sent questionnaires for the current study by InContact. Given that this is a self-selected sample of women suffering from SUI and not a random sample of the population, it is not known how representative this sample is of the wider population.

## Ethical issues

The 2006 survey in which the participants were originally identified was a service evaluation in which The Bladder and Bowel Foundation surveyed people who had previously been in touch with the charity. As such, no ethical approval was necessary. The 2006 survey materials contained an explicit assurance that confidentiality would be maintained and that identifiable data would not be passed on to third parties. Respondents were asked if they were willing to be contacted in the future for research purposes. For this study questionnaires were sent in July 2007 to 188 women with SUI who gave their consent for further contact relating to research. The questionnaires were returned directly to the charity and, after screening only anonymous data, were subsequently forwarded to the authors in accordance with the Medical Research Council's guidance on the use of personal information in medical research and the Data Protection Act 1998.[101,102]

## Results

All data were analysed in SPSS version 17.0. Descriptive statistics and correlations of the sample were analysed and EQ-5D and PGI scores were calculated. In total, 105 out of 188 respondents (55.9%) completed and returned the questionnaire. *Table 3* shows the areas of an individual's life that they reported to be affected by their SUI, divided into four different themes. These themes were: (1) activities of daily living (work, home and social); (2) sex, hygiene and lifestyle issues; (3) emotional health; and (4) services. In total, 38 different areas were reported by respondents. Activities of daily living were the most frequently reported areas to be affected by SUI, followed by sex, hygiene and lifestyle issues and emotional health.

Out of 105 respondents, 73 respondents were categorised as having answered the PGI correctly. A further nine respondents made mistakes in the PGI and 23 respondents did not fully complete it (*Table 4*). Of the 73 respondents who correctly completed the questionnaire, 61 answered the PGI with no mistakes (all sections were completed satisfactorily). The remaining 12 respondents made a small error in completion of the PGI. This small error always occurred in section three of the PGI, where respondents had to spend 10 points. These respondents did in fact spend 10 points but they missed out spending points in area 6 (all other areas of their life affected by SUI) and totalled to 10 in box 6. This error is likely to have occurred due to the layout of the PGI. An example of the PGI used can be seen in Appendix 1.

*Table 5* shows the demographic information of the sample, as a whole and for those individuals who correctly and incorrectly completed the PGI. The mean age for the sample as a whole was 57 years

***TABLE 3*** *Area of life identified by respondents as being affected by stress urinary incontinence*

| Theme/specific issue | *N* | % | Theme/specific issue | *N* | % |
|---|---|---|---|---|---|
| ***Activities of daily living: work, home and social*** | | | | | |
| Going out/socialising[a] | 58 | 13.7 | Continually going to toilet when not necessary | 1 | 0.2 |
| Sleep[a] | 47 | 11 | Feeling cold | 1 | 0.2 |
| Shopping[a] | 33 | 7.8 | Worry about leaving wet stains | 1 | 0.2 |
| Physical activity | 30 | 7.1 | **Total** | | **22.4** |
| Work[a] | 24 | 5.7 | ***Emotional health*** | | |
| Travel | 18 | 4.2 | Depression[a] | 32 | 7.5 |
| Going on holiday/staying away from home | 12 | 2.8 | Anxiety[a] | 24 | 5.7 |
| Household tasks | 10 | 2.4 | Bladder controlling life | 2 | 0.5 |
| Family activities | 4 | 0.9 | Embarrassment | 2 | 0.5 |
| Travelling on public transport | 1 | 0.2 | Affecting confidence | 1 | 0.2 |
| Being housebound | 1 | 0.2 | Body image | 1 | 0.2 |
| Inability to study/write | 1 | 0.2 | Feeling unfeminine | 1 | 0.2 |
| Activities outside the home | 1 | 0.2 | It annoys me | 1 | 0.2 |
| **Total** | | **56.6** | Long-term effect it is having on me | 1 | 0.2 |
| ***Sex, hygiene, lifestyle issues*** | | | Failure | 1 | 0.2 |
| Personal hygiene[a] | 53 | 12.5 | **Total** | | **15.6** |
| Sexual relationships | 10 | 2.4 | ***Services*** | | |
| Personal relationships | 7 | 1.7 | Lack of public toilets | 11 | 2.6 |
| Sneezing/coughing/laughing | 7 | 1.7 | Need to use products/pads | 8 | 1.9 |
| Affecting choice of clothes | 6 | 1.4 | Time spent at doctor's surgery/hospital | 3 | 0.7 |
| Infections/skin irritations | 4 | 0.9 | Public queues | 1 | 0.2 |
| Loss of independence | 3 | 0.7 | **Total** | | **5.4** |
| Limiting liquid intake | 2 | 0.5 | | | |

a Areas provided in prompt list in the PGI.

***TABLE 4*** *Patient Generated Index responses*

| Responses | Frequency | Percentage | Notes |
|---|---|---|---|
| PGI answered correctly | 73 | 69.5 | PGI correct: 61<br>PGI put total in box 6: 12 |
| Mistake in PGI | 9 | 8.6 | |
| PGI not fully completed | 23 | 21.9 | |
| Total | 105 | 100.0 | |

'PGI answered correctly', those respondents who had fully completed PGI (outcomes, scores and points); includes those who mistakenly totalled their points in box 6, but points summed to 10; 'Mistake in PGI', those respondents who fully competed the PGI but who did not sum to 10; 'PGI not fully completed', not all sections of the PGI were completed.

(range 28–89). As can be seen in *Table 5*, those respondents who correctly completed the PGI were, on average, younger than those who completed it incorrectly. In addition, those who correctly completed the PGI appear to be better educated and in higher-income groups.

In addition to listing the outcomes of importance to women who suffer from SUI, a score of overall quality of life can also be calculated from the PGI. The score ranges from 0 to 6, with 0 reflecting a very low quality of life ('it's as bad as it could possibly be') and 6 reflecting a very high quality of life ('it's as high as it could possibly be'). An

***TABLE 5*** *Demographic and socioeconomic information*

| Variable | Total sample (*n* = 105) | Correct PGI (*n* = 73) | Incorrect PGI (*n* = 32) |
|---|---|---|---|
| Mean age of respondents (range, years) | 56.90 (28–89) | 55.16 (28–89) | 60.84 (37–87) |
| ***Age ranges (%)*** | | | |
| 25–34 | 3 (2) | 3 (4) | – |
| 35–44 | 15 (14) | 11 (15) | 4 (13) |
| 45–54 | 39 (37) | 28 (38) | 11 (35) |
| 55–64 | 21 (20) | 15 (21) | 6 (19) |
| 65–74 | 8 (8) | 6 (8) | 2 (6) |
| 75+ | 19 (18) | 10 (14) | 9 (28) |
| ***Income (valid %)*** | | | |
| £6000 | 10 (11) | 7 (11) | 3 (11) |
| £6001–10,000 | 16 (17) | 12 (19) | 4 (15) |
| £10,001–15,000 | 20 (22) | 11 (17) | 9 (33) |
| £15,001–20,000 | 13 (14) | 9 (14) | 4 (15) |
| £20,001–25,000 | 5 (5) | 3 (5) | 2 (7) |
| £25,001–30,000 | 10 (11) | 7 (11) | 3 (11) |
| £30,001–35,000 | 8 (9) | 6 (9) | 2 (7) |
| £35,001+ | 10 (11) | 10 (15) | – |
| ***Education (%)*** | | | |
| None | 2 (2) | 1 (1) | 1 (3) |
| Secondary school | 39 (37) | 22 (30) | 17 (53) |
| College | 29 (28) | 21 (29) | 8 (25) |
| University | 35 (33) | 29 (40) | 6 (19) |

example of the PGI and the method used to calculate the score is given in *Table 6*. For the respondents who successfully completed the PGI the mean score was 2.4 (SD 1.4, range 0–6). Given that a score of 6 on the PGI reflects the highest quality of life, a mean score of 2.4 in this population reflects that their quality of life falls significantly short of their hopes and expectations. In total, 101 out of 105 returned questionnaires had a fully completed EQ-5D. Scores on the EQ-5D ranged from –0.17 to 1. The mean EQ-5D score was 0.598 (SD 0.339). Correlation between the mean PGI score and the mean EQ-5D score was, as expected, positive and statistically significant.

Scores (out of 100) for each domain in the King's Health Questionnaire can be seen in *Table 7*. The higher the score, the worse off an individual feels. In addition to the domains of the King's Health Questionnaire, it also contains a section detailing the respondent's bladder problems and how much they affect the individual's life.

Correlations of the PGI and seven domains of the King's Health Questionnaire were also performed. Given the scoring system of the King's Health Questionnaire we would expect to find a negative correlation between the PGI and King's Health Questionnaire. All correlations were negative but only two were statistically significant: personal relationships ($p = 0.004$) and severity measures ($p = 0.003$).

In addition, correlations between the EQ-5D score and the domains of the King's Health Questionnaire were also calculated. We found all seven of the King's Health Questionnaire domains to be significantly (negatively) correlated with the EQ-5D. This result is to be expected, as many of the EQ-5D and King's Health Questionnaire domains are similar.

## Summary

The PGI has been used to quantify the effect of SUI on the quality of women's lives for the first time. In stage one of the PGI, 38 different areas of a woman's life affected by SUI were reported. The most frequently mentioned areas were: going out or socialising, with 14% of all respondents listing this as one of the areas of their life affected by their condition; personal hygiene (13%); and the effect their condition has on their sleep (11%). Shopping (8%), depression (8%), physical activity (6%), work (6%), anxiety (6%), travel (4%), household tasks (2%), personal (1%) and sexual relationships (2%) were all also listed as areas of their life affected by SUI.

The respondents are a self-selected sample of women who had previously been in touch with a patient support charity and who may be considered to be active help-seekers. However, there is no reason to suspect that their experience of SUI and the relative perceived impact of SUI on various aspects of their lives are different from the wider population of women affected. Nearly 70% of respondents successfully completed the questionnaire. A further 9% attempted the PGI but made mistakes in its completion, and 22% failed to fully complete the PGI (the majority of these respondents completed stage one of the PGI but failed to complete stages two or three). Those respondents who successfully completed the questionnaire were found to be younger, in

***TABLE 6*** *Example of Patient Generated Index scoring*

| Part 1: list areas of life affected by urinary incontinence | Part 2: score (0–6) | Part 3: spend your 10 points | Final PGI score |
|---|---|---|---|
| 1. Interrupted sleep | 1 | 3 | 0.3 |
| 2. Affects my social life | 6 | 1 | 0.6 |
| 3. Affects my work | 3 | 2 | 0.6 |
| 4. Personal relationships | 2 | 2 | 0.4 |
| 5. It makes me feel depressed | 4 | 1 | 0.4 |
| 6. All other areas of your life affected by your urinary incontinence | 5 | 1 | 0.5 |
| **Total** | | | **2.8** |
| Notes: [1 × 3/10] + [6 × 1/10] + [3 × 2/10] + [2 × 2/10] + [4 × 1/10] + [5 × 1/10] = 2.8. | | | |

***TABLE 7*** *King's Health Questionnaire – descriptive statistics*

| | *N* | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|---|
| KHQ scores for role limitation | 101 | 0.00 | 100.00 | 53.30 | 30.64 |
| KHQ physical limitation scores | 100 | 0.00 | 100.00 | 61.83 | 30.09 |
| KHQ social limitation | 95 | 0.00 | 100.00 | 45.61 | 30.98 |
| KHQ score for personal relationships | 73 | 0.00 | 100.00 | 37.90 | 35.92 |
| KHQ score for emotions | 98 | 0.00 | 100.00 | 60.32 | 31.67 |
| Sleep energy | 100 | 0.00 | 100.00 | 60.67 | 31.02 |
| Severity measures | 98 | 6.67 | 100.00 | 68.50 | 22.55 |

KHQ, King's Health Questionnaire.

higher-income groups and to have a higher level of education. For the PGI to be used as a valid and reliable measure of outcomes of importance to women with SUI and to be able to accurately quantify the effect of SUI on their lives, the response rate and successful completion of the PGI would need to be improved. Of the respondents, 31% had difficulty in completing the questionnaire and there was also a low response rate to the survey in general (56%).

In order to improve this response rate and the chance of successful completion, alterations could be made to the layout of the PGI to make it more user-friendly. The PGI, or instruments like it, have been criticised in the past. Some authors question whether they reflect the patient's view point or, conversely, whether they are simply reflecting the views of the researchers who designed the questionnaire.[103] In this survey, while we did find a varied response in the number of outcomes listed by respondents, the majority of these did in fact come from the prompt list provided in the PGI. Of the 10 most mentioned areas, eight of these were from the prompt list. Other studies have found similar associations between the prompt list and final outcomes listed by respondents. However, it is unclear whether this association is due to the most relevant examples being selected from the prompt list, or due to respondents being unwilling or unable to think of their own examples because the prompt list is already comprehensive.[104]

We correlated the mean PGI score with the mean EQ-5D scores. This correlation was, as expected, found to be positive and statistically significant. In addition to this, correlations between the King's Health Questionnaire and the PGI were performed. Although all correlations of the PGI and King's Health Questionnaire were as expected (negative), only two were found to be statistically significant. Given that the PGI outcomes and the domains of the King's Health Questionnaire do not correlate well, and that many of the aspects respondents mentioned in the PGI list of outcomes do not map very well on to the dimensions of the EQ-5D, this might suggest that generic measures, like the EQ-5D, may not be a very good reflection of the preferences of people with incontinence. The PGI in this instance may therefore be capturing concerns of women who suffer from SUI which are not adequately captured by generic instruments, such as the EQ-5D. This is of particular interest in the context of health technology appraisals such as this, where EQ-5D has become the accepted standard for calculation of quality-adjusted life-year (QALY) indices for use in determination of cost-effectiveness.[105] As will be described in later chapters, health-state utilities derived from the EQ-5D have been used to estimate QALYs in the economic evaluation. Hence, in the light of findings reported in this chapter, evidence on cost-effectiveness of interventions needs careful consideration.

## Conclusion

Much of the available literature on SUI focuses on doctor-selected clinical outcomes. Given the undoubted social and personal impact of SUI, these outcomes may have limited relevance to the women who suffer this condition. Thirty-eight different areas of an individual's life affected by SUI were identified by the PGI. The PGI succeeded in capturing a diverse range of outcomes of importance to women suffering from SUI, although some respondents found the PGI difficult to complete.

The PGI was not found to correlate well with the domains of the King's Health Questionnaire, nor to map well on to the dimensions of the EQ-5D or the King's Health Questionnaire. This suggests that generic measures may not be a very good reflection of the preferences of people with incontinence.

Ideally, the information obtained from this survey would be used to help define outcome measures for the systematic review of clinical effectiveness. However, these outcomes were often not considered in primary studies and hence their inclusion in a systematic review was not possible. Nevertheless, it would be important to include them in future research in this area.

# Chapter 5

# Methods for reviewing clinical effectiveness

The next four chapters present the systematic review of clinical effectiveness. This includes the review methods (this chapter), characteristics of the included studies (Chapter 6), direct head-to-head comparisons (Chapter 7), followed by MTC models (Chapter 8).

## Inclusion and exclusion criteria

### Types of studies

The types of studies considered were RCTs and quasi-RCTs (alternate allocation). Trial data reported in conference abstracts, as well as full-text papers, were included. For abstracts, solely those identified from the Cochrane Incontinence Group Specialised Register of trials were used.

### Types of participants

The participants were women with SUI or incontinence that was predominantly SUI (however diagnosed). Classification of diagnoses was accepted as defined by the trialists.

Owing to the small number of studies per intervention available, a pragmatic decision was made to include studies where the majority (≥ 50%) of the sample consisted of women with SUI or predominant SUI. Studies were therefore included if:

- all women had SUI alone (type-1 population)
- at least 50% of women had SUI alone; the remainder could have UUI or MUI (type-2 population)
- under 50% of women had stress incontinence alone but the majority (50% or more) had MUI with stress symptoms as a predominant pattern; the remainder could have SUI, UUI or MUI (type-3 population).

Studies were excluded if the proportion of women with predominantly SUI was not reported, if the type of incontinence (stress, urge, mixed) was unknown or undiagnosed, or if predominant symptoms (stress or urgency) of women with MUI were not specified.

Women with urinary incontinence whose symptoms might be due to significant factors outside the urinary tract were excluded, for example neurological disorders, cognitive impairment, and lack of independent mobility. Studies investigating nocturnal enuresis in women were also excluded.

Incontinent women during pregnancy or in the early postpartum period were considered for inclusion. Data from these childbearing women were analysed separately on the assumption that the effect of PFMT might differ in this group due to the physiological changes of pregnancy and in the postpartum period. Studies investigating prevention of incontinence among childbearing women were excluded.

Studies that recruited mixed populations of men and women with different types of urinary incontinence were eligible for inclusion, providing that demographic and outcome data were reported separately for women with predominantly SUI.

### Types of interventions

We defined non-surgical treatment as that which could be undertaken in a heath-care professional's office or clinic and patients' homes. Any of the following interventions, alone or in combination, were included. Treatment definitions used were as according to Cochrane Reviews where possible.

#### *Lifestyle interventions*

- Weight loss, decreased physical exertion, fluid manipulation, decreased caffeine, nicotine or alcohol consumption, treatment of constipation and dietary interventions.[106]

#### *Physical or behavioural therapy*

- Pelvic floor muscle training, with or without biofeedback – defined as 'a programme of repeated voluntary pelvic floor muscle contractions taught and supervised by a health care professional'.[83] This includes 'The Knack', the use of a timed contraction of the pelvic floor muscles before and during a cough (Miller 1998).[107] However, it excludes PFMT introduced by a leaflet only, without any contact with a health-care professional

(which was classified as being equivalent to no treatment).
- Electrical stimulation (non-implanted) – local stimulation of pelvic floor muscles. Electrical nerve stimulation (e.g. sacral nerve) was excluded.
- Weighted vaginal cones.
- Bladder training, either described by trialists as bladder training, bladder retraining, bladder drill or bladder re-education or an intervention 'which included mandatory schedule or self schedule with the aim of increasing the interval between voids'.[53] Prompted or timed voiding or urge suppression techniques alone with no mention of mandatory schedule or self-schedule were not considered as BT.

***Pharmacotherapy***
- SNRIs.
- Local administration (in form of cream or pessaries) of intravaginal low-dose estrogens, given as an adjunct to other therapy (e.g. PFMT) in postmenopausal women. Hormonal treatment (estrogens) given on its own was excluded.

Trials comparing methods of delivering services (e.g. nurse-led care) were considered for inclusion if they involved one of the included interventions listed above. The use of non-surgical therapies for prevention of incontinence was excluded. Complementary therapies, such as acupuncture, hypnosis and herbal medicines, were also excluded.

Where studies reported a comparison involving a programme of interventions (e.g. PFMT plus BT), then these studies were included, provided that every participant in the intervention arm received all of the specified treatments. If, on the other hand, treatments were tailored according to participants' diagnosis (e.g. PFMT for participants with stress incontinence alone and PFMT plus BT for participants with mixed or urge incontinence) and some participants did not receive all components available, studies were excluded, as it was not possible to distinguish effects of individual treatments for SUI.

A valid comparator was one of the included interventions or no treatment. Studies that compared non-surgical with surgical interventions were included in order to enable the performance of MTCs of non-surgical treatment. However, studies were excluded if the comparator was an excluded intervention (e.g. PFMT vs adrenergic agonists).

## Types of outcome measures

The standardisation committee of the International Continence Society recommended that research investigating the effect of therapeutic interventions for urinary incontinence in adult women should incorporate outcome measurements in the following five domains: (1) the patient's observations (symptoms); (2) quantification of symptoms (e.g. urine loss); (3) the clinician's observations (anatomical or functional); (4) quality of life; and (5) socioeconomic measures.[108] Following this recommendation, the following measures of outcomes were sought in this review:

*Primary outcomes*
- Number of women cured.
- Number of women cured or improved (this outcome is henceforth referred to in the text as improvement).
- Adverse events.
- Condition-specific (and generic measures of health-related) quality of life.

*Secondary outcomes*
- Quantification of symptoms:
  - number of incontinent episodes over 24 hours
  - number of pad changes over 24 hours
  - mean volume or weight of urine loss on pad test
  - number of micturitions over 24 hours.
- Participant satisfaction or desire for further treatment.
- Long-term data:
  - number of women having incontinence surgery
  - return of symptoms/recurrence.
- Socioeconomic measures.
- Other intermediate, explanatory or treatment-specific outcomes:
  - measure of pelvic floor muscle function
  - treatment adherence
  - volume and type of fluid intake or change in body mass index.

The cure and improvement rate may be ascertained via women's observation (self-report), quantification of symptoms (typically based on incontinence diaries or pad tests) or clinician's observation. There was a considerable variability in the way these outcomes were defined by the trialists, which limited the possibilities for quantitative synthesis. We therefore chose to combine data on the cure and improvement rate from different sources. The women's observation was given priority but for studies in which it was not reported, the rate based

on diaries was used as a proxy. Where diary data were also not reported, the rate based on pad tests or any other definitions chosen by the trialists was used.

The choice of quality of life measures again varied across studies. In addition, scores were reported either as final values or changes from baseline. Final values were preferred, but where these were not reported, a change score was used. Quantitative synthesis was performed separately for final values and change scores.

## Search methods for identification of studies

Literature searching was performed in two stages. First, relevant trials were identified from the Cochrane Incontinence Group Specialised Register of controlled trials of interventions for urinary incontinence (last searched 20 March 2008). When last searched for this project, the Register contained trials identified from: MEDLINE (covering January 1966 to week 4 of January 2008), the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 1, 2008), CINAHL (covering January 1982 to December 2000), and from hand searching relevant journals and conference proceedings.

Second, an extensive electronic search was carried out to identify reports of relevant published and ongoing studies, as well as grey literature and recent meeting abstracts from sources that are not currently covered for the Cochrane Incontinence Group Specialised Register of trials. A highly sensitive search strategy based upon the one developed for the Cochrane Incontinence Review Group was adopted.[109] This strategy used controlled vocabulary and text word terms that reflected the clinical condition, interventional procedures and study designs that were considered within the scope of this project. The following additional databases were searched:

- CINAHL (January 1982 to week 1 of December 2007)
- EMBASE (January 1980 to week 49 2007)
- BIOSIS (January 1985 to 13 March 2008)
- Science Citation Index and Social Science Citation Index (1970 to 2 February 2008)
- Current Controlled Trials (searched on 29 May 2008)
- ClinicalTrials.gov (searched on 9 June 2008)
- UKCRN Portfolio Database (replaces UK National Research Register).

An Internet search included the websites of relevant professional organisations and manufacturers that had not been covered by the Specialised Register or the other bibliographic database searches. No language or date restrictions were applied to the searches.

Searches were run for the intervention areas listed above on each of the databases listed. The main searches were run during September to November 2007, with updates in December 2007/January–February 2008. A set of urinary incontinence terms was combined with a set of terms to cover the main interventions listed above. These terms were combined with a study design filter as appropriate for each database. InterTasc website design filters were assessed and adapted if suitable.[110] Full details of the search strategies used are provided in Appendix 2.

## Data collection and analysis

### Selection of studies

The titles and abstracts identified by the searches were assessed by one reviewer, having already been assessed by the Cochrane Incontinence Group Trials Search Co-ordinator. Full-text copies of all potentially relevant reports were obtained and independently assessed by two reviewers, using a form developed to determine whether the reports met the inclusion criteria (Appendix 3). Any disagreements were resolved by consensus or arbitration by a third person.

### Data extraction

A data extraction form was developed to record details of study design, methods, participants, interventions and outcomes (Appendix 4). One reviewer extracted data and another reviewer checked the extracted data. Any disagreements that could not be resolved by discussion were referred to an arbiter.

For studies in which the majority of participants had stress incontinence alone (types 1 and 2 above), data were extracted for both primary and secondary outcomes. For studies where stress-predominant MUI was the majority (type 3) and studies of childbearing women, data were extracted for primary outcomes only. General background

and methodological information was collected from all studies.

## Assessment of risk of bias in included studies

Two reviewers independently assessed all of the studies that met selection criteria for potential risk of bias. The assessment used the adapted version of a checklist developed by the Cochrane Incontinence Group (Appendix 5).[109]

## Data synthesis

Data analysis was performed in two stages: (1) pairwise (head-to-head) comparison (Chapter 7), and (2) a mixed-treatments comparison (Chapter 8).

### *Pairwise comparisons*

For trials with multiple publications, only the most up-to-date or complete data for each outcome were included. Overall, there was inconsistency in outcome measures chosen by the trialists. For this reason, quantitative synthesis was performed on primary outcomes only. A random effects model was used to derive summary estimates with 95% CI of odds ratio (OR) for dichotomous variables (cure and improvement rates) and standardised mean difference (SMD) for continuous variables (quality-of-life measures). The random effects model was chosen because of variability in the characteristics of included studies in terms of participants' diagnoses (inclusion of women with stress, urge or mixed incontinence), variation in the treatment programmes, and the frequency and duration of treatment. Odds ratios were used because of their symmetry compared with relative risks and were therefore unaffected by outcome definitions (e.g. number of women cured or not cured). Odds ratios were also chosen to fulfil a requirement of the MTC model.

Publication bias was not formally assessed in the analysis, as the number of studies available for each comparison was very limited. Heterogeneity between studies was assessed by visual inspection of plots of the data, the chi-squared test for heterogeneity and the $I^2$ statistic.[111] Possible reasons for heterogeneity were explored, such as differences in the populations studied, the treatment given or the way in which the outcomes were assessed. Studies were grouped and sorted by types of participants: studies solely comprising women with SUI alone (type 1), studies where the majority of participants (50% or more) had stress incontinence alone (type 2) and studies where the majority (50% or more) of participants had MUI with stress as the predominant pattern (type 3). Where a quantitative synthesis was considered to be inappropriate or not feasible, then a narrative synthesis of the results was provided. Analysis was performed in STATA.[112]

The duration of treatment varied between studies. No attempt was made to standardise the treatment duration. Data at the end of the prescribed treatment phase, or at the first outcome assessment, if later, were used in quantitative synthesis. This may mean that any treatment effects shown were measured when they may be considered to be showing the maximum effects. Data from further follow-ups after the end of the initial treatment phase are reported in the text but are not included in the meta-analysis.

Data from primary studies were often reported ambiguously, particularly the number of people contributing data for an outcome (i.e. there were problems caused by missing data). For example, some studies had reported percentages without reference to an actual number of participants, or where studies claimed to have used an 'intention-to-treat' method but this was not clearly described. Where possible, we used the number of participants with available outcome data as the denominator for the relevant time point (i.e. we did not make the assumption that all participants who dropped out 'failed' and were not cured). We did consider the reasons for missing data caused by withdrawal/dropout reported by the trialists and these are highlighted (Chapter 7) where these appear to be treatment related. This is particularly problematic where there is differential withdrawal between trial arms.

Further analysis was planned on the following patient subgroups:

- nature of presentation – postpartum (within 12 months of childbirth) versus at any other time
- nature of the incontinence – stress urinary incontinence alone versus mixed/any urinary incontinence
- presence or absence of a co-existing anterior vaginal wall prolapse.

In the event this was not performed due to a lack of available data.

### *Mixed-treatment comparison*

This review aimed to assess the effectiveness of several treatments for SUI. With direct, head-to-head, comparisons alone it is often not clear which treatment is the most effective.[113] Multiple treatment comparison models attempt to address this problem by analysing all of the treatments and all of the trials together in one single model. In such a model it is possible to estimate the OR of all pairs of treatments, using direct and indirect evidence.

Multiple treatment comparison models were used for key treatments and outcomes (i.e. cure and improvement rates). The models were evaluated using Bayesian methods within WINBUGS software.[114] A full description is given in Chapter 8.

# Chapter 6
# Description of studies

## Results of the search

### Number of studies identified

The results of the initial searches are summarised in *Table 8*. These results were then assessed for potential relevance to the project and to remove duplicates already present in the Specialised Register that could not be removed by REFERENCE MANAGER duplicate checking. As described above, the numbers retrieved for CINAHL, EMBASE, BIOSIS and Science Citation Index include only the additional reports identified after excluding those identified in the Cochrane Incontinence Register. A total of 7103 titles and abstracts were identified, of which 378 were selected for full assessment.

### Number and type of studies included

Of the papers selected for full text assessment the level of agreement between reviewers about whether a paper met the inclusion criteria was very high, and 176 papers from the search met the inclusion criteria for the review. These described 88 studies, which covered 37 distinct treatments (*Table 9*) and 68 treatment comparisons (*Table 10*). The list of included studies and associated references are listed in Appendix 6.

### Excluded studies, with reasons for specific exclusions

A total of 199 papers were obtained but did not meet the inclusion criteria (*Figure* 7). Of these, 113 were excluded on the basis of study design, populations, interventions or outcomes. A further 86 papers (describing 56 studies) that did include relevant populations or interventions as part of the study were retained for further assessment and subsequently excluded through the consensus within the research team that it was impossible to attribute an effect to a particular intervention for women with SUI. Reasons for exclusions for the 86 papers excluded on further assessment are described in more detail in Appendix 7.

### Ongoing studies

A list of ongoing trials is provided in Appendix 8.

## Risk of bias in included studies

A summary of the assessment of risk of bias for the 88 included RCTs is presented in *Table 11*, and a detailed assessment for each of the included studies is reported in Appendix 9.

Fourteen studies (15.9%) reported both adequate random allocation sequence generation and concealment.[57,115,117,129,137,139–141,143,144,164,181,182,199] A further two studies reported adequate allocation concealment, although the method of allocation sequence generation was not clear.[133,153] Five studies reported inadequate methods of sequence generation and allocation concealment, namely consecutive/alternate assignment,[157,162,190] assignment based on hospital casenote number[116] or assignment based on time of arrival at the clinic and severity of incontinence.[127] Allocation concealment was also considered to be suboptimal (sealed envelopes with no indication of third party involvement) in a further five studies.[120,147,150,172,183] The remainder ($n = 47$, 53.4%) did not describe the methods used in sufficient detail to assess proneness to selection bias related to random allocation sequence generation and concealment.

The majority of studies did not clearly stipulate whether participants, health-care providers or outcome assessors were 'blinded' to participants' treatment status. For example, some studies would state 'double blind' but would not detail whether this referred to participants, health-care providers or outcome assessors. In addition, for some treatments (e.g. PFMT) it was not considered feasible to blind the health-care providers or participants to group allocation.

Nevertheless, 19 studies (21.6%) reported participant blinding.[57,117,128,130–134,136–145,189] Twelve of these involved drug therapy and used a placebo to blind participants.[57,117,136–145] In the other seven studies, participants were blinded through sham ES,[130–134,189] or imitation or placebo PFMT.[57,128] Six studies (6.8%) reported that health-care providers were blinded.[57,133,140,144,183,189] However, in one of these, which was a four-arm trial comparing drug therapy with active or imitation PFMT versus PFMT with active or placebo drug,[57] blinding

***TABLE 8*** *Search results – numbers of hits retrieved*

| Database | Number of hits | Number of full text papers selected for assessment | Number of reports included in final review |
|---|---|---|---|
| ***Published reports*** | | | |
| Cochrane SR | 645 (date of last search: 20 March 2008) | 322 | 175 |
| CINAHL | 1115 (date of last search: 5 February 2008) | 4 | 0 |
| EMBASE | 1031 (date of last search: 10 December 2007) | 23 | 0 |
| BIOSIS | 204 (date of last search: 13 March 2008) | 9 | 3[a] |
| SCI, SSCI | 3228 (date of last search: 6 February 2008) | 5 | 1[b] |
| Eli Lilly website | 15 (date of last search: 29 May 2008) | 15 | 0 |
| Subtotal | 6238 | 378 | 179 |
| ***Ongoing trial list*** | | | |
| UKCRN Portfolio Database[c] | 34 (date of last search: 9 June 2008) | NA | NA |
| CCT | 549 (date of last search: 29 May 2008) | NA | NA |
| ClinicalTrials | 282 (date of last search: 9 June 2008) | NA | NA |
| Subtotal | 865 | | |
| **Total** | **7013** | **378** | **179** |

CCT, Current Controlled Trials; Cochrane SR, Cochrane Incontinence Group Specialised Register of trials; NA, not applicable; SCI, Science Citation Index; SSCI, Social Science Citation Index.

a EAU conference abstracts – 12 reports of this trial had already been identified in the SR (Bø and colleagues, 1990)[115] and full text reports of these trials had already been identified in the SR.[116,117]

b This was a new trial but also picked up by SR MEDLINE search shortly after – related to timing of searches.[118]

c Replaces National Research Register.

was only possible for the drug treatment aspect of the study and not for PFMT. Blinded outcome assessment should be possible but only 17 studies (19.3%) reported that this was done.[115,121,122,127,128,130,131,133,134,147,153,163,164,166,182,189,199] Based on the available information on blinding, the majority of studies may be considered to be at modest risk of performance and detection bias.

While no study reported that groups had been treated differently in any other way apart from the named intervention, in two studies[140,181] it was doubtful whether groups had been treated the same in all other ways. In one of these studies this was due to a large proportion of participants in one arm opting out of the allocated treatment (weighted VCs) and receiving the comparator treatment (PFMT).[181] In the other, participants randomised to drug therapy were permitted to reduce their dosage, suspend their treatment or augment it with other treatments.[140]

Thirty-three studies (37.5%) stated numbers and reasons for withdrawals in sufficient detail,[57,115–118,123,127,128,131,133,134,137–140,143,146,147,153,156,159,164,166,167,175,178,181,183,187,189,197–199] while another 33 studies (37.5%) stated the number of withdrawals but did not describe reasons for withdrawals.[107,119,121,122,129,130,132,135,141,142,144,145,150,152,154,155,162,163,165,168,172,176,179,180,184,185,188,190–193,196] The remaining 22 studies (25.0%) did not provide sufficient information about withdrawals, dropouts and those lost to follow-up.

The majority of studies (52.3%) failed to report results for everyone who entered into the trial,[57,115–119,122,124,129–133,135,137–141,143–145,150,152,154,156,159,162,164,166–168,176,178,180,183,185,187–190,196–199] while in 24 studies (27.3%), it was unclear whether results accounted for all participants originally randomised.[107,120,121,134,136,142,148,153,157,158,160,161,165,169–174,179,186,193–195] Few studies explicitly stated that participants were analysed in the groups that they had been originally allocated to but no study showed clear evidence that this was not done.

***TABLE 9*** *Included interventions with available data*

| Type of interventions |
|---|
| NT |
| PFMT |
| PFMT + BF |
| ES |
| VC |
| BT |
| SNRI 80 mg |
| SNRI 40 mg |
| SNRI 30 mg |
| SNRI 20 mg |
| SNRI 40 mg b.i.d., starting with 40 mg b.i.d. |
| SNRI 40 mg b.i.d., starting with 40 mg q.d. |
| SNRI 40 mg b.i.d., starting with 20 mg b.i.d. |
| PFMT + ES |
| PFMT + VC |
| PFMT + BF + BT |
| PFMT + SNRI |
| PFMT with additional sessions |
| PFMT with audiocassette |
| Strength and motor relearning PFMT |
| Motor relearning PFMT |
| PFMT in supine position |
| PFMT in supine and upright position |
| Modified pilates |
| PFMT (maximal contraction) + BF |
| PFMT (submaximal contraction) + BF |
| PFMT + urethral electrical conductance |
| PFMT + BF (vaginal) |
| PFMT + BF (vaginal and abdominal) |
| PFMT + BF + ES (faradism) |
| PFMT + BF + ES (IFT) |
| PFMT+BF + ES (maximal intensity at clinic) |
| PFMT + BF + ES (low intensity at home) |
| VC passive |
| VC active |
| PFMT + VC + BF |
| Surgery |

b.i.d., twice daily; IFT, inferential therapy; NT, no treatment; q.d., once daily.

## Characteristics of included studies

The sample size ranged from 11 to 683, with a total of 9721 participants.[139,166] This includes 9163 non-childbearing women and 558 childbearing women (*Table 12*). A large proportion of the participants ($n = 4197$) came from 11 pharmaceutical trials comparing SNRI with placebo. Trials of physical or behavioural interventions for non-childbearing women were generally small; only four trials[57,123,129,183] had 200 or more participants and this included one trial[57] comparing PFMT with SNRI. Participants' baseline characteristics are provided in Appendix 10. A brief summary of the baseline characteristics of the participants in the included studies, such as mean age, is also provided in Chapter 7, although it was not possible to summarise severity of incontinence of the participants in the included studies in any meaningful way because this was reported using diverse measures.

The main characteristics of active treatments are summarised in Appendices 11–15. The majority of included studies involved PFMT as part of their interventions. The PFMT programme that was used varied in a number of ways: for example, whether a correct pelvic floor muscle contraction was confirmed prior to training, the frequency and type (e.g. strength and endurance) of contractions performed per day, the duration of training, the number of clinic sessions provided and whether training was provided individually or in groups. Advice on lifestyle change or strategies for symptoms of urge and/or frequency may also be given. However, without any structured regimen, such advice was considered as part of a broad PFMT programme and not a separate treatment.

Biofeedback may also be provided for the purpose of teaching a voluntary pelvic muscle floor contraction. A single episode of BF in the initial teaching but not thereafter was similarly considered as part of a broad PFMT programme. This excludes BF that was used *repeatedly* to monitor or assist PFMT, which was classified separately as an adjunct treatment (PFMT with BF). An intravaginal device is also included in the BF comparison.

While it is likely that the success or otherwise of PFMT may be contingent on the level of intensity of the training programme, characterising or categorising PFMT is difficult. We chose supervisory intensity (the frequency of clinic visits or any face-to-face contacts with health-care professionals) as a crude measure of differentiating PFMT programmes. The current guidelines[43] of the National Institute for Health and Clinical Excellence (NICE) estimated from the Guidance Development Group members that four to eight sessions were typically offered for PFMT over 3 months (six visits over 3 months or two visits per month). Following this guideline, in this

***TABLE 10*** *Number of studies and participants for each intervention assessed*

| Comparison | Number of trials | Participants | References |
|---|---|---|---|
| Lifestyle change | 1 | 84 | 119 |
| ***Comparison with no treatment*** | | | |
| PFMT vs NT | 14 | 958 | 57, 107, 115, 118, 120–129 |
| PFMT + BF vs NT | 2 | 110 | 120, 122 |
| ES vs NT | 8 | 446 | 115, 124, 126, 130–134 |
| VC vs NT | 2 | 220 | 115, 129 |
| BT vs NT | 1 | 131 | 135 |
| SNRI 80 mg vs NT | 11 | 3891 | 57, 117, 136–144 |
| SNRI 40 mg vs NT | 2 | 342 | 144, 145 |
| SNRI 30 mg vs NT | 1 | 60 | 145 |
| SNRI 20 mg vs NT | 2 | 344 | 144, 145 |
| SNRI 40 mg b.i.d., starting with 40 mg b.i.d. vs NT | 1 | 256 | 138 |
| SNRI 40 mg b.i.d., starting with 40 mg q.d. vs NT | 1 | 247 | 138 |
| SNRI 40 mg b.i.d., starting with 20 mg b.i.d. vs NT | 1 | 253 | 138 |
| PFMT + ES vs NT | 3 | 257 | 121, 123, 126 |
| PFMT + SNRI vs NT | 1 | 99 | 57 |
| ***Comparison of different PFMT variants*** | | | |
| PFMT vs PFMT + BF | 15 | 609 | 120, 122, 146–158 |
| PFMT vs PFMT with additional sessions | 4 | 178 | 116, 159–161 |
| PFMT vs PFMT with audiocassette | 2 | 157 | 162, 163 |
| Strength and motor relearning PFMT vs motor relearning PFMT | 1 | 128 | 164 |
| PFMT in supine position vs PFMT in supine and upright position | 1 | 44 | 165 |
| PFMT vs modified pilates | 1 | 11 | 166 |
| PFMT (maximal contraction) + BF vs PFMT (submaximal contraction) + BF | 1 | 37 | 167 |
| PFMT + perineometer vs PFMT + urethral electrical conductance | 1 | 34 | 168 |
| PFMT + BF (vaginal) vs PFMT + BF (vaginal and abdominal) | 1 | 38 | 169 |
| PFMT + BF vs PFMT + ES | 2 | 90 | 170, 171 |
| ***Comparison of different variants of ES*** | | | |
| PFMT + BF + ES (faradism) vs PFMT + BF + ES (IFT) | 1 | 30 | 157 |
| PFMT+BF + ES (maximal intensity at clinic) vs PFMT+BF + ES (low intensity at home) | 1 | 49 | 172 |
| ***Comparison of different variants of VC*** | | | |
| VC passive vs VC active | 1 | 61 | 173 |
| ***Comparison of different SNRI doses*** | | | |
| SNRI 80 mg vs SNRI 40 mg | 1 | 277 | 144 |
| SNRI 80 mg vs SNRI 20 mg | 1 | 278 | 144 |
| SNRI 40 mg vs SNRI 30 mg | 1 | 59 | 145 |
| SNRI 40 mg vs SNRI 20 mg | 2 | 342 | 144, 145 |
| SNRI 30 mg vs SNRI 20 mg | 1 | 60 | 145 |
| SNRI 40 mg b.i.d., starting with 40 mg b.i.d. vs SNRI 40 mg b.i.d., starting with 40 mg q.d. | 1 | 263 | 138 |

***TABLE 10*** *Number of studies and participants for each intervention assessed (continued)*

| Comparison | Number of trials | Participants | References |
|---|---|---|---|
| SNRI 40 mg b.i.d., starting with 40 mg b.i.d. vs SNRI 40 mg b.i.d., starting with 20 mg b.i.d. | 1 | 269 | 138 |
| SNRI 40 mg b.i.d., starting with 40 mg q.d. vs SNRI 40 mg b.i.d., starting with 20 mg b.i.d. | 1 | 260 | 138 |
| ***Comparison of different treatments (single modality)*** | | | |
| PFMT vs ES | 7 | 222 | 115, 124, 126, 174–177 |
| PFMT vs VC | 6 | 426 | 115, 129, 152, 178–180 |
| PFMT + BF vs VC | 2 | 141 | 152, 181 |
| PFMT vs BT | 1 | 84 | 182 |
| PFMT + BF vs BT | 1 | 137 | 183 |
| PFMT vs SNRI | 1 | 102 | 57 |
| PFMT vs surgery | 2 | 105 | 184, 185 |
| ES vs VC | 4 | 191 | 115, 186–188 |
| ***Comparison of different treatments (dual modality)*** | | | |
| PFMT vs PFMT + ES | 7 | 473 | 121, 123, 126, 185, 189–191 |
| PFMT + BF vs PFMT + BF + ES | 2 | 115 | 157, 172 |
| PFMT + BF vs PFMT + BF + ES (faradism)[a] | 1 | 30 | 157 |
| PFMT + BF vs PFMT + BF + ES (IFT)[a] | 1 | 30 | 157 |
| PFMT + BF vs PFMT + BF + ES (maximal intensity at clinic)[a] | 1 | 45 | 172 |
| PFMT + BF vs PFMT + BF + ES (low intensity at home)[a] | 1 | 46 | 172 |
| PFMT vs PFMT + VC | 1 | 46 | 192 |
| PFMT vs PFMT + SNRI | 1 | 102 | 57 |
| PFMT + BF vs PFMT + BF + BT | 1 | 136 | 183 |
| PFMT + ES vs ES | 1 | 22 | 126 |
| PFMT + VC vs VC | 1 | 42 | 188 |
| PFMT + BF + BT vs BT | 1 | 135 | 183 |
| PFMT + SNRI vs SNRI | 1 | 104 | 57 |
| ***Comparisons considered not relevant for direct head-to-head comparisons***[b] | | | |
| PFMT vs PFMT + BF + ES (faradism) | 1 | 30 | 157 |
| PFMT vs PFMT + BF + ES (IFT) | 1 | 30 | 157 |
| PFMT + ES vs VC | 1 | 60 | 193 |
| PFMT + ES vs surgery | 1 | 54 | 185 |
| PFMT + VC vs ES | 1 | 41 | 188 |
| PFMT + BF + VC vs ES | 1 | 46 | 132 |
| PFMT + SNRI vs surgery | 1 | 197 | 194 |
| PFMT + ES + BF vs VC | 1 | 120 | 195 |
| PFMT + ES + BF vs PFMT + VC | 1 | 102 | 196 |
| ***Childbearing women only*** | | | |
| PFMT, VC or both vs NT | 1 | 230 | 197 |
| PFMT vs NT | 1 | 264 | 198 |
| PFMT vs PFMT + abdominal training vs NT | 1 | 68 | 199 |

a Included in comparison of PFMT + BF vs PFMT + BF + ES noted above
b Results reported in Appendix 17, Comparison 23; some comparisons were included in the MTC analysis.

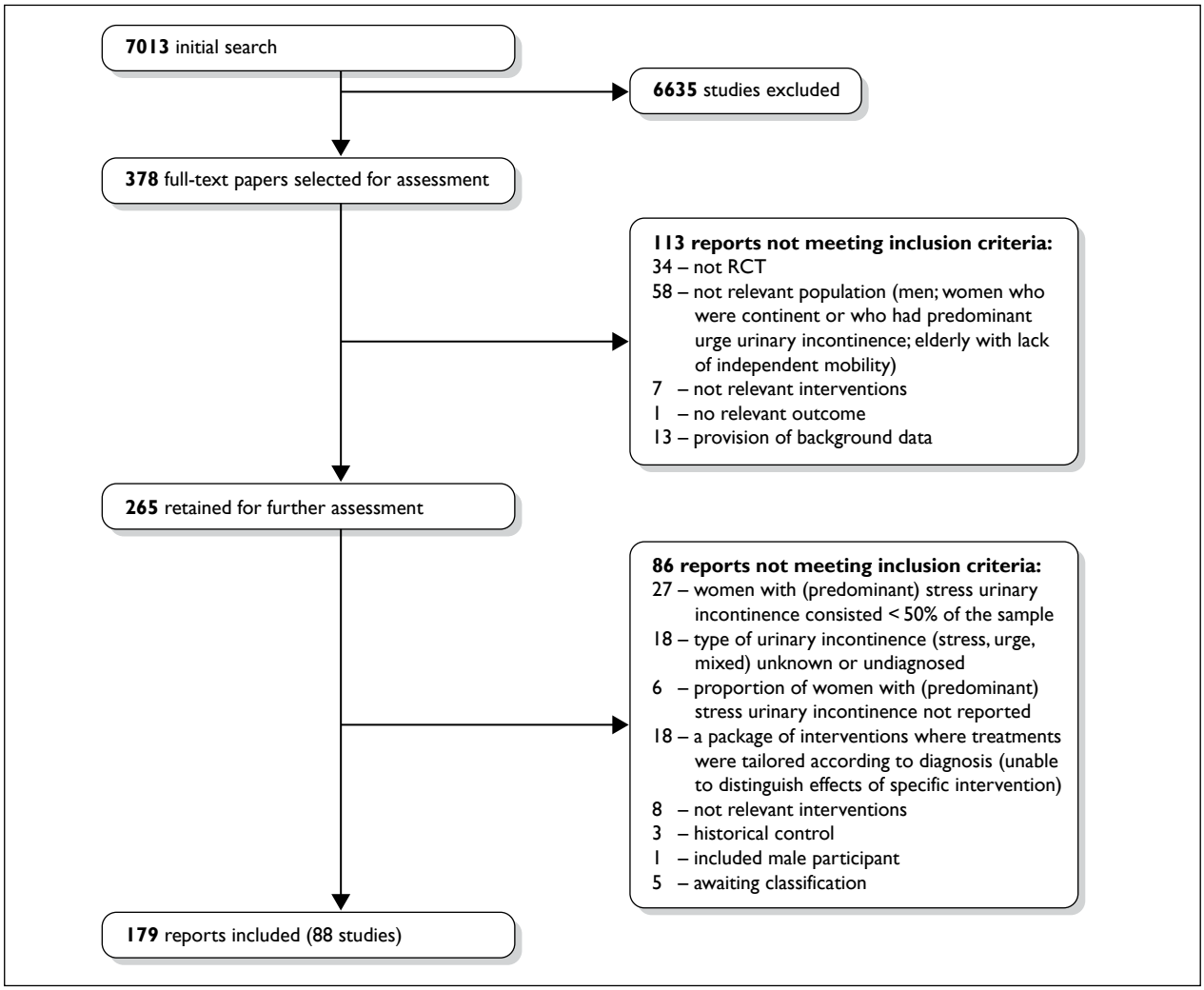



***FIGURE 7*** *Flow chart for study selection.*

***TABLE 11*** *Summary of assessment of risk of bias for the included randomised controlled trials (*N = *88)*

| Criteria | Yes (*n*, %) | Unclear (*n*, %) | No (*n*, %) |
|---|---|---|---|
| 1. Was the allocation sequence adequately generated? | 30 (34.1) | 53 (60.2) | 5 (5.7) |
| 2. Was allocation adequately concealed? | 16 (18.2) | 63 (71.6) | 9 (10.2) |
| 3. Were participants 'blind' to treatment status? | 19 (21.6) | 56 (63.6) | 13 (14.8) |
| 4. Were health-care providers 'blind' to treatment status? | 6 (6.8) | 63 (71.6) | 19 (21.6) |
| 5. Were outcome assessors 'blind' to treatment status? | 17 (19.3) | 65 (73.9) | 6 (6.8) |
| 6. Were the groups treated identically other than for the named intervention? | 86 (97.7) | 0 (0.0) | 2 (2.3) |
| 7. Was there a description of withdrawals, dropouts and those lost to follow-up? | 33 (37.5) | 33 (37.5) | 22 (25.0) |
| 8. Was the analysis on intention to treat? That is: | | | |
| (a) Were trial results reported for everyone who entered the trial? | 18 (20.5) | 24 (27.3) | 46 (52.3) |
| (b) Were participants analysed in the groups they were originally allocated to? | 75 (85.2) | 13 (14.8) | 0 (0.0) |

***TABLE 12*** *Number of studies and participants included in the review by study size*

| | Number of studies | | | Number of participants |
|---|---|---|---|---|
| | Type 1 | Type 2 | Type 3 | |
| Lifestyle | 0 | 1 | 0 | 84 |
| Physical/behavioural, ≥ 200 participants per trial | 1 | 2 | 1 | 843 |
| Physical/behavioural, 100–199 participants per trial | 6 | 4 | 1 | 1459 |
| Physical/behavioural, < 100 participants per trial | 56 | 1 | 1 | 2583 |
| Pharmaceutical (SNRI vs placebo)[a] | 3 | 1 | 7 | 4194 |
| Studies with childbearing women only | 1 | 2 | 0 | 558 |
| **Total** | **67** | **11** | **10** | **9721** |

a No studies meeting the inclusion criteria were identified involving intravaginal low-dose estrogens.
Type 1, studies solely comprising women with SUI alone; type 2, studies where ≥ 50% of women had SUI alone; type 3, studies where 50% of women had stress-predominant MUI (see Chapter 5, Types of participants).

review a PFMT programme with up to two clinic visits per month is considered as PFMT with basic supervisory intensity (or 'PFMT basic'), and the programme with more than two clinic visits per month is considered as PFMT with intensive supervision (or 'PFMT extra sessions') (Appendices 11 and 12). This is regardless of the amount or type of pelvic floor muscle contractions performed per day or the duration and precise nature of supervision; such data were poorly reported and hence could not be incorporated into our analysis.

The comparison group may be another active treatment or no treatment. No treatment in this review is equivalent to no *active* treatment. Leaflet-only PFMT, which was not taught by a health-care professional, is also considered as 'no treatment', based on the assumption that the distribution of guidelines has a small effect on behaviour[200] and also that patients are not naive and can obtain knowledge of PFMT from anywhere (e.g. internet). Within the 30 studies of non-childbearing women classified as having a 'no-treatment' arm, participants received no treatment,[107,118,120–122,124,125,135] advice on continence device or pads,[115,127] sham ES,[126,130–134] placebo PFMT,[128] imitation PFMT with placebo drug,[57] placebo drug alone,[117,136–142,144,145] a booklet including the entire training programme for self-administration[123] or an educational leaflet, encouragement to keep an exercise diary and an equal number of clinic visits to the comparator arm.[129] Of the three studies of childbearing women, one[199] provided a relaxation massage, whereas the other two[197,198] provided standard or routine care for the 'no-treatment' arm.

The treatment protocol for ES varied widely between studies. A common problem associated with ES is that there is no consistency in the criteria used to describe ES.[201] Treatment could be described on the basis of the type of current being used (e.g. faradic stimulation, interferential therapy), the structure being targeted (e.g. neuromuscular ES), or the current intensity, etc. No attempt was made in this review to categorise different treatment protocols.

The VCs treatment was relatively homogeneous and so was SNRI drug therapy, which was based on duloxetine. Nevertheless, one study by Kinchen and colleagues[140] was a 'naturalistic' study, for which participants could, at any point after randomisation, choose to remain on SNRI as randomised, reduce drug doses, add other treatments to SNRI, or suspend SNRI and receive other treatments. The additional treatments used by the study participants included estrogen products, anticholinergic medications and PFMT. There was differential withdrawal due to adverse events between SNRI and placebo groups in all 10 studies with available data (see Chapter 7, Serotonin–noradrenaline reuptake inhibitors drug therapy).[117,137–145] Nine studies[117,136–139,142–145] stated that they had either received sponsorship, funding or support from the manufacturer of duloxetine (Eli Lilly and Company).

# Chapter 7

# Assessment of clinical effectiveness

This chapter describes the results from direct pairwise (head-to-head) comparisons. Results are grouped into three sections: comparison with no treatment and variation within comparators, comparison between different treatments (single modality), and comparison between different treatments (dual modality).

A summary of the baseline characteristics of the participants and interventions in the included studies is provided at the beginning of each section. This is described in more detail in Appendix 10.

The focus is on the primary outcome data (cure, improvement, adverse events and quality of life) and, in particular, those that are relevant to the MTC analysis in the following chapter (Chapter 7). There was a great variability in the way cure and improvement was defined by the trialists. This is detailed in Appendix 16. As noted in Chapter 5 (see Types of outcome measures), we chose to substitute woman's observation (measurement type 1) with quantified symptoms or clinician's observation (measurement type 2), if the former was missing. The type of outcome measurement for each study is shown on the right hand side of the quantitative synthesis figure (measurement type – see *Box 8*). For quantitative synthesis, data at the end of the prescribed treatment phase, or at the first outcome assessment, if later, were used. Data from further follow-ups and other relevant primary outcome data are reported in the text and also in Appendix 17.

Studies with different population types are analysed together. The type of population included in each trial is also shown on the right hand side of the figure (population type – *Box 8*). The quantitative analysis for cure and improvement rates was also performed with studies that included women diagnosed as having SUI only (population type 1); the results are presented in Appendix 18. Quantitative data syntheses for condition-specific quality of life were limited due to lack of available data; these are given in Appendix 19. Studies of childbearing women were analysed separately and provided in Appendix 20. Secondary outcome data of all relevant comparisons are reported in Appendix 21.

***BOX 8*** *Classification of sample populations and outcome measurements*

***Type of outcome measurement***

1. Women's observation
2. Quantification of symptoms or clinician's observation

***Type of population***

1. All women had SUI alone
2. ≥ 50% of women had SUI alone; the remainder could have UUI or MUI
3. ≥ 50% of women had MUI with stress symptoms as a predominant pattern; the remainder could have SUI, UUI or MUI

## Comparison with no treatment and variation within comparators

### Lifestyle change

No studies were found comparing lifestyle change with no treatment. The only relevant study[119] was a crossover trial evaluating the effect of increasing or decreasing fluid intake on urinary symptoms in women (*Table 13*). Women were randomised in the order in which they increased or decreased fluids. All women were instructed to restrict caffeine. No information was available on any of the specified outcomes.

### PFMT with and without BF

#### *PFMT, with or without BF, vs no treatment*

The characteristics of included studies comparing PFMT (with and without BF) and no treatment are summarised in *Table 14*. Fourteen studies were eligible for this comparison, in which a total of 958 participants were randomised. Studies varied widely in terms of the duration of treatment prescribed by the trialists, as well as supervisory intensity (measured in terms of the number of clinic visits or any face-to-face contacts with a health-care professional). No studies reported data on further follow-up after the end of the prescribed

***TABLE 13*** *Baseline characteristics of randomised controlled trials comparing lifestyle changes to no treatment*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age (years) | Supervisory intensity[a] |
|---|---|---|---|---|---|---|
| Swithinbank 2005[119] | 2 | 2 | Increase fluid | 84 (crossover trial) | 54.8 | Intensive |
| | | | Decrease fluid | 84 (crossover trial) | | Intensive |

a Intensive, more than two clinic visits per month.

treatment phase. The comparison groups received no treatment,[107,118,120–122,124,125] advice on continence device or pads,[115,127] sham ES,[126] placebo PFMT,[128] imitation PFMT with placebo drug,[57] a booklet including the entire behavioural training programme for self-administration[123] or an educational leaflet, the equal number of clinic visits as the PFMT arm and encouragement to keep an exercise diary.[129]

Pelvic floor muscle training plus sham ES was classified as being equivalent to PFMT. Where both PFMT and PFMT plus sham ES were present in a trial,[121] the dichotomous data were combined (added up).

**Cure and improvement rate**

*Figures 8* and *9* show the number of women who were either cured or improved, respectively, in the PFMT group (with or without BF) versus the no-treatment group at the end of the prescribed treatment phase. Pooled data for cure rates showed higher cure rates for PFMT with or without BF, but with significant heterogeneity (*Figure 8*: PFMT vs no treatment – 23% vs 7%, OR 5.41, 95% CI 1.64 to 17.82; PFMT with BF vs no treatment – 42% vs 2%, OR 21.54, 95% CI 3.65 to 126.98). The source of the heterogeneity appeared to be the inclusion of studies with women with SUI with or without UUI symptoms (population types 2 or 3). In these studies the direction and magnitude of effect varied across studies. Of note is that the two studies reporting the lowest effect size[123,129] not only included women with different types of urinary incontinence, but also had the largest sample size, less intensive supervision (fewer clinic visits) and relatively substantial provision of care for the no-treatment group (e.g. self-administered behavioural training, clinic visits), which may have contributed to the relatively small effect size.

Removing these studies reduced the statistical heterogeneity but also widened the CI (as fewer data were available for meta-analysis) (Appendix 18, Comparison 01: PFMT vs no treatment – 39% vs 3%, OR 15.15, 95% CI 5.50 to 41.75; PFMT with BF vs no treatment – 80% vs 0%, OR 77.00, 95% CI 3.75 to 1581.71).

Results for improvement rates similarly favoured PFMT with or without BF compared with no treatment, though statistical heterogeneity was again evident across studies (*Figure 9*: no BF, OR 11.75, 95% CI 3.49 to 39.55; with BF, OR 24.20, 95% CI 2.02 to 290.58). One additional cause of heterogeneity for this outcome was the greater variability in the way 'improvement' was defined between studies, as the heterogeneity remained even after removing studies with mixed diagnoses (Appendix 18, Comparison 02: OR 27.07, 95 CI 4.72 to 155.35). Crucially, the smallest effects were found in those studies with placebo or imitation PFMT[57,128] in the no-treatment arm and with women with mixed types of urinary incontinence.[123,129]

**Adverse events**

Adverse events were uncommon in the PFMT group (*Table 15*). Nevertheless, two studies[127,129] reported that up to 12% of women experienced adverse events during PFMT.

**Quality of life**

Condition-specific quality of life was reported using various measures, including the Social Activity Index, the Urinary Incontinence Quality of Life (I-QoL) scale, the Leicester Impact Scale, the Incontinence Impact Questionnaire (IIQ) and the Bristol Female Lower Urinary Tract Symptoms (B-FLUTS) (Appendix 19, Comparison 01). In all but two trials,[123,129] results were better for the PFMT group (with or without BF). One study[115] reported this outcome using two instruments (Social Activity Index and B-FLUTS), with results consistently favouring PFMT. As the outcome measures varied between studies and not all studies reported data amenable to meta-analysis, quantitative synthesis was not performed.

***TABLE 14*** *Background characteristics of studies comparing pelvic floor muscle training (plus biofeedback) with no treatment or comparing variation within comparators*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age | Supervisory intensity[a] | Notes |
|---|---|---|---|---|---|---|---|
| Aksac 2003[120] | 1 | 2 | PFMT | 20 | 52.5 | Intensive | |
| | | | PFMT + BF | 20 | 51.6 | Intensive | |
| | | | NT | 10 | 54.7 | None | |
| Bidmead 2002[121] | 1 | 3.5 | PFMT | 40[b] | 46.2 | Basic | |
| | | | PFMT + sham ES | 42[b] | 51.5 | Basic | |
| | | | NT | 20[b] | 47.5 | None | |
| Bø 1999[115] | 1 | 6 | PFMT | 29 | 49.6 | Intensive | |
| | | | NT | 32 | 51.7 | None | Advice on Continence Guard™ |
| Burns 1993[122] | 2 | 2 | PFMT | 43[c] | 63.0 | Intensive | |
| | | | PFMT + BF | 40[c] | 63.0 | Intensive | |
| | | | NT | 40[c] | 63.0 | None | |
| Ghoniem 2005[57] | 1 | 3 | PFMT | 50 | 54.0 | Basic | Placebo drug |
| | | | NT | 47 | 51.0 | Basic | Placebo drug and imitation PFMT |
| Goode 2003[123] | 3 | 2 | PFMT | 66 | 57.7 | Basic | 'Behavioural training' |
| | | | NT | 67 | 55.9 | None | Self-administered behavioural training |
| Henalla 1989[124] | 1 | 3 | PFMT | 26 | NR | Intensive | |
| | | | NT | 25 | NR | None | |
| Henalla 1990[125] | 1 | 1.5 | PFMT | 8 | 54 | NR | |
| | | | NT | 7 | | NR | |
| Hofbauer 1990[126] | 1 | 1.5 | PFMT | 11 | 51.0 | Intensive | |
| | | | NT | 10 | 59.8 | Intensive | Sham ES |
| Kim 2007[118] | 1 | 3 | PFMT | 35 | 76.6 | Intensive | |
| | | | NT | 35 | 76.6 | None | |
| Lagro-Janssen 1991[127] | 1 | 3 | PFMT | 33 | 46.1 | Basic | |
| | | | NT | 33 | 44.6 | None | Advice on continence pads |
| Miller 1998[107] | 1 | 0.25 | PFMT | 13 | 68.4 | Intensive | The Knack |
| | | | NT | 14 | | None | |
| Ramsay 1990[128] | 1 | 3 | PFMT | 22 | NR | NR | |
| | | | NT | 22 | NR | NR | Placebo PFMT |
| Williams 2006[129] | 2 | 3 | PFMT | 79 | 55.9 | Basic | |
| | | | NT | 79 | 56.7 | Basic | Leaflet, clinic visits and exercise diary |

NR, not reported.
a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.
b *N* randomised unclear due to poor reporting.
c *N* in analysis; *N* randomised in each group unclear.

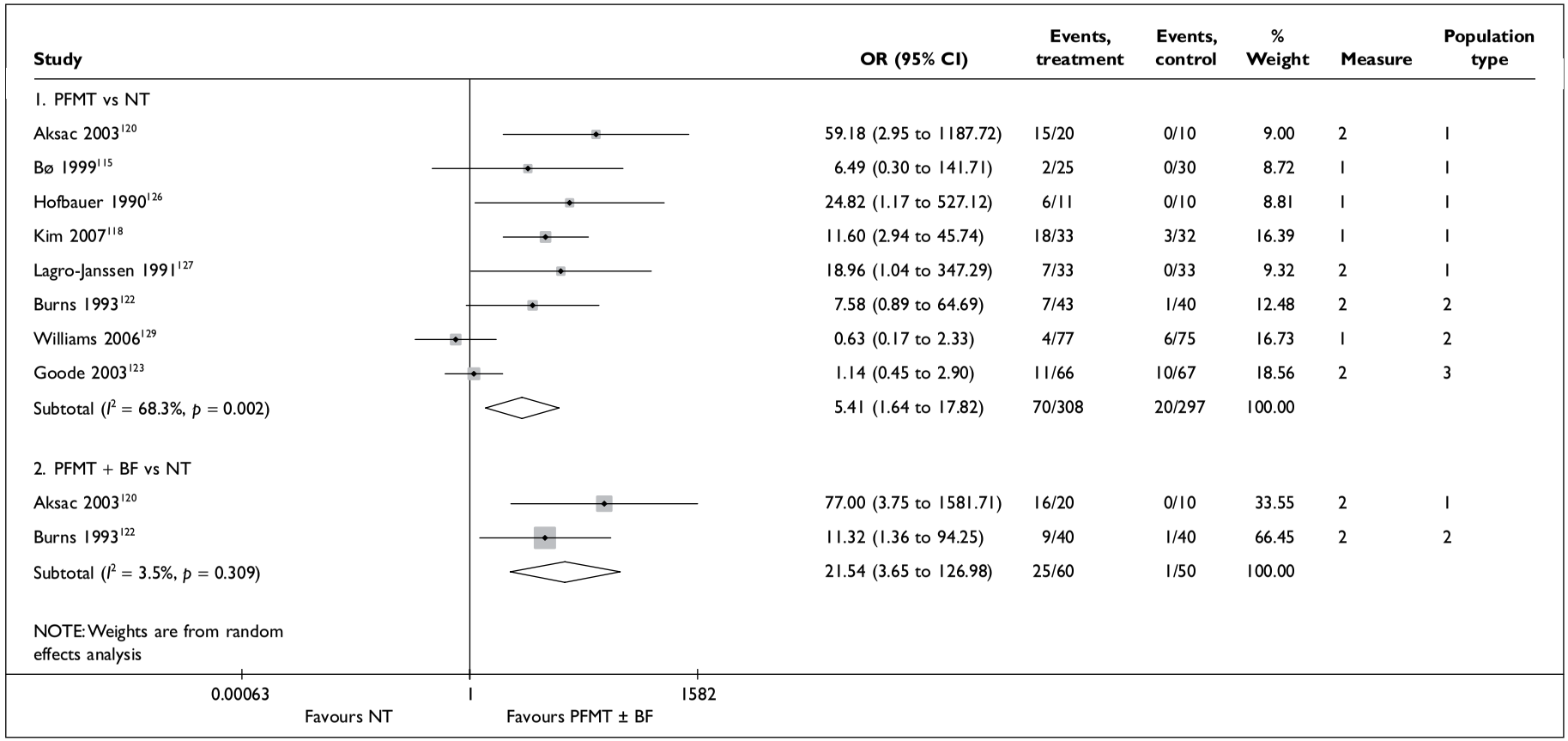



***FIGURE 8*** *Cure rates for pelvic floor muscle training, with or without biofeedback, versus no training.*

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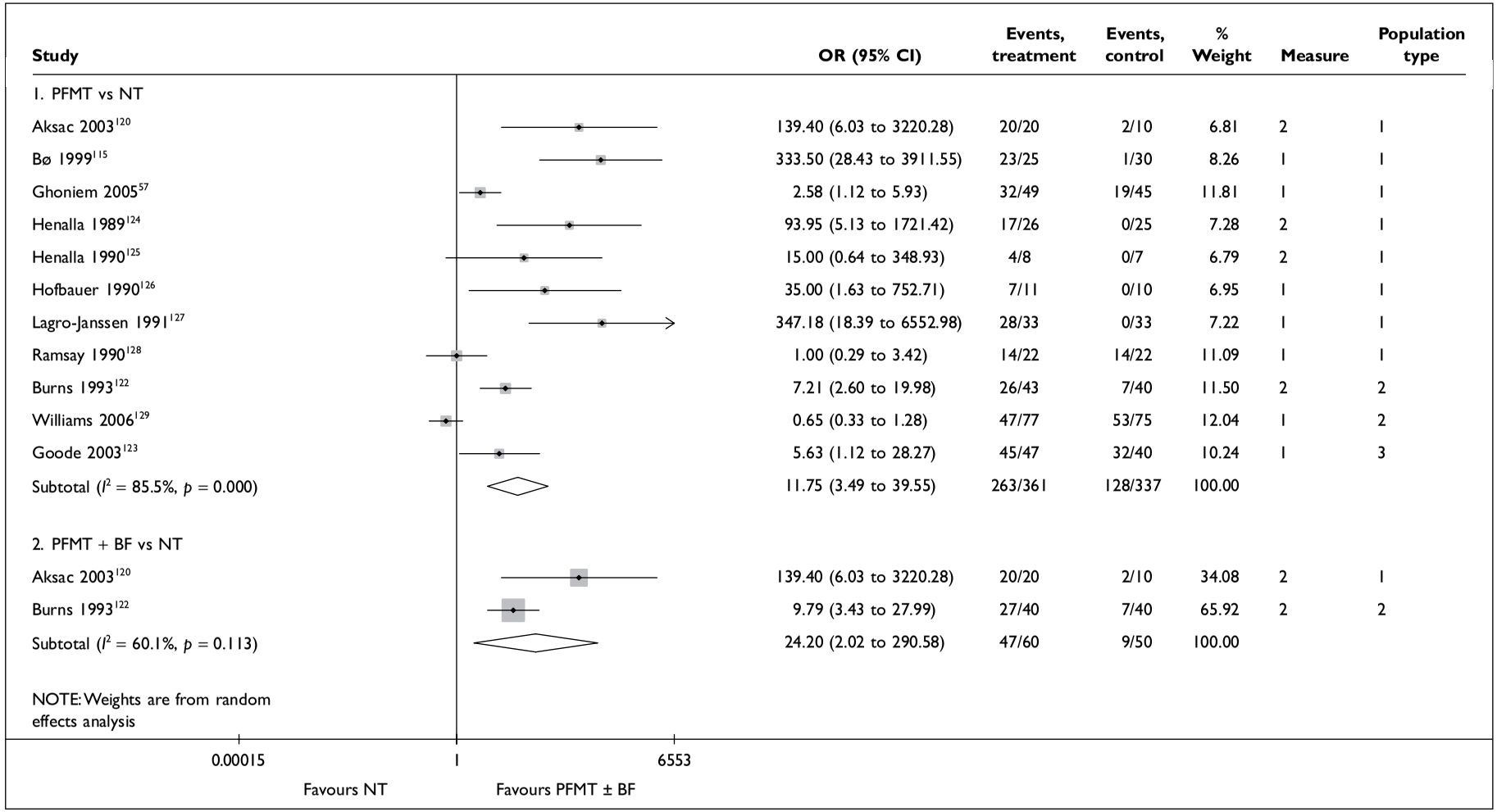


***FIGURE 9*** *Improvement rates for pelvic floor muscle training, with or without biofeedback, versus no training.*

***TABLE 15*** *Adverse events: pelvic floor muscle training versus no treatment*

| | PFMT | | NT | | | |
|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **Notes** | **Population type** |
| Lagro-Janssen 1991[127] | 4/33 | 12 | 0/33 | 0 | Pain, uncomfortable feeling during exercise | 1 |
| Williams 2006[129] | 2/79 | 3 | 0/79 | 0 | Urinary tract infection | 2 |

Two studies[115,123] reported general health-related quality of life (HRQoL) using SF-36 and the Norwegian version of the Quality of Life Scale (QoLS-*N*). One of these studies[115] reported higher quality of life for the PFMT group, whereas the other[123] reported no statistically significant difference between the groups (Appendix 17, Comparison 01).

### *PFMT vs PFMT plus BF*

Fifteen studies[120,122,146–158] evaluated the effect of adding BF to PFMT (*Table 16*). In two studies by Glavind and colleagues[150] and Wilson and colleagues,[157] the women randomised to use BF had more clinic visits than the PFMT group. There was also a potential difference in supervisory intensity in a further study by Pages and colleagues,[154] in which the PFMT group had group therapy for 60 minutes, five times a week, whereas the BF group had individual therapy for 15 minutes, five times a week.

In addition to devices specifically designed to provide visual and/or audio BF, the use of intravaginal resistance device,[149] an endotrainer[151] and an exerciser[155] were also classified as BF for the purpose of this review.

#### Cure and improvement rate

Pooled data showed that at the end of the prescribed treatment phase the addition of BF to PFMT resulted in significantly higher cure and improvements than with PFMT alone (*Figures 10* and *11*: cure rates 34% vs 49%, OR 0.48, 95% CI 0.30 to 0.77; improvement rates 76% vs 86%, OR 0.41, 95% CI 0.18 to 0.97). Among the studies showing the largest effect size were studies by Glavind and colleagues[150] and Wilson and colleagues,[157] which had additional supervisory visits in the BF group relative to the PFMT group. The study by Pages and colleagues,[154] which was also a trial with a potential difference in supervisory intensity, also suggested a large treatment effect in the cure data.

Two studies[150,157] conducted a further follow-up after the end of the supervised treatment in which all women were advised to continue PFMT at home without BF or any close supervision by a health-care professional. The first study[157] with 6-month follow-up (4.5 months after the end of 6-week treatment) reported that women who did not use BF in the treatment phase were significantly less likely to improve than those who trained with BF (Appendix 17, Comparison 02, 4/15 vs 9/14, OR 0.20, 95% CI 0.04 to 0.98). In the second study[150] with 2.5 years of follow-up, the results for cure and improvement also favoured the BF group, although the differences were not statistically significant (Appendix 17, Comparison 02, cure 0/14 vs 5/19, OR 0.09, 95% CI 0.01 to 1.80; improvement 4/14 vs 8/19, OR 0.55, 95% CI 0.13 to 2.40).

#### Adverse events

Adverse events were uncommon but in two studies[146,153] that did report incidents, more participants (15–27%) experienced adverse events if they were using BF. Some women found the device unpleasant or painful (*Table 17*).

#### Quality of life

Five studies[120,147,152,153,158] reported condition-specific quality of life using four different measures (*Table 17*). In four of these studies results were similar for both groups, but in one study,[158] women reported statistically significantly better quality of life in the PFMT group than with those using BF. Quantitative synthesis did not demonstrate a statistically significant difference between the groups (Appendix 19, Comparison 01, SMD for total score, –0.29, 95% CI –0.62 to 0.03; SMD for change in score, 0.49, 95% CI –0.14 to 1.12).

### *PFMT vs PFMT with additional sessions*

The characteristics of included studies comparing PFMT with and without additional supervisory clinical sessions are summarised in *Table 18*.

#### Cure and improvement rate

Cure and improvement rates were consistently higher for women who received additional supervisory sessions (*Figures 12* and *13*: cure rate, 15% vs 43%, OR 0.11, 95% CI 0.03 to 0.43;

***TABLE 16*** *Baseline characteristics of studies comparing pelvic floor muscle training (PFMT) with PFMT plus biofeedback*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age | Supervisory intensity[a] | Notes |
|---|---|---|---|---|---|---|---|
| Aksac 2003[120] | 1 | 2 | PFMT | 20 | 52.5 | Intensive | |
| | | | PFMT + BF | 20 | 51.6 | Intensive | |
| Aukee 2002[146] | 1 | 3 | PFMT | 15 | 50.8 | Basic | |
| | | | PFMT + BF | 15 | 51.8 | Basic | Home BF |
| Berghmans 1996[147] | 1 | 1 | PFMT | 20 | 50.4 | Intensive | |
| | | | PFMT + BF | 20 | 46.4 | Intensive | |
| Burns 1993[122] | 2 | 2 | PFMT | 43 | 63.0 | Intensive | |
| | | | PFMT + BF | 40 | 63.0 | Intensive | Clinic BF |
| Castleden 1984[148] | 1 | 1 | PFMT | 19 (crossover) | 55.0 | NR | |
| | | | PFMT + BF | 19 (crossover) | | NR | Home BF |
| Ferguson 1990[149] | 1 | 1.5 | PFMT | 10 | 35.8 | Basic | |
| | | | PFMT + BF | 10 | 37.1 | Basic | IVRD |
| Glavind 1996[150] | 1 | 3[b] | PFMT | 20 | 45.0 | Basic | |
| | | | PFMT + BF | 20 | | Basic | Additional visits for clinic BF |
| Klingler 1995[151] | 1 | 3 | PFMT | 21 | 53.0 | Intensive | |
| | | | PFMT + BF | 20 | 51.8 | Intensive | Endotrainer |
| Laycock 2001[152] | 1 | 3 | PFMT | 20 | NR | Basic | |
| | | | PFMT + BF | 40 | NR | Basic | Home BF |
| Mørkved 2002[153] | 2 | 6 | PFMT | 50 | 45.4 | Intensive | |
| | | | PFMT + BF | 53 | 47.8 | Intensive | Home + clinic BF |
| Pages 2001[154] | 1 | 3 | PFMT | 27 | 51.1 | Intensive | Group therapy |
| | | | PFMT + BF | 24 | | Intensive | Individual therapy; clinic BF |
| Shepherd 1983[155] | 1 | 4.5[c] | PFMT | 11 | 48.4 | Basic | |
| | | | PFMT + BF | 11 | 48.2 | Basic | Exerciser |
| Taylor 1986[156] | 1 | 2.25 | PFMT | 13 (number in each group unclear) | NR | Intensive | |
| | | | PFMT + BF | | NR | Intensive | Clinic BF |
| | | | PFMT + BF | | NR | Intensive | Clinic + home BF |
| | | | PFMT + BF | | NR | Intensive | Home BF without vaginal sensor to be used as a resistive device |
| Wilson 1987[157] | 1 | 1.5 | PFMT | 15 | 46.8 | Basic | |
| | | | PFMT + BF | 15 | | Intensive | Clinic BF |
| Wong 1997a[158] | 1 | 2 | PFMT | 7 | 48.2 | Intensive | |
| | | | PFMT + BF | 10 | | Intensive | |

IVRD, intravaginal resistance device.

a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.

b Treatment for 4 weeks, and measurement at 3 months.

c Treatment for 6 weeks, and measurement at 3 months after end of treatment.

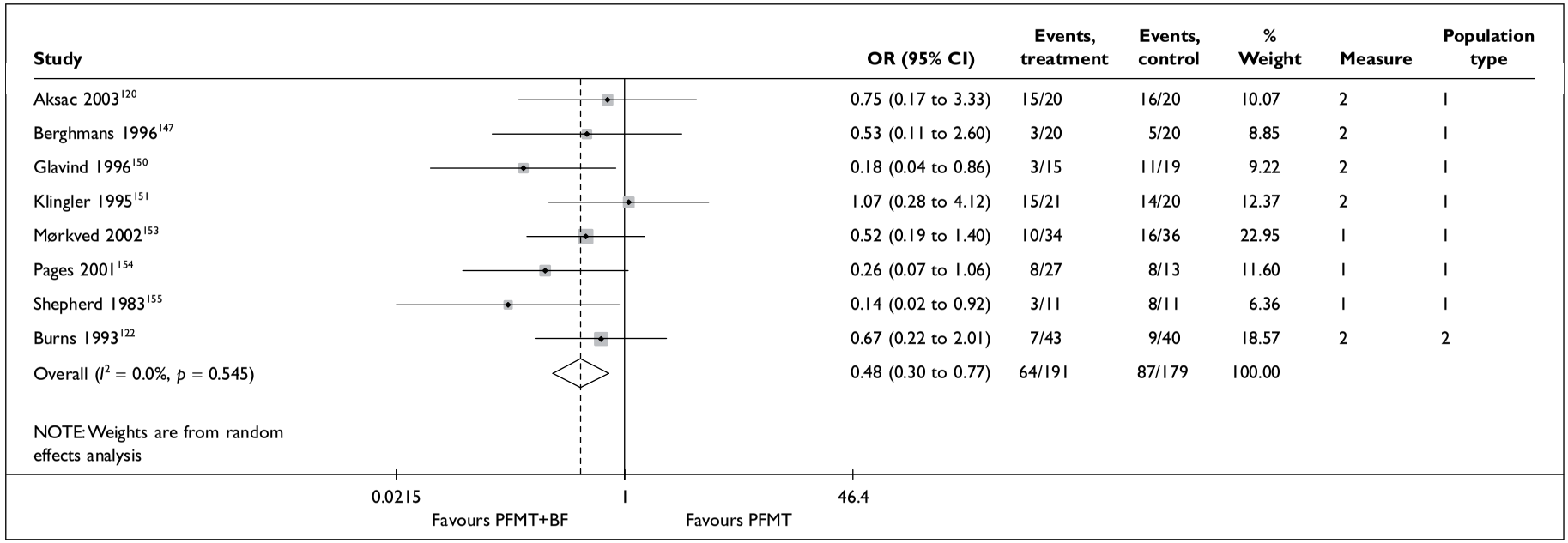


***FIGURE 10*** *Cure rates: pelvic floor muscle training (PFMT) versus PFMT plus biofeedback.*

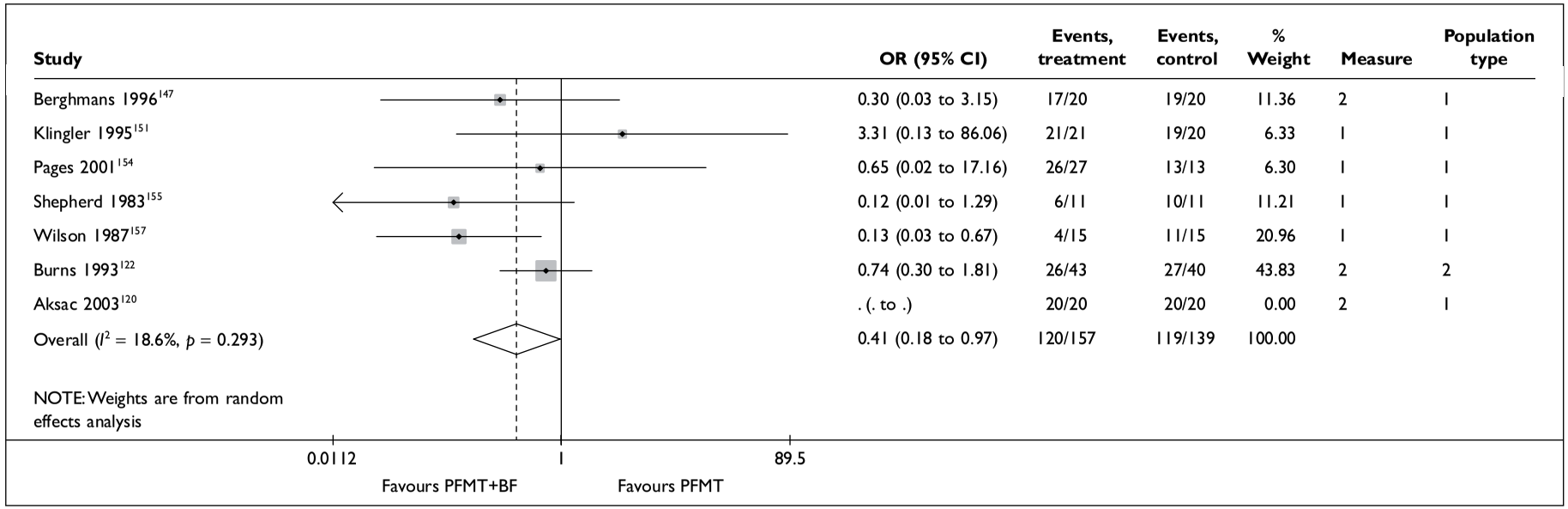


***FIGURE 11*** *Improvement rates: pelvic floor muscle training (PFMT) versus PFMT plus biofeedback.*

***TABLE 17a*** *Adverse events: pelvic floor muscle training (PFMT) versus PFMT plus biofeedback*

| | PFMT | | PFMT + BF | | | |
|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | Notes | Population type |
| Aukee 2002[146] | 3/15 | 20 | 4/15 | 27 | Pain while training (of which 3/7 premenopausal) | 1 |
| Mørkved 2002[153] | 3/46 | 7 | 7/48 | 15 | PFMT + BF: 7/48 found use of apparatus 'unpleasant'; PFMT: 3/46 found PFMT itself 'unpleasant'; 'However, they all followed the training protocol in spite of this' | 2 |

***TABLE 17b*** *Quality of life: pelvic floor muscle training (PFMT) versus PFMT plus biofeedback*

| | PFMT | | PFMT + BF | | | | |
|---|---|---|---|---|---|---|---|
| | *N* | Value | *N* | Value | Reported *p*-value | Notes | Population type |
| ***Social Activity Index*** | | | | | | | |
| Aksac 2003[120] | 20 | 7.5 (1.2) | 20 | 8.1 (0.8) | | Score (median, SD) | 1 |
| Mørkved 2002[153] | 34 | 9.5 (0.74) | 36 | 9.6 (0.61) | | Score (mean, SD) at 6 months | 1 |
| ***Modified PRAFAB*** | | | | | | | |
| [a]Berghmans 1996[147] | 20 | 13.1 (8.6) | 20 | 11.1 (5.9) | NS | Score (mean, SD) | 1 |
| ***King's Health Questionnaire*** | | | | | | | |
| Laycock 2001[152] | 16 | 8.13 (9.06) | 22 | 6.14 (6.20) | NS | Change in score (mean increase, SD) | 1 |
| ***Incontinence Impact Questionnaire*** | | | | | | | |
| Wong 1997a[158] | 7 | 24.5 (10.8) | 10 | 8.5 (19.9) | < 0.05 | Change in score (mean reduction, SD) | 1 |

NS, not statistically significant.
a Lower scores reflect better quality of life.

improvement rate, 54% vs 97%, OR 0.05, 95% CI 0.01 to 0.28).

One small study[159] with 15 years of follow-up also reported that the number of women who remained continent (cured) after they were left to continue PFMT on their own was higher in the group who had additional sessions during the initial supervised treatment phase, although this difference was not statistically significant (Appendix 17, Comparison 03, 16% vs 30%, OR 0.44, 95% CI 0.11 to 1.87).

### Adverse events

No studies reported any adverse events.

### Quality of life

Condition-specific quality of life measures varied, but all studies consistently reported that PFMT with additional sessions was associated with better quality of life (*Table 19*). Two studies[116,159] provided data amenable to quantitative synthesis; results showed a statistically significant difference between the groups favouring PFMT with additional sessions (Appendix 19, Comparison 02, SMD –1.07, 95% CI –1.98 to –0.15).

#### *Comparisons of other PFMT variants*

A further 10 studies[162–171] compared other variations in the method of delivering PFMT (*Table 20*). Not all studies collected data for the

***TABLE 18*** *Baseline characteristics of studies comparing pelvic floor muscle training (PFMT) and PFMT with additional supervisory clinical sessions*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age | Supervisory intensity[a] |
|---|---|---|---|---|---|---|
| Bø 1990[159] | I | 6 | PFMT | 31 | 45.9 | Basic |
| | | | PFMT with additional sessions | 26 | 44.9 | Intensive |
| Konstantinidou 2007[116] | I | 3 | PFMT | 15 | 47.8 | Basic |
| | | | PFMT with additional sessions | 15 | | Intensive |
| Wong 1997b[160] | I | 1 | PFMT | 26 | 48.8 | Basic |
| | | | PFMT with additional sessions | 21 | | Intensive |
| Zanetti 2007[161] | I | 3 | PFMT | 21 | 54.0 | Basic |
| | | | PFMT with additional sessions | 23 | 56.0 | Intensive |

a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.

same outcome and it was therefore not possible to combine results in a meaningful way. The detailed information for comparators is reported in Appendix 17, Comparisons 04–09. Within the data available from the six studies that reported at least one of the specified primary outcomes,[164–169] there was insufficient evidence to suggest that any of these variants of PFMT were more effective than the comparator treatment shown in *Table 20*.

## Other physical and behavioural interventions

The characteristics of included studies comparing physical or behavioural interventions other than PFMT (with and without BF) are summarised in *Table 21*.

### *Electrical stimulation vs no treatment*

Eight studies[115,124,126,130–134] compared ES with no active treatment. Five studies provided treatment by means of a device for home use, and compared it with either sham treatment[130,131,133,134] or no treatment.[115] The other studies provided treatment at clinic, compared with sham treatment[126,132] or no treatment.[124]

#### Cure and improvement rate

Pooled data showed no statistically significant difference between the groups in the cure rate (6% vs 6%, OR 1.10, 95% CI 0.41 to 2.94), but ES showed a significantly higher rate for improvement (37% vs 13%, OR 3.93, 95% CI 1.43 to 10.80) compared with no active treatment, although there was some evidence of heterogeneity (*Figures 14* and *15*). The source of heterogeneity is unclear but it appears to be caused by the study by Bø and colleagues.[115] Removal of this study reduced statistical heterogeneity and the difference between the groups was still statistically significant (OR 2.46, 95% CI 1.14 to 5.30, figure not shown).

#### Adverse events

Only two studies[115,134] reported any incidence of adverse events (*Table 22*). All recorded cases were attributed to the treatment device, whether it was used for active or sham ES. In the study by Bø and colleagues,[115] seven of the 32 participants in the ES group stopped treatment due to adverse events.

#### Quality of life

Two studies[115,131] reported condition-specific quality of life, with one of these studies[131] using two instruments (questionnaires). Results were inconsistent across and within studies (*Table 22* and Appendix 19, Comparison 03).

There were no statistically significant differences in general HRQoL scores (SF-36) between the groups in two studies (Appendix 17, Comparison 10).[131,134]

### *Comparison of different variants of ES*

Two studies[157,172] assessed different variants of ESs. One of these studies[157] compared faradism and interferential therapy (IFT), both as an adjunct treatment to PFMT with clinic-based BF, for a period of 6 weeks. After this initial supervised treatment phase, all participants ($N = 30$) continued with PFMT and were followed up for 6 months.

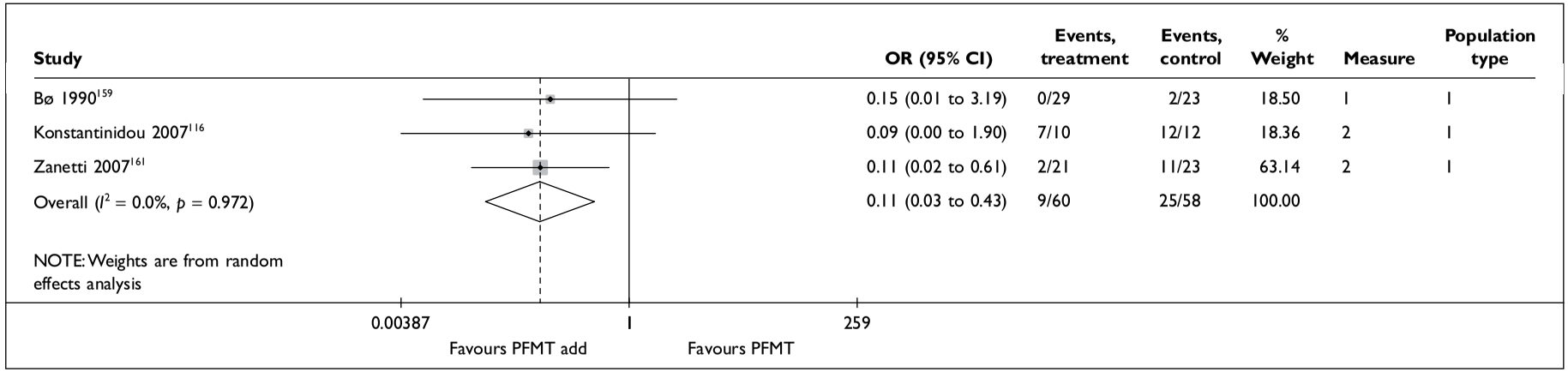


***FIGURE 12*** *Cure rates: pelvic floor muscle training (PFMT) versus PFMT with additional sessions.*

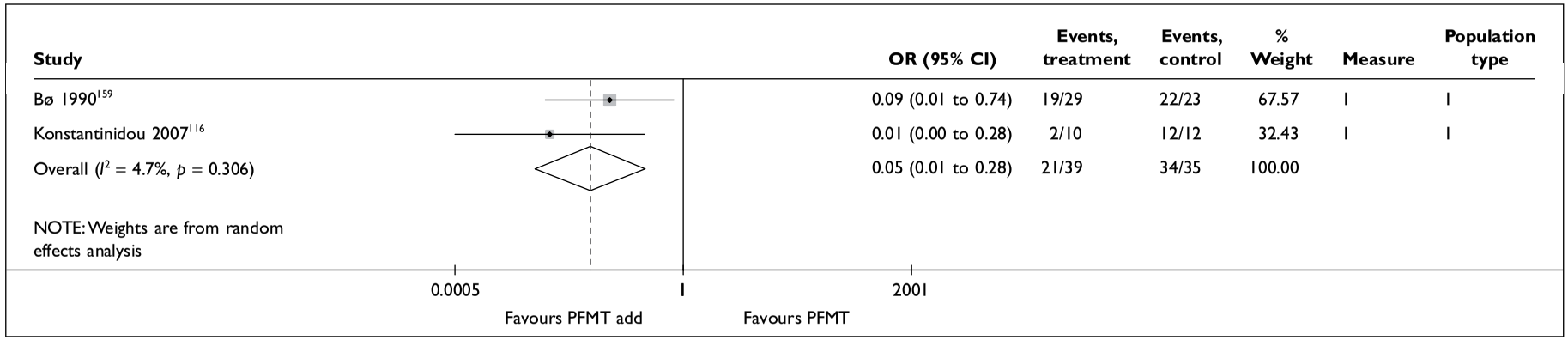


***FIGURE 13*** *Improvement rates: pelvic floor muscle training (PFMT) versus PFMT with additional sessions.*

***TABLE 19*** *Pelvic floor muscle training (PFMT) versus PFMT with additional sessions*

| | PFMT | | PFMT + additional sessions | | Reported *p*-value | Notes | Population type |
|---|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | | | |
| ***Social Activity Index*** | | | | | | | |
| Bø 1990[159] | 29 | 8.2 (2.06) | 23 | 9.3 (0.73) | < 0.01 | Sum score (mean, SD) at 6 months | I |
| ***Quality-of-life index*** | | | | | | | |
| [a]Konstantinidou 2007[116] | 10 | 3.6 (1.5) | 12 | 1.7 (0.8) | 0.000 | Score (mean, SD) | I |
| ***Incontinence Quality of Life*** | | | | | | | |
| Zanetti 2007[161] | 21 | 79 | 23 | 89 | 0.0456 | Score (median) | I |

a Lower scores reflect better quality of life.

***TABLE 20*** *Baseline characteristics of studies comparing different variants of pelvic floor muscle training*

| Study ID | Population type | Duration (months) | Comparator | *N* randomised | Age | Supervisory intensity[a] |
|---|---|---|---|---|---|---|
| Borello-France 2006[165] | I | 2.25–3 | PFMT in supine position | 22 | 51.7 | Intensive |
| | | | PFMT in supine and upright position | 22 | 53.6 | Intensive |
| Edwards 2000[170] | I | 3 | PFMT + BF | 10? | 46 | NR |
| | | | PFMT + ES | 10? | | NR |
| Gallo 1997[162] | I | 1–1.5 | PFMT | 43 | 60 | Basic |
| | | | PFMT with audiocassette | 43 | | Basic |
| Hay-Smith 2003[164] | 3 | 5 | Strength and motor relearning PFMT | 64 | 48.7 | Basic |
| | | | Motor relearning PFMT | 64 | 48.9 | Basic |
| Johnson 2001[167] | I | 1.5 | PFMT (maximal contraction) + BF | 37 | 49.5 | NR |
| | | | PFMT (submaximal contraction) + BF | | 51.0 | NR |
| Mayne 1988[168] | I | 4 | PFMT + perineometer | 34 | 45.0 | Basic |
| | | | PFMT + urethral electrical conductance | | 56.0 | Basic |
| Nygaard 1996[163] | 2 | 3 | PFMT | 71 | 53.0 | Basic |
| | | | PFMT with audiocassette | | | Basic |
| Pohl 2004[171] | I | 3 | PFMT + BF | 70 | NR | NR |
| | | | PFMT + ES | | NR | NR |
| Savage 2005[166] | I | 3 | PFMT | 5 | 54.6 | Basic |
| | | | Modified pilates | 6 | 48.2 | Basic |
| Wong 2001[169] | I | 3 | PFMT + BF (vaginal) | 19 | 47.6 | Basic |
| | | | PFMT + BF (vaginal and abdominal) | 19 | 44.4 | Basic |

a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.

***TABLE 21*** *Baseline characteristics of physical and behavioural interventions other than pelvic floor muscle training and lifestyle change*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age | Supervisory intensity[a] | Notes |
|---|---|---|---|---|---|---|---|
| Bø 1999[115] | 1 | 6 | ES | 32 | 47.2 | Basic | Maximum intermittent vaginal stimulation |
| | | | VC | 29 | 49.2 | Basic | |
| | | | NT | 32 | 51.7 | None | |
| Brubaker 1997[130] | 2 | 2 | ES | 148 | 56.0 | Basic | Transvaginal stimulation |
| | | | NT | | 57.7 | None | Sham ES |
| Burton 1993[173] | 1 | NR | VC passive | 31 | NR | NR | VC in static position |
| | | | VC active | 30 | NR | NR | VC while doing activities |
| Fantl 1991[135] | 2 | 1.5 | BT | 65 | 66.0 | Intensive | |
| | | | NT | 66 | 68.0 | None | |
| Henalla 1989[124] | 1 | 3 | ES | 25 | NR | Intensive | IFT |
| | | | NT | 25 | NR | None | |
| Hofbauer 1990[126] | 1 | 1.5 | ES | 11 | 59.7 | Intensive | Faradic |
| | | | NT | 10 | 59.8 | Intensive | Sham ES |
| Jeyaseelan 2000[131] | 1 | 2 | ES | 14 | NR | NR | Patterned neuromuscular stimulation |
| | | | NT | 13 | NR | NR | Sham ES |
| Knight 1998[172] | 1 | 6 | PFMT+BF+ES (max) | 24 | NR | Intensive | ES = maximal stimulation at clinic |
| | | | PFMT+BF+ES (low) | 25 | NR | Intensive | ES = overnight at low intensity at home |
| Laycock Trial 2 1993[132] | 1 | 2–3 | ES | 15 | 43.7 | Intensive | IFT |
| | | | NT | 15 | 46.2 | Intensive | Sham ES |
| Luber 1997[133] | 1 | 3 | ES | 26 | 54.1 | Basic | |
| | | | NT | 28 | 53.6 | Basic | Sham ES |
| Sand 1995[134] | 1 | 3 | ES | 35 | 50.9 | Basic | |
| | | | NT | 17 | 57.7 | Basic | Sham ES |
| Williams 2006[129] | 2 | 3 | VC | 80 | 58.2 | Basic | |
| | | | NT | 79 | 56.7 | Basic | Leaflet, clinic visits and exercise diary |
| Wilson 1987[157] | 1 | 1.5 | PFMT+BF+ES (faradism) | 15 | 46.8 | Intensive | |
| | | | PFMT+BF+ES (IFT) | 15 | | Intensive | |

a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.

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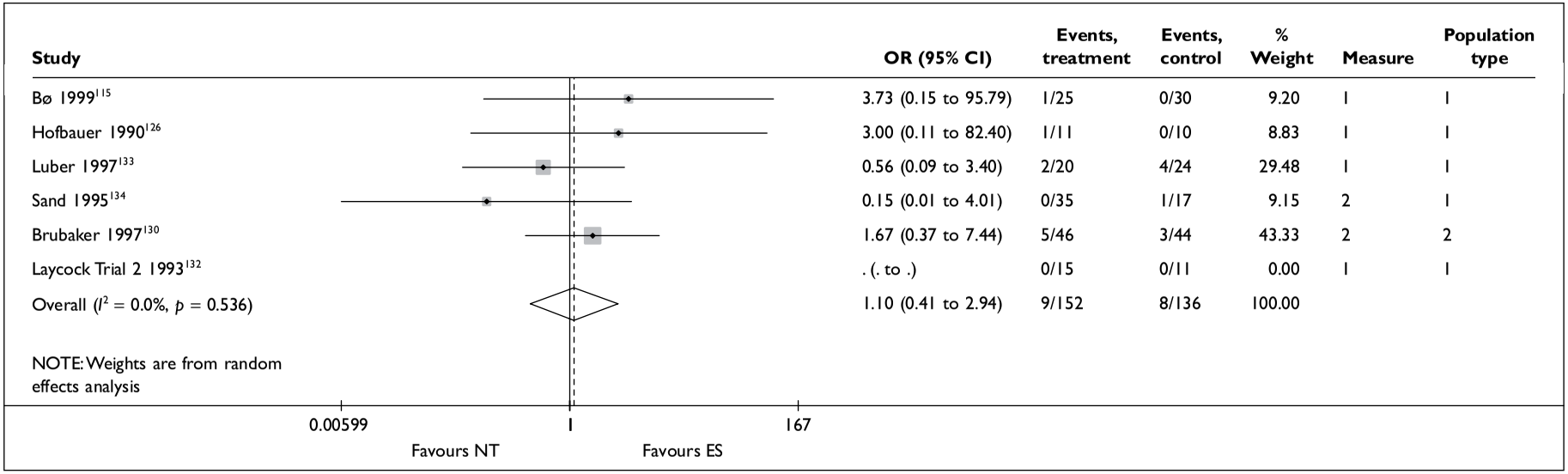


***FIGURE 14*** *Cure rates: electrical stimulation versus no treatment.*

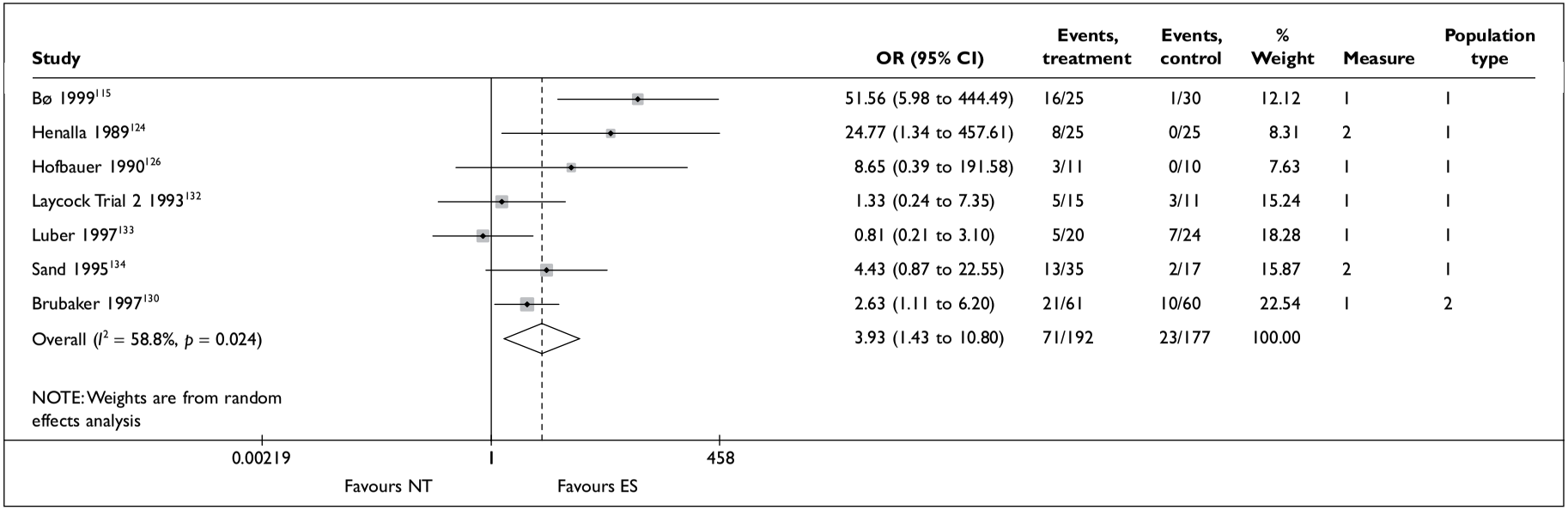


***FIGURE 15*** *Improvement rates: electrical stimulation versus no treatment.*

***TABLE 22a*** *Adverse events: electrical stimulation versus no treatment*

| | ES | | NT | | | Population type |
|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | Type of AEs | |
| ***N experiencing AEs*** | | | | | | |
| Bø 1999[115] | 10/32 | 31 | 0/32 | 0 | Smarting (tenderness, bleeding, discomfort), motivation problem, difficulty in using the stimulator | I |
| Sand 1995[134] | 14/35 | 40 | 7/17 | 41 | All cases added up, although unclear if the same patient experienced more than one adverse event; vaginal irritation: ES 5/35, NT 2/17; occasional pain: ES 3/35, NT 1/17; vaginal infection: ES 4/35, NT 2/17; urinary tract infection: ES 1/35, NT 2/17 | I |

***TABLE 22b*** *Quality of life: electrical stimulation versus no treatment*

| | ES | | NT | | Reported *p*-value | Notes | Population type |
|---|---|---|---|---|---|---|---|
| | *N* | Value | *N* | Value | | | |
| ***Social Activity Index*** | | | | | | | |
| Bø 1999[115] | 25 | 0.6 (1.02) | 30 | –0.2 (1.68) | | Change in score (mean, SD) | I |
| ***Incontinence Impact Questionnaire*** | | | | | | | |
| [a]Jeyaseelan 2000[131] | 12 | –4.1 (16.4) | 12 | –9.1 (17.1) | NS | Change in score (mean, SD) | I |
| ***Urogenital Distress Inventory*** | | | | | | | |
| [a]Jeyaseelan 2000[131] | 12 | –11.8 (15.9) | 12 | –3.3 (8.3) | 0.01 | Change in score (mean, SD) | I |

a Lower scores reflect better quality of life.

The other study[172] compared maximal ES (provided at clinic) with low intensity ES (provided overnight at home), both performed in conjunction with PFMT and a home BF device. Participants ($N = 49$) received these treatments with supervision for 6 months and were then instructed to perform PFMT with BF for a further 6 months.

Results showed that improvement was more likely for faradism and clinic-based maximal stimulation than for interferential therapy and home-based low-intensity stimulation, respectively, both after the supervised treatment phase and at 6 months after the end of the supervised phase (Appendix 17, Comparisons 11–12). However, CIs were wide and did not rule out clinically important differences that could favour either treatment. No information was available on cure, adverse events or quality of life.

### *VCs vs no treatment*

#### Cure and improvement rate

Two studies[115,129] comparing VCs with no treatment reported conflicting data on improvement (*Figure 16*). This may stem from a range of factors such as difference in study populations (SUI with or without UUI symptoms) and sample size, duration of treatment and supervisory intensity. The intervention for the 'no-treatment' group also differed, with one study by Bø and colleagues[115] offering instructions on a disposable vaginal device (Continence Guard™) only, whereas the other study by Williams and colleagues[129] provided the same number of clinic visits as the treatment group, with leaflets giving advice on the pelvic floor muscles. Cure rates were not reported.

#### Adverse events

In one study[115] 62% (18/29) of the women who used weighted VCs reported abdominal pain

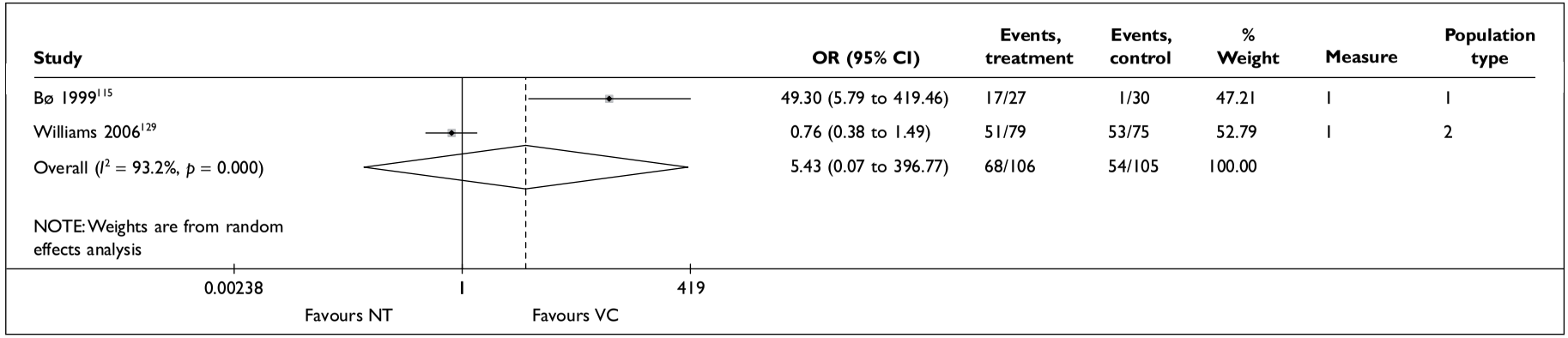


***FIGURE 16*** *Improvement rates: vaginal cones versus no treatment.*

and vaginitis, as well as difficulty in using cones and motivational problems. In the other study,[129] 3% (2/80) in the cones group reported urinary infection. No adverse events were reported for women receiving no treatment (*Table 23*).

### Quality of life

There was no evidence of a difference between the groups in either study (*Table 23*).

#### *Comparison of different variants of VC*

One study[173] of 61 women with SUI compared VCs used in a static position ('passive cones') with VCs used while doing activities that previously made them incontinent ('active cones'). The results showed a slightly higher cure rate for the active cones (Appendix 17, Comparison 13, 58% vs 70%, OR 0.59, 95% CI 0.21 to 1.71).

#### *BT vs no treatment*

Only one study[135] compared BT with no treatment among women with different types of urinary incontinence (SUI with or without UUI symptoms). The results favoured BT in terms of both cure and improvement, although CIs were wide (*Table 24*). Condition-specific quality of life similarly favoured BT. The study reported no significant difference by incontinence diagnosis (stress, mixed or urge incontinence) (*Table 24*).

## SNRI drug therapy

The characteristics of included studies comparing SNRI drug therapy (duloxetine) with no treatment are summarised in *Table 25*.

#### *SNRI vs no treatment*

All but one[57] of the 12 trials compared SNRI (duloxetine) with placebo. The other study by Ghoniem and colleagues[57] was a four-arm trial comparing duloxetine with placebo, both combined with either active or imitation PFMT. For cure and improvement as well as quality of life, data from two arms were compared (SNRI with imitation PFMT vs placebo with imitation PFMT), while for adverse events, data from all four arms were combined (SNRI with active or imitation PFMT vs placebo with active or imitation PFMT). All but three studies[57,136,137] included women with SUI with UUI symptoms (population types 2 and 3).

The majority of studies used a daily dose of 80 mg, although participants in the SNRI group

***TABLE 23a*** *Adverse events: vaginal cones versus no treatment*

| | VC | | NT | | | |
|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | Notes | Population type |
| Bø 1999[115] | 18/29 | 62 | 0/32 | 0 | Abdominal pain, vaginitis, bleeding, motivation problems, trouble in using the cones | 1 |
| Williams 2006[129] | 2/80 | 3 | 0/79 | 0 | Urinary tract infection | 2 |

***TABLE 23b*** *Quality of life: vaginal cones versus no treatment*

| | VC | | NT | | | | |
|---|---|---|---|---|---|---|---|
| | *N* | Value | *N* | Value | Reported *p*-value | Notes | Population type |
| ***Social Activity Index*** | | | | | | | |
| Bø 1999[115] | 27 | 0.1 (1.06) | 30 | –0.2 (1.68) | | Change in score (mean, SD) | 1 |
| ***The Leicester Impact Scale*** | | | | | | | |
| [a]Williams 2006[129] | 79 | 2 (0.0 to 5.0) | 75 | 1.5 (0.0 to 5.0) | 0.658 | Score (0–42, median, interquartile range) | 2 |

a Lower scores reflect better quality of life.

***TABLE 24a*** *Cure and improvement rates: bladder training versus no treatment*

| | BT | | NT | | | | |
|---|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **OR (95% CI)** | **Measure** | **Population type** |
| ***Cure rate*** | | | | | | | |
| Fantl 1991[135] | 7/60 | 12 | 2/63 | 3 | 4.03 (0.80 to 20.23), $p = 0.091$ | 2 | 2 |
| ***Improvement*** | | | | | | | |
| Fantl 1991[135] | 45/60 | 75 | 15/63 | 24 | 9.60 (4.22 to 21.87), $p < 0.001$ | 2 | 2 |

***TABLE 24b*** *Quality of life: bladder training versus no treatment*

| | BT | | NT | | | | |
|---|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Reported *p*-value** | **Notes** | **Population type** |
| ***Incontinence Impact Questionnaire*** | | | | | | | |
| [a]Fantl 1991[135] | 39 | 0.25 (0.29) | 39 | 0.5 (0.59) | 0.0001 | Composite score (range 0–3, mean, SD) | 2 |

a Lower scores reflect better quality of life.

in the Cardozo and colleagues study[137] ingested 80 mg daily for 4 weeks, escalating to 120 mg daily for another 4 weeks. Another four-arm trial by Castro-Diaz and colleagues[138] varied a starting dose in the first 2 weeks (20 mg twice a day, 40 mg once a day or 40 mg twice a day), with all participants in the SNRI group taking 40 mg twice daily in the subsequent weeks. In this study, cure and improvement rates and quality of life were measured at the end of 8 weeks, whereas adverse events were reported at the end of 4 weeks when all participants had at least 2 weeks of ingesting 40 mg twice a day. In the study by Kinchen and colleagues,[140] the participants were allowed to reduce or suspend study drug or use other modalities of treatment (e.g. PFMT) simultaneously with SNRI. One study by Manning and colleagues[142] did not specify dosage and this was assumed to be 80 mg per day.

### Cure and improvement rate

Cure and improvement rates were consistently higher across studies for SNRI than with placebo, regardless of the dosage (80, 40 or 20 mg per day) (*Figures 17* and *18*). Pooled data for a daily dosage of 80 mg showed that cure was reported in 11% (67/609) of the participants using SNRI compared with 8% (53/683) for placebo, and improvement was reported in 65% (1254/1939) for SNRI compared with 46% (803/1733) for placebo. The difference between the groups in improvement reached statistical significance (*Figure 18*: OR 2.02, 95% CI 1.67 to 2.44) but for cure this was not the case. The results also appeared to show a noticeable placebo effect. The study by Cardozo and colleagues[137] showed a higher OR for improvement than other studies. The reason for this is unclear, but may partly stem from the fact that the study recruited women with SUI only and also provided a higher drug dosage.

While most studies provided treatment for a period of 2–3 months, one study[140] continued treatment for a total of 9 months and provided data on improvement; the results favoured the treatment group, although the difference was not statistically significant (Appendix 17, Comparison 14, 49% vs 41%, OR 1.37, 95% CI 0.93 to 2.01).

A small number of studies using a daily dosage of 40, 30 or 20 mg reported similar results. Pooled data for improvement from two studies[144,145] using a daily dosage of 40 and 20 mg showed statistical heterogeneity, which may be partly explained by different sample populations, with one study[145] recruiting women with stress incontinence alone and the other[144] including women with different types of incontinence.

### Adverse events

*Table 26* shows the number of participants who experienced *any* treatment-related adverse events

***TABLE 25*** *Baseline characteristics of studies comparing serotonin–noradrenaline reuptake inhibitor drug therapy (duloxetine) with no treatment*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age | Supervisory intensity |
|---|---|---|---|---|---|---|
| Bump 2004[136] | 1 | 1 | SNRI80 | 34 | NR | NA |
| | | | NT | 31 | NR | NA |
| Cardozo 2004[137] | 1 | 2 | SNRI80 | 55 | 54.5 | NA |
| | | | NT | 54 | 52.4 | NA |
| Castro-Diaz 2007[138] | 3 | 2 | SNRI40 b.i.d., starting with 40 b.i.d. | 136 | 53.3 | NA |
| | | | SNRI40 b.i.d., starting with 40 q.d. | 127 | 52.3 | NA |
| | | | SNRI40 b.i.d., starting with 20 b.i.d. | 133 | 53.5 | NA |
| | | | NT | 120 | 52.7 | NA |
| Dmochowski 2003[139] | 3 | 3 | SNRI80 | 344 | 52.3 | NA |
| | | | NT | 339 | 53.3 | NA |
| Ghoniem 2005[57] | 1 | 3 | SNRI | 52 | 53.0 | NA |
| | | | NT | 47 | 51.0 | NA |
| Kinchen 2005[140] | 3 | 3 | SNRI80 | 224 | 52.7 | NA |
| | | | NT | 227 | 53.5 | NA |
| Mah 2006[141] | 3 | 2 | SNRI80 | 61 | 50.7 | NA |
| | | | NT | 60 | 48.5 | NA |
| Manning 2005[142] | 3 | 2 | SNRI80 | 306 | NR | NA |
| | | | NT | 311 | NR | NA |
| Millard 2004[143] | 3 | 3 | SNRI80 | 227 | 53.7 | NA |
| | | | NT | 231 | 52.6 | NA |
| Norton 2002[144] | 2 | 3 | SNRI80 | 140 | 49.3 | NA |
| | | | SNRI40 | 137 | 49.4 | NA |
| | | | SNRI20 | 138 | 49.4 | NA |
| | | | NT | 138 | 50.2 | NA |
| van Kerrebroeck 2004[117] | 3 | 3 | SNRI80 | 247 | 52.0 | NA |
| | | | NT | 247 | 54.0 | NA |
| Zinner 1998[145] | 1 | 1.5 | SNRI40 | 33[a] | NR | NA |
| | | | SNRI30 | 26[a] | NR | NA |
| | | | SNRI20 | 34[a] | NR | NA |
| | | | NT | 34[a] | NR | NA |

NT, no treatment; SNRI80, serotonin–noradrenaline reuptake inhibitors 80 mg per day.
a *n* in analysis; total *N* randomised = 140.

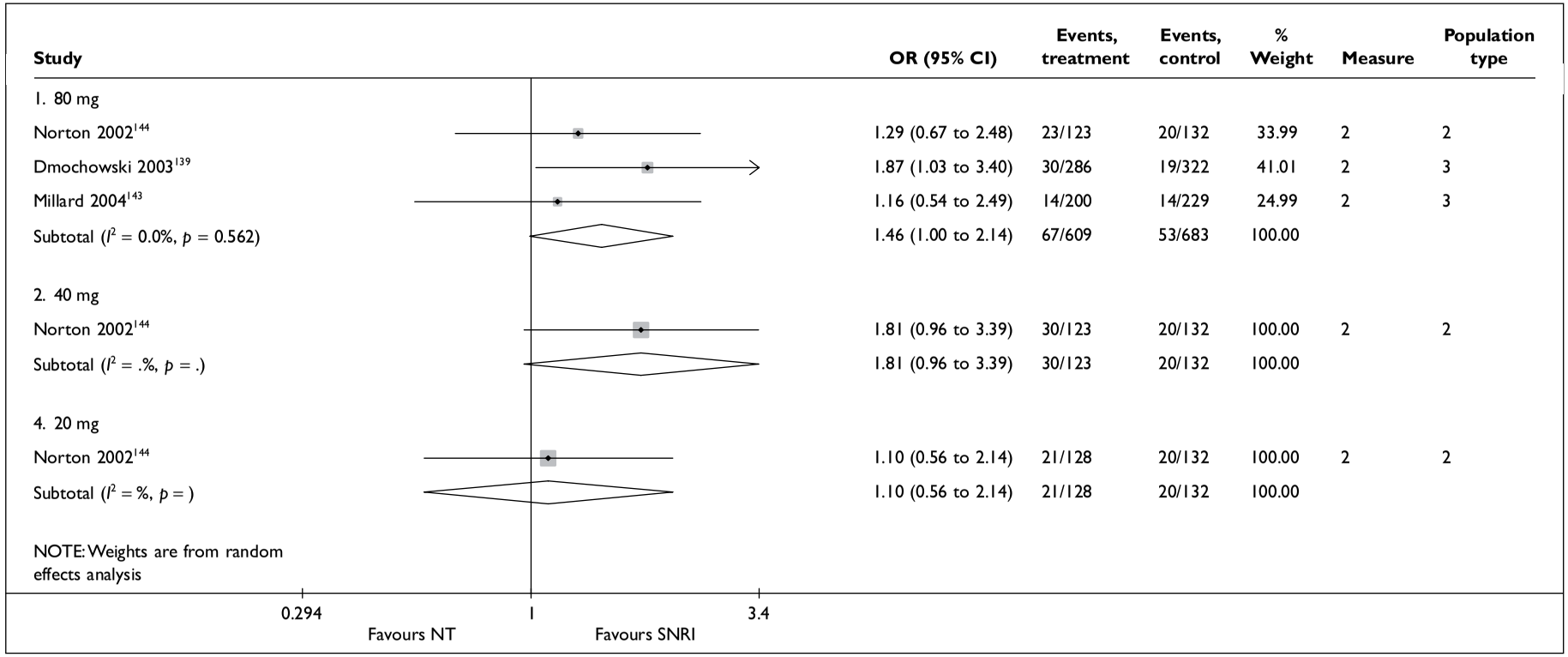


***FIGURE 17*** *Cure rates: serotonin–noradrenaline reuptake inhibitors versus no treatment.*

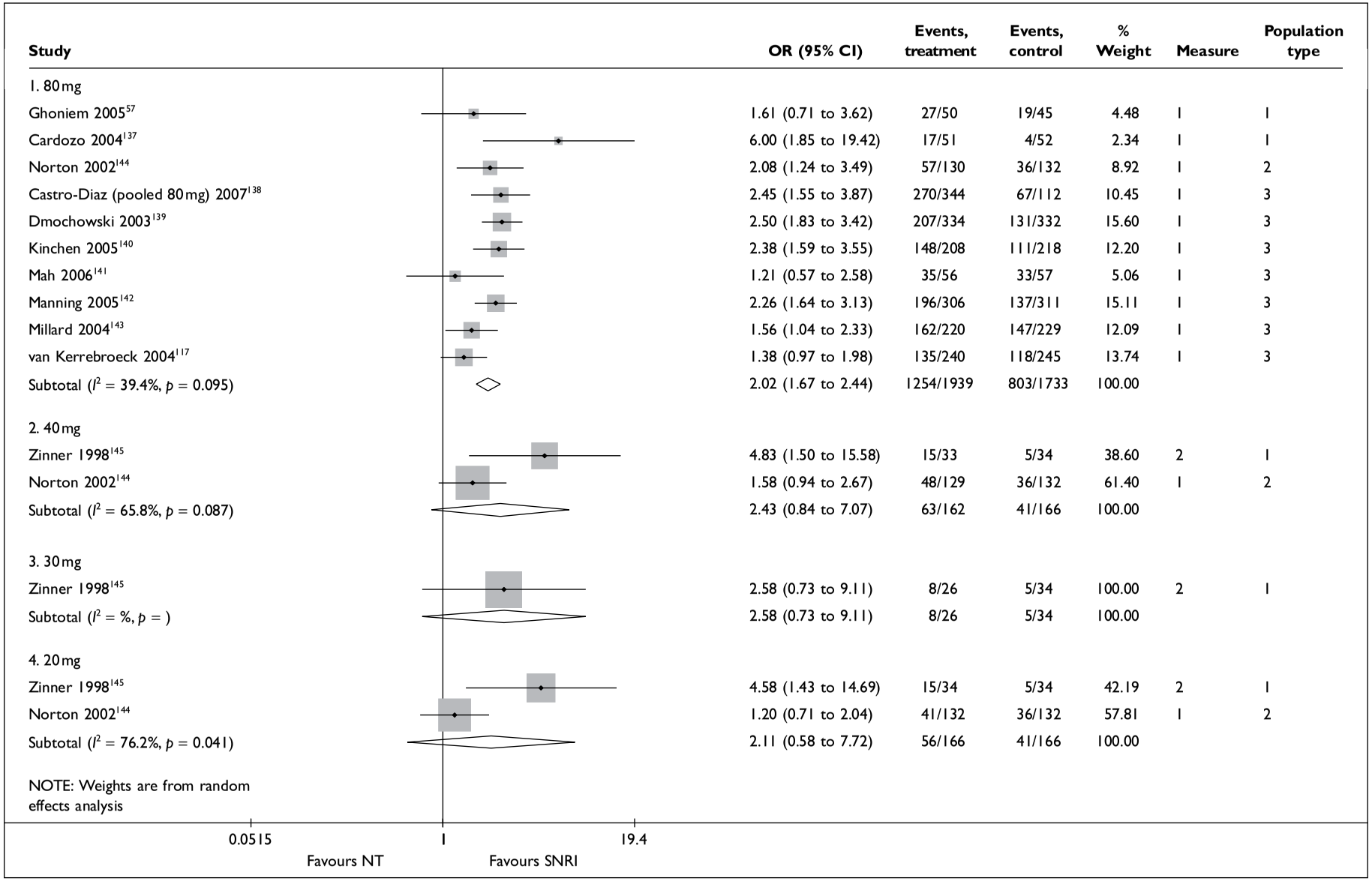


***FIGURE 18*** *Improvement rates: serotonin–noradrenaline reuptake inhibitors versus no treatment.*

***TABLE 26*** *Adverse events: serotonin–noradrenaline reuptake inhibitors versus no treatment*

| | SNRI | | NT | | | Population type |
|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **Notes** | |
| ***N experiencing adverse events*** | | | | | | |
| *SNRI 80 mg vs NT* | | | | | | |
| Cardozo 2004[137] | 43/46 | 93 | 37/52 | 71 | Adverse events that occurred in more than 10% of participants: nausea, constipation, headache, dry mouth, fatigue, dizziness, insomnia, somnolence and vomiting; *serious adverse events*: cardiovascular (not significantly different in both arms); increasing the dose from 80 mg to 120 mg daily did not increase efficacy or side effects | 1 |
| Ghoniem 2005[57] | 85/104 | 82 | 58/97 | 60 | Adverse events that were significantly more common with SNRI than with placebo (with PFMT or imitation PFMT): nausea, dizziness, dry mouth, constipation, insomnia, somnolence, aesthesia | 1 |
| Norton 2002[144] | 102/140 | 73 | 84/138 | 61 | Adverse events that occurred in ≥ 5% of subjects in any treatment arm: nausea, headache, diarrhoea, constipation, dry mouth, dizziness, insomnia, sinusitis, fatigue, nasopharyngitis | 2 |
| Castro-Diaz 2007[138] (40 mg b.i.d. starting dose) | 87/136 | 64 | 53/120 | 44 | Adverse events that occurred in ≥ 2 patients in first 4 weeks: nausea, dry mouth, constipation, somnolence, dizziness, insomnia, fatigue, headache, diarrhoea | 3 |
| Castro-Diaz 2007[138] (40 mg q.d. starting dose) | 76/127 | 60 | 53/120 | 44 | As above | 3 |
| Castro-Diaz 2007[138] (20 mg b.i.d. starting dose) | 69/133 | 52 | 53/120 | 44 | As above | 3 |
| Dmochowski 2003[139] | 255/344 | 74 | 170/339 | 50 | Adverse events significantly more common with SNRI and occurring in ≥ 5% of subjects on SNRI: nausea, fatigue, insomnia, dry mouth, constipation, somnolence, dizziness, headache, diarrhoea | 3 |
| Kinchen 2005[140] | 198/224 | 88 | 159/227 | 70 | Adverse events for which there are statistically significant differences between groups: nausea, fatigue, insomnia, dizziness, headache, somnolence, dry mouth, constipation, diarrhoea, vomiting, increased sweating, decreased appetite, anxiety, tremor, decreased libido, lethargy, nightmare, fungal infection | 3 |
| Mah 2006[141] | 50/61 | 82 | 19/60 | 32 | Adverse events that occurred in ≥ 5% of the women randomised to the SNRI group or which occurred significantly more often with SNRI than with placebo: nausea, dizziness, anorexia, fatigue, lethargy, abdominal discomfort, somnolence, constipation, headache, dry mouth | 3 |
| Millard 2004[143] | 173/227 | 76 | 137/231 | 59 | Adverse events: significantly more common with, and occurring in, ≥ 5% of subjects with SNRI: nausea, headache, insomnia, constipation, dry mouth, dizziness, fatigue, somnolence, anorexia, vomiting, increased sweating, anxiety | 3 |

*continued*

***TABLE 26*** *Adverse events: serotonin–noradrenaline reuptake inhibitors versus no treatment (continued)*

| | SNRI | | NT | | | Population type |
|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | **Notes** | |
| van Kerrebroeck 2004[117] | 200/247 | 81 | 158/247 | 64 | Adverse events occurring in at least 5% of patients on SNRI or occurring significantly more often with SNRI than placebo: nausea, dry mouth, constipation, fatigue, insomnia, dizziness, headache, increased sweating, vomiting, somnolence, tremor | 3 |
| *SNRI 40 mg vs NT* | | | | | | |
| Norton 2002[144] | 93/137 | 68 | 84/138 | 61 | Adverse events that occurred in ≥ 5% of subjects in any treatment arm: nausea, headache, diarrhoea, constipation, dry mouth, dizziness, insomnia, sinusitis, fatigue, nasopharyngitis | 2 |
| *SNRI 20 mg vs NT* | | | | | | |
| Norton 2002[144] | 86/138 | 62 | 84/138 | 61 | Adverse events that occurred in ≥ 5% of subjects in any treatment arm: nausea, headache, diarrhoea, constipation, dry mouth, dizziness, insomnia, sinusitis, fatigue, nasopharyngitis | 2 |
| ***Discontinuation due to adverse events*** | | | | | | |
| *SNRI 80 mg vs NT* | | | | | | |
| Cardozo 2004[137] | 18/55 | 33 | 3/54 | 6 | | 1 |
| Castro-Diaz 2007[138] (40 mg b.i.d. starting dose) | 22/136 | 16 | 7/120 | 6 | | 3 |
| Castro-Diaz 2007[138] (40 mg q.d. starting dose) | 15/127 | 12 | 7/120 | 6 | | 3 |
| Castro-Diaz 2007[138] (20 mg b.i.d. starting dose) | 10/133 | 8 | 7/120 | 6 | | 3 |
| Dmochowski 2003[139] | 83/344 | 24 | 14/339 | 4 | | 3 |
| Ghoniem 2005[57] | 28/104 | 27 | 8/97 | 8 | | 1 |
| Kinchen 2005[140] | 20/224 | 9 | 5/227 | 2 | | 3 |
| Mah 2006[141] | 21/61 | 34 | 5/60 | 8 | | 3 |
| Manning 2005[142] | 53/306 | 17 | 9/311 | 3 | | 3 |
| Millard 2004[143] | 39/227 | 17 | 4/231 | 2 | | 3 |
| Norton 2002[144] | 21/140 | 15 | 7/138 | 5 | | 2 |
| van Kerrebroeck2004[117] | 53/247 | 21 | 12/247 | 5 | | 3 |
| *SNRI 40 mg vs NT* | | | | | | |
| Norton 2002[144] | 17/137 | 12 | 7/138 | 5 | | 2 |
| *SNRI 20 mg vs NT* | | | | | | |
| Norton 2002[144] | 13/138 | 9 | 7/138 | 5 | | 2 |

***TABLE 27*** *Quality of life: serotonin–noradrenaline reuptake inhibitors versus no treatment*

| | SNRI | | NT | | Reported *p*-value | Notes | Population type |
|---|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | | | |
| ***I-QoL*** | | | | | | | |
| *SNRI80 vs NT* | | | | | | | |
| Cardozo 2004[137] | 52 | 10.6 (19.1) | 52 | 2.4 (9.4) | 0.003 | Change in score (mean, SD) | 1 |
| Ghoniem 2005[57] | 50 | 8.3 | 45 | 4.8 | | Mean percentage score increase | 1 |
| Norton 2002[144] | 130 | 9.3 | 132 | 5.8 | 0.03 | Change in score (mean) | 2 |
| [a]Castro-Diaz 2007[138] | 344 | 12.9 | 112 | 5.7 | <0.001 | Change in score (mean). | 3 |
| Dmochowski 2003[139] | 334 | 11.1 (14.8) | 332 | 6.8 (13.8) | <0.001 | Change in score (mean, SD) | 3 |
| Kinchen 2005[140] | 208 | 13 | 218 | 10.4 | 0.07 | Change in score (mean) | 3 |
| Mah 2006[141] | 56 | 63.41 | 57 | 60.23 | | Total score (mean) | 3 |
| Millard 2004[143] | 220 | 69.2 (23.8) | 229 | 64.7 (24.9) | | Total score (mean, SD) | 3 |
| van Kerrebroeck 2004[117] | 240 | 72.2 | 245 | 68.5 | 0.127 | Total score (mean) | 3 |
| *SNRI40 vs NT* | | | | | | | |
| Zinner 1998[145] | 33 | 8.2 (10.8) | 34 | 2.6 (8.8) | <0.05 | Change in score (mean, SD) | 1 |
| Norton 2002[144] | 129 | 7.8 | 132 | 5.8 | 0.16 | Change in score (mean) | 2 |
| *SNRI30 vs NT* | | | | | | | |
| Zinner 1998[145] | 26 | 10 (6.4) | 34 | 2.6 (8.8) | <0.05 | Change in score (mean, SD) | 1 |
| *SNRI20 vs NT* | | | | | | | |
| Zinner 1998[145] | 34 | 12 (16) | 34 | 2.6 (8.8) | <0.05 | Change in score (mean, SD) | 1 |
| Norton 2002[144] | 132 | 5.3 | 132 | 5.8 | 0.6 | Change in score (mean) | 2 |
| ***King's Health Questionnaire*** | | | | | | | |
| *SNRI80 vs NT* | | | | | | | |
| [b]Manning 2005[142] | 306 | –9.2 | 311 | –2.6 | <0.0001 | Change in score (mean) | 3 |
| ***ICIQ-UI SF*** | | | | | | | |
| *SNRI80 vs NT* | | | | | | | |
| [b]Castro-Diaz 2007[138] | 344 | –2.8 | 112 | –1.7 | 0.004 | Change in score (mean) | 3 |

ICIQ-UI SF, International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form; I-QoL, Urinary Incontinence Quality of Life Scale.
a No significant difference among the three groups with different starting dose.
b Lower scores reflect better quality of life.

***TABLE 28*** *Baseline characteristics of studies comparing pelvic floor muscle training plus adjunct treatment versus no treatment*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age | Supervisory intensity[a] | Notes |
|---|---|---|---|---|---|---|---|
| Bidmead 2002[121] | I | 3.5 | PFMT + ES | 82? | 50.4 | Basic | |
| | | | NT | 20? | 47.5 | None | |
| Ghoniem 2005[57] | I | 3 | PFMT + SNRI | 52 | 54.0 | Basic | |
| | | | NT | 47 | 51.0 | Basic | Placebo drug and imitation PFMT |
| Goode 2003[123] | 3 | 2 | PFMT + ES | 67 | 54.9 | Basic | |
| | | | NT | 67 | 55.9 | None | Self-administered behavioural training |
| Hofbauer 1990[126] | I | 1.5 | PFMT + ES | 11 | 62.9 | Intensive | |
| | | | NT | 10 | 59.8 | Intensive | Sham ES |

a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.

and also lists *all* adverse events that were defined by trialists as being significant (in terms of quantity rather than severity): the latter is not a list of all adverse events. adverse events were experienced by 52–93% of participants in the SNRI group.[137,138] Notably, 32–64% of participants in the placebo group also reported adverse events.[117,141] Nausea was the most commonly reported adverse event with SNRI. Castro-Diaz and colleagues[138] reported that at 4 weeks (when all SNRI-treated participants had had at least 2 weeks' use of 40 mg twice a day) a low starting dose of 20 mg, twice daily, significantly reduced the incidence of nausea and dizziness compared with other drug regimens.

It should be noted that the discontinuation rate among participants due to adverse events was high, at 8–34% in the SNRI group, compared with 2–8% in the placebo group (*Table 26*).

Serious adverse events were reported by three studies. One of these studies[57] reported one case of rectal bleeding in the SNRI group but this was not attributed to the study drug. The second study[144] reported that five subjects had adverse events that required hospitalisation (one event before randomisation, one event in the group taking SNRI 20 mg per day, two events in the group taking SNRI 40 mg per day, and one event in the group taking SNRI 80 mg per day): only one of these events (a rash) was judged by the study authors to be related to the study drug. The third study[140] recorded serious adverse events (details not reported) in eight of the 224 participants (16 events) in the SNRI group and seven of the 227 participants (eight events) in the placebo group. Of these, two of the events in the placebo group but none in the SNRI group was considered by the study author to be related to the study drug (active or placebo).

### Quality of life

A total of 11 studies provided information on condition-specific quality of life using various outcome measures and drug doses (*Table 27*). With respect to studies using a daily dosage of 80 mg, all 10 studies favoured SNRI-treated participants. This difference was reported to be statistically significant in all but two studies[117,140] that performed a statistical test. One study[138] using two outcome measures reported consistent results favouring duloxetine. Only three studies reported data amenable to meta-analysis, with one reporting a total score at the final evaluation,[143] and the other two reporting a change in score from baseline to the final evaluation.[137,139] Pooled data from the two studies[137,139] reporting a change in score found a statistically significant difference between the groups (Appendix 19, Comparison 04, OR 0.35. 95% CI 0.16 to 0.55).

One study[140] provided information for a longer treatment duration of 9 months; no significant difference between the groups was reported (Appendix 17, Comparison 14).

Two studies[144,145] used a daily dose of 40, 30 and 20 mg, with one study[145] favouring duloxetine and the other[144] reporting no statistically significant difference between SNRI and placebo (*Table 27*).

#### *Comparison of different SNRI doses*

Two small studies[144,145] compared different doses of SNRI. Data on cure and improvement rates are reported in Appendix 17, Comparison 15. In one study,[144] slightly more participants taking a higher dose of SNRI were improved than those taking a lower dose (80 mg: 44%, 57/130; 40 mg: 37%, 48/129; 20 mg: 31%, 41/132), but no such pattern was found for cure rates (80 mg: 19%, 23/123; 40 mg: 24%, 30/123; 20 mg: 16%, 21/128). The other smaller study[145] also did not find any dose dependence for improvement rates (40 mg: 45%, 15/33; 30 mg: 31%, 8/26; 20 mg: 44%, 15/34).

With respect to adverse events, the direction of effect was consistent across all comparisons, with more participants experiencing adverse events with a higher dose than with a lower dose (Appendix 17, Comparison 15).

There is no strong evidence to say whether a lower dose is associated with a better quality of life (Appendix 17, Comparison 16).

## PFMT with adjunct treatment

The characteristics of included studies comparing PFMT with adjunct treatment versus no treatment are summarised in *Table 28*.

#### *PFMT plus ES vs no treatment*

**Cure and improvement**

Three studies[121,123,126] compared PFMT with adjunct ES versus no treatment (*Figures 19* and *20*). Pooled data from two of these studies with data[123,126] showed a higher improvement rate (but not cure rate) in the intervention group, although the CI was wide (*Figure 20*: OR 8.69, 95% CI 1.87 to 40.32).

**Adverse events**

Only one study[123] reported adverse events: 6% (4/67) of the participants using ES experienced vaginal irritation (*Table 29*).

**Quality of life**

The same study[123] found no significant difference between the groups in condition-specific quality of life (*Table 29*) and general quality of life (Appendix 17, Comparison 17).

#### *PFMT plus SNRIs vs no treatment*

One four-arm trial[57] reported data for a combination of PFMT plus a drug therapy (SNRI) compared with no treatment (*Table 30*). The 'no-treatment' arm received placebo drugs and also performed imitation PFMT. The PFMT-plus-SNRI group was associated with higher improvement rates and higher (better) quality of life than the no-treatment group. adverse events associated with SNRI (with PFMT or imitation PFMT) are reported separately in *Table 27*. No adverse events associated with PFMT were reported.

## Comparison between different treatments: single modality

*Table 31* summarises the characteristics of included studies comparing different single interventions. PFMT augmented with BF is included here as a 'single' intervention.

## PFMT vs ES

Seven studies provided at least one of the specified primary outcomes.[115,124,126,174–177] Of these, five studies, namely Bernardes and colleagues (2000),[174] Bø and colleagues (1999),[115] Henalla and colleagues (1989),[124] Hofbauer and colleagues (1990)[126] and Laycock and colleagues (1988),[176] provided intensive supervision (more than two sessions per month) for both groups. In addition, the study by Bø and colleagues (1999)[115] also provided intensive supervision for the PFMT group but basic supervision (two or fewer sessions per month) for the comparator group.

**Cure and improvement**

Pooled data for cure and improvement indicated that PFMT was more effective than ES in terms of both cure (*Figure 21*: OR 2.65, 95% CI 0.82 to 8.60) and improvement (*Figure 22*: OR 2.18, 95% CI 0.76 to 6.28). The direction and magnitude of effects varied across studies, particularly for the improvement rate which displayed statistical heterogeneity at the 10% level ($p = 0.070$). The source of heterogeneity was unclear. However, it is noteworthy that all but one study (Laycock 1988)[176] that provided intensive supervision for the PFMT group showed ORs (point estimate) of greater than one (favouring PFMT on average) for both cure and improvement data.

#### *Adverse events and quality of life*

Information on adverse events and condition-specific quality of life was provided by one small study only[115] (*Table 32*). In this study, adverse events were experienced in 31% (10/32) of the participants using ES but none in the PFMT group. Seven participants in the ES group withdrew. Condition-specific quality-of-life scores were similar for both groups (*Table 32*).

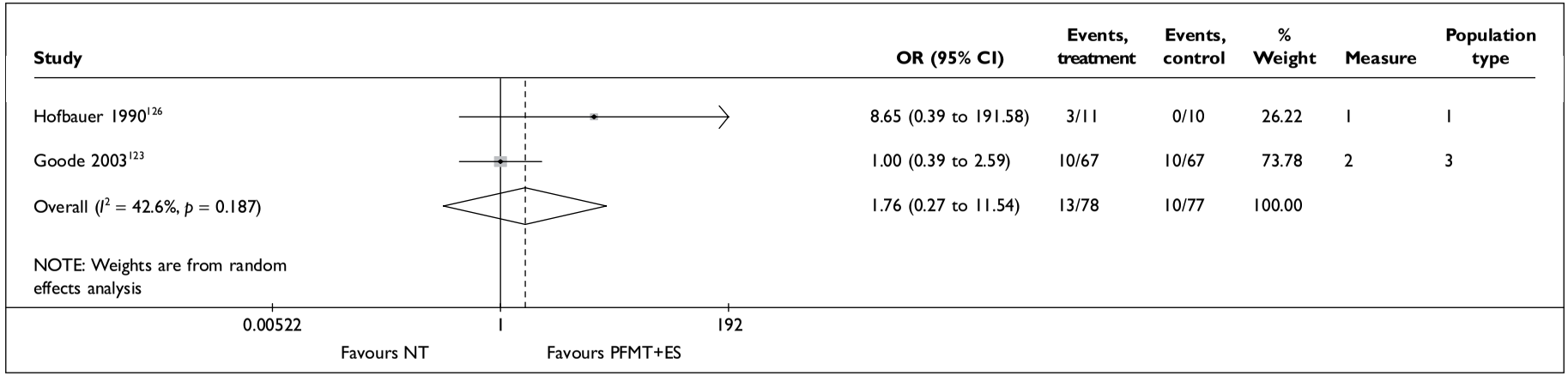


***FIGURE 19*** *Cure rates: pelvic floor muscle training and electrical stimulation versus no treatment.*

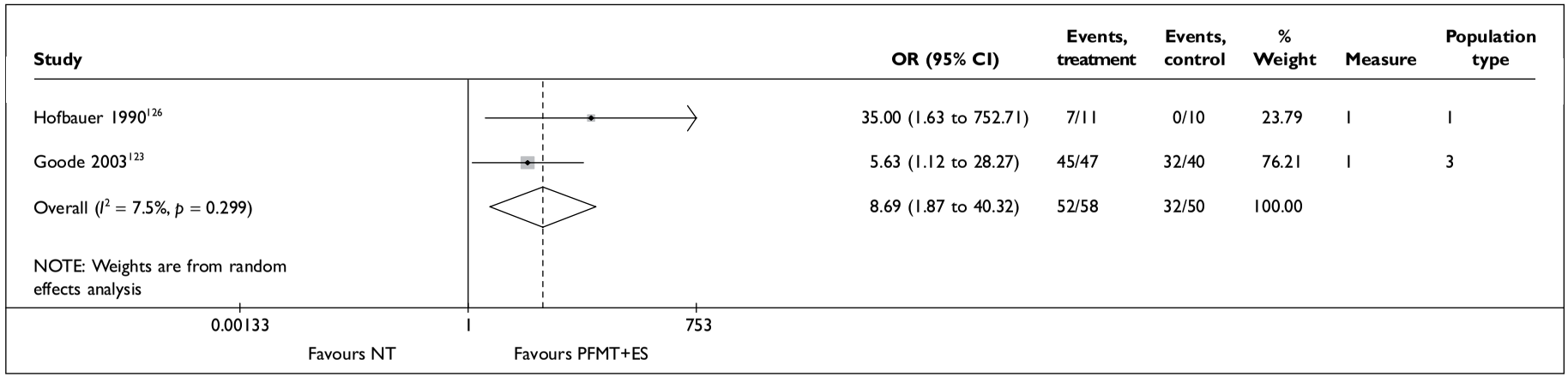


***FIGURE 20*** *Improvement rates: pelvic floor muscle training and electrical stimulation versus no treatment.*

***TABLE 29a*** *Adverse events: pelvic floor muscle training plus electrical stimulation versus no treatment*

| | PFMT + ES | | NT | | | |
|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **Notes** | **Population type** |
| Goode 2003[123] | 4/67 | 6 | 0/67 | 0 | Vaginal irritation | 3 |

***TABLE 29b*** *Quality of life: pelvic floor muscle training plus electrical stimulation versus no treatment*

| | PFMT + ES | | NT | | | |
|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Notes** | **Population type** |
| ***Incontinence Impact Questionnaire*** | | | | | | |
| Goode 2003[123] | 67 | No difference | 67 | No difference | Total score | 3 |

***TABLE 30a*** *Improvement rate: pelvic floor muscle training plus serotonin–noradrenaline reuptake inhibitors versus no treatment*

| | PFMT + SNRI | | NT | | | | |
|---|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **OR (95% CI)** | **Measure** | **Population type** |
| ***Improvement rate*** | | | | | | | |
| Ghoniem 2005[57] | 36/51 | 71 | 19/45 | 42 | 3.28 (1.41 to 7.64), $p = 0.006$ | 1 | 1 |

***TABLE 30b*** *Quality of life: pelvic floor muscle training plus serotonin–noradrenaline reuptake inhibitors versus no treatment*

| | PFMT + SNRI | | NT | | | |
|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Notes** | **Population type** |
| ***I-QoL*** | | | | | | |
| Ghoniem 2005[57] | 51 | 13.1 | 50 | 8.3 | Change in score (mean percentage score increase) | 1 |

***TABLE 31*** *Background characteristics of studies comparing different treatments (single modality)*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age (years) | Supervisory intensity[a] | Notes |
|---|---|---|---|---|---|---|---|
| Arvonen 2001[178] | 1 | 4 | PFMT | 20 | 47.0 | Basic | |
| | | | VC | 20 | 49.0 | Basic | |
| Bernardes 2000[174] | 1 | 0.3 | PFMT | 7 | 44.1 | Intensive | |
| | | | ES | 7 | 53.3 | Intensive | |
| Bø 1999[115] | 1 | 6 | PFMT | 29 | 49.6 | Intensive | |
| | | | ES | 32 | 47.2 | Basic | Maximum intermittent vaginal stimulation |
| | | | VC | 29 | 49.2 | Basic | |

*continued*

***TABLE 31*** *Background characteristics of studies comparing different treatments (single modality) (continued)*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age (years) | Supervisory intensity[a] | Notes |
|---|---|---|---|---|---|---|---|
| Cammu 1998[181] | 1 | 3 | PFMT + BF | 30 | 55.9 | Intensive | |
| | | | VC | 30 | 56.3 | Basic | |
| Delneri 2000[186] | 1 | 0.5 | ES | 10 | 49.5 | Intensive | Functional ES |
| | | 1 | VC | 10 | 41.5 | NR | |
| Ghoniem 2005[57] | 1 | 3 | PFMT | 50 | 54.0 | Basic | Placebo drug |
| | | | SNRI | 52 | 53.0 | Basic | Imitation PFMT |
| Hahn 1991[175] | 1 | 6 | PFMT | 10 | 47.2 | Basic | IFT |
| | | | ES | 10 | | Basic | |
| Haken 1991[179] | 1 | 2.5 | PFMT | 33 | 48.0 | Basic | |
| | | | VC | 31 | | Basic | |
| Henalla 1989[124] | 1 | 3 | PFMT | 26 | NR | Intensive | |
| | | | ES | 25 | NR | Intensive | IFT |
| Hofbauer 1990[126] | 1 | 1.5 | PFMT | 11 | 51.0 | Intensive | 12 visits |
| | | | ES | 11 | 59.7 | Intensive | 18 visits; faradism |
| Klarskov 1986[184] | 1 | 4 | PFMT | 24 | 48.0 | Basic | |
| | | | Surgery | 26 | | NR | |
| Laycock 1988[176] | 1 | 1–2? | PFMT | 16 | 44.0 | Intensive | Weekly visit |
| | | | ES | 20 | | Intensive | 2–3 visits per week; IFT |
| Laycock 2001[152] | 1 | 3 | PFMT | 20 | NR | Basic | |
| | | | PFMT + BF | 40 | NR | Basic | |
| | | | VC | 41 | NR | Basic | |
| Oláh 1990[187] | 3 | 1 | ES | 36 | 47.9 | Intensive | 12 visits |
| | | | VC | 33 | 43.2 | Intensive | 4 visits; IFT |
| Peattie 1988[180] | 1 | 1 | PFMT | 22 | NR | Intensive | |
| | | | VC | 22 | NR | Basic | |
| Sherburn 2007[182] | 1 | 5 | PFMT | 43 | 72.0 | Intensive | |
| | | | BT | 41 | | Intensive | |
| Smith 1996[177] | 1 | 4 | PFMT | 9 | 48.0 | Basic? | |
| | | | ES | 9 | 53.0 | Basic? | Intravaginal neuromuscular stimulation |
| Tapp 1989[185] | 1 | 3 | PFMT | 27 | NR | Intensive | |
| | | | Surgery | 28 | NR | NR | |
| Williams 2006[129] | 2 | 3 | PFMT | 79 | 55.9 | Basic | |
| | | | VC | 80 | 58.2 | Basic | |
| Wise 1993[188] | 1 | 3 | ES | 20 | NR | Basic | Maximal vaginal ES |
| | | | VC | 21 | NR | Basic | |
| Wyman 1998[183] | 2 | 3 | PFMT + BF | 69 | 62.0 | Basic | |
| | | | BT | 68 | 60.0 | Basic | |

a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.

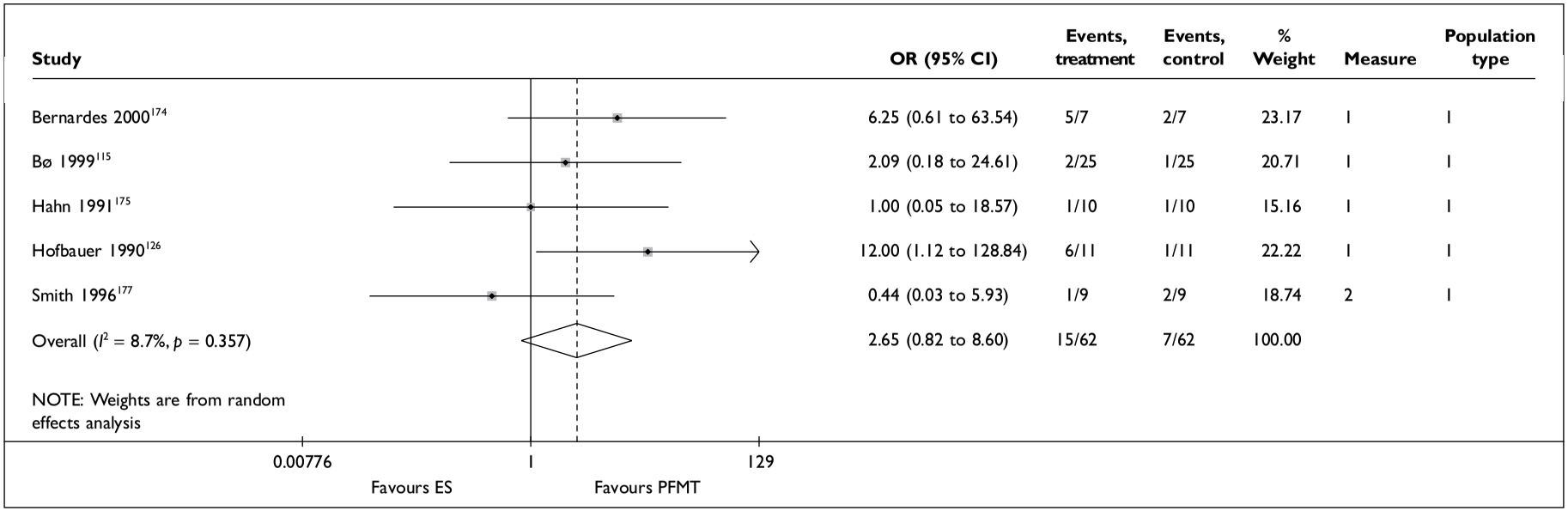


***FIGURE 21*** *Cure rates: pelvic floor muscle training versus electrical stimulation.*

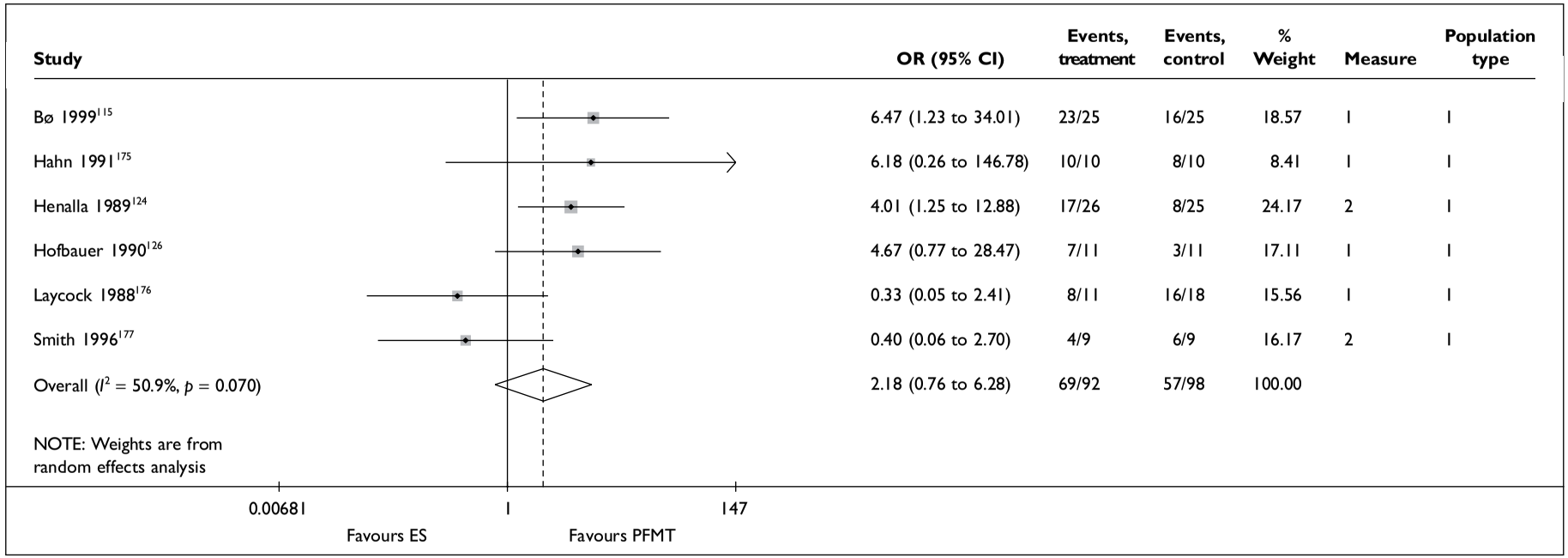


***FIGURE 22*** *Improvement rates: pelvic floor muscle training versus electrical stimulation.*

***TABLE 32a*** *Adverse events: pelvic floor muscle training versus electrical stimulation*

| | PFMT | | ES | | | |
|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **Notes** | **Population type** |
| ***N experiencing AEs*** | | | | | | |
| Bø 1999[115] | 0/29 | 0 | 10/32 | 31 | Smarting (tenderness, bleeding, discomfort), motivation problem, difficulty in using the stimulator | 1 |

***TABLE 32b*** *Quality of life: pelvic floor muscle training versus electrical stimulation*

| | PFMT | | ES | | | |
|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Notes** | **Population type** |
| ***Social Activity Index*** | | | | | | |
| Bø 1999[115] | 25 | 0.6 (1.02) | 25 | 0.6 (1.02) | Change in score (mean, SD) | 1 |

## PFMT, with or without BF, vs VC

Seven studies provided information on at least one of the specified primary outcomes.[115,129,152,178–181] Three of these studies, namely Bø and colleagues (1999),[115] Cammu and colleagues (1998)[181] and Peattie and colleagues (1988),[180] provided intensive supervision (more than two sessions per month) for the PFMT group (with or without BF) but basic supervision (two or fewer sessions per month) for the VCs group. The other studies provided basic supervision for both groups.

### *Cure and improvement*

There appeared to be no clear differences between PFMT, with or without BF, and VCs (*Figures 23* and *24*). One study by Bø and colleagues (1999)[115] stands out, showing a relatively higher OR favouring PFMT. It is not clear why this is the case. One explanation may be a longer training duration and more supervisory sessions for the PFMT group relative to other studies.

### *Adverse events*

Four studies[115,129,179,181] reported adverse events (*Table 33*). The first study[115] reported that 62% (18/29) of participants in the VCs group experienced adverse events, compared with none in the PFMT group. The second study[179] did not report any data but noted that PFMT was associated with difficulty remembering to use the technique, whereas participants using cones reported aesthetic dislike of the technique as well as difficulties associated with vaginal prolapse, resulting for some in discontinuation of the cone treatment. In the third study,[129] there were two cases of urinary tract infection in both groups but no other side effects were reported by the participants. The fourth study[181] reported that 47% (14/30) in the cones group experienced adverse events and subsequently discontinued treatment, compared with none in the PFMT-plus-BF group.

### *Quality of life*

Two studies[129,152] found no statistically significant differences between groups in condition-specific quality of life (*Table 33*).

## PFMT, with or without BF, vs BT

### *Cure and improvement*

Two studies[182,183] compared PFMT (with or without BF) with BT (*Table 34*). The first study[182] recruited women with SUI only (population type 1) and reported cure rates of 48% (19/40) for PFMT and 26% (9/35) for BT immediately after the supervised treatment phase (OR 2.61, 95% CI 0.98 to 6.96). The difference was not statistically significant. The other study[183] included women with other urinary incontinence symptoms (population type 2) and similarly found no clear difference between groups in cure and improvement at the end of the supervised treatment phase (*Table 34*: cure 13% vs 18%; improvement 76% vs 65%), and 3 months after the end of the treatment phase (Appendix 17, Comparison 18: cure 20% vs 16%; improvement 70% vs 62%). In this second study,[183] a large proportion of participants from both groups appeared to have sought alternative treatments by

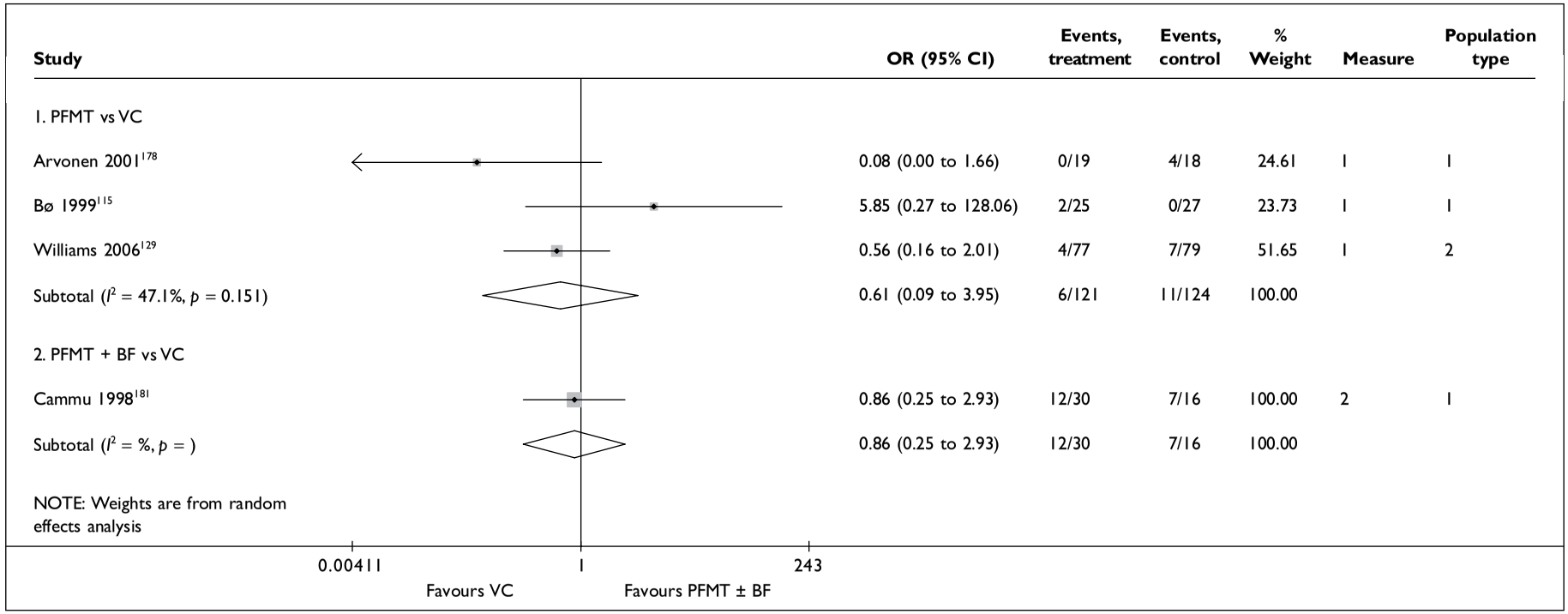


***FIGURE 23*** *Cure rates: pelvic floor muscle training, with or without biofeedback, versus vaginal cones.*

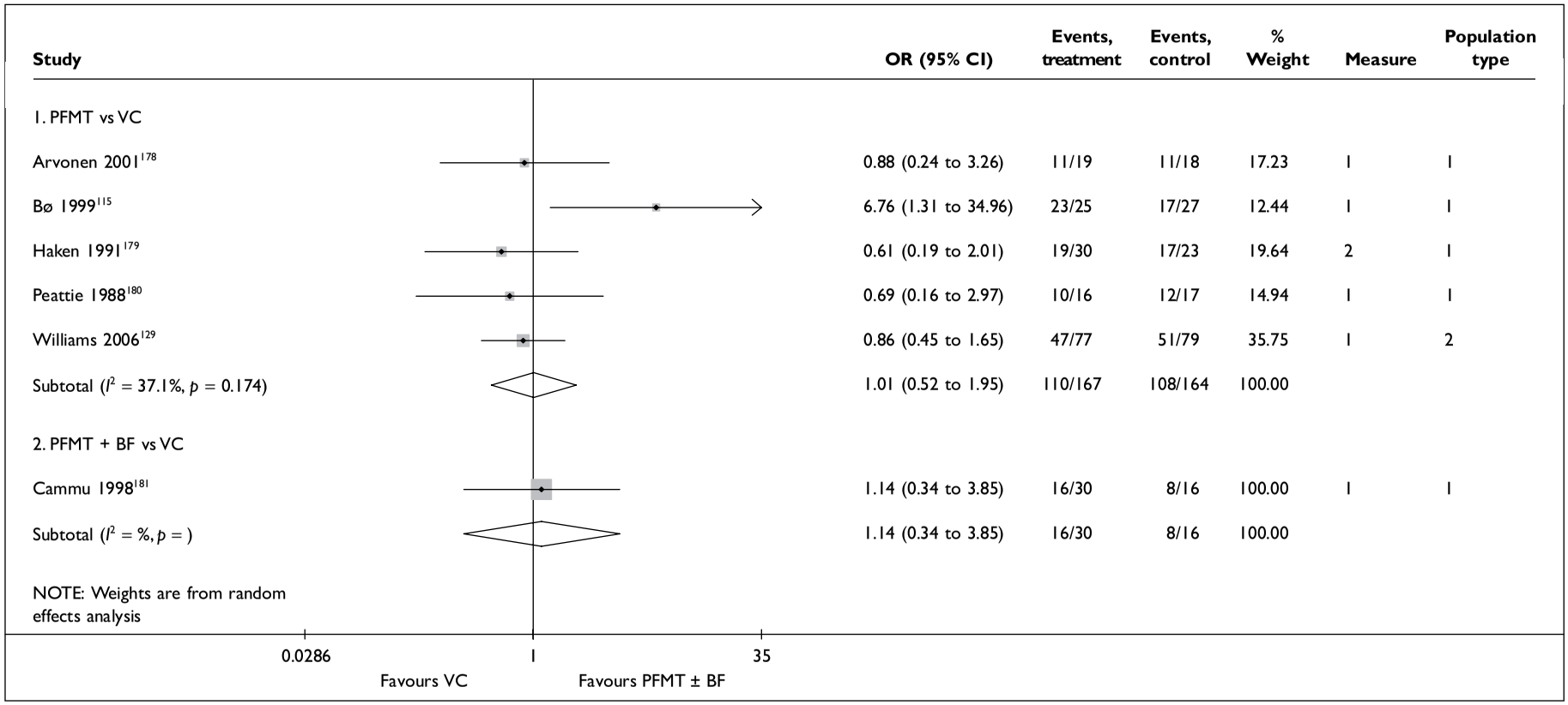


***FIGURE 24*** *Improvement rates: pelvic floor muscle training, with or without biofeedback, versus vaginal cones.*

***TABLE 33a*** *Adverse events: pelvic floor muscle training with or without biofeedback versus vaginal cones*

| | PFMT ± BF | | VC | | | Population type |
|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | Notes | |
| ***PFMT vs VC*** | | | | | | |
| Bø 1999[115] | 0/29 | 0 | 18/29 | 62 | Abdominal pain, vaginitis, bleeding, motivation problems, trouble in using the cones | 1 |
| Haken 1991[179] | ND/33 | | ND/31 | | 'Difficulty remembering to use the technique was a significant feature in the [PFMT] group which was not apparent in those using cones. Causes of withdrawal in the cones group were predominantly aesthetic dislike of the technique and difficulties associated with vaginal prolapse'; number lost to follow-up for PFMT = 3/33, for cones = 8/31 | 1 |
| Williams 2006[129] | 2/79 | 3 | 2/80 | 3 | Urinary tract infection | 2 |
| ***PFMT + BF vs VC*** | | | | | | |
| Cammu 1998[181] | 0/30 | 0 | 14/30 | 47 | Unpleasant feeling ($n = 5$), time consuming ($n = 3$), inability to introduce the cone when too nervous or when in a hurry ($n = 2$), interference with menstrual cycle ($n = 2$), a certain cone held in the morning could not be held any longer in the evening (muscle fatigue) ($n = 2$) | 1 |

ND, no data.

***TABLE 33b*** *Quality of life: pelvic floor muscle training with or without biofeedback versus vaginal cones*

| | PFMT ± BF | | VC | | Reported *p*-value | Notes | Population type |
|---|---|---|---|---|---|---|---|
| | *N* | Value | *N* | Value | | | |
| ***Social Activity Index – PFMT vs VC*** | | | | | | | |
| Bø 1999[115] | 25 | 0.6 (1.02) | 27 | 0.1 (1.06) | | Change in score (mean, SD) | 1 |
| ***King's Health Questionnaire – PFMT vs VC*** | | | | | | | |
| Laycock 2001[152] | 16 | 8.13 (9.06) | 30 | 7.03 (7.74) | NS | Change in score (mean increase, SD) | 1 |
| ***King's Health Questionnaire – PFMT + BF vs VC*** | | | | | | | |
| Laycock 2001[152] | 22 | 6.14 (6.2) | 30 | 7.03 (7.74) | NS | Change in score (mean increase, SD) | 1 |
| ***The Leicester Impact Scale – PFMT vs VC*** | | | | | | | |
| [a]Williams 2006[129] | 77 | 2 (0.0 to 5.0) | 79 | 2 (0.0 to 5.0) | 0.729 | Score (median interquartile range) | 2 |

a Lower scores reflect better quality of life.

the end of the 3-year follow-up; of those who did not receive any additional treatment, cure rates were 9% (1/11) in the PFMT group and 18% (4/22) in the BT group (Appendix 17, Comparison 18).

#### *Adverse events*

No data were available on adverse events.

#### *Quality of life*

Condition-specific quality of life was better for women having PFMT with or without BF, compared with BT (*Table 34*). In one study[182] that performed a statistical test, the difference was found to be statistically significant. General HRQoL scores [Assessment of Quality of Life (AQoL)] were similar for both groups in one study[182] that reported this outcome (Appendix 17, Comparison 18).

### PFMT vs SNRI (80 mg)

One study[57] compared PFMT (with placebo drug) with SNRI (with imitation PFMT). The results showed greater improvement and better condition-specific quality of life in the PFMT group, although the difference was not statistically significant (*Table 35*).

### PFMT vs surgery

Data on cure and improvement from two studies[184,185] comparing PFMT with surgery are shown in *Figures 25* and *26*. One of these studies[184] compared PFMT with either Burch colposuspension, vaginal repair or combined procedures, whereas the other study[185] compared PFMT with Burch colposuspension. The results for both cure and improvement favoured surgery (*Figures 25* and *26*: OR for cure 0.08, 95% CI 0.03 to 0.23; OR for improvement 0.19, 95% CI 0.04 to 0.77). However, no information was reported on adverse events or quality of life.

### ES vs VC: cure and improvement

*Figures 27* and *28* show pooled data from three studies[115,187,188] reporting the number of women cured or improved after treatment with ES compared with VCs. No statistically significant difference between the groups was found (*Figures 27* and *28*: OR for cure 1.00, 95% CI 0.26 to 3.91, OR for improvement 1.30, 95% CI 0.59 to 2.84).

One of these studies[187] provided data at 6 months after the initial treatment phase had finished and found no statistically significant difference between the groups in terms of cure (OR 0.93, 95% CI 0.31 to 2.78) or improvement (OR 0.54, 95% CI 0.17 to 1.68) (Appendix 17, Comparison 19).

### ES vs VC: adverse events

One study[115] indicated that more participants experienced adverse events in the VC group (62%) than in the ES group (31%), although discontinuation due to adverse events was more common in the ES group (7/32) than in the VC group (1/29) (*Table 36*). Another study,[187] which used cones to assess pelvic floor muscle strength in both groups, reported that nine women withdrew because of a failure to tolerate the cones during pretreatment assessment. In seven of these women, the vagina was too narrow and the cones 'wedged'. The same study[187] reported a further two adverse events (one psychiatric disorder and one death) in the cones group, which were considered by the study author to be unrelated to the study intervention.

### ES vs VC: quality of life

The information on condition-specific quality of life was available from one study only.[115] The results were similar for both groups (*Table 36*).

## Comparison between different treatments: dual modality

The characteristics of included studies comparing a single intervention with an intervention combined with an adjunct treatment are summarised in *Table 37*. Pelvic floor muscle training with sham ES was classified as being equivalent to PFMT. Where both PFMT and PFMT with sham ES were present within a trial, the dichotomous data were combined (added up).[121,190] In two three-arm trials examining the addition of ES to PFMT plus BF,[157,172] the trial arms involving different types of ES (PFMT plus BF and ES) were combined for dichotomous data.

### PFMT (with or without BF) vs PFMT (with or without BF) and adjunct treatment

#### *PFMT (with or without BF) vs PFMT (with or without BF) and ES*

**Cure and improvement**

Pooled data on cure and improvement showed that all trial estimates overlapped, and there was significant statistical heterogeneity for the cure rate at the 10% level (*Figures 29* and *30*: OR for cure without BF 1.02, 95% CI 0.29 to 3.55; OR

***TABLE 34a*** *Cure rates and improvement rates: pelvic floor muscle training, with or without biofeedback, versus bladder training*

| | PFMT ± BF | | BT | | | | |
|---|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **OR (95% CI)** | **Measure** | **Population type** |
| ***Cure rate*** | | | | | | | |
| *PFMT vs BT* | | | | | | | |
| Sherburn 2007[182] | 19/40 | 48 | 9/35 | 26 | 2.61 (0.98 to 6.96), $p = 0.055$ | 2 | 1 |
| *PFMT + BF vs BT* | | | | | | | |
| Wyman 1998[183] | 8/64 | 13 | 12/68 | 18 | 0.67 (0.25 to 1.76), $p = 0.412$ | 2 | 2 |
| ***Improvement*** | | | | | | | |
| *PFMT + BF vs BT* | | | | | | | |
| Wyman 1998[183] | 48/63 | 76 | 43/66 | 65 | 1.71 (0.79 to 3.70), $p = 0.171$ | 1 | 2 |

***TABLE 34b*** *Quality of life: pelvic floor muscle training, with or without biofeedback, versus bladder training*

| | PFMT ± BF | | BT | | | | |
|---|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Reported *p*-value** | **Notes** | **Population type** |
| ***ICIQ-UI SF – PFMT vs BT*** | | | | | | | |
| [a]Sherburn 2007[182] | 43 | 5 (4) | 41 | 8 (7) | 0.003 | Score (median interquartile range) | 1 |
| ***Urogenital Distress Inventory – PFMT + BF vs BT*** | | | | | | | |
| [a]Wyman 1998[183] | 45 | 81.2 (39.6) | 47 | 99.2 (54.4) | | Score (mean, SD) | 1 |
| ***Incontinence Impact Questionnaire-Revised – PFMT + BF vs BT*** | | | | | | | |
| [a]Wyman 1998[183] | 45 | 43.5 (47.4) | 47 | 68.4 (69.7) | | Score (mean, SD) | 1 |

ICIQ-UI SF, International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form.
a Lower scores reflect better quality of life.

***TABLE 35a*** *Improvement rate: pelvic floor muscle training versus serotonin–noradrenaline reuptake inhibitor (80 mg)*

| | PFMT | | SNRI | | | | |
|---|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **OR (95% CI)** | **Measure** | **Population type** |
| Ghoniem 2005[57] | 32/49 | 65 | 27/50 | 54 | 1.60 (0.71 to 3.60), $p = 0.253$ | 1 | 1 |

***TABLE 35b*** *Quality of life: pelvic floor muscle training versus serotonin–noradrenaline reuptake inhibitor (80 mg)*

| | PFMT | | SNRI | | | | |
|---|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Reported *p*-value** | **Notes** | **Population type** |
| ***I-QoL*** | | | | | | | |
| Ghoniem 2005[57] | 49 | 7.8 | 50 | 8.3 | 0.979 | Change in score (mean percentage score increase) | 1 |

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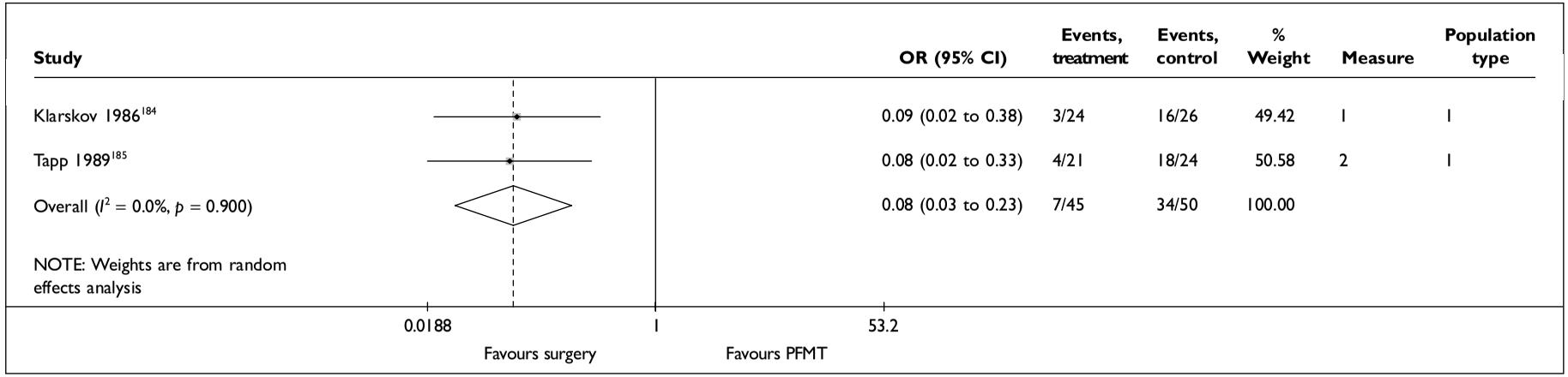


***FIGURE 25*** *Cure rates: pelvic floor muscle training versus surgery.*

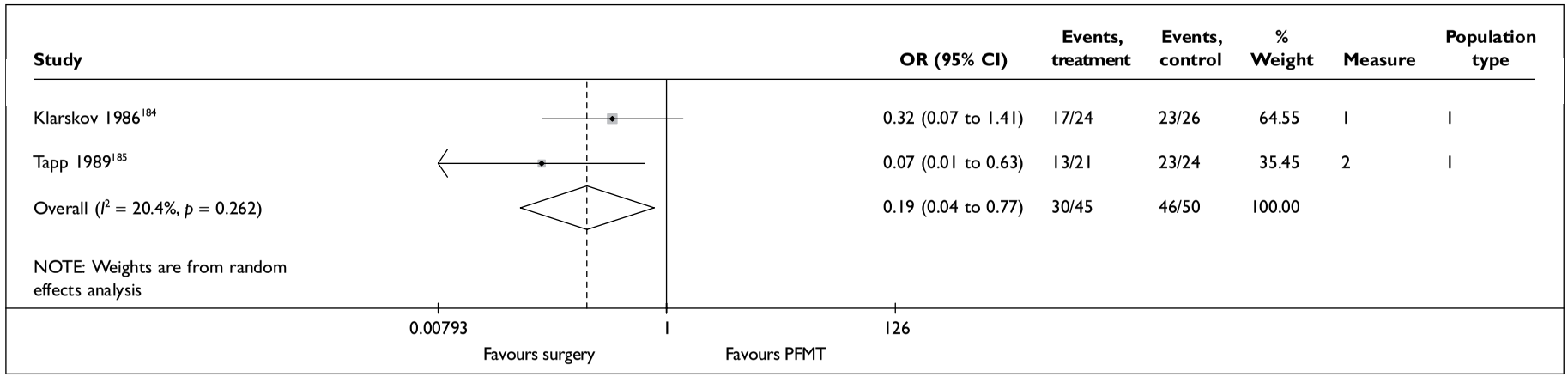


***FIGURE 26*** *Improvement rates: pelvic floor muscle training versus surgery.*

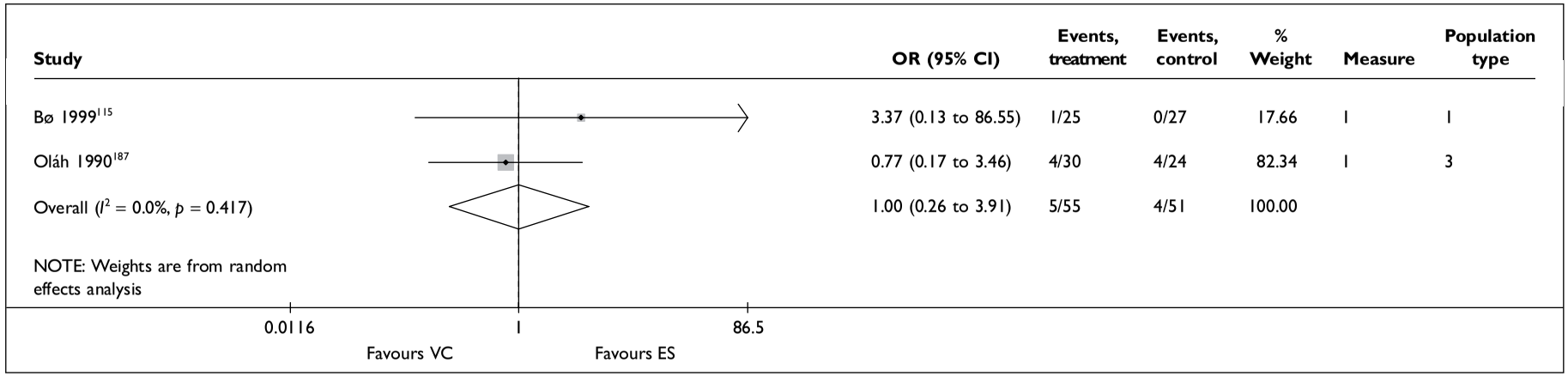


***FIGURE 27*** *Cure rates: electrical stimulation versus vaginal cones.*

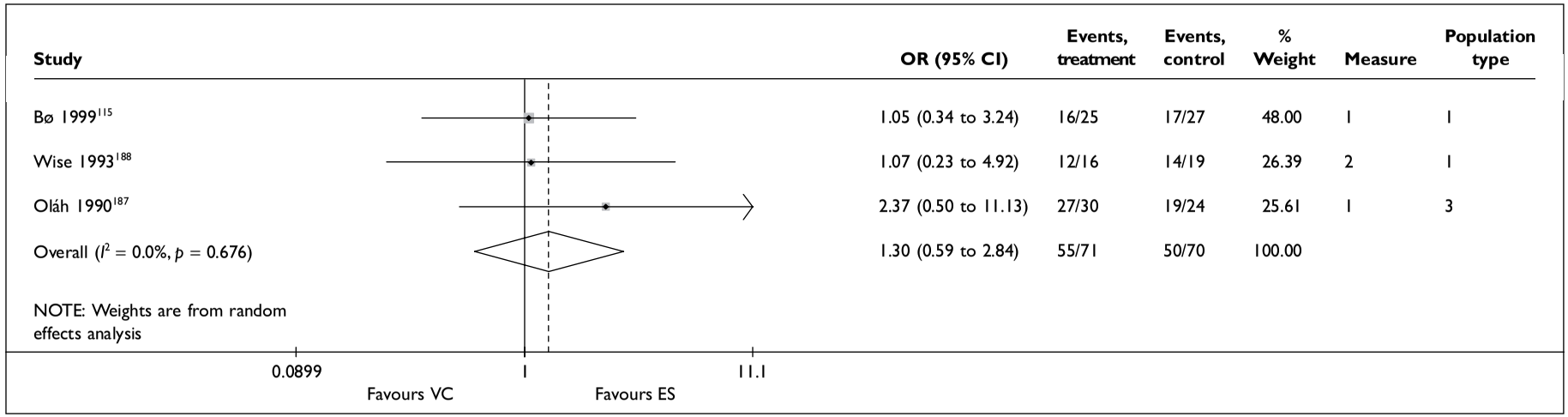


***FIGURE 28*** *Improvement rates: electrical stimulation versus vaginal cones.*

***TABLE 36a*** *Adverse events: electrical stimulation versus vaginal cone*

| | ES | | VC | | | |
|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **Notes** | **Population type** |
| ***N experiencing AEs*** | | | | | | |
| Bø 1999[115] | 10/32 | 31 | 18/29 | 62 | ES: Smarting (tenderness, bleeding, discomfort), motivation problem, difficulty in using the stimulator<br>VC: Abdominal pain, vaginitis, bleeding, motivation problems, trouble in using the cones | 1 |
| Oláh 1990[187] | 4/36 | 11 | 5/33 | 15 | Unable to tolerate cones (used to assess pelvic floor muscle strength in both groups): the vagina was too narrow and the cones 'wedged'; irregular uterine bleeding preventing cone use; discomfort experienced during use because of excessive scar tissue in the vagina | 3 |

***TABLE 36b*** *Quality of life: electrical stimulation versus vaginal cone*

| | ES | | VC | | | |
|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Notes** | **Population type** |
| ***Social Activity Index*** | | | | | | |
| Bø 1999[115] | 25 | 0.6 (1.02) | 27 | 0.1 (1.06) | Change in score (mean, SD) | 1 |

for improvement without BF 0.84, 95% CI 0.34 to 2.07; OR for improvement with BF 0.86, 95% CI 0.36 to 2.08). The source of heterogeneity appears to be the study by Blowman and colleagues,[189] which suggested that adding ES to PFMT was significantly better than PFMT alone. The reason for this is unclear.

Two studies[157,172] reported the improvement rate at 6 months after the end of the initial treatment phase (Appendix 17, Comparison 20). No differences between the treatment groups were found.

### Adverse events

Only one study[123] reported any adverse events (*Table 38*). The combined treatment group recorded four (6%) occurrences of vaginal irritation due to application of ES devices, compared with none in the PFMT group.

### Quality of life

Condition-specific (Incontinence Impact Questionnaire) (*Table 38*) and general HRQoL (SF-36) (Appendix 17, Comparison 20) was reported by one study only.[123] The results did not differ by treatment group.

### *PFMT vs PFMT plus VC*

One study[192] reported cure and improvement rates for PFMT compared with PFMT with adjunct VCs (*Table 39*). The results were slightly better for the combined treatment group, but these differences were not statistically significant.

### *PFMT plus BF vs PFMT plus BF and BT*

#### Cure and improvement

One study[183] of 136 women with different types of incontinence reported cure and improvement at the end of the 3-month treatment phase, at 6 months (3 months after the end of treatment) and at 3.2 years (*Table 40*). Both cure and improvement rates were consistently higher in the combined treatment group at 3 months (*Table 40*: cure OR 0.32, 95% CI 0.13 to 0.79; improvement OR 0.35, 95% CI 0.13 to 0.97) and 6 months (Appendix 17, Comparison 21: cure OR 0.69, 95% CI 0.30 to 1.58; improvement OR 0.75, 95% CI 0.34 to 1.69). However, the differences were not statistically significant at follow-up at 6 months. The percentage of participants who

***TABLE 37*** *Background characteristics of studies comparing different treatments (dual modality)*

| Study ID | Population type | Duration (month) | Comparator | *N* randomised | Age | Supervisory intensity[a] | Notes |
|---|---|---|---|---|---|---|---|
| Bidmead 2002[121] | 1 | 3.5 | PFMT | 40? | 46.2 | Basic | |
| | | | PFMT + sham ES | 42? | 51.5 | Basic | |
| | | | PFMT + ES | 82? | 50.4 | Basic | |
| Blowman 1991[189] | 1 | ?1 | PFMT | 7 | 42.5 | Basic | With sham ES |
| | | | PFMT + ES | 7 | 45.0 | Basic | ES = neurotrophic stimulation |
| Ghoniem 2005[57] | 1 | 3 | PFMT | 50 | 54.0 | Basic | |
| | | | SNRI | 52 | 53.0 | Basic | |
| | | | PFMT + SNRI | 52 | 54.0 | Basic | |
| Goode 2003[123] | 3 | 2 | PFMT | 66 | 57.7 | Basic | |
| | | | PFMT + ES | 67 | 54.9 | Basic | ES = biphasic pulses |
| Haig 1995[190] | 1 | 3 | PFMT | 20 | 55.0 | Intensive | |
| | | | PFMT + sham ES | 18 | 51.0 | Intensive | |
| | | | PFMT + ES | 20 | 51.0 | Intensive | |
| Hofbauer 1990[126] | 1 | 1.5 | PFMT | 11 | 51.0 | Intensive | |
| | | | ES | 11 | 59.7 | Intensive | Faradic |
| | | | PFMT + ES | 11 | 62.9 | Intensive | |
| Knight 1998[172] | 1 | 6 | PFMT + BF | 21 | NR | Intensive | ES = maximal stimulation at clinic |
| | | | PFMT + BF + ES (maximal) | 24 | NR | Intensive | |
| | | | PFMT + BF + ES (low) | 25 | NR | Intensive | ES = overnight at low intensity at home |
| Pieber 1995[192] | 1 | 3 | PFMT | 25 | 44.3 | Basic | |
| | | | PFMT + VC | 21 | 41.7 | Basic | |
| Tapp 1987[191] | 1 | 3 | PFMT | 15 | NR | Intensive | |
| | | | PFMT + ES | 14 | NR | Intensive | |
| Tapp 1989[185] | 1 | 3 | PFMT | 27 | NR | Intensive | |
| | | | PFMT + ES | 26 | NR | Intensive | Faradic |
| Wilson 1987[157] | 1 | 1.5 | PFMT + BF | 15 | 46.8 | Intensive | |
| | | | PFMT + BF + ES (faradism) | 15 | | Intensive | |
| | | | PFMT + BF + ES (IFT) | 15 | | Intensive | |
| Wise 1993[188] | 1 | 3 | PFMT + VC | 21 | NR | Basic | |
| | | | VC | 21 | NR | Basic | |
| Wyman 1998[183] | 2 | 3 | PFMT + BF | 69 | 62.0 | Basic | |
| | | | BT | 68 | 60.0 | Basic | |
| | | | PFMT + BF + BT | 67 | 61.0 | Basic | |

a None, no clinic visit for training, treatment or supervision; basic, up to two clinic visits per month; intensive, more than two clinic visits per month.

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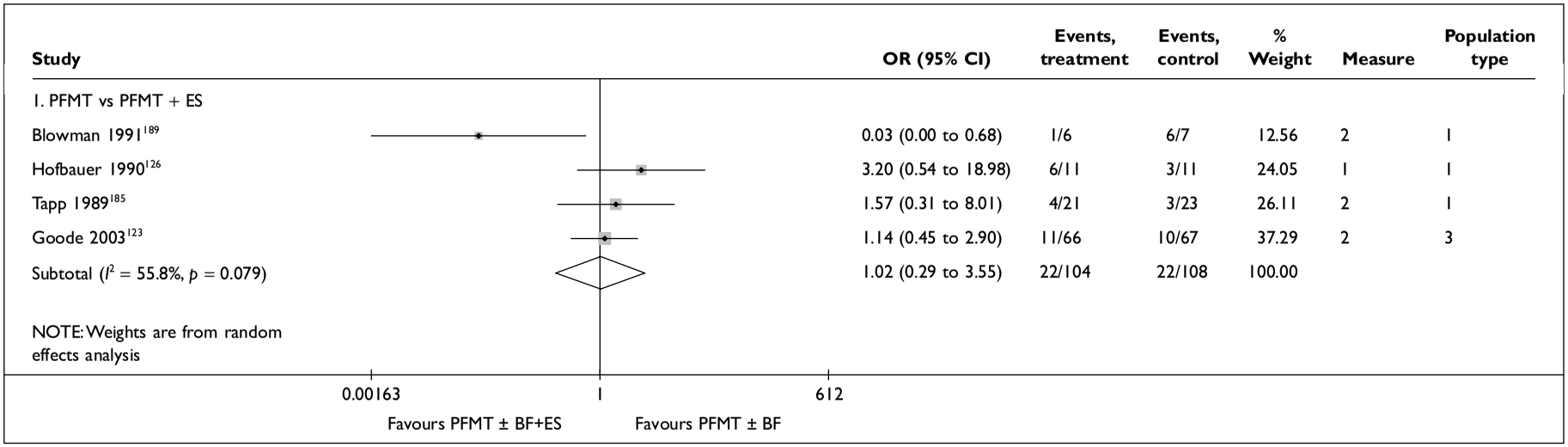


***FIGURE 29*** *Cure rates: pelvic floor muscle training (PFMT) [± biofeedback (BF)] versus PFMT (± BF) plus electrical stimulation.*

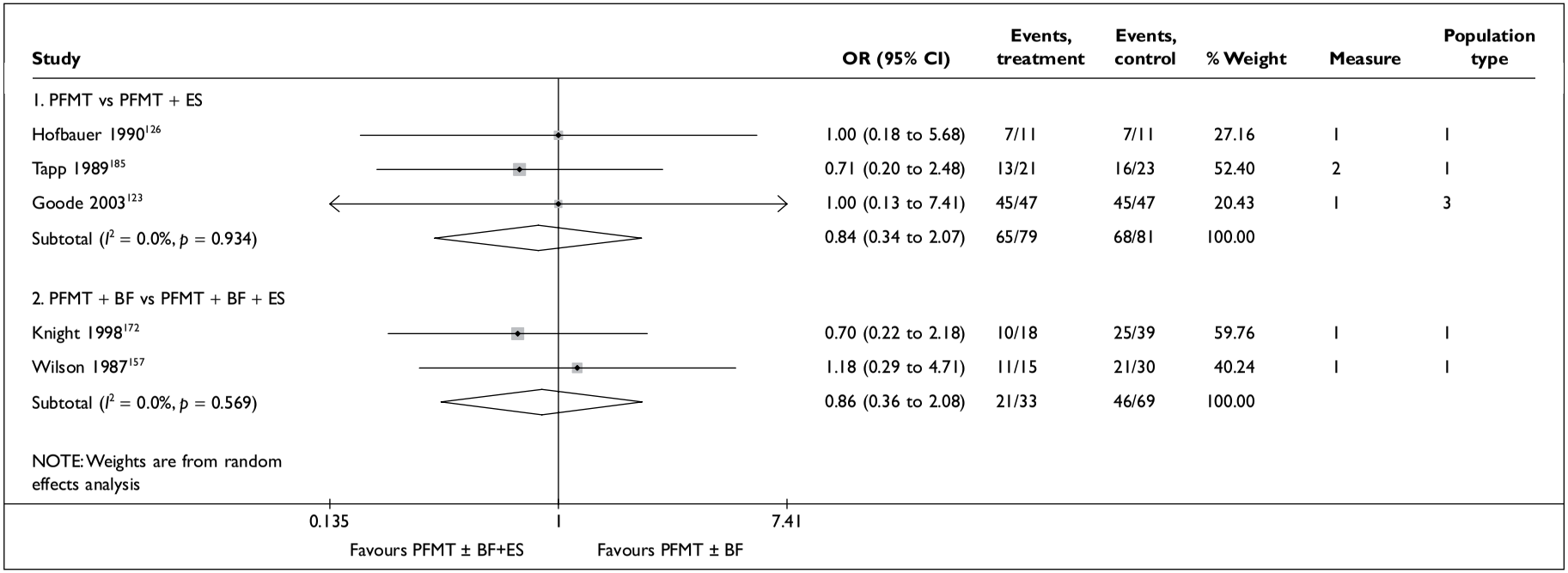


***FIGURE 30*** *Improvement rates: pelvic floor muscle training (PFMT) [± biofeedback (BF)] versus PFMT (± BF) plus electrical stimulation.*

***TABLE 38a*** *Number experiencing adverse effects: pelvic floor muscle training (PFMT) versus PFMT plus electrical stimulation*

| | PFMT | | PFMT + ES | | | |
|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | Notes | Population type |
| Goode 2003[123] | 0/66 | 0 | 4/67 | 6 | Vaginal irritation | 3 |

***TABLE 38b*** *Quality of life: pelvic floor muscle training (PFMT) versus PFMT plus electrical stimulation*

| | PFMT | | PFMT + ES | | | |
|---|---|---|---|---|---|---|
| | *N* | Value | *N* | Value | Notes | Population type |
| ***Incontinence Impact Questionnaire*** | | | | | | |
| Goode 2003[123] | 66 | No difference | 67 | No difference | Total score | 3 |

***TABLE 39*** *Cure and improvement rates: pelvic floor muscle training (PFMT) versus PFMT plus vaginal cone*

| | PFMT | | PFMT + VC | | | | |
|---|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | OR (95% CI) | Measure | Population type |
| ***Cure rate*** | | | | | | | |
| Pieber 1995[192] | 3/25 | 12 | 5/21 | 24 | 0.44 (0.09 to 2.10), $p = 0.300$ | 1 | 1 |
| ***Improvement rate*** | | | | | | | |
| Pieber 1995[192] | 12/25 | 48 | 11/21 | 52 | 0.84 (0.26 to 2.68), $p = 0.767$ | 1 | 1 |

***TABLE 40a*** *Cure and improvement rates: pelvic floor muscle training (PFMT) plus biofeedback (BF) versus PFMT plus BF and bladder training*

| | PFMT + BF | | PFMT + BF + BT | | | | |
|---|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | OR (95% CI) | Measure | Population type |
| ***Cure rate*** | | | | | | | |
| Wyman 1998[183] | 8/64 | 13 | 19/61 | 31 | 0.32 (0.13 to 0.79), $p = 0.014$ | 2 | 2 |
| ***Improvement rate*** | | | | | | | |
| Wyman 1998[183] | 48/63 | 76 | 55/61 | 90 | 0.35 (0.13 to 0.97), $p = 0.044$ | 1 | 2 |

remained cured at 3.2 years was 50% (8/16) for the combined treatment and 9% (1/11) for the comparator, although the number available for long-term assessment was very small (Appendix 17, Comparison 21).

### Quality of life

The same study[183] measured condition-specific quality of life using two instruments (*Table 40*). The data at the end of the 3-month treatment phase were reported separately for women with SUI alone: one instrument (Urogenital Distress Inventory) favoured the group with adjunct BT, and the other (Incontinence Impact Questionnaire Revised) favoured the group without BT. The data with longer follow-up were reported combined for all participants with SUI, UUI and MUI (Appendix 17, Comparison 21). The results were again contradictory according to the different instruments.

#### *PFMT vs PFMT plus SNRI*

One study[57] reported improvement and condition-specific quality of life for PFMT compared with

***TABLE 40b*** *Quality of life: pelvic floor muscle training (PFMT) plus biofeedback (BF) versus PFMT plus BF and bladder training*

| | PFMT + BF | | PFMT + BF + BT | | | |
|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Notes** | **Population type** |
| ***Urogenital Distress Inventory*** | | | | | | |
| [a]Wyman 1998[183] | 45 | 81.2 (39.6) | 44 | 63.2 (49.2) | Score (mean, SD) | I |
| ***Incontinence Impact Questionnaire-Revised*** | | | | | | |
| [a]Wyman 1998[183] | 45 | 43.5 (47.4) | 44 | 52.3 (73.4) | Score (mean, SD) | I |

a Lower scores reflect better quality of life.

women having a combination of PFMT plus adjunct drug therapy (*Table 41*). The results were slightly better for the combined treatment, but these differences were not statistically significant. adverse events associated with SNRI (with PFMT or imitation PFMT) are reported separately in *Table 27*.

## PFMT plus adjunct treatment vs the adjunct treatment

### *PFMT plus ES vs ES*

One study[126] reported the number of women cured or improved for PFMT plus ES compared with ES alone (*Table 42*). The ORs (point estimate) favoured the combined treatment for both cure and improvement, but CIs were wide and included one (no difference).

### *PFMT plus VC vs VC*

One study[188] compared a combination of PFMT plus VCs with VCs alone (*Table 43*). Between 74% and 93% of participants improved after treatment but there was no clear difference between the groups.

### *PFMT plus BF and BT vs BT*

#### Cure and improvement

One study[183] of 135 women with different types of urinary incontinence reported cure and improvement at the end of the 3-month treatment phase, at 6 months (3 months after the end of treatment) and 3.2 years (*Table 44*). The results showed higher cure and improvement rates for the combined treatment group at the end of the initial treatment phase (*Table 44*: cure OR 2.11, 95% CI 0.92 to 4.82; improvement OR 4.90, 95% CI 1.84 to 13.10), and at 6 months (Appendix 17, Comparison 22; cure OR 1.89,

***TABLE 41a*** *Improvement rates: pelvic floor muscle training (PFMT) versus PFMT plus serotonin–noradrenaline reuptake inhibitor*

| | PFMT | | PFMT + SNRI | | | | |
|---|---|---|---|---|---|---|---|
| | ***n/N*** | **%** | ***n/N*** | **%** | **OR (95% CI)** | **Measure** | **Population type** |
| Ghoniem 2005[57] | 32/49 | 65 | 36/51 | 71 | 0.78 (0.34 to 1.82), $p = 0.572$ | I | I |

***TABLE 41b*** *Quality of life: pelvic floor muscle training (PFMT) versus PFMT plus serotonin–noradrenaline reuptake inhibitor*

| | PFMT | | PFMT + SNRI | | | | |
|---|---|---|---|---|---|---|---|
| | ***N*** | **Value** | ***N*** | **Value** | **Reported *p*-value** | **Notes** | **Population type** |
| ***I-QoL*** | | | | | | | |
| Ghoniem 2005[57] | 49 | 7.8 | 51 | 13.1 | 0.063 | Mean percentage score increase | I |

***TABLE 42*** *Cure and improvement rates: pelvic floor muscle training plus electrical stimulation (ES) versus ES*

| | PFMT+ES | | ES | | | | |
|---|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | OR (95% CI) | Measure | Population type |
| ***Cure rate*** | | | | | | | |
| Hofbauer 1990[126] | 3/11 | 27 | 1/11 | 9 | 3.75 (0.33 to 43.31), $p = 0.290$ | 1 | 1 |
| ***Improvement rate*** | | | | | | | |
| Hofbauer 1990[126] | 7/11 | 64 | 3/11 | 27 | 4.67 (0.77 to 28.47), $p = 0.095$ | 1 | 1 |

***TABLE 43*** *Improvement rates: pelvic floor muscle training plus vaginal cone (VC) versus VC*

| | PFMT+VC | | VC | | | | |
|---|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | OR (95% CI) | Measure | Population type |
| ***Improvement rate*** | | | | | | | |
| Wise 1993[188] | 14/15 | 93 | 14/19 | 74 | 5.00 (0.52 to 48.46), $p = 0.165$ | 2 | 1 |

***TABLE 44a*** *Cure and improvement rates: pelvic floor muscle training plus biofeedback and bladder training (BT) versus BT*

| | PFMT+BF+BT | | BT | | | | |
|---|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | OR (95% CI) | Measure | Population type |
| ***Cure rate*** | | | | | | | |
| Wyman 1998[183] | 19/61 | 31 | 12/68 | 18 | 2.11 (0.92 to 4.82), $p = 0.076$ | 2 | 2 |
| ***Improvement rate*** | | | | | | | |
| Wyman 1998[183] | 55/61 | 90 | 43/66 | 65 | 4.90 (1.84 to 13.10), $p = 0.002$ | 1 | 2 |

***TABLE 44b*** *Quality of life: pelvic floor muscle training plus biofeedback and bladder training (BT) versus BT*

| | PFMT+BF+BT | | BT | | | |
|---|---|---|---|---|---|---|
| | *N* | Value | *N* | Value | Measure | Population type |
| ***Urogenital Distress Inventory*** | | | | | | |
| [a]Wyman 1998[183] | 44 | 63.2 (49.2) | 47 | 99.2 (54.4) | Score (mean, SD) | 1 |
| ***Incontinence Impact Questionnaire-Revised*** | | | | | | |
| [a]Wyman 1998[183] | 44 | 52.3 (73.4) | 47 | 68.4 (69.7) | Score (mean, SD) | 1 |

a Lower scores reflect better quality of life.

95% CI 0.78 to 4.59; improvement OR 1.95, 95% CI 0.88 to 4.33). The difference in improvement at 3 months reached statistical significance but the CIs were wide. At 3.2 years, 50% (8/16) of the women receiving the combined treatment and 18% (4/22) receiving BT alone were continent (cured), although the number available for long-term assessment was very small (Appendix 17, Comparison 22).

**Quality of life**

The same study[183] measured condition-specific quality of life using two instruments. The data immediately after the 3-month treatment phase were reported separately for women with stress incontinence alone and suggested higher quality of life for the combined treatment compared with BT without PFMT and BF (*Table 44*). The data at 6 months (3 months after the end of 3-month treatment) were reported for all participants with SUI, UUI and MUI; the direction of effect remained in favour of the combined treatment (Appendix 17, Comparison 22). Among 38 women who did not seek additional treatment before the 3.2 years' follow-up, however, quality of life did not differ significantly between groups (Appendix 17, Comparison 22).

***PFMT plus SNRI vs SNRI***

One study[57] compared PFMT plus drug therapy (SNRI) with drug therapy alone (*Table 45*). The apparent greater improvement and better quality of life in the combined therapy group was not statistically different from the group using drug therapy alone.

## Summary

A summary of the effect sizes based on meta-analyses of cure and improvement data are given in *Tables 46* and *47*. Overall, it appears that most standalone interventions had, on average, higher cure and improvement rates than no (active) treatment. In particular, PFMT with or without BF was more effective than no treatment.

There was insufficient evidence from direct comparisons to say whether PFMT was more effective than other modalities of treatment or which of the PFMT programmes was the most effective. Nevertheless, PFMT with additional supervisory sessions (or any face-to-face contacts with health-care professionals) appeared more effective than PFMT alone. PFMT augmented with BF was also associated with higher cure and improvement rates. With respect to PFMT combined with adjunct treatment (e.g. PFMT plus ES), it was not possible to draw firm conclusions due to the small number of studies identified from our searches.

Quality-of-life measures reported in included studies were highly variable, which made

***TABLE 45a*** *Improvement rates: pelvic floor muscle training plus serotonin–noradrenaline reuptake inhibitor (SNRI) versus SNRI*

| | PFMT + SNRI | | SNRI | | | | |
|---|---|---|---|---|---|---|---|
| | *n/N* | % | *n/N* | % | OR (95% CI) | Measure | Population type |
| Ghoniem 2005[57] | 36/51 | 71 | 27/50 | 54 | 2.04 (0.90 to 4.64), $p = 0.087$ | I | I |

***TABLE 45b*** *Quality of life: improvement rates: pelvic floor muscle training plus serotonin–noradrenaline reuptake inhibitors (SNRI) versus SNRI*

| | PFMT + SNRI | | SNRI | | | |
|---|---|---|---|---|---|---|
| | *N* | Value | *N* | Value | Notes | Population type |
| ***I-QoL*** | | | | | | |
| Ghoniem 2005[57] | 51 | 13.1 | 50 | 8.3 | Change in score (mean percentage score increase) | I |

***TABLE 46*** *Summary table: odds ratio for cure rate*

| Intervention 1 | Intervention 2 | Number of trials in MA (total) | Number of participants in MA | OR | 95% CI | *p*-value |
|---|---|---|---|---|---|---|
| ***Comparison with no treatment*** | | | | | | |
| PFMT | NT | 8 (14) | 605 | 5.41 | 1.64 to 17.82 | 0.005 |
| PFMT + BF | NT | 2 (2) | 110 | 21.54 | 3.65 to 126.98 | 0.001 |
| ES | NT | 6 (8) | 288 | 1.10 | 0.41 to 2.94 | 0.849 |
| VC | NT | 0 (2) | | | | |
| SNRI80 | NT | 3 (11) | 1292 | 1.46 | 1.00 to 2.14 | 0.053 |
| SNRI40 | NT | 1 (2) | 255 | 1.81 | 0.96 to 3.39 | 0.065 |
| SNRI30 | NT | 0 (1) | | | | |
| SNRI20 | NT | 1 (2) | 260 | 1.10 | 0.56 to 2.14 | 0.781 |
| BT | NT | 1 (1) | 123 | 4.03 | 0.80 to 20.23 | 0.091 |
| PFMT + ES | NT | 2 (3) | 155 | 1.76 | 0.27 to 11.54 | 0.556 |
| PFMT + SNRI | NT | 0 (1) | | | | |
| ***Single modality*** | | | | | | |
| PFMT | ES | 5 (7) | 124 | 2.65 | 0.82 to 8.60 | 0.105 |
| PFMT | VC | 3 (6) | 245 | 0.61 | 0.09 to 3.95 | 0.606 |
| PFMT + BF | VC | 1 (2) | 46 | 0.86 | 0.25 to 2.93 | 0.806 |
| PFMT | BT | 1 (1) | 75 | 2.61 | 0.98 to 6.96 | 0.055 |
| PFMT + BF | BT | 1 (1) | 132 | 0.67 | 0.25 to 1.76 | 0.412 |
| PFMT | SNRI | 0 (1) | | | | |
| PFMT | Surgery | 2 (2) | 95 | 0.08 | 0.03 to 0.23 | <0.001 |
| ES | VC | 2 (4) | 106 | 1.00 | 0.26 to 3.91 | 0.998 |
| ***Dual modality*** | | | | | | |
| PFMT | PFMT + ES | 4 (7) | 133 | 1.02 | 0.29 to 3.55 | 0.976 |
| PFMT + BF | PFMT + BF + ES | 0 (2) | | | | |
| PFMT | PFMT + VC | 1 (1) | 46 | 0.44 | 0.09 to 2.10 | 0.300 |
| PFMT + BF | PFMT + BF + BT | 1 (1) | 125 | 0.32 | 0.13 to 0.79 | 0.014 |
| PFMT | PFMT + SNRI | 0 (1) | | | | |
| PFMT + ES | ES | 1 (1) | 22 | 3.75 | 0.33 to 43.31 | 0.290 |
| PFMT + VC | VC | 0 (1) | | | | |
| PFMT + BF + BT | BT | 1 (1) | 129 | 2.11 | 0.92 to 4.82 | 0.076 |
| PFMT + SNRI80 | SNRI80 | 0 (1) | | | | |
| ***Variation within comparators*** | | | | | | |
| Fluid increase then decrease | Fluid, decrease then increase | 0 (1) | | | | |
| PFMT | PFMT + BF | 8 (15) | 370 | 0.48 | 0.30 to 0.77 | 0.002 |
| PFMT | PFMT with additional sessions | 3 (4) | 118 | 0.11 | 0.03 to 0.43 | 0.001 |
| PFMT | PFMT with audiotape | 0 (2) | | | | |
| Strength and motor learning PFMT | Mortor learning PFMT alone | 1 (1) | 123 | 0.24 | 0.03 to 2.23 | 0.210 |
| PFMT (in supine) + BF | PFMT (in supine and upright) + BF | 0 (1) | | | | |
| PFMT | Modified pilates | 0 (1) | | | | |

***TABLE 46*** *Summary table: odds ratio for cure rate (continued)*

| Intervention 1 | Intervention 2 | Number of trials in MA (total) | Number of participants in MA | OR | 95% CI | *p*-value |
|---|---|---|---|---|---|---|
| PFMT (maximal contraction) + BF | PFMT (submaximal contraction) + BF | 1 (1) | 32 | 1.80 | 0.39 to 8.22 | 0.448 |
| PFMT + perineometer | PFMT + urethral conductance | 1 (1) | 27 | 1.09 | 0.13 to 9.12 | 0.936 |
| PFMT + BF (vaginal) | PFMT + BF (vaginal and abdominal) | 0 (1) | | | | |
| PFMT + BF | PFMT + ES | 0 (2) | | | | |
| PFMT + BF + ES (faradism) | PFMT + BF + ES (interferential) | 0 (1) | | | | |
| PFMT + BF + ES (maximal) | PFMT + BF + ES (low) | 0 (1) | | | | |
| VC passive | VC active | 0 (1) | | | | |
| SNRI 80 mg | SNRI 40 mg | 1 (1) | 246 | 0.71 | 0.39 to 1.32 | 0.279 |
| SNRI 80 mg | SNRI 20 mg | 1 (1) | 251 | 1.17 | 0.61 to 2.25 | 0.633 |
| SNRI 40 mg | SNRI 30 mg | 0 (1) | | | | |
| SNRI 40 mg | SNRI 20 mg | 1 (2) | 251 | 1.64 | 0.88 to 3.07 | 0.118 |
| SNRI 30 mg | SNRI 20 mg | 0 (1) | | | | |

MA, meta-analysis.

***TABLE 47*** *Summary table: odds ratio for improvement rate*

| Intervention 1 | Intervention 2 | Number of trials in meta-analysis (total) | Number of participants in meta-analysis | OR | 95% CI | *p*-value |
|---|---|---|---|---|---|---|
| ***Comparison with no treatment*** | | | | | | |
| PFMT | NT | 11 (14) | 689 | 11.75 | 3.49 to 39.55 | <0.001 |
| PFMT + BF | NT | 2 (2) | 110 | 24.20 | 2.02 to 290.58 | 0.012 |
| ES | NT | 7 (8) | 369 | 3.93 | 1.43 to 10.80 | 0.008 |
| VC | NT | 2 (2) | 212 | 5.43 | 0.07 to 396.77 | 0.439 |
| SNRI80 | NT | 10 (11) | 3672 | 2.02 | 1.67 to 2.44 | <0.001 |
| SNRI40 | NT | 2 (2) | 328 | 2.43 | 0.84 to 7.07 | 0.103 |
| SNRI30 | NT | 1 (1) | 60 | 2.58 | 0.73 to 9.11 | 0.142 |
| SNRI20 | NT | 2 (2) | 332 | 2.11 | 0.56 to 7.72 | 0.258 |
| BT | NT | 1 (1) | 123 | 9.60 | 4.22 to 21.87 | <0.001 |
| PFMT + ES | NT | 2 (3) | 108 | 8.69 | 1.87 to 40.32 | 0.006 |
| PFMT + SNRI | NT | 1 (1) | 96 | 3.28 | 1.41 to 7.64 | 0.006 |
| ***Single modality*** | | | | | | |
| PFMT | ES | 6 (7) | 190 | 2.18 | 0.76 to 6.28 | 0.148 |
| PFMT | VC | 5 (6) | 331 | 1.01 | 0.52 to 1.95 | 0.978 |
| PFMT + BF | VC | 1 (2) | 46 | 1.14 | 0.34 to 3.85 | 0.829 |
| PFMT | BT | 0 (1) | | | | |

*continued*

***TABLE 47*** *Summary table: odds ratio for improvement rate (continued)*

| Intervention 1 | Intervention 2 | Number of trials in meta-analysis (total) | Number of participants in meta-analysis | OR | 95% CI | *p*-value |
|---|---|---|---|---|---|---|
| PFMT + BF | BT | 1 (1) | 129 | 1.71 | 0.79 to 3.70 | 0.171 |
| PFMT | SNRI | 1 (1) | 99 | 1.60 | 0.71 to 3.60 | 0.253 |
| PFMT | Surgery | 2 (2) | 95 | 0.19 | 0.04 to 0.77 | 0.020 |
| ES | VC | 3 (4) | 141 | 1.30 | 0.59 to 2.84 | 0.514 |
| ***Dual modality*** | | | | | | |
| PFMT | PFMT + ES | 3 (7) | 160 | 0.84 | 0.34 to 2.07 | 0.699 |
| PFMT + BF | PFMT + BF + ES | 2 (2) | 102 | 0.86 | 0.36 to 2.08 | 0.743 |
| PFMT | PFMT + VC | 1 (1) | 46 | 0.84 | 0.26 to 2.68 | 0.767 |
| PFMT + BF | PFMT + BF + BT | 1 (1) | 124 | 0.35 | 0.13 to 0.97 | 0.044 |
| PFMT | PFMT + SNRI | 1 (1) | 100 | 0.78 | 0.34 to 1.82 | 0.572 |
| PFMT + ES | ES | 1 (1) | 22 | 4.67 | 0.77 to 28.47 | 0.095 |
| PFMT + VC | VC | 1 (1) | 34 | 5.00 | 0.52 to 48.46 | 0.165 |
| PFMT + BF + BT | BT | 1 (1) | 127 | 4.90 | 1.84 to 13.10 | 0.002 |
| PFMT + SNRI80 | SNRI80 | 1 (1) | 101 | 2.04 | 0.90 to 4.64 | 0.087 |
| ***Variation within comparators*** | | | | | | |
| Fluid, increase then decrease | Fluid, decrease then increase | 0 (1) | | | | |
| PFMT | PFMT + BF | 7 (15) | 296 | 0.41 | 0.18 to 0.97 | 0.042 |
| PFMT | PFMT with additional sessions | 2 (4) | 74 | 0.05 | 0.01 to 0.28 | 0.001 |
| PFMT | PFMT with audiotape | 0 (2) | | | | |
| Strength and motor learning PFMT | Motor learning PFMT alone | 1 (1) | 123 | 1.69 | 0.67 to 4.25 | 0.269 |
| PFMT (in supine) + BF | PFMT (in supine and upright) + BF | 0 (1) | | | | |
| PFMT | Modified pilates | 0 (1) | | | | |
| PFMT (maximal contraction) + BF | PFMT (submaximal contraction) + BF | 0 (1) | | | | |
| PFMT + perineometer | PFMT + urethral conductance | 1 (1) | 20 | 1.17 | 0.26 to 5.29 | 0.842 |
| PFMT + BF (vaginal) | PFMT + BF (vaginal and abdominal) | 0 (1) | | | | |
| PFMT + BF | PFMT + ES | 0 (2) | | | | |
| PFMT + BF + ES (faradism) | PFMT + BF + ES (interferential) | 1 (1) | 30 | 1.38 | 0.29 to 6.60 | 0.691 |
| PFMT + BF + ES (maximal) | PFMT + BF + ES (low) | 1 (1) | 39 | 4.44 | 1.08 to 18.36 | 0.039 |
| VC passive | VC active | 1 (1) | 61 | 0.59 | 0.21 to 1.71 | 0.334 |
| SNRI 80 mg | SNRI 40 mg | 1 (1) | 259 | 1.32 | 0.80 to 2.17 | 0.277 |
| SNRI 80 mg | SNRI 20 mg | 1 (1) | 262 | 1.73 | 1.05 to 2.87 | 0.033 |
| SNRI 40 mg | SNRI 30 mg | 1 (1) | 59 | 1.88 | 0.64 to 5.51 | 0.253 |
| SNRI 40 mg | SNRI 20 mg | 2 (2) | 328 | 1.25 | 0.80 to 1.97 | 0.329 |
| SNRI 30 mg | SNRI 20 mg | 1 (1) | 60 | 0.56 | 0.19 to 1.65 | 0.294 |

comparison across studies difficult. There were few major safety concerns for most non-surgical interventions, although some instances were reported which were related to the treatment device for BF, ES or weighted VCs. However, one notable exception was SNRI drug therapy, for which the majority of participants experienced adverse events and up to one-third of the participants discontinued treatment due to adverse events. It is unclear whether the potential mood-enhancing effect of SNRIs might or might not affect its measured effect on SUI. It is also worth mentioning the apparent placebo effects of the SNRI drug as noted above under SNRI drug therapy.

A key issue for all non-surgical interventions is their long-term performance. Data beyond the supervised treatment phase were sparse. The extent to which women continued to adhere to treatment after active supervision finished may also be an important confounding factor, although such data were poorly reported and could not be incorporated into the analysis.

# Chapter 8

# Mixed-treatment comparisons (direct and indirect)

## Introduction

The review of effectiveness data presented in the preceding chapters has revealed that several treatments are used for SUI, with many variations and combinations of them also being used. Mixed treatment comparison (MTC) models analyse all of the treatments in one model, allowing indirect evidence to supplement direct, head-to-head evidence and thereby making comparison of treatments easier than via multiple head-to-head analyses.[113] The model produces estimates (from direct and indirect evidence) of the OR for each pair of treatments and then the cure and improvement rates of each individual treatment. Cure and improvement are defined in Chapter 5 (see Types of outcome measures). The rest of this chapter describes the data used, discusses the technical issues surrounding the application of a MTC model to these data and gives some definitions of important terms in Bayesian statistics that are used in the chapter, followed by results, discussion and summary of the work.

## The data

The cured and improved outcomes were analysed in separate models. The searches identified 61 trials which have data on either or both of these outcomes. Fourteen treatments were included in the MTC analysis. The standard abbreviations for the treatments are used throughout this chapter (see List of abbreviations). Six trials (*Table 48*) were removed from the data set either because they compared one treatment on the list of treatments selected with one that was not, for example Klarskov and colleagues (1986),[184] or because they compared two varieties of the same treatment and it was decided that separating treatments down to that level of detail was unhelpful, for example Burton (1993).[173] Some trials included some treatments that did not meet the inclusion criteria of this review, for example Tapp and colleagues (1989),[185] compares PFMT, PFMT plus ES, and surgery. In this case the surgery arm was not included in the analysis.

Removing these six trials resulted in 55 trials being used; of which eight reported cure results only, 17 reported improved results only and 30 reported both. Therefore, 38 trials were included in the cured analysis and 47 in the improved analysis.

The success rates in each trial were assessed by either the patient or by a clinician, with some trials reporting both. As for the direct, head-to-head meta-analyses, the patient-reported measure was used when it was available, with the clinician-reported measure being used as a proxy for it when the patient-reported measure was unavailable (see Model assumptions). The time between intervention and measurement of success varied across trials from 10 days to 6 months. Some trials also reported additional, long-term follow-up.[150,157,172,183,187] Each trial appears once in the model, using the data collected at the first time that the outcome was measured. This assumes that the measurement was taken at the point in time when the trialists believed that the treatments would have their maximal effect.

*Table 49* shows which treatments are compared in each trial and the number of patients in each arm. A MTC model requires all treatments of interest to be connected to each other, which was the case for both the cured and the improved data sets (i.e. if trial 1 compares treatments A and B, trial 2 compares treatments B and C, and trial 3 compares treatments C and D, then A is connected to C through a path of trial 1, then trial 2 and A is connected to D through a path of trial 1, trial 2 and trial 3; an MTC model can only be applied if all pairs of treatments in a model have a path of trials that connect them). A total of 6608 patients were involved in the 55 trials, with 3560 providing data for cure and 6140 for improvement. It should be noted that a large proportion of these patients (36.3%, 1292/3560 for cure and 61.4%, 3772/6140 for improvement) come from the 10 trials testing SNRIs against a placebo (placebo being considered equivalent to 'no treatment'). The cure model considered 13 treatments and the improvement model considered 14 treatments, as there were no cure data for the PFMT plus SNRI treatment.

***TABLE 48*** *Trials not used in the models, with reasons*

| Trial | Reason |
|---|---|
| Burton 1993[173] | Comparison of 'passive' VC and 'active' VC |
| Hay-Smith 2003[164] | Comparison of 'motor learning' with and without PFMT |
| Johnson 2001[167] | Comparison of PFMT + BF with maximal contraction and submaximal contraction |
| Klarskov 1986[184] | Comparison of PFMT and surgery; surgery not included in the data set |
| Mayne 1998[168] | Comparison of PFMT with perineometer and PFMT with urethral conductance |
| Zinner 1998[145] | Comparison of no treatment with 20- and 40-mg doses of SNRI |

An important difference between the MTC model and the head-to-head comparisons is that PFMT has been separated into two treatments: 'PFMT basic' and 'PFMT extra sessions', where 'PFMT extra sessions' is defined as having more than two supervised sessions per month (see Chapter 6, Characteristics of included studies).[43] The models for each outcome were analysed twice, once with PFMT split into the two categories and once with it together as one treatment. This latter model is to facilitate comparison with the direct, head-to-head analyses. However, three trials[116,159,161] are solely comparisons of the two intensities of PFMT, and as they provide no comparison with any other treatments they were removed from the data set when considering PFMT as one treatment. Hence, the former model, which considers the two intensities of PFMT separately, is taken as the base-case analysis and is presented in this chapter. The results from the models with PFMT considered as one treatment (regardless of the number of sessions) are shown in Appendix 23.

## The model

The model used was developed by the Multi-parameter Evidence Synthesis (MPES) Programme at the University of Bristol.[202] The statistical theory behind the code can be found in Lu and Ades (2004),[203] Caldwell and colleagues (2005),[113] Lu and Ades (2006),[204] and Ades and colleagues (2006).[205] Its main parameters are the log ORs of each treatment compared to a reference treatment, for which we used 'no treatment'. A random effects model was adopted, and, as some of the trials involved had three or four arms that were relevant to the study, the multiarm version of the MTC model was used. This incorporates adjustments for the correlation between arms of the same trial. The model parameters are estimated within Bayesian methodology by the use of WINBUGS software.[114] The model code, currently available from the MPES website,[202] is given in Appendix 22, alongside the data used from the individual trials.

### Model assumptions

The data that were available required the following two key additional assumptions to be made before using the model (as previously suggested – see The data):

1. that the log OR of the success of any treatment compared to the no-treatment reference is the same when success is assessed using the clinician methods as when it is assessed by the patient
2. that the log OR of the success of any treatment compared to the no-treatment reference is independent of the time period at which the outcome was assessed.

### 'No-treatment' cure rate and improvement rate

Although the main parameters of the model are the log ORs of pairs of treatments, other statistics can be calculated from the parameters. The cure and improvement rates for each treatment can be calculated from the ORs if the success rate for one treatment is known. The distribution of the success rate of the reference treatment was estimated by applying a normal distribution to the log odds of the probability of success, with its mean and variance being estimated from a random effects model of the no-treatment arms of the studies involved (see Appendix 22).

### Technical information about the running of the model

Vague prior distributions are used on the necessary parameters: the log ORs of treatment to no treatment, the individual trial baselines and the random effects standard deviation – see Appendix 22 for further details. The model was run on four different data sets; the cure and improvement data sets, with and without the PFMT treatment being split into basic and extra sessions. For the cure data set, a burn-in period of 20,000 iterations

was used to ensure convergence, whereas for the improvement data set a burn-in period of 10,000 iterations was sufficient for convergence. The results were sampled for a further 100,000 iterations in both cases.

## Bayesian terminology

For those who are unfamiliar with Bayesian methodology, a few terms used in the results section need to be explained. A good introduction to Bayesian methods can be found in O'Hagan and Luce's primer for health economics.[206]

- *Distribution* The Bayesian method uses probability distributions to describe the uncertainty about a parameter, for example the OR between two treatments. The *posterior distribution* is the probability distribution gained from applying the data to the model. The posterior distribution is described through its summary statistics, such as the mean, median and percentiles. The phrase 'the median odds ratio between …' should be interpreted as 'the median of the posterior distribution of the odds ratio between …'.
- *Ninety-five per cent central credible interval* A 95% credible interval is one where the probability that the true value for the parameter is within that interval is 95%. The interval is central if, in addition, the probability of being below the credible interval is 2.5% and being above it is 2.5%. Bayesian analyses report credible intervals for similar reasons to the reporting of CIs in frequentist analysis (e.g. the direct, pairwise, meta-analyses in this report are performed using frequentist statistical inference), i.e. to give an indication of the uncertainty surrounding the estimate. The abbreviation CrI is used for (central) credible interval.

## Results

In this section we report the ORs between treatments. The posterior distributions of the ORs are generally skewed. Therefore, we report the median OR as the point estimate. As the log ORs are roughly symmetrical, *Figures 31* and *32* are plotted on the log odds scale, although labelled with the ORs.

*Table 50* shows the posterior distribution of the ORs for each treatment compared with no treatment for both the cure and the improvement models. These are shown graphically in *Figures 31* and *32*. Tables showing the distributions of the ORs for each pair of treatments are given in Appendix 23. For cure, all treatments when compared to no treatment have a median OR greater than one, indicating that on average they have higher cure rates than no treatment. PFMT extra sessions, PFMT plus BF, VCs, BT, PFMT plus ES and PFMT plus BT and BF all have their 2.5th percentile greater than one, indicating a benefit from the treatment. For improvement, the median ORs for all treatments compared with no treatment were greater than one, with all 2.5th percentiles being greater than one, except for PFMT plus VCs and BF, and PFMT plus SNRI. For both outcomes the treatment with the highest median OR is PFMT plus BT and BF. This treatment, however, appears in only one trial[183] and has 61 participants in the PFMT-plus-BT-and-BF arm. Its success rate is high for both cure (19/61, 31.1%) and improvement (55/61, 90.2%). Given that the data come from only one trial, further research is needed.

### Splitting of PFMT into basic and extra sessions

The results show that the number of sessions of PFMT does have an effect. For cure, the combined PFMT has an OR of 4.56 (95% CrI 1.95 to12.4) against no treatment, but on splitting by number of sessions, PFMT basic (two or fewer sessions per month) has an OR of 1.28 (95% CrI 0.554 to 2.92), whereas PFMT with extra sessions (more than two sessions per month) has an OR of 10.7 (95% CrI 5.03 to 26.2). The OR for PFMT with extra sessions compared with PFMT basic is 8.36 (95% CrI 3.74 to 21.7). For improvement a similar relationship appears, with combined PFMT having an OR compared with no treatment of 8.97 (95% CrI 4.4 to 20.8), whereas the model with PFMT separated into basic or with extra sessions has an OR for PFMT basic of 4.47 (95% CrI 2.03 to 10.9) and for PFMT extra sessions of 25.7 (95% CrI 10.3 to 73.1). The OR between PFMT with extra sessions and PFMT basic is 5.75 (95% CrI 2.11 to 16.2). The results from the combined PFMT models are given in Appendix 23.

### Treatment success rates

The cure and improvement rates for each individual treatment are shown in *Table 51*, and, graphically, in *Figures 33* and *34*. These are calculated by combining the treatment to no-treatment ORs with the success rate for no

***TABLE 49*** *List of trials showing which treatments each compares and the number of patients in each arm of the trial*

| Trial ID | Outcome | NT | PFMT basic | PFMT extra | PFMT + BF | ES | VC | SNRI |
|---|---|---|---|---|---|---|---|---|
| Aksac 2003[120] | C/I | 10 | | 20 | 20 | | | |
| Arvonen 2001[178] | C/I | | 19 | | | | 18 | |
| Berghmans 1996[147] | C/I | | | 20 | 20 | | | |
| Bernardes 2000[174] | C | | | 7 | | 7 | | |
| Blowman 1991[189] | C | | 6 | | | | | |
| Bø 1990[159] | C/I | | 29 | 23 | | | | |
| Bø 1999[115] | C/I | 30 | | 25 | | 25 | 27 | |
| Bourcier 1994[196] | C | | | | | | | |
| Brubaker 1997[130] | C | 44 | | | | 46 | | |
| | I | 60 | | | | 61 | | |
| Burns 1993[122] | C/I | 40 | | 43 | 40 | | | |
| Cammu 1998[181] | C/I | | | | 30 | | 16 | |
| Cardozo 2004[137] | I | 52 | | | | | | 51 |
| Castro-Diaz 2007[138] | I | 112 | | | | | | 344 |
| Dmochowski 2003[139] | C | 322 | | | | | | 286 |
| | I | 332 | | | | | | 334 |
| Fantl 1991[135] | C/I | 63 | | | | | | |
| Ghoniem 2005[57] | I | 45 | 49 | | | | | 50 |
| Glavind 1996[150] | C | | 15 | | 19 | | | |
| Goode 2003[123] | C | 67 | 66 | | | | | |
| | I | 40 | 47 | | | | | |
| Hahn 1991[175] | C/I | | 10 | | | 10 | | |
| Haken 1991[179] | I | | 30 | | | | 23 | |
| Henalla 1989[124] | I | 25 | | 26 | | 25 | | |
| Henalla 1990[125] | I | 7 | 8 | | | | | |
| Hofbaur 1990[126] | C/I | 10 | | 11 | | 11 | | |
| Kim 2007[118] | C | 32 | | 33 | | | | |
| Kinchen 2005[140] | I | 218 | | | | | | 208 |
| Klingler 1995[151] | C/I | | | 21 | 20 | | | |
| Knight 1998[172] | I | | | | 18 | | | |
| Konstantinidou 2007[116] | C/I | | 10 | 12 | | | | |
| Lagro-Janssen 1991[127] | C/I | 33 | 33 | | | | | |
| Laycock 1988[176] | I | | | 11 | | 18 | | |
| Laycock Trial 1 1993[132] | C/I | | | | | 23 | | |
| Laycock Trial 2 1993[132] | C/I | 11 | | | | 15 | | |
| Luber 1997[133] | C/I | 24 | | | | 20 | | |
| Mah 2006[141] | I | 57 | | | | | | 56 |
| Manning 2005[142] | I | 311 | | | | | | 306 |
| Millard 2004[143] | C | 229 | | | | | | 200 |
| | I | 229 | | | | | | 220 |
| Mørkved 2002[153] | C | | | 34 | 36 | | | |

| BT | PFMT + ES | PFMT + ES + BF | PFMT + VC | PFMT + VC + BF | PFMT + BF + BT | PFMT + SNRI | Source of outcome | Number of patients in trial |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Clinician | 50 |
| | | | | | | | Patient | 37 |
| | | | | | | | Clinician | 40 |
| | | | | | | | Patient | 14 |
| | 7 | | | | | | Clinician | 13 |
| | | | | | | | Patient | 52 |
| | | | | | | | Patient | 107 |
| | | 46 | 38 | | | | Patient | 84 |
| | | | | | | | Clinician | 90 |
| | | | | | | | Clinician | 121 |
| | | | | | | | Clinician | 123 |
| | | | | | | | Clinician | 46 |
| | | | | | | | Patient | 103 |
| | | | | | | | Patient | 456 |
| | | | | | | | Clinician | 608 |
| | | | | | | | Patient | 666 |
| 60 | | | | | | | Clinician | 123 |
| | | | | | | 51 | Patient | 195 |
| | | | | | | | Clinician | 34 |
| | 67 | | | | | | Clinician | 200 |
| | 47 | | | | | | Patient | 134 |
| | | | | | | | Patient | 20 |
| | | | | | | | Clinician | 53 |
| | | | | | | | Clinician | 76 |
| | | | | | | | Clinician | 15 |
| | 11 | | | | | | Patient | 43 |
| | | | | | | | Patient | 65 |
| | | | | | | | Patient | 426 |
| | | | | | | | Clinician (C) / patient (I) | 41 |
| | | 39 | | | | | Patient | 57 |
| | | | | | | | Clinician | 22 |
| | | | | | | | Clinician | 66 |
| | | | | | | | Patient | 29 |
| | | | | 16 | | | Patient | 39 |
| | | | | | | | Patient | 26 |
| | | | | | | | Patient | 44 |
| | | | | | | | Patient | 113 |
| | | | | | | | Patient | 617 |
| | | | | | | | Clinician | 429 |
| | | | | | | | Patient | 449 |
| | | | | | | | Patient | 70 |

*continued*

***TABLE 49*** *List of trials showing which treatments each compares and the number of patients in each arm of the trial (continued)*

| Trial ID | Outcome | NT | PFMT basic | PFMT extra | PFMT + BF | ES | VC | SNRI |
|---|---|---|---|---|---|---|---|---|
| Norton 2002[144] | C | 132 | | | | | | 123 |
| | I | 132 | | | | | | 130 |
| Oláh 1990[187] | C/I | | | | | 30 | 24 | |
| Pages 2001[154] | C/I | | | 27 | 13 | | | |
| Peattie 1988[180] | I | | | 16 | | | 17 | |
| Pieber 1995[192] | C/I | | 25 | | | | | |
| Ramsay 1990[128] | I | 22 | 22 | | | | | |
| Sand 1995[134] | C/I | 17 | | | | 35 | | |
| Seo 2004[195] | I | | | | | | 60 | |
| Shepherd 2003[155] | C/I | | 11 | | 11 | | | |
| Sherburn 2007[182] | C | | | 40 | | | | |
| Smith 1996[177] | C/I | | 9 | | | 9 | | |
| Tapp 1989[185] | C/I | | | 21 | | | | |
| van Kerrebroeck 2004[117] | I | 245 | | | | | | 240 |
| Williams 2006[129] | C/I | 75 | 77 | | | | 79 | |
| Wilson 1987[157] | I | | 15 | | 15 | | | |
| Wise 1993[188] | I | | | | | 16 | 19 | |
| Wyman 1998[183] | C | | | | 64 | | | |
| | I | | | | 63 | | | |
| Zanetti 2007[161] | C | | 21 | 23 | | | | |
| **Totals** | C | 1139 | 331 | 360 | 273 | 231 | 164 | 609 |
| | I | 2200 | 394 | 276 | 250 | 298 | 283 | 1939 |
| | All | 2259 | 455 | 413 | 306 | 305 | 283 | 1939 |

C, cured; I, improvement.
Note: The second column indicates whether a trial records the cure outcome (C), the improvement outcome (I) or both. In cases where both are reported, and the number of patients recording each outcome varies, the trial is recorded on two lines. The source of outcome (patient or clinician) is also recorded (see Chapter 5, Types of outcome measures). The total rows show the number of patients for each treatment that provided cure outcome data (C), improvement outcome data (I) and the number in total.

treatment (obtained from modelling the no-treatment arms). The width of the 95% CrIs suggests that there is still considerable uncertainty surrounding the success rates.

Nevertheless, PFMT extra sessions appears to have a higher cure rate than PFMT basic and a similar rate to PFMT plus BF. In fact, PFMT extra sessions, PFMT plus BF, and PFMT plus BT and BF appear to be the best treatments in terms of cure, bearing in mind that PFMT plus BT and BF is assessed in only one trial. These three treatments also have the highest median improvement rate.

## Sensitivity analysis

In the cure model, two treatments, 'PFMT plus VCs and BF' and 'PFMT plus BT and BF', appear in only one trial. PFMT plus SNRI, which appears only in the improvement model, was also only reported in one trial. As a sensitivity analysis to the inclusion of these three treatments, the cure and improvement models were run without them. This resulted in one trial[132] being removed from the data set. The log ORs between the treatments and no treatment and the individual treatment success rates were satisfactorily similar to those of the original models.

| BT | PFMT + ES | PFMT + ES + BF | PFMT + VC | PFMT + VC + BF | PFMT + BF + BT | PFMT + SNRI | Source of outcome | Number of patients in trial |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Clinician | 255 |
| | | | | | | | Patient | 262 |
| | | | | | | | Patient | 54 |
| | | | | | | | Patient | 40 |
| | | | | | | | Patient | 33 |
| | | | 21 | | | | Patient | 46 |
| | | | | | | | Patient | 44 |
| | | | | | | | Clinician | 52 |
| | | 60 | | | | | Patient | 120 |
| | | | | | | | Patient | 22 |
| 35 | | | | | | | Clinician | 75 |
| | | | | | | | Clinician | 18 |
| | 23 | | | | | | Clinician | 44 |
| | | | | | | | Patient | 485 |
| | | | | | | | Patient | 231 |
| | | 30 | | | | | Patient | 60 |
| | | | 15 | | | | Clinician | 50 |
| 68 | | | | | 61 | | Clinician | 193 |
| 66 | | | | | 61 | | Patient | 190 |
| | | | | | | | Clinician | 44 |
| 163 | 108 | 46 | 59 | 16 | 61 | 0 | | 3560 |
| 126 | 81 | 129 | 36 | 16 | 61 | 51 | | 6140 |
| 163 | 108 | 175 | 74 | 16 | 61 | 51 | | 6608 |

## Probability that each treatment is the most effective

Another measure that can be calculated from the results is the probability that each treatment is the best. In the cure model, 'PFMT plus BT and BF' has the highest probability (0.54) of being the best treatment, with 'PFMT plus ES and BF' (0.20) and 'PFMT plus VCs and BF' (0.17) the next highest. 'PFMT plus BF' (0.047) and 'PFMT with extra sessions' (0.025) come fourth and fifth in the ranking. For improvement, 'PFMT plus BT and BF' stands out as the treatment that is most likely to be the best (0.64), with 'PFMT plus ES' (0.092), 'PFMT plus ES and BF' (0.083), 'PFMT with extra sessions' (0.060), 'PFMT plus VCs' (0.052) and 'PFMT plus BF' (0.043) coming next.

These results need to be interpreted with caution, as 'PFMT plus BT and BF' appears in only one trial. In the models used in the sensitivity analysis (see Sensitivity analysis), excluding 'PFMT plus VCs and BF', 'PFMT plus BT and BF' and 'PFMT plus SNRI' (the interventions with only one trial) produces the following probabilities that each treatment is the most effective:

***TABLE 50*** *Posterior distribution of the odds ratio for each treatment compared to no treatment*

| Treatment | Sample | Mean | SD | Median | 2.5th percentile | 97.5th percentile |
|---|---|---|---|---|---|---|
| ***Cure*** | | | | | | |
| PFMT basic | 331 | 1.4 | 0.627 | 1.28 | 0.554 | 2.92 |
| PFMT extra sessions | 360 | 12 | 5.7 | 10.7 | 5.03 | 26.2 |
| PFMT + BF | 273 | 14 | 7.38 | 12.3 | 5.35 | 32.7 |
| ES | 231 | 1.64 | 0.88 | 1.45 | 0.55 | 3.86 |
| VC | 164 | 4.18 | 2.62 | 3.55 | 1.23 | 10.9 |
| SNRI | 609 | 1.57 | 0.771 | 1.43 | 0.582 | 3.46 |
| BT | 163 | 9.34 | 7.17 | 7.53 | 2.34 | 27 |
| PFMT + ES | 108 | 3.78 | 2.84 | 3.05 | 1.09 | 10.7 |
| PFMT + ES + BF | 46 | 30.7 | 182 | 9.21 | 0.569 | 172 |
| PFMT + VC | 59 | 6.89 | 18 | 3.13 | 0.324 | 36 |
| PFMT + VC + BF | 16 | 86.4 | 2750 | 5.82 | 0.245 | 263 |
| PFMT + BT + BF | 61 | 37.8 | 55.1 | 25.2 | 4.94 | 146 |
| ***Improvement*** | | | | | | |
| PFMT basic | 394 | 4.97 | 2.37 | 4.47 | 2.03 | 10.9 |
| PFMT extra sessions | 276 | 29.8 | 17 | 25.7 | 10.3 | 73.1 |
| PFMT + BF | 250 | 31 | 21.8 | 25.4 | 8.68 | 86.9 |
| ES | 298 | 6.14 | 3 | 5.49 | 2.39 | 13.7 |
| VC | 283 | 7.86 | 4.65 | 6.77 | 2.6 | 19.4 |
| SNRI | 1939 | 2.29 | 0.87 | 2.14 | 1.06 | 4.4 |
| BT | 126 | 18.3 | 23.4 | 12 | 2.16 | 73.3 |
| PFMT + ES | 81 | 29.6 | 31 | 20.7 | 4.51 | 108 |
| PFMT + ES + BF | 129 | 31.2 | 35.3 | 21.6 | 4.5 | 116 |
| PFMT + VC | 36 | 21.7 | 35.6 | 12.2 | 1.83 | 99.2 |
| PFMT + VC + BF | 16 | 7.44 | 28.4 | 2.66 | 0.181 | 42 |
| PFMT + BT + BF | 61 | 160 | 401 | 69.8 | 6.59 | 852 |
| PFMT + SNRI | 51 | 7.37 | 11.8 | 4.42 | 0.646 | 31.8 |

Note: Each treatment is being compared to no treatment, so an OR of greater than one implies that the odds of success for the active treatment are better than the odds for no treatment. The no-treatment arms had a total of 1139 patients in the cure model and 2200 patients in the improvement model.

- *Cure* PFMT + ES + BF (0.384), PFMT + BF (0.354), PFMT extra (0.158)
- *Improvement* PFMT + ES (0.215), PFMT + ES + BF(0.212), PFMT extra (0.198), PFMT (0.186)

The results suggest that adding an adjunct (such as ES) or making PFMT more intensive in another way is likely to be the most effective. However, of the different options considered, several resulted in similar probabilities of being the most effective.

## Discussion

Mixed-treatment comparison models are an effective method of handling evidence from many trials on several treatments in one analysis. Like all models, they require assumptions to be made that may or may not be reasonable. In this case, the assumptions used in this analysis indicate that the results should be interpreted with a degree of caution.

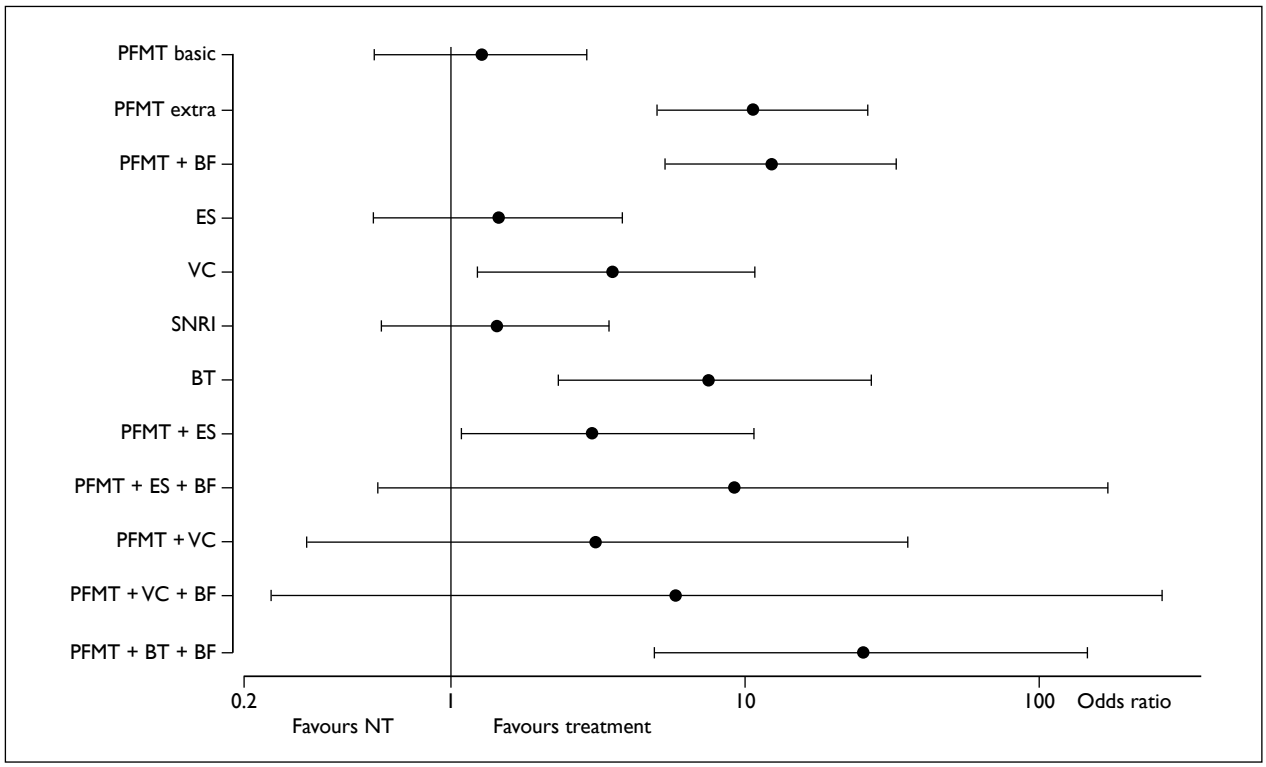


***FIGURE 31*** *Cure: odds ratio of each treatment versus no treatment. Note: posterior distribution median (circle) with 95% central credible intervals. The horizontal axis is plotted on the log scale.*

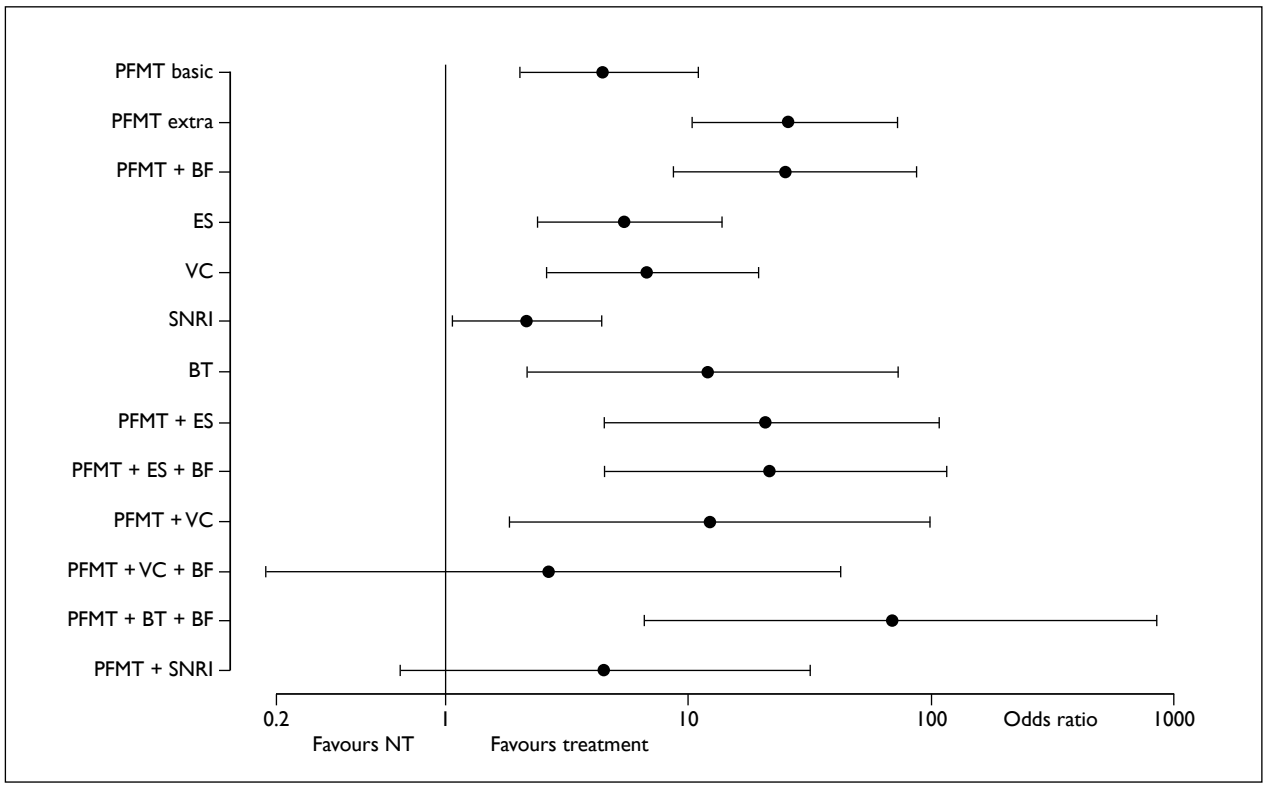


***FIGURE 32*** *Improvement: odds ratio of each treatment versus no treatment. Note: posterior distribution median (circle) with 95% central credible intervals. The horizontal axis is plotted on the log scale.*

The output from the MTC model shows wide credible intervals for some treatments. For example, the intervals for the cure rates for 'PFMT plus ES and BF' and 'PFMT plus VCs and BF' are so wide (on a bounded scale) that we know very little about the effectiveness of these treatments. This is due to there being very few data about the cure rates for these treatments; the data for each treatment come from only one trial, with 'PFMT plus ES and BF' having 46 participants in its arm and 'PFMT plus VCs and BF' having 16.

There are some results that are quite clear and useful. There is clear evidence that both 'PFMT with extra sessions' and 'PFMT with BF' are better at cure than the following: no treatment; PFMT basic; ES; VCs; SNRI; and PFMT plus ES. Both 'PFMT with extra sessions' and 'PFMT with BF' are also better at improvement than: no treatment; PFMT basic; ES; VCs; and SNRI. The evidence also suggests that 'PFMT plus BT and BF' is better than each of the above listed treatments for cure and improvement, respectively, except for VCs, for which there is no clear evidence of a difference in improvement rates. However, conclusions about 'PFMT plus BT and BF' must be considered with caution, as this appears as a treatment in only one trial.

The results of the model indicate where further research might be beneficial, for example 'PFMT plus BT and BF' had reasonable success in the one trial that is in the data set, and its comparisons with other treatments look promising.

Comparison of the results from the model with PFMT, separated into basic and extra sessions with the combined PFMT model, shows that the median ORs between the other treatments can be different. The nature of the MTC model is such that splitting a treatment into two has an effect on the comparisons between other treatments. However, the split PFMT models do include additional trials (three for cure and two for improvement) that compare the two PFMT intensities alone, which were not used in the combined PFMT model. This appears to account for most of the discrepancies between the results of the split PFMT model compared with the combined PFMT model.

## Summary

PFMT appears to be more effective when delivered with extra sessions (more than two sessions per month). Using this format of PFMT or adding BF to PFMT appears to be more effective than the other standalone treatments that have been

***TABLE 51*** *Cure and improvement success rates for each treatment, as percentages*

| | Cure | | | | Improvement | | | |
|---|---|---|---|---|---|---|---|---|
| | *N* | Median | 95% central CrI | | *N* | Median | 95% central CrI | |
| NT | 1139 | 5.8 | 3.3 | 9.9 | 2200 | 26.3 | 15.7 | 40.5 |
| PFMT basic | 331 | 7.3 | 2.8 | 17.8 | 394 | 61.5 | 36.4 | 82.7 |
| PFMT extra sessions | 360 | 39.9 | 20.2 | 65.8 | 276 | 90.2 | 74.9 | 96.9 |
| PFMT + BF | 273 | 43.3 | 21.5 | 70.2 | 250 | 90.1 | 72.0 | 97.3 |
| ES | 231 | 8.2 | 2.8 | 21.9 | 298 | 66.3 | 40.6 | 85.8 |
| VC | 164 | 18.0 | 6.1 | 43.5 | 283 | 70.8 | 43.1 | 89.3 |
| SNRI | 609 | 8.1 | 2.9 | 20.1 | 1939 | 43.3 | 22.7 | 66.7 |
| BT | 163 | 31.8 | 11.2 | 65.3 | 126 | 81.1 | 40.5 | 96.7 |
| PFMT + ES | 108 | 15.9 | 5.4 | 42.8 | 81 | 88.1 | 58.3 | 97.8 |
| PFMT + ES + BF | 46 | 36.1 | 3.2 | 91.8 | 129 | 88.5 | 58.5 | 97.9 |
| PFMT + VC | 59 | 16.1 | 1.8 | 70.3 | 36 | 81.4 | 36.7 | 97.5 |
| PFMT + VC + BF | 16 | 26.4 | 1.4 | 94.4 | 16 | 48.7 | 5.7 | 94.1 |
| PFMT + BT | 61 | 60.8 | 21.8 | 90.7 | 61 | 96.1 | 68.4 | 99.7 |
| PFMT + SNRI | 331 | | | | 51 | 61.2 | 17.1 | 92.5 |

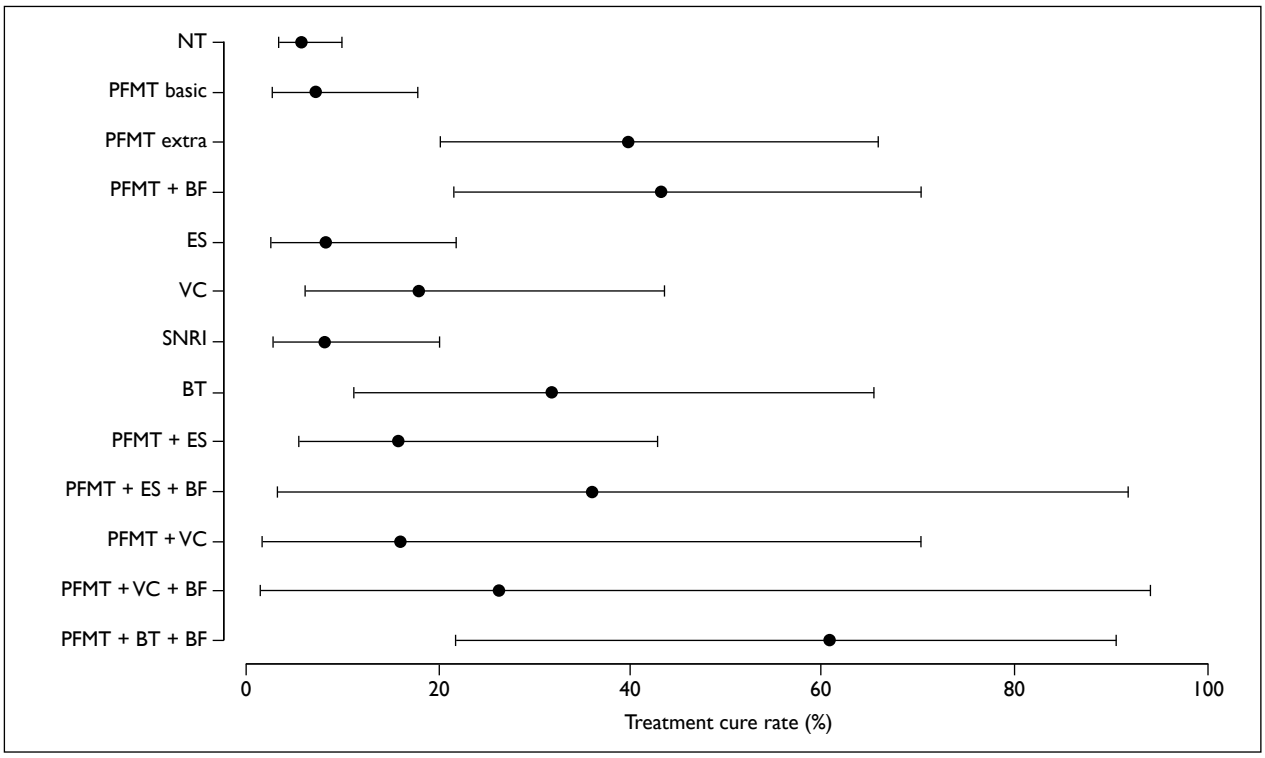


***FIGURE 33*** *Cure rate for each treatment. Note: posterior distribution median (circle) with 95% central credible intervals.*

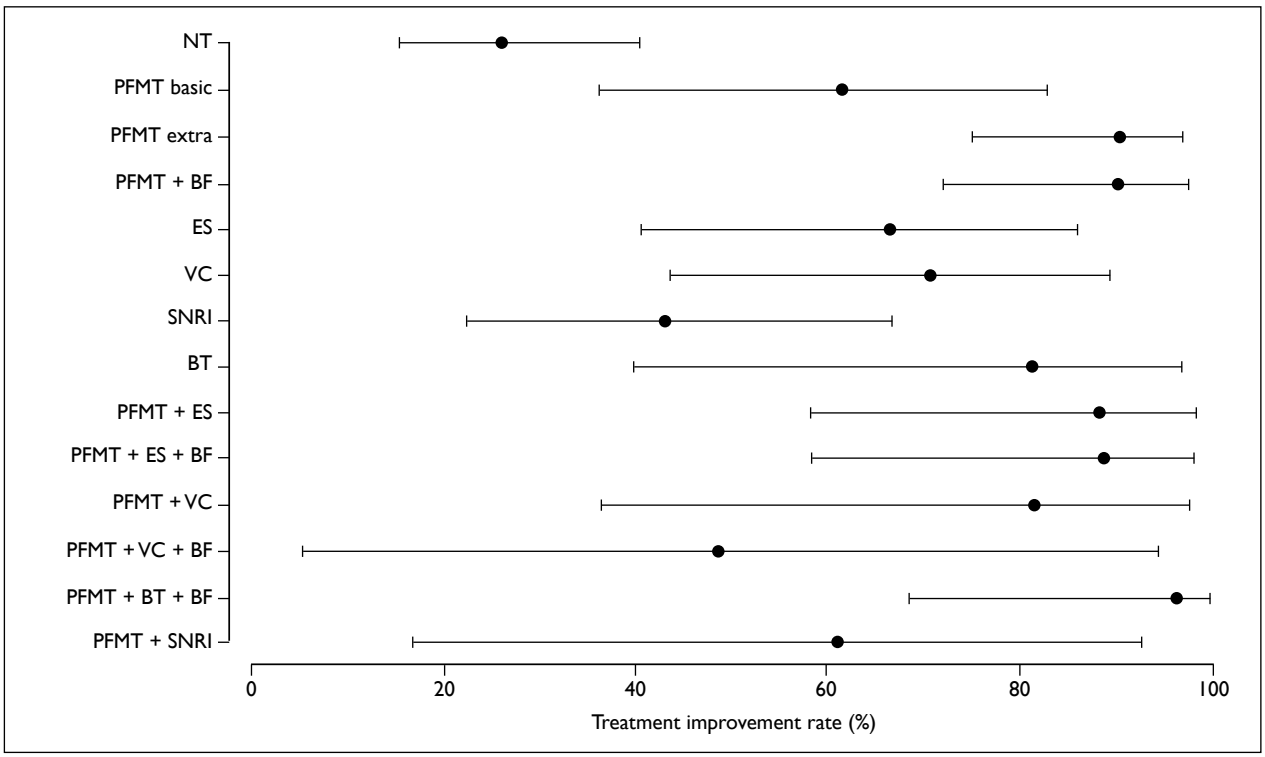


***FIGURE 34*** *Improvement rate for each treatment. Note: posterior distribution median (circle) with 95% central credible intervals.*

analysed: no treatment, PFMT basic, ES, VCs, and SNRIs. Adding ES as an adjunct may also be effective.

The strengths of this approach are that all of the treatments of interest are compared in one analysis, facilitating indirect evidence to support direct evidence.

The limitations of the models lie in the assumptions taken about the equivalence of patient- and clinician-assessed success, and that the different time intervals over which the outcome is assessed within the separate trials is unimportant. The credible intervals around the estimates are often wide, indicating that there is still considerable uncertainty about the values of some parameters.

# Chapter 9
# Assessment of cost-effectiveness

A formal systematic review of existing economic evaluations was not attempted, as initial scoping searches failed to identify any existing prior economic evaluations that considered all comparators from the perspective of the UK NHS. Therefore, this chapter focuses on presenting the methods and results of a de novo economic model.

The subsections 'Model framework' and 'Summary of key assumptions made in the economic model' (see Methods, below) describe the basics of the modelling approach and the key assumptions underpinning the estimates of cost-effectiveness results. The remainder of the Methods section describes, in detail, how parameter estimates for the economic model were derived and how these data were used to estimate cost-effectiveness. The results from the economic model are presented in three sections. In the first section, the results of the economic model are presented in terms of number of people cured, cured or improved (referred to in the text as '*improvement*') or incontinent in the model at different time horizons (see Results of the model presented in terms of costs and consequences). In the second section the results are based upon patients being cured of incontinence (see Cost–utility analysis based upon cure rates). In the third section (see Results based upon improvement rates), results are presented when successful treatment is defined as being either cured or improved. The final section of this chapter provides a short summary of the results.

## Methods

As explained in Chapter 3, the economic model described the pathways of care for alternative management strategies of SUI. The perspective adopted for the analysis is that of the NHS (the main health service provider within the UK).

### Model framework

A Markov model portraying the temporal and logical sequence of the clinical decision problem was used to provide estimates of costs, effectiveness (measured in QALYs) and cost-effectiveness. The health states within the model are considered to reflect possible outcomes of therapy, for example successful treatment (i.e. cure or improvement), failure (i.e. incontinence) and recurrence of incontinence. Graduation in the severity of incontinence was otherwise not considered in the model due to paucity of the available data on effectiveness.

In the model, women receive an initial treatment and then move into one of three states: success, failure or death. If a woman considers herself cured (or sufficiently improved so that she no longer feels the need for further treatment) then the treatment is successful. If the treatment does not result in cure (or sufficient improvement) then the woman enters the failure state. There is always a chance that over any period of time that a woman would die. If this should happen, they then move into an absorbing state (a state from which they cannot move): death. Death takes into account that patients are exposed to a very small risk of death when they are undergo surgery as well as a chance of dying from other causes at any point in time, assumed to be equivalent to all-cause mortality.

In a Markov model, people stay in a state for a minimum period of time (called the cycle length). In this model the cycle length was 3 months. This cycle length was chosen as it represents the recommended/widely used duration of PFMT before reassessment. Women who enter into the success state, stay in that state for 3 months, after which time, if they are still alive, they either continue to stay in this state or suffer a recurrence and go to the next available treatment. If a woman becomes incontinent after previously being cured, or after a treatment has failed, she proceeds to the next treatment in the strategy.

Women can continue moving through states in the model for a maximum of 40 years (equivalent to 160 cycles). This time horizon was chosen as it takes into account the average life expectancy of women who enter the model at the age of 45, which, as *Figure 1* shows, is that age of peak incidence of SUI. Costs and benefits that occur in the future are discounted following standard practice. The discount rate used is the recommended rate of 3.5% for both costs and benefits.[105]

It is assumed that all women are initially given advice, if appropriate, about modifying their lifestyles. The interventions included in the management strategies are thus: lifestyle changes (LS); basic PFMT (PFMT basic); PFMT with extra sessions (PFMT extra sessions); PFMT plus BF; PFMT plus ES; ES; VCs; drug treatment (SNRI), surgery [tension-free vaginal tape (TVT) or other similar self-fixing sling, e.g. transvaginal obturator tape], and the second surgery. Once all of the treatments are exhausted, it is assumed that women have to manage their symptoms using containment products. *Table 52* summarises the potential strategies that are considered in the model.

The difference between basic PFMT and PFMT with extra sessions was based upon the number of supervisory sessions that a woman had per month. For basic PFMT it was assumed that the woman would have six sessions in 3 months, whereas PFMT with extra sessions was defined as having 12 sessions in 3 months.[43]

Pelvic floor muscle training with BF has not been explicitly included in this model, as its effectiveness is similar to the effectiveness of PFMT with extra sessions and it is plausible that the costs of the two types of therapy are similar. The impact of difference in costs for PFMT with BF is explored within a sensitivity analysis.

*Figure 35* depicts an example of one of the management strategies used in the model (a more detailed description of the model is provided in Appendix 24). A woman that is diagnosed with SUI is offered PFMT. If this treatment is successful then the patient stays in a success state. When a treatment fails the woman is offered the next available treatment in that particular strategy. In this example, if PFMT fails in the next cycle the woman is offered PFMT plus an adjunct. If this fails, the woman is offered the next available treatment, drug therapy, and so on. If necessary the woman will receive each treatment until the treatment options are exhausted and their incontinence has to be managed with containment products.

## Summary of key assumptions made in the economic model

Outlined below are the key assumptions that are made within the economic model. Details about how these assumptions were arrived at and their justifications are provided in the remainder of this section.

### *Assumptions related to the structure of the model*

1. The age of the women considered in the model is 45 years. In sensitivity analysis, different starting ages were considered.

***TABLE 52*** *Management strategies*

| | Treatment sequence | | | | | |
|---|---|---|---|---|---|---|
| | **First treatment** | **Second treatment** | **Third treatment** | **Fourth treatment** | **Fifth treatment** | **Sixth treatment** |
| 1 | Lifestyle + PFMT basic | TVT/TVT-O | Second surgery | Containment | | |
| 2 | Lifestyle + PFMT basic | PFMT extra sessions | TVT/TVT-O | Second surgery | Containment | |
| 3 | Lifestyle + PFMT basic | PFMT extra sessions | SNRI | TVT/TVT-O | Second surgery | Containment |
| 4 | Lifestyle + PFMT extra sessions | TVT/TVT-O | Second surgery | Containment | | |
| 5 | Lifestyle + PFMT extra sessions | SNRI | TVT/TVT-O | Second surgery | Containment | |
| 6 | Lifestyle | TVT/TVT-O | Second surgery | Containment | | |
| 7[a] | Lifestyle + PFMT basic | VC | TVT/TVT-O | Second surgery | Containment | |
| 8[a] | Lifestyle + PFMT basic | ES | TVT/TVT-O | Second surgery | Containment | |

TVT, tension-free vaginal tape; TVT-O, transvaginal obturator tape.
a Two strategies reported in sensitivity analyses only.

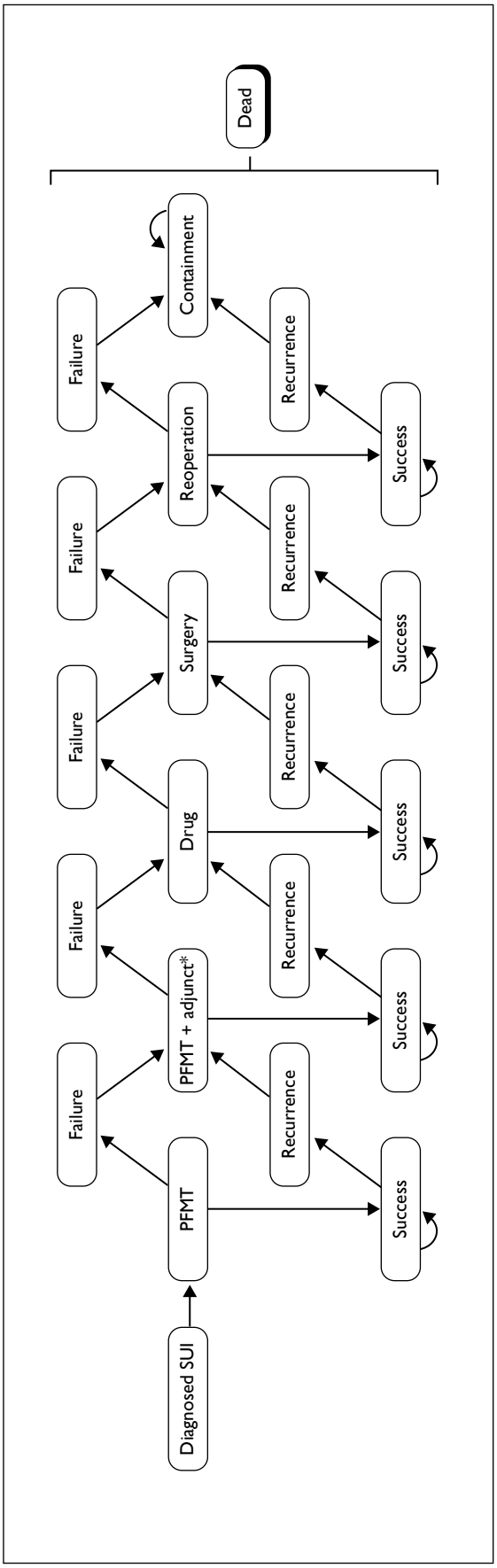


***FIGURE 35*** *Markov model for one of the strategies. *Adjuncts include, for example, biofeedback and electrical stimulation.*

2. Cumulative costs and effectiveness were estimated for a 40-year time horizon. This would cover the average life expectancy of women aged 45 years. In sensitivity analyses the effect of shorter time horizons on costs, effects and cost-effectiveness was considered.
3. Costs and effects that occur in the future are given less weight in the analysis than costs and effects that occur in the present, i.e. they are discounted. This is recommended practice for any economic evaluation. Different discount rates were considered in a sensitivity analysis.
4. The cycle length of the model is 3 months. This cycle length determines the minimum period of time over which a woman's continence status might change or over which treatments might change. This period was chosen as it represents the recommended/ widely used duration of PFMT before reassessment.
5. Within the model, women can either be cured (or improved in the version of the model based on improvement rates) or be incontinent. Severity of disease is not otherwise considered in the model because of lack of data.

#### *Assumptions related to the treatment strategies compared*

1. The treatment strategies compared consist of a finite number of treatments. In reality women whose symptoms are not controlled to their satisfaction could continue seeking treatment until they have what they consider adequate control of their symptoms.
2. All women are initially given advice, if appropriate, about modifying their lifestyles.
3. If a woman becomes incontinent after previously been cured, or after a treatment failed, she would proceed to the next treatment in the strategy. Sensitivity analysis was performed to explore the relaxation of this assumption.
4. In the cure model analysis women were assumed not to use containment products until they had exhausted all treatments in a treatment strategy. Sensitivity analysis was performed to explore the relaxation of this assumption.
5. In the improvement model all women were assumed to use containment products. Those women who were improved used less containment products than those who were not improved. Sensitivity analysis was performed to explore the relaxation of this assumption.
6. The probability of drug therapy being successful after suffering an adverse event was assumed to be zero as we expected the woman to stop taking the drug when she suffered an adverse event.

#### *Assumptions relating to effectiveness*

1. The median values of cure and improvement rates were used in the economic model, as the data were highly skewed and the median was believed to provide a better representation of the actual difference.
2. Long-term cure rates of all interventions were based on extrapolation of available data.
3. When making an extrapolation from these data, it was assumed, for drug therapy, that at 12 months only 5.8% of those initially cured remain cured, which is equivalent to the spontaneous cure estimated for no treatment.
4. The estimates of cure and improvement rates for all treatments were assigned log-normal or normal distributions, based on the assumptions made for the mixed-treatment model in Chapter 8.

#### *Assumptions relating to costs*

1. The difference between basic PFMT and PFMT with extra sessions was based upon the number of sessions that a woman had per month.
2. The resources used in PFMT plus BF were based on the assumption that the staff providing the service was the same as those providing PFMT and that the number of sessions were the same as those for PFMT.
3. The costs of VCs were based on the assumption that the labour costs were one-third of those for PFMT (i.e. two visits with the physiotherapist).
4. The costs of exercise dairies and leaflets were considered to be negligible and it was also assumed that all patients would receive them. Therefore, their costs were not included.
5. All treatment costs were assigned log-normal distributions, as this distribution appeared to best fit the data that have skewed or symmetric ranges.

## Estimation of model probabilities

The main probabilities for the model are the cure rates, improvement rates and recurrence rates of different interventions and mortality rates.

#### *Relative differences in cure and improvement rates*

The estimates of cure and improvement rates for the interventions considered in the model are based on the results of the mixed-treatment model reported in Chapter 8. *Table 53* describes the median ORs for the comparison with either no

***TABLE 53*** *Odds ratios of intervention compared with no treatment or basic pelvic floor muscle training*

| | Cure rates | | Improvement rates | |
|---|---|---|---|---|
| **Intervention vs comparison** | **Median** | **95% CrI** | **Median** | **95% CrI** |
| ***Used in base-case analysis*** | | | | |
| PFMT basic vs NT | 1.28 | 0.55 to 2.92 | 4.47 | 2.03 to 10.9 |
| PFMT extra sessions vs NT | 10.7 | 5.03 to 26.2 | 25.7 | 10.3 to 73.1 |
| SNRI vs NT | 1.43 | 0.58 to 3.46 | 2.14 | 1.06 to 4.4 |
| ***Used only in sensitivity analysis*** | | | | |
| ES vs NT | 1.45 | 0.55 to 3.86 | 5.49 | 2.39 to 13.7 |
| VC vs NT | 3.55 | 1.23 to 10.9 | 6.77 | 2.6 to 19.4 |
| ES vs PFMT basic | 1.13 | 0.39 to 3.32 | 1.23 | 0.45 to 3.25 |
| VC vs PFMTbasic | 2.77 | 0.98 to 8.51 | 1.52 | 0.58 to 3.97 |

CrI, credible interval.

treatment or PFMT. The median values were used in the economic model, as the data were highly skewed and the median was believed to provide a better representation of the actual difference.

### *Absolute cure and improvement rates*

As mentioned in Chapter 8, while the main parameters of the model are the log ORs of the treatments, the absolute success rate for each treatment can be calculated from the relative success rates, if the absolute success rate for one treatment is known. The absolute cure and improvement rates were calculated in the model by combining the information on relative cure and improvement rates described in *Table 53*, above, with the absolute cure and improvement rates for no treatment which was taken to be the reference treatment. The absolute cure rate at 3 months for no treatment was median 5.8% (95% CrI: 3.3% to 9.9%) and the improvement rate at 3 months was 26.3% (95% CrI: 15.7% to 40.5%) (Chapter 8).

### *Transition probabilities*

#### Recurrence rates of PFMT

Despite extensive searching, few data were identified on the long-term effectiveness (greater than 1 year) for any of the interventions. Therefore, estimates used in the model were based on extrapolations of the available data.

Only four reports[159,207–209] provided long-term follow-up of women who had received PFMT. One report[209] indicated that at 6 years no significant differences were found in urinary incontinence prevalence, severity or leakage episodes in the women who responded to the questionnaire between groups for PFMT with extra sessions and basic PFMT. However, this study was based on postnatal women, whom we regarded as not being representative of women with SUI. A further three reports published by other authors provided outcome data at 5 years[207] and 15 years[208] after receiving PFMT were identified. One report[208] looked at two different intensities of pelvic floor muscle exercises over a period of 15 years. Hence, data from these three reports have been used in the model, although the sample sizes were small. Details of the values taken from these papers are described in *Table 54*.

Extrapolation of the long-term cure rates used in the model was generated from Kaplan–Meier survival curves, using a linear exponential distribution that manipulated by adjusting the two parameters (defined below). Using this process it is possible to estimate a hazard function using the values reported in *Table 55*.

The formula used to extrapolate the survival function [$S(t)$] is:

$$S(t) = \exp(-(\lambda t + \gamma t^2/2))$$

$$\lambda = 0.001372, \gamma = 0.006308$$

where:

- $S(t)$ is the probability of cure at any given time $t$
- $t$ is time (measured in terms of the number of cycles, where each cycle is equivalent to 12 weeks)

***TABLE 54*** *Values used in the estimation of long-term recurrence rates of pelvic floor muscle training*[a]

| Values | Number of patients | |
|---|---|---|
| | **PFMT basic** | **PFMT extra sessions** |
| Randomised | 31 | 26 |
| At 6 months | 29 | 23 |
| At 5 years | NR | 20 |
| At 15 years | 26 | 21 |
| Surgical interventions at 5 years | 9 | 3 (3/23) |
| Surgical interventions at 15 years | 4 | 8 (8/21) |
| Pad test <2 g (cure) at 5 years | NR | 6 (6/20) |
| No visible leakage on stress pad test at 6 months | NR | 17 (17/20) |
| No visible leakage on stress pad test at 5 years | NR | 15 (15/20) |
| Dry on severity index at 15 years | 4 (4/25) | 6 (6/20) |

a PFMT follow-up rates (home vs intensive) – Bø and colleagues (1990);[159] (1996);[207] (2005).[208]

- λ is the scale parameter, which describes the probability that a woman will remain/become incontinent during the next time period, given that she was continent in the current period
- γ is the shape parameter, which, in simple terms, describes the rate of change in the probability that a woman will become incontinent over time.

Appendix 25 described how the transition probabilities (i.e. the chance or remaining cured or suffering a recurrence of symptoms) were calculated using the above formula. *Figure 36* shows the shape of the linear exponential curve that was fitted to the data reported in *Table 55*.

### Recurrence rates for other physical therapies

The recurrence rate for physical therapies was generated by multiplying the failure of PFMT by the relative effect sizes derived in the MTC reported in Chapter 8 and summarised in *Table 50*.

***TABLE 55*** *Values used in the estimation of long-term cure rate after receiving pelvic floor muscle training*

| Time (years) | Probability of cure for: | |
|---|---|---|
| | **PFMT basic** | **PFMT extra sessions** |
| 0 | 1 | 1 |
| 5 | 0.67[a] | 0.75[b] |
| 15 | 0.16[b] | 0.30[b] |

a Value based on Lagro-Janssen and van Weel (1998).[210]
b Value based on results of Bø and colleagues (2005).[208]

### Recurrence rates for drug (SNRI) therapy

As with the PFMT, there were very few studies that had long-term follow-up of women who were using drugs to treat their incontinence. Four relevant studies were identified as part of the systematic review studies[57,136–138] and an unpublished study from Eli Lilly and Company.[211] These studies had an unclear length of follow-up, a follow-up of less than 1 year or were unpublished. One study was identified that reported recurrence rates for a cohort of women at different time points after the initiation of drug treatment.[212] In making an extrapolation from these data it was assumed that at 12 months only 5.8% of those initially cured remain cured, which is equivalent to the spontaneous cure estimated for no treatment. This rate is lower than the 9% cure rate reported by Vella and colleagues.[212]

Extrapolation of cure rate (disease free) was estimated from a Kaplan–Meier curve using a Weibull survival model from the data reported in *Table 56*. The Weibull distribution was chosen for this extrapolation as it was felt to have a suitable functional form to estimate a survival. The Weibull distribution is defined by two parameters: the scale parameter (λ) and the shape parameter (γ). The scale parameter describes the probability that the woman becomes incontinent during the next time period, given that she is continent during the current time period. The shape parameter describes the hazard function of Weibull function for the survival time. The hazard function for Weibull survival time could be increasing or

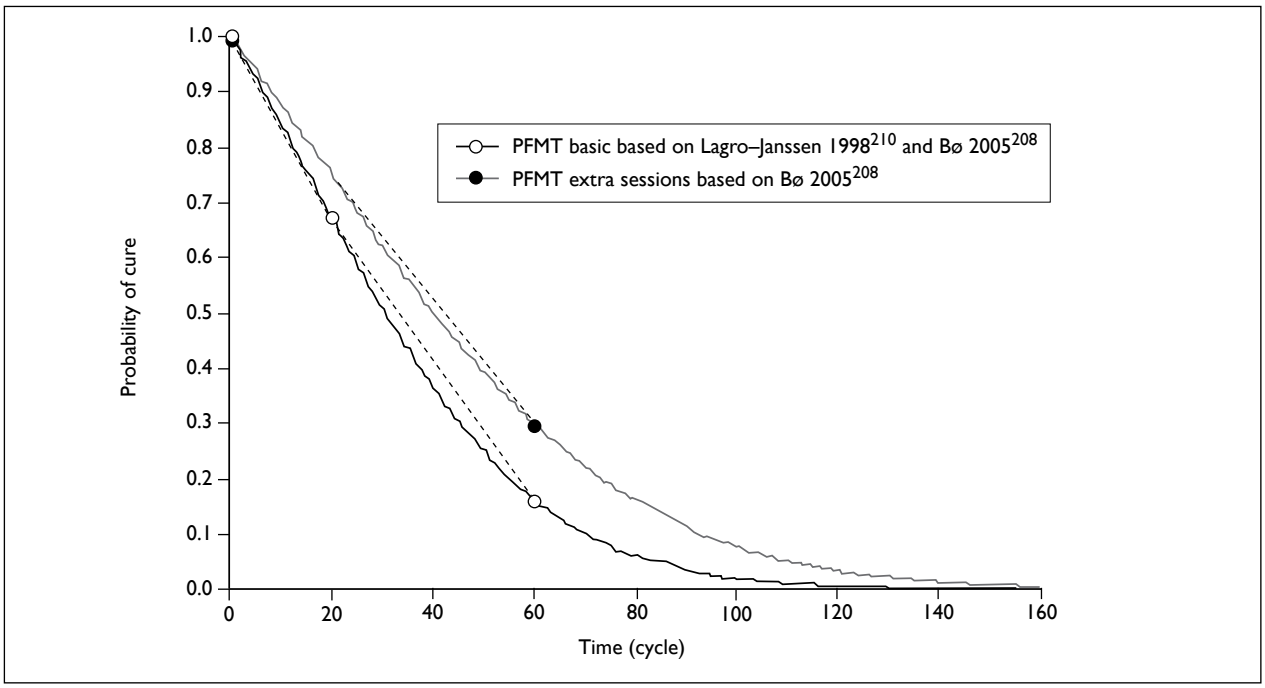


***FIGURE 36*** *Extrapolated cure rates after pelvic floor muscle training. Note that each cycle is 3 months long. Based on Lagro-Janssen and van Weel (1998)[210] and Bø and colleagues (2005).[208]*

decreasing with time, depending on the value of parameter γ. If the value is greater than 1, the hazard rate increases with time. If the shape parameter is less than 1, the hazard decreases with time. If the shape parameter is equal to 1, then the Weibull distribution is equivalent to an exponential distribution. *Figure 37* describes the curve fitted to the data reported in *Table 56*. An approximate hazard function for the curve is given by:

$$S(t) = \exp(-\lambda t^{\gamma}): \text{ where } \lambda = 1.73459, \gamma = 0.36$$

where:

- $S(t)$ is the probability of cure in any given cycle
- $t$ is time (measured in terms of the number of cycles, where each cycle is equivalent to 12 weeks)
- λ is the scale parameter that describes the probability that the woman becomes incontinent during the next time period, given that she is continent during the current time period
- γ is the shape parameter, which describes the hazard function of Weibull function for the survival time.

***TABLE 56*** *Values used in the estimation of long-term cure rates after drug therapy*

| Time (months) | Cure rate |
|---|---|
| 0 | 1 |
| 1 | 0.31 |
| 4 | 0.12 |
| 6 | 0.1 |
| 12 | 0.09[a] |

a Value from Vella and colleagues (2008).[212]

Appendix 25 describes how the above equation was used to calculate the transition probabilities required for the model (e.g. the probability of a woman who is currently cured suffering a recurrence in the next cycle and the probability of remaining cured).

**Recurrence rates of TVT**

The long-term recurrence rates of TVT were derived using the long-term cure rates of a recent trial conducted in the UK, comparing TVT with Burch colposuspension.[213] The data from reported cure rates for up to 5 years were used to estimate longer-term recurrence rates using a Weibull survival model (*Figure 38*), from the data reported in *Table 57*. As was the case for drug treatment, this model was chosen because it was felt to provide a reasonable representation of the estimated long-term recurrence rates.

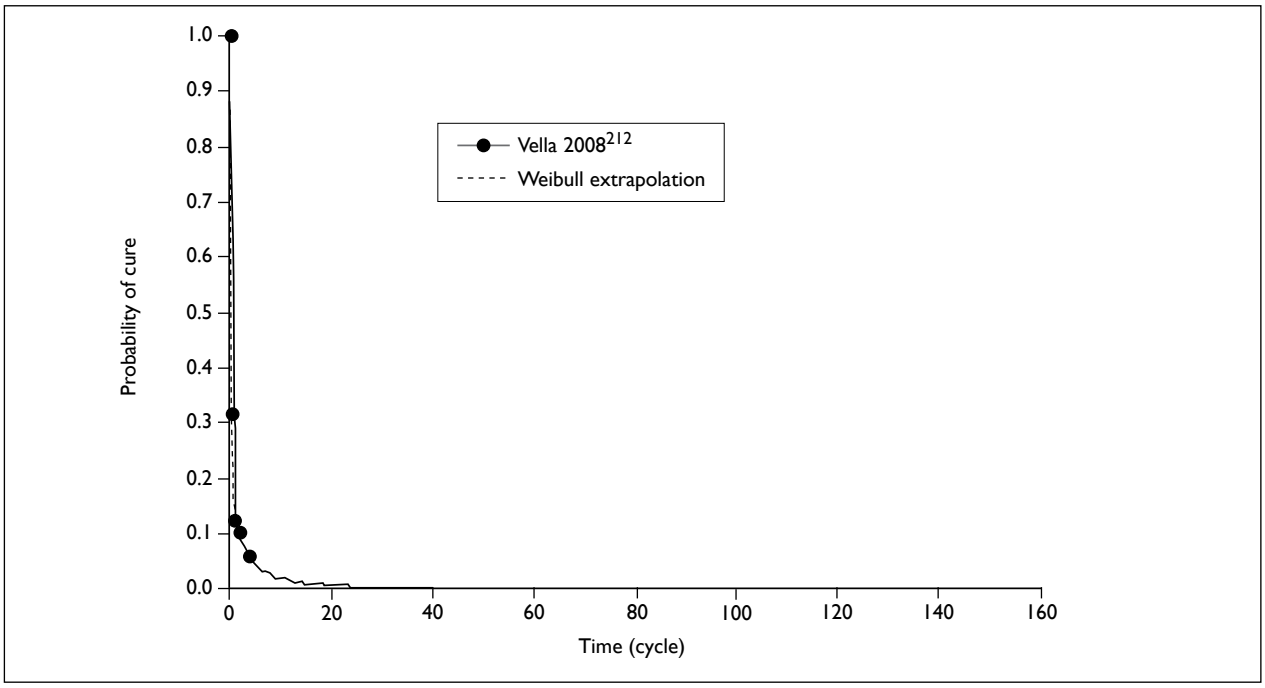


***FIGURE 37*** *Extrapolated long-term cure rates after drug therapy. Note that each cycle is 3 months long. Based on Vella and colleagues (2008).*[212]

***TABLE 57*** *Values used in the estimation of long-term cure rates after being treated with tension-free vaginal tape*

| Time (years) | Rate of continence |
|---|---|
| 0 | 1 |
| 0.5 | 0.85 |
| 2 | 0.80 |

In this trial the cure rate at 5 years was 0.81, which is 0.01 higher than it was at 2 years, which is likely to be caused by women being lost to follow-up. Therefore, the reported data at 5 years were not used in the extrapolation, although it did help inform assumptions about what proportion of women might remain cured at 5 years.

The following survival hazard formula was defined:

$$S(t) = \exp(-\lambda t^{\gamma}): \ \lambda = 0.138696, \gamma = 0.228682$$

where:

- $S(t)$ is the probability of cure
- $t$ is time (measured in terms of the number of cycles, where each cycle is equivalent to 12 weeks)
- $\lambda$ is the scale parameter, which describes the probability that the woman becomes incontinent during the next time period, given that she is continent during the current time period
- $\gamma$ is the shape parameter, which describes the hazard function of Weibull function for the survival time.

The transition probabilities used in the model were calculated using the formula shown in Appendix 25.

### *Other parameters*

The other parameters (*Table 58*) considered in the model were:

- The probability of adverse events (drugs only). The estimate used in the model was generated from the systematic review reported in Chapter 7 (see SNRI drug therapy).
- The chance that women may still need to use containment products when undergoing any of the interventions. In the base-case analysis it was assumed that if women were cured then they did not need to use containment products. This assumption was tested in a sensitivity analysis. In the improvement model all women were assumed to use containment products. The cost of the containment product used by those who were improved was based on the

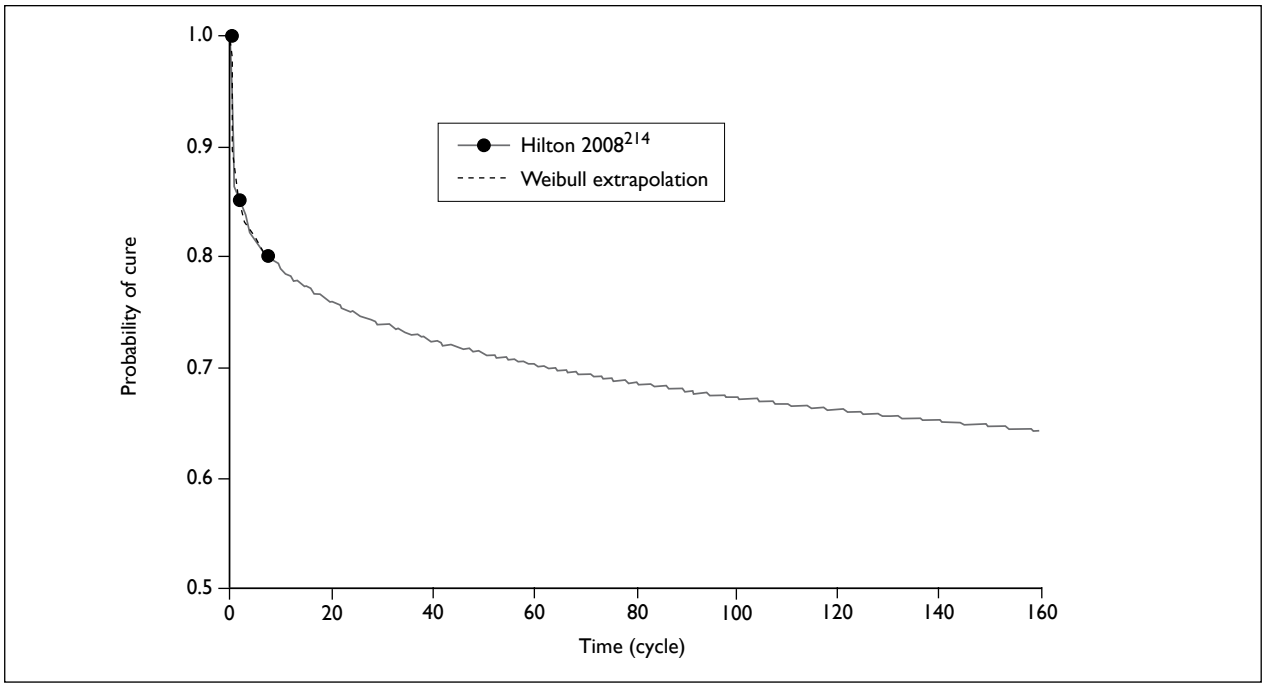


***FIGURE 38*** *Extrapolated long-term cure rates after tension-free vaginal tape surgery. Note that each cycle is 3 months long. Based on Hilton and colleagues (2008),[214] which summarises data reported in Ward and colleagues (2002);[213] (2004);[215] (2008).[216]*

least expensive type of containment product used (menstrual pads).[84]
- Risk of death attached to surgery. This information was taken from a previous systematic review that reported the risk of death from open colposuspension surgery.[80]

**All-cause mortality rates in the UK**
As a woman moves through the model there will be some chance of that the woman might die. The likelihood that a woman might die was based upon the annual rates of age-specific all-cause mortality for women [based on the Office for National Statistics (ONS) interim life tables 2004–06 (database on the Internet)].[217] *Figure 39* shows the survival curve for females for the UK and Appendix 25 reports the rates of all-cause mortality used in the model.

## Resource utilisation and cost estimation

Resource use data was identified from existing studies,[43] relevant literature (e.g. reports from manufacturers) and advice from experts in this field. The resources used to provide the non-surgical interventions included:

- the number of visits to the practitioners for the sessions of therapy
- the staff time, the appropriate grade and direct overheads associated with delivering health care, such as clerical support and administration of the sessions of therapy
- the consumables required to provide service
- the reusable equipment used.

The costs of exercise dairies and leaflets were considered to be negligible and it was also assumed that all patients would receive them. Therefore, their costs were not included.

### *Lifestyle changes*
The cost of lifestyle changes were based on the cost of a single visit to the GP.

### *PFMT basic*
As indicated in the recent NICE guidance,[43] it was assumed that PFMT comprised six sessions. As acknowledged in the guidance, it is difficult to define a 'standard' or 'typical' PFMT session, and, hence, in reality, costs will vary according to the actual care provided. Within the model it was assumed that the first session of PFMT would last for 1 hour and the other five sessions would last for 30 minutes each. Each session would be conducted by a senior grade 1 women's health physiotherapist in a hospital physiotherapy department. The consumables that would be required per session would be: gloves, KY Jelly, wipes and paper towels.

***TABLE 58*** *Other parameters used in the economic model*

| Probability | Value | Source |
|---|---|---|
| Probability of adverse event while on drug therapy | 0.45 | Estimated from systematic review[a] |
| Probability that women who failed PFMT, or for whom symptoms recurred, managed their symptoms thereafter with containment products | 0 | Assumption |
| Probability of continuing to use containment products after PFMT has failed or symptoms have recurred | 0 | Assumption |
| Probability that women who failed PFMT + adjunct, or for whom symptoms recurred, managed their symptoms thereafter with containment products | 0 | Assumption |
| Probability of continuing to use containment products after PFMT + adjunct has failed or symptoms have recurred | 0 | Assumption |
| Probability that women who failed PFMT, etc., or for whom symptoms recurred, managed their symptoms thereafter with containment products | 0 | Assumption |
| Probability of continuing to use containment management after PFMT, etc. has failed or symptoms have recurred | 0 | Assumption |
| Probability that women who failed with drugs, or for whom symptoms recurred, managed their symptoms thereafter with containment products | 0 | Assumption |
| Probability of continuing to use containment products after drugs have failed or symptoms have recurred | 0 | Assumption |
| Probability that women who failed following surgery, or for whom symptoms recurred, managed their symptoms thereafter with containment products | 0 | Assumption |
| Probability of continuing to use containment products after surgery has failed or symptoms have recurred | 0 | Assumption |
| Probability of the first surgery being successful | 0.87 | Estimated in the model |
| Probability of a second surgery being successful | 0.85 | Estimated in the model |
| Probability of drug therapy being successful after suffering an adverse event | 0 | Urinary incontinence guideline, 2006[43] |
| Mortality rates of surgery | 0.0005 | Cody 2003[80] |

a See Chapter 7.

### *PFMT with extra sessions*

The costs of PFMT with extra sessions were derived in the same way as those of basic PFMT described above, but the number of sessions was increased from six to 12.

### *PFMT plus BF*

The resources used for PFMT plus BF were based on the assumption that the staff providing the service was the same as those providing PFMT alone, and that the number of sessions were the same as those for PFMT. Additional resources required for the BF were the equipment used, for example the hand-held single-channel EMG channel, the Neen Educator® and Neen Periform vaginal probe. The educators and the probes were treated as consumables, as they were used by only one woman over all of the sessions. However, the NeuroTrac device™ was loaned to women for 3 months. Based upon information from manufacturers and from NHS users, this piece of equipment was considered to have a lifespan of 5 years, the equivalent annual cost of the equipment was calculated (using a 3.5% discount rate as recommended by the UK Treasury) and the cost per woman took into account that the equipment was used by four women per year. These data were used to help interpret the results of 'PFMT with extra sessions' only when it was used in the model. This is because the effectiveness of PFMT with extra sessions was similar to PFMT plus BF, and it is plausible that the costs of the two types of therapy were similar.

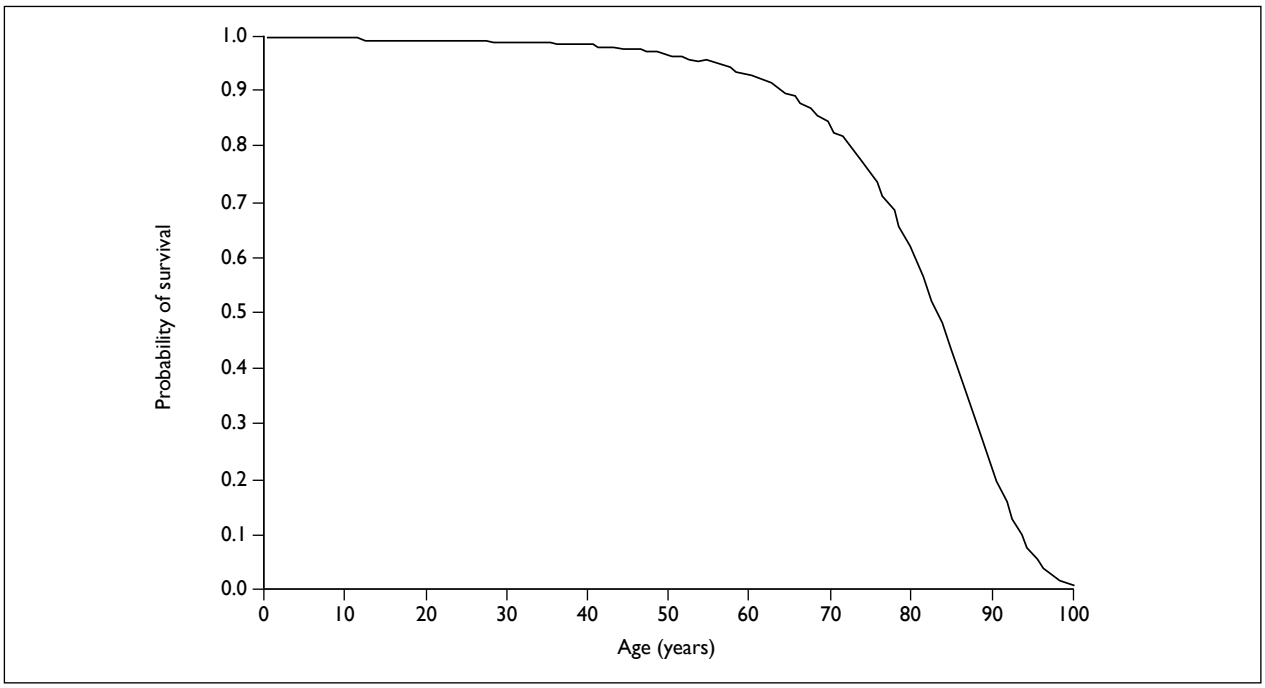


***FIGURE 39*** *Age-adjusted survival Kaplan–Meier curve for females in the UK.*

### *Vaginal cones*

Although VCs are recommended as a first-line treatment, they are not routinely provided by the NHS. Cones are often bought over the counter after GP advice. The cost of VCs was based on the assumption that the labour costs were one-third of those for PFMT (i.e. two visits with the physiotherapist). Although VCs are not currently provided by the NHS, the women using VCs would still have two visits with the physiotherapist. The consumables required and consumables used were cones, gloves, paper towels and KY Jelly.

### *Electrical stimulation*

Electrical stimulation can be provided either at home or in a clinic. The difference between the two ways of providing the therapy relates to the number of sessions that the woman receives. Home-based ES has three sessions, whereas the clinic-based therapy has 13 sessions (although this may vary in practice), with the first session lasting 1 hour and the remainder lasting 30 minutes. For the home-based ES, the woman has a 1-hour-long session in the hospital physiotherapy department to determine an appropriate programme and then two follow-up sessions. The Neen Pericalm device is loaned to women for home use for 3 months. In this analysis it was assumed that 13 sessions would be provided by a physiotherapist in a hospital department. The resources used included a Neen Periform vaginal electrode and data-reading clinical equipment, along with the same consumables that were used in the provision of PFMT (gloves, KY Jelly, couch roll, wipes and paper towels). Based upon information from manufacturers and from NHS users, the equipment was assumed to have a lifespan of 5 years and an equivalent annual cost of the equipment was calculated (using a 3.5% discount rate as recommended by the UK Treasury). A total of 200 women would be able to use it each year in a clinical setting.

### *Medical therapy*

The cost of drug treatment was based on two consultations (an initial consultation and a review consultation) with the GP, and the drug costs for each cycle (3 months).

### *Surgical interventions*

Surgical costs were based on the average costs of an elective minor lower urinary tract procedure without complications.[54]

### *Containment products*

The costs of containment products (such as disposable insert and menstrual pads, and washable pants with and without insert pads) were based on information reported in a systematic review of containment products.[84] The cost of other containment products, such as urethral plugs, were not included in the base analysis.

### Cost estimation

As described above, costs focused on the direct health service costs that were associated with each treatment. Unit cost data were extracted from the literature or from relevant sources, such as manufacturer price lists and NHS reference costs. The year of the cost data is 2008 and the currency is pounds sterling (£). *Table 59* provides a summary of the costs for each intervention.

## Quality of life

### Summary of a structured review of reports on health-state utilities

The primary outcome for the economic analysis was QALYs. The QALY estimates within the model analysis are mainly determined by whether a woman was continent or not, as the risk of death from SUI or any of the treatment options is very low. Although there is considerable evidence about the quality of life of women with SUI, this tends to be measured using condition-specific tools, such as the I-QoL. Such data are not ideal for incorporation into an economic evaluation. As an economic evaluation seeks to inform choices about how best to allocate society's scarce resources, it has been argued that changes in quality of life should reflect society's valuation. One quality-of-life instrument that has a scoring system based on the preferences of the UK population is the EQ-5D. This method is the approach preferred by NICE[105] in HTAs, although there may be some concerns that it is not sufficiently sensitive to changes in the symptoms of incontinence.

Estimates of the EQ-5D scores for a sample of women suffering from SUI were reported in Chapter 4. Further data were identified from the literature search that was performed for the effectiveness review and these were supplemented by information from NHS Economic Evaluation Database (EED) and the Cost-Effectiveness Analysis (CEA) Registry at Tufts Medical Center.[218] From this search, only three published studies

***TABLE 59*** *Cost of each intervention*

| Intervention | Cost per cycle (£)[a] | Range (£) | Notes and comments |
|---|---|---|---|
| ***Lifestyle changes*** | | | |
| Cost per visit | 27 | 13–40 | Range based on 1 or 3 visits to GP (Curtis 2008)[46] |
| ***PFMT*** | | | |
| PFMT basic | 189 | 135–243 | Range based on 4 and 8 sessions |
| PFMT + BF | 224 | 175–388 | Range based on 4 and 8 sessions |
| ES | 398 | 206–481 | Range based on 8 and 16 sessions |
| VCs | 93 | 83–103 | Assumed provided at the hospital |
| PFMT extra sessions | 351 | 243–459 | Based on 8 and 16 sessions |
| ***Drug therapy (SNRI)*** | | | |
| Appointments and drugs for 12 weeks | 164 | 128–200 | Initial cost based on 2 appointments (initial and review) and the range is based on 1 or 3 visits to GP |
| Surgical therapy | | | |
| TVT/TVT-O | 1135 | 741–1357 | Based on lower and upper interquartile range of reference costs (2008) for elective surgery on lower-tract minor procedures without complications |
| Colposuspension | 1396 | 1002–1618 | Range estimation based on TVT range |
| ***Containment products*** | | | |
| Washable inserts | 39 | 9–75 | Initial cost based on cost per month for washable insert pants; range based on the minimum (menstrual pads) and maximum (disposable insert pants) cost of containment |

a Log-normal probability distribution was attached to all these costs.

***TABLE 60*** *EQ-5D values used in the model*

| EQ-5D score | Value | Source |
|---|---|---|
| The baseline of SUI (pretreatment) | 0.78 | Manca and colleagues (2003)[220] |
| The failure of treatment | 0.74 | Haywood and colleagues (2008)[219] |
| The success of treatment | 0.85 | Haywood and colleagues (2008)[219] |

were identified.[219–221] The first study[221] was a pan-European study of women with urinary incontinence, who sought treatment, the second study[219] was a clinical trial of group versus individual physiotherapy for women with SUI and the final study[220] was an economic evaluation alongside an RCT, conducted in the UK, of TVT compared with Burch colposuspension.

In the first study, conducted in 14 European countries, the median EQ-5D score of women with urinary incontinence that sought treatment was 0.85. The mean score for women in the UK was 0.73 and the median 0.85.[221] Another study on the same population of women reported 0.76 as the adjusted OR for EQ-5D health-state index score.[222]

Haywood and colleagues[219] reported EQ-5D scores for women based on the number of incontinence episodes at baseline. Those with no episodes has a mean score of 0.85 (SD 0.24). When incontinence was suffered on a few days the mean score was 0.85 (SD 0.16). As would be anticipated, the mean score declined as severity of incontinence increased. For example, when incontinence was suffered for 'about half the week' the mean score was 0.81 (SD 0.20); for 'most days' the mean score was 0.79 (SD 0.23) and for 'everyday' the mean score was 0.75 (SD 0.32).[219] This study[219] also reported EQ-5D scores based upon the perceived benefit from physiotherapy at 6 weeks and 5 months. At 6 weeks the mean score from those who said they had benefited was 0.85 (SD 0.23) and for those who said that they had no benefit was 0.73 (SD 0.31). At 5 months the mean scores were 0.85 (SD 0.24) and 0.74 (SD 0.38) for those who said they did and did not benefit from physiotherapy, respectively.

The third study published on women who were receiving surgery for SUI reported quality of life at baseline and at trial follow-up.[220] These data were subsequently manipulated in an HTA trial comparing different surgical treatments.[80] The EQ-5D score for women prior to surgery was 0.778 for women randomised to TVT, and 0.785 for women randomised to colposuspension.[220] Finally, as reported in Chapter 4, the survey of members of InContact previously identified as suffering from SUI reported a mean EQ-5D score of 0.598 (SD 0.339). The mean age for the women involved in this sample was 57 years (range 28–89).

### *Derivation of values used in the model*

It was thought possible that the women involved in the survey reported in Chapter 4 might be atypical of the average woman with SUI, as they were part of a self-selected patient group. Therefore, in the economic model the utility score was based on the study by Manca and colleagues,[220] and failure after treatment was based on the study by Haywood and colleagues.[219] This value was that of women who perceived that they did not benefit from physiotherapy treatment, thus indicating that it had failed. The utility assigned to successful treatment was taken as 0.85. This value was based on the women who perceived that they benefited from physiotherapy treatment at 6 months after treatment (*Table 60*).

## Data analysis

### *Cost–utility analysis*

As women with SUI might be either cured or 'cured or improved' (i.e. not requiring further treatment but possibly still having some degree of incontinence), two separate analyses were conducted. One analysis was based upon the reported cure rates (see Cost–utility analysis based upon cure rates, below) and a second analysis based upon improvement rates (see Results based upon improvement rates, below).

The estimation of the costs and consequences of the different management strategies was performed using a hypothetical cohort of 1000 women, starting at age of 45 years (the identified prevalence average age of women with SUI in Chapter 1) over a 40-year horizon. Results are presented as incremental cost per QALY. These are ratios of the differences in costs of the interventions divided by the differences in effectiveness between the different strategies. These data show the rate of return (in QALYs) to the quantity of resources used (measured in monetary terms). If for any given

incremental cost-effectiveness ratio (ICER) it is judged that a treatment is efficient then it implies that society is willing to pay at least that amount to obtain an additional QALY. The value society is willing to pay for a QALY is unclear, but, typically, NICE, within the UK, recommends interventions when the incremental cost per QALY is less than £20,000–30,000.[105]

## Sensitivity analyses

With all parameter estimates there are elements of uncertainty owing to the lack of available information. In order to explore the importance of such uncertainties and assumptions, various sensitivity analyses were conducted by varying some of the assumptions or parameters made in the model. Two types of sensitivity analyses were performed: a probabilistic sensitivity analysis and a deterministic sensitivity analysis.

### *Probabilistic sensitivity analysis*

One area of uncertainty within the economic model is precision of the parameter estimates used. Many of the parameters are not precisely known but the uncertainty surrounding a point estimate can be described using a statistical distribution. Probability distributions were applied to the specific ranges of the key parameters (*Table 61*), such as costs and samples drawn at random from these distributions to generate an empirical distribution of the cost-effectiveness ratios. All treatment costs were assigned log-normal distributions, as this distribution appeared to best fit the data that have skewed or symmetric ranges. There was no distribution to be assigned for probabilities of recurrence of all treatment (PFMT, drug and TVT surgery) due to the paucity of data. There was also no distribution to all-cause mortality rate as the number of observation used to calculate the risk was very large. The estimates of cure and improvement rates for all treatments were assigned log-normal or normal distributions based on the assumptions made in the mixed-treatment model in Chapter 8.

### *Deterministic sensitivity analysis*

The second type of analysis undertaken to handle parameter uncertainty was to consider changes in one or more parameter value at the same time. This was used to explore structural uncertainty, extrapolations, methodological uncertainty, etc. This deterministic sensitivity analysis had been combined with probabilistic sensitivity analysis so that the joint effect of using different values (and distributions) and statistical imprecision surrounding estimates is explored. Outlined below are the details of the specific sensitivity analyses performed.

### *Recurrence rates of PFMT*

As there were limited data relating to the long-term follow-up of PFMT, the long-term recurrence rates of PFMT in the base-case analysis were produced based on the values at 5 years[210] and 15 years.[208] However, the identified data at 15 years in the study by Bø and colleagues[208] was varied as in *Table 55*. Changes to the recurrence rates of PFMT are likely to alter cost-effectiveness of the strategies related to PFMT. *Figure 40* describes the alternative long-term recurrence rates considered in the sensitivity analysis.

As described in the section Estimation of model probabilities, data on the long-term effectiveness of all physical interventions were not readily available. In the base-case model it was assumed that the recurrence rates for physical therapies could be derived by multiplying the recurrence of PFMT by the relative effect sizes derived in the MTC, reported in Chapter 8 and summarised in *Table 50*. The recurrence rates for PFMT came from Bø and colleagues.[208] Bø and colleagues[208] reported that there was no difference at 15 years in the effectiveness of the two forms of PFMT compared. Therefore, in this sensitivity analysis it was assumed that the recurrence rates for all different physical treatments (PFMT plus BF, VCs and ES) had the same recurrence rate as PFMT.

### *Recurrence rates of TVT*

As explained in Estimation of model probabilities, there was no reliable evidence related to the long-term follow-up of recurrence rate of TVT surgery. The trial by Ward and colleagues,[213] which reported recurrence rates for up to 5 years' follow-up, was used to estimate the recurrence rates of TVT surgery in the base-case analysis. This sensitivity analysis used the recurrence rates estimated in an earlier HTA that compared TVT surgery with other surgical treatments.[80] In the sensitivity analysis the long-term cure rates for TVT surgery were increased to 81% and reduced to 65% in the first year and 61% in the second year.

### *Starting age and time horizon*

The incidence rate of SUI is likely to increase as age increases. The mean age of women with SUI in the UK is 45 years and this was taken to be the age of women in the cohort modelled. Women included in the trials included in the systematic review of effectiveness tended to be slightly older, with

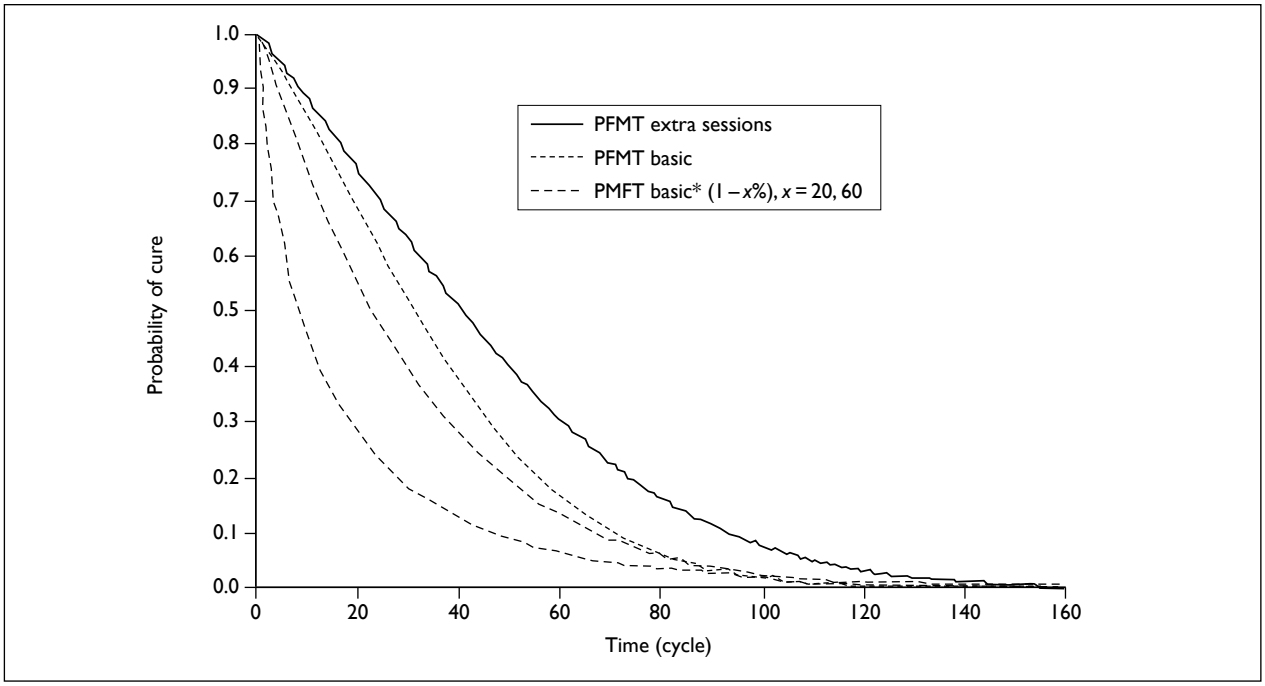


***FIGURE 40*** *Linear exponential curves with variation of recurrence rates of pelvic floor muscle training. Note that each cycle is 3 months long.*

average ages varying from 50 to 60 years. The costs and effects in the model were estimated for a 40-year time horizon. This time horizon was chosen as it was felt to cover the expected life expectancy of women aged 45. However, few robust data are available for such a long follow-up.

In this sensitivity analysis the implications of varying the age of women at the start of treatment and the impact of adopting a shorter time horizon were explored. Therefore, the starting age of women was changed to 50, 55, and 60 years in the sensitivity analyses. The time horizons were likewise reduced to 10, 20 and 30 years.

### *Quality of life*

As mentioned previously (see Quality of life), data from Manca and colleagues[220] and Haywood and colleagues[219] were used in the base-case analysis. Sensitivity analysis was performed using the EQ-5D scores derived in the survey reported in Chapter 4 to weight the utility scores taken from the study by Haywood and colleagues[219] (*Table 61*).

The impact of the natural decline in quality of life over time was also considered in further sensitivity analysis. The values for the age-related reduction was derived based on published values for age-related quality of life.[223] The extrapolated values are illustrated in *Figure 41* and Appendix 25.

### *Discount rate*

As recommended in the NICE guidelines, an annual discount rate of 3.5% for costs and benefits was used in the base-case analyses.[105] A range of 1–6% for discount rate was considered in this sensitivity analysis.

### *Probability of moving to the next treatment following failure of prior treatment*

Considerable efforts were made to identify the estimates for a probability that women would not seek further treatment should a treatment fail or symptoms recur, and would manage their incontinence using containment products, but few data are available. In the base-case analyses it was assumed that the women would go immediately to the next treatment after failure or recurrence. In this sensitivity analysis, the impact of allowing between 10% and 50% of women who experience a treatment failure or recurrence of symptoms not to seek further treatment was explored.

### *Use of containment products*

Although there is anecdotal evidence that women use containment even when they are undergoing treatment, there were no data to inform what proportion of the women use containment products

***TABLE 61*** *EQ-5D values weighted by the utilities reported in Chapter 4*

| EQ-5D score | Value | Source |
|---|---|---|
| The baseline of SUI (pretreatment) | 0.60 | Chapter 4 |
| The failure of treatment | 0.57 | Haywood and colleagues (2008),[219] weighted by utilities reported in Chapter 4 |
| The success of treatment | 0.65 | Haywood and colleagues (2008),[219] weighted by utilities reported in Chapter 4 |

and what type of products they use. Therefore, in the cure and improvement model it was assumed all women used containment products, although the quantity/type used varied according to symptoms.

#### *Mortality and success rate of TVT*

Further sensitivity analyses were conducted by varying the mortality risk and success rates related to TVT in base case. In the base-case analysis a mortality risk based on the risk of undergoing open surgery (0.0005) was attached to TVT. In the sensitivity analysis this was reduced to zero. Sensitivity analysis was also performed to estimate the impact of an increase in the success rate of TVT by 5%.

#### *Costs*

As indicated earlier, it is difficult to define a 'standard' intervention, as practice varies greatly. The costs of interventions are dependent on the assumptions made about the number of sessions of therapy a woman could get. Maximum and minimum costs were derived by increasing and reducing the number of sessions. For example, the minimum cost of basic PFMT was derived by reducing the number of sessions to four and the maximum cost was derived by increasing the number of sessions to eight. Distributions were used in the analysis to incorporate the minimum and maximum values attached to the costs.

## Results of the model presented in terms of costs and consequences

The results of the base-case deterministic analyses for 1000 women are presented in terms of summaries of the time spent cured (or improved for the improvement model), with incontinence and also the cumulative number of women who have received surgery. The results are also presented in terms of the cumulative QALYs and cost.

### Analysis based on cure rates

For the analyses based on the cure rates, the strategy that used lifestyle changes and PFMT basic followed by PFMT with extra sessions followed by TVT surgery (LS–PFMT basic–PFMT extra sessions–TVT) had the best performance in terms of the highest number of successes (939 and 953) and lowest number of failures (59 and 36) at the 1- and 10-year time horizons, whereas the strategy that used lifestyle changes and PFMT basic followed by TVT surgery (LS–PMT basic–TVT) had the highest number of success at the 40-year time horizon (398). The strategy that had the least number of failures (28) was the one that used the lifestyle changes and PFMT basic followed by PFMT with extra sessions followed by SNRI followed by TVT surgery (LS–PFMT basic–PFMT extra sessions–SNRI–TVT). The strategy of lifestyle change and TVT surgery (LS–TVT) has the worst performance in terms of the lowest number of successes (726, 907 and 363) and the highest number of failures (272, 82 and 57) at all three time horizons. This strategy had the highest number of patients (998 and 989) receiving surgery at 1- and 10-year time horizons, and the strategy that used lifestyle changes and PFMT basic followed by TVT surgery (LS–PFMT basic–TVT) had the highest number (443) of patients receiving surgery at the 40-year time horizon (*Table 62*).

### Analysis based on improvement rates

For the analysis based on improvement rates, the strategy that used LS–PFMT with extra sessions followed by TVT surgery had the best performance in terms of the highest number of successes (985, 951 and 410) at all the three time horizons and the lowest number of failures (13 and 22) at 1 and 10 years (*Table 63*). The strategy that used lifestyle changes and PFMT basic followed by PFMT with extra sessions followed by drug therapy followed by TVT surgery (LS–PFMT basic–PFMT extra sessions–SNRI–TVT) had the least number

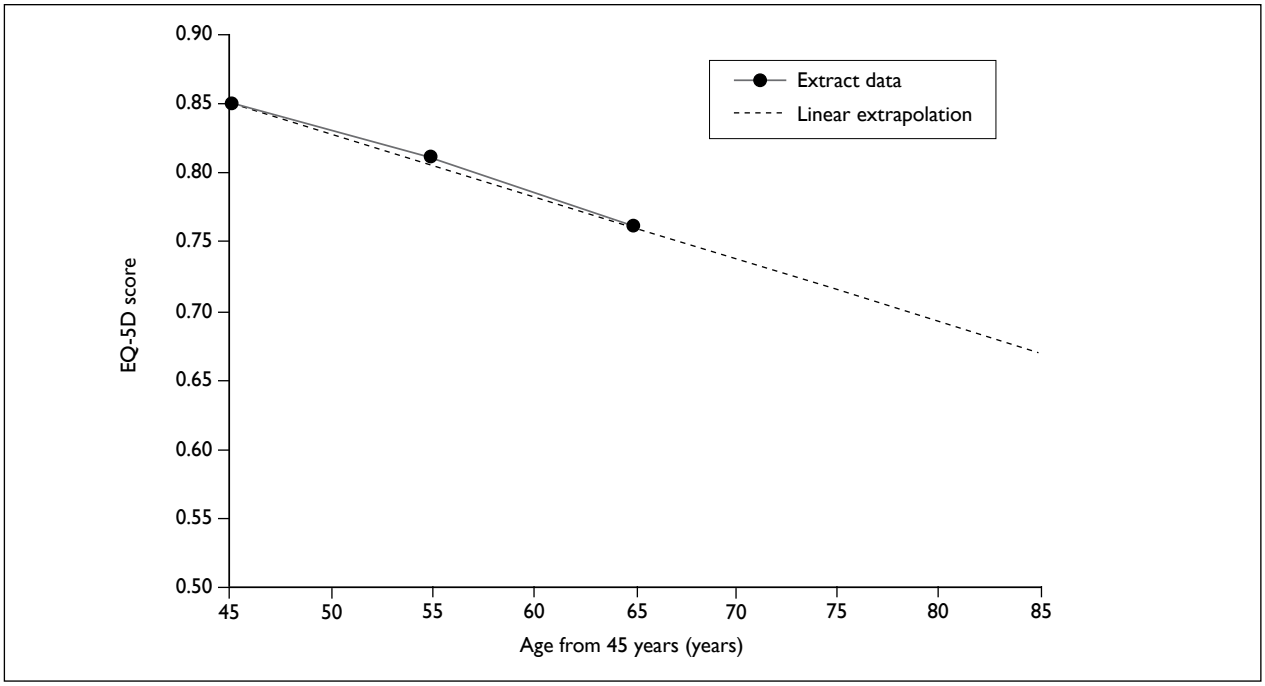


***FIGURE 41*** *Linear extrapolation of EQ-5D score using EQ-5D adjusted by age. Note that extracted data refers to data taken from Kind and colleagues (1999).*[223]

of failures (8). The strategy of lifestyle changes followed by TVT surgery (LS–TVT) had the worst performance in terms of the lowest number of successes (793, 913 and 382) and the highest number of failures (205, 60 and 40) at all three time horizons. This strategy also had the highest number of patients (998, 973 and 422) having had surgery at all three time horizons.

# Cost–utility analysis based upon cure rates

## Deterministic results

*Table 64* details the results of the mean cost and treatment effects of the model using cure rates from the mixed-treatment model in a hypothetical cohort with 1000 samples. The table reports performance of the strategies from the least to the most costly. The lower part of the table reports the ICERs when dominated and extendedly dominated strategies are omitted. The strategy that used lifestyle changes and PFMT with extra sessions followed by TVT surgery (LS–PFMT extra sessions–TVT) was the least costly (£1644) and the most effective (16.20 QALYs). The strategy that had lifestyle changes followed by TVT surgery (LS–TVT) was the most costly (£1973), and the strategy that used lifestyle changes and PFMT basic followed by PFMT with extra sessions followed by SNRI and then TVT surgery (LS–PFMT basic–PFMT extra sessions–SNRI–TVT) was the least effective (15.89 QALYs).

## Probabilistic results

As the cost-effectiveness point estimates do not provide any information of uncertainty surrounding the model parameters, probabilistic sensitivity analysis using Monte Carlo simulations was also performed using these strategies. The results of the probabilistic analysis are presented in the form of cost-effectiveness acceptability curves in *Figure 42*. The strategy employing lifestyle changes and PFMT with extra sessions followed by TVT surgery (LS-PFMT extra sessions-TVT) has a more than 70% probability of being considered cost-effective for all threshold values for willingness to pay for a QALY presented. The other five strategies each have a probability of less than 20% of being considered cost-effective.

## Sensitivity analyses

### *Changes to the effectiveness and cost of PFMT basic and PFMT with extra sessions*

#### Change in the long-term recurrence rates of PFMT basic and PFMT with extra sessions

As mentioned previously (under Summary of key assumptions made in the economic model), the

***TABLE 62*** *Results of the deterministic model based on cure rates for 1-, 10- and 40-year time horizons*[a]

| Year | Strategy | Success performance | | Receiving surgery | Population | QALYs/costs | |
|---|---|---|---|---|---|---|---|
| | | Success | Failure | | | QALYs | Costs (£) |
| 1 | LS–PFMT extra sessions–TVT | 927 | 71 | 393 | 1000 | 0.8 | 821 |
| | LS–PFMT extra sessions–SNRI–TVT | 927 | 71 | 375 | 1000 | 0.79 | 855 |
| | LS–PFMT basic–PFMT extra sessions–TVT | 939 | 59 | 357 | 1000 | 0.78 | 930 |
| | LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 936 | 62 | 333 | 1000 | 0.77 | 954 |
| | LS–PFMT basic–TVT | 845 | 153 | 926 | 1000 | 0.78 | 1261 |
| | LS–TVT | 726 | 272 | 998 | 1000 | 0.8 | 1186 |
| 10 | LS–PFMT extra sessions–TVT | 950 | 39 | 512 | 1000 | 6.97 | 1290 |
| | LS–PFMT extra sessions–SNRI–TVT | 946 | 43 | 500 | 1000 | 6.93 | 1349 |
| | LS–PFMT basic–PFMT extra sessions–TVT | 953 | 36 | 478 | 1000 | 6.90 | 1391 |
| | LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 947 | 42 | 466 | 1000 | 6.86 | 1449 |
| | LS–PFMT basic–TVT | 932 | 57 | 937 | 1000 | 6.89 | 1676 |
| | LS–TVT | 907 | 82 | 989 | 1000 | 6.91 | 1733 |
| 40 | LS–PFMT extra sessions–TVT | 386 | 31 | 416 | 1000 | 16.2 | 1644 |
| | LS–PFMT extra sessions–SNRI–TVT | 380 | 28 | 406 | 1000 | 16.06 | 1727 |
| | LS–PFMT basic–PFMT extra sessions–TVT | 379 | 29 | 407 | 1000 | 16.02 | 1758 |
| | LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 373 | 27 | 398 | 1000 | 15.89 | 1842 |
| | LS–PFMT basic–TVT | 398 | 45 | 443 | 1000 | 16.03 | 1886 |
| | LS–TVT | 363 | 57 | 420 | 1000 | 16.08 | 1973 |

a The addition of success and failure rates does not equal 1000, as in any given year some women in the original cohort will have died.

recurrence rates of PFMT basic and PFMT with extra sessions were estimated from the study by Bø and colleagues[208] and it is possible that this value is overestimated. As long-term cure rates of PFMT basic and PFMT with extra sessions decreased, the costs of the strategies associated with long-term PFMT basic and PFMT with extra sessions are increased because the long-term recurrence estimation for PFMT basic and PFMT with extra sessions is increased. However, the outcomes associated with long-term PFMT basic and PFMT with extra sessions are decreased. The results of the sensitivity analyses of variations of long-term of recurrence rates for PFMT basic and PFMT with extra sessions are presented in *Table 65*.

The probability that society is willing to pay for an additional QALY for the strategies associated with PFMT basic and PFMT with extra sessions generally decreases as the long-term cure rate of PFMT decreases.

### Changes to the ORs of PFMT basic and PFMT with extra sessions compared with no treatment

The results of the sensitivity analysis performed using different point estimates in clinical effectiveness for cure rates of PFMT with extra sessions and PFMT basic are reported in *Table 66*. When the ORs of PFMT with extra sessions were compared with no treatment decreased,

***TABLE 63*** *Results of the deterministic model in terms based on improvement rates for 1-, 10- and 40-year time horizons*[a]

| | | Success performance | | | | QALYs/costs | |
|---|---|---|---|---|---|---|---|
| Year | Strategy | Success | Failure | Receiving surgery | Population | QALYs | Costs (£) |
| 1 | LS–PFMT extra sessions–TVT | 985 | 13 | 23 | 1000 | 0.82 | 430 |
| | LS–PFMT extra sessions–SNRI–TVT | 977 | 21 | 8 | 1000 | 0.81 | 416 |
| | LS–PFMT basic–PFMT extra sessions–TVT | 983 | 15 | 0 | 1000 | 0.81 | 252 |
| | LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 983 | 15 | 0 | 1000 | 0.81 | 252 |
| | LS–PFMT basic–TVT | 981 | 17 | 30 | 1000 | 0.81 | 275 |
| | LS–TVT | 793 | 205 | 998 | 1000 | 0.8 | 1200 |
| 10 | LS–PFMT extra sessions–TVT | 951 | 22 | 462 | 1000 | 7.04 | 1159 |
| | LS–PFMT extra sessions–SNRI–TVT | 942 | 31 | 401 | 1000 | 7.02 | 1145 |
| | LS–PFMT basic–PFMT extra sessions–TVT | 947 | 26 | 162 | 1000 | 7.03 | 833 |
| | LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 940 | 33 | 127 | 1000 | 7.03 | 818 |
| | LS–PFMT basic–TVT | 947 | 26 | 593 | 1000 | 7.03 | 1139 |
| | LS–TVT | 913 | 60 | 973 | 1000 | 6.96 | 1883 |
| 40 | LS–PFMT extra sessions–TVT | 410 | 12 | 420 | 1000 | 16.37 | 1938 |
| | LS–PFMT extra sessions–SNRI–TVT | 403 | 11 | 404 | 1000 | 16.27 | 1965 |
| | LS–PFMT basic–PFMT extra sessions–TVT | 406 | 9 | 410 | 1000 | 16.31 | 1795 |
| | LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 400 | 8 | 386 | 1000 | 16.24 | 1803 |
| | LS–PFMT basic–TVT | 408 | 13 | 421 | 1000 | 16.34 | 1873 |
| | LS–TVT | 382 | 40 | 422 | 1000 | 16.2 | 2425 |

a The addition of success and failure rates does not equal 1000, as in any given year some women in the original cohort will have died.

the probability that the strategies associated with PFMT with extra sessions were cost-effective was also reduced. When the ORs compared with no treatment reduced to four (the value used in base case was 10.7), the likelihood that lifestyles followed by PFMT with extra sessions followed by TVT surgery (LS–PFMT extra sessions–TVT) was cost-effective fell to approximately 40%. The main strategy that gained was 'lifestyles', followed by 'TVT surgery', which has a 50% chance of being considered cost-effective over the range of values for a cost per QALY considered.

When the OR of PFMT basic compared with no treatment varied (*Table 67*), the results were broadly similar to the best case analysis.

### Changes to the cost of PFMT with extra sessions

As indicated in Resource utilisation and cost estimation, the cost of PFMT with extra sessions may be underestimated. As shown in *Table 68*, the probability that lifestyle–PFMT extra sessions–TVT was most cost-effective decreased and the probability that LV–TVT was cost-effective increased. However, PFMT with extra sessions would need to increase in cost by more than £400 before the base-case conclusions would substantially change.

***TABLE 64*** *Base-case results of costs and effects using cure rates from the mixed-treatment model*

| Strategy | Cost (£) | Incremental cost (£) | QALYS | Incremental QALY | ICER |
|---|---|---|---|---|---|
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated |
| LS–PFMT basic–PFMT extra sessions –TVT | 1758 | 113 | 16.02 | –0.17 | Dominated |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | –0.3 | Dominated |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated |
| ***Results without dominated and extendedly dominated options*** | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | |

### *Changes to the effectiveness of surgery*

#### Changes to the recurrence rates of TVT surgery

As indicated in Estimation of model probabilities, the long-term recurrence rates of incontinence after TVT surgery were estimated from the trial by Hilton and colleagues (2008).[214] There is some uncertainty attached to this estimate and it is probable that this value could be either an over- or underestimate. As long-term cure rates of TVT surgery increases, the costs for each strategy are decreased and QALYs increase, as women spend more time continent over the 40-year time horizon.

When the probability of recurrence of TVT surgery was increased to 81%, the probability that LS–PFMT extra sessions–TVT would be considered to be cost-effective was reduced, and the probability that lifestyle changes followed by TVT surgery (LS–TVT) was cost-effective increases. When the TVT surgery cure rate was reduced to 65%, the probability that the strategy that uses lifestyle changes followed by TVT surgery (LS–TVT), was considered to be cost-effective was also reduced (*Table 69*).

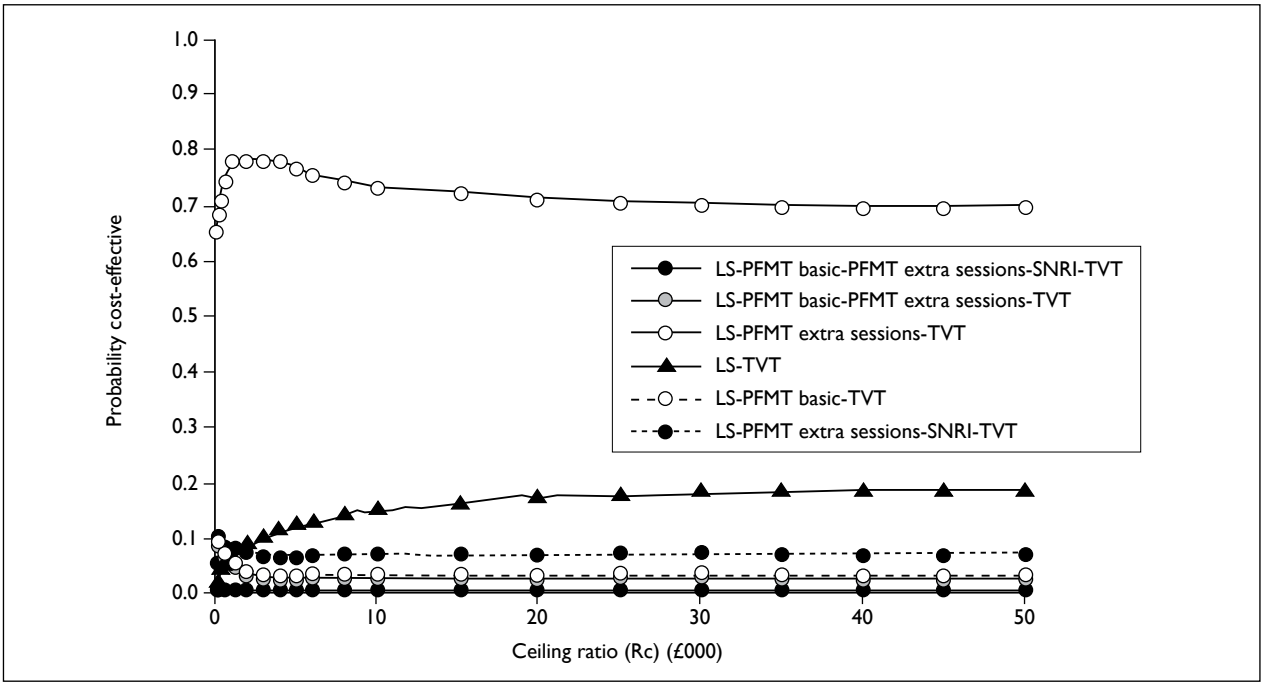


***FIGURE 42*** *Cost-effectiveness acceptability curves determined by society's willingness to pay for a quality-adjusted life-year for the six strategies.*

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**TABLE 65** *Sensitivity analyses associated with recurrence of pelvic floor muscle training (PFMT) with extra sessions and PFMT basic*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Strategy | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | Incremental cost per QALY (£) | 10,000 | 20,000 | 30,000 | 40,000 | 50,000 |
| ***Base case [cure rates of PFMT basic and PFMT with extra sessions at 5 and 15 years in the Lagro-Janssen (1998)[210] and Bø (2005)[208] studies]*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***Long-term cure rates of PFMT with extra sessions were the same as the that of PFMT basic*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1715 | | 16.17 | | | 66 | 65 | 64 | 63 | 63 |
| LS–PFMT extra sessions–SNRI–TVT | 1802 | 88 | 16.03 | –0.14 | Dominated | 5 | 5 | 5 | 5 | 5 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1826 | 111 | 16.00 | –0.17 | Dominated | 3 | 3 | 3 | 3 | 3 |
| LS–PFMT basic–TVT | 1886 | 172 | 16.03 | –0.15 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1915 | 200 | 15.86 | –0.31 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 258 | 16.08 | –0.09 | Dominated | 24 | 26 | 27 | 27 | 27 |

*continued*

***TABLE 65*** *Sensitivity analyses associated with recurrence of pelvic floor muscle training (PFMT) with extra sessions and PFMT basic (continued)*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Long-term cure rate of PFMT with extra sessions and PFMT basic is reduced by 20%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1763 | | 16.15 | | | 64 | 62 | 62 | 61 | 64 |
| LS–PFMT extra sessions–SNRI–TVT | 1853 | 90 | 16.00 | –0.15 | Dominated | 4 | 4 | 4 | 4 | 4 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1871 | 109 | 15.98 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic–TVT | 1892 | 129 | 16.02 | –0.13 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1963 | 201 | 15.84 | –0.32 | Dominated | 3 | 3 | 3 | 3 | 3 |
| LS–TVT | 1973 | 210 | 16.08 | –0.07 | Dominated | 27 | 29 | 30 | 30 | 27 |
| ***Long-term cure rate of PFMT with extra sessions and PFMT basic is reduced by 60%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1879 | | 16.10 | | | 48 | 48 | 48 | 47 | 47 |
| LS–PFMT basic–TVT | 1906 | 27 | 16.02 | –0.09 | Dominated | 9 | 8 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1969 | 90 | 15.94 | –0.16 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 94 | 16.08 | –0.02 | Dominated | 39 | 40 | 41 | 41 | 41 |
| LS–PFMT extra sessions–SNRI–TVT | 1974 | 95 | 15.94 | –0.16 | Dominated | 3 | 3 | 3 | 3 | 3 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2065 | 186 | 15.79 | –0.32 | Dominated | 0 | 0 | 0 | 0 | 0 |

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**TABLE 66** *Sensitivity analyses associated with changes to the odds ratio of pelvic floor muscle training with extra sessions compared with no treatment*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (OR of PFMT with extra sessions compared with no treatment is 10.7)*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | −0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | −0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | −0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | −0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | −0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***OR of PFMT with extra sessions compared with no treatment is 8*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1758 | | 16.15 | | | 66 | 63 | 63 | 63 | 62 |
| LS–PFMT extra sessions–SNRI–TVT | 1842 | 84 | 16.01 | −0.14 | Dominated | 6 | 6 | 6 | 6 | 6 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1860 | 102 | 15.98 | −0.17 | Dominated | 2 | 3 | 3 | 3 | 2 |
| LS–PFMT basic–TVT | 1886 | 128 | 16.03 | −0.12 | Dominated | 3 | 3 | 3 | 3 | 3 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1947 | 190 | 15.84 | −0.31 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–TVT | 1973 | 215 | 16.08 | −0.07 | Dominated | 24 | 26 | 26 | 26 | 27 |
| ***OR of PFMT with extra sessions compared with no treatment is 4*** | | | | | | | | | | |
| LS–PFMT basic–TVT | 1886 | | 16.03 | | | 8 | 6 | 5 | 5 | 5 |
| LS–PFMT extra sessions–TVT | 1926 | 39 | 16.08 | 0.05 | 769 | 39 | 40 | 41 | 40 | 41 |
| LS–TVT | 1973 | 47 | 16.08 | <0.01 | 13,249 | 50 | 51 | 51 | 52 | 52 |
| LS–PFMT basic–PFMT extra sessions–TVT | 2011 | 38 | 15.92 | −0.16 | Dominated | 2 | 2 | 1 | 1 | 1 |
| LS–PFMT extra sessions–SNRI–TVT | 2013 | 40 | 15.92 | −0.16 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2104 | 131 | 15.77 | −0.32 | Dominated | 1 | 1 | 1 | 1 | 1 |

***TABLE 67*** *Sensitivity analyses associated with changes to the odds ratio of pelvic floor muscle training basic compared with no treatment*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (OR of PFMT basic compared with no treatment is 1.28)*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***OR of PFMT basic compared with no treatment is 4*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 75 | 72 | 71 | 71 | 71 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1685 | 41 | 16.06 | –0.14 | Dominated | 4 | 4 | 4 | 4 | 4 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 5 | 5 | 5 | 5 | 5 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1767 | 122 | 15.93 | –0.26 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1790 | 145 | 16.07 | –0.13 | Dominated | 4 | 3 | 3 | 3 | 3 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 13 | 16 | 17 | 17 | 17 |
| ***OR of PFMT basic compared with no treatment is 8*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1579 | | 16.11 | | | 11 | 10 | 10 | 9 | 9 |
| LS–PFMT extra sessions–TVT | 1644 | 65 | 16.20 | 0.09 | 726 | 58 | 59 | 59 | 60 | 60 |
| LS–PFMT basic–TVT | 1648 | 4 | 16.13 | –0.07 | Dominated | 15 | 12 | 11 | 11 | 11 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1656 | 12 | 15.99 | –0.21 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 3 | 3 | 3 | 3 | 3 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 12 | 14 | 16 | 16 | 16 |

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***TABLE 68*** *Sensitivity analyses associated with changes to the cost of pelvic floor muscle training with extra sessions*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (cost of PFMT with extra sessions is based on 12 visits per cycle)*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***Cost of PFMT with extra sessions is increased by 200*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1844 | | 16.20 | | | 70 | 71 | 71 | 71 | 71 |
| LS–PFMT basic–TVT | 1886 | 42 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT extra sessions–SNRI–TVT | 1927 | 82 | 16.06 | –0.13 | Dominated | 6 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1950 | 106 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 128 | 16.08 | –0.12 | Dominated | 19 | 19 | 19 | 19 | 19 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2034 | 190 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |

*continued*

***TABLE 68*** *Sensitivity analyses associated with changes to the cost of pelvic floor muscle training with extra sessions (continued)*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Cost of PFMT with extra sessions is increased by 400*** | | | | | | | | | | |
| LS–PFMT basic–TVT | 1886 | | 16.03 | | | 4 | 3 | 3 | 2 | 4 |
| LS–TVT | 1973 | 86 | 16.08 | 0.05 | Extendedly dominated | 24 | 22 | 22 | 22 | 24 |
| LS–PFMT extra sessions–TVT | 2044 | 72 | 16.20 | 0.17 | 1059 | 65 | 67 | 68 | 68 | 65 |
| LS–PFMT extra sessions–SNRI–TVT | 2127 | 82 | 16.06 | –0.13 | Dominated | 6 | 7 | 7 | 7 | 6 |
| LS–PFMT basic–PFMT extra sessions–TVT | 2143 | 98 | 16.03 | –0.17 | Dominated | 2 | 1 | 2 | 2 | 2 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2227 | 182 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| ***Cost of PFMT with extra sessions is increased by 1000*** | | | | | | | | | | |
| LS–PFMT basic–TVT | 1886 | | 16.03 | | | 10 | 4 | 3 | 3 | 2 |
| LS–TVT | 1973 | 86 | 16.08 | 0.05 | 1577 | 36 | 28 | 25 | 24 | 23 |
| LS–PFMT extra sessions–TVT | 2644 | 672 | 16.20 | 0.12 | 5820 | 48 | 60 | 62 | 64 | 65 |
| LS–PFMT basic–PFMT extra sessions–TVT | 2721 | 76 | 16.02 | –0.17 | Dominated | 5 | 6 | 7 | 7 | 7 |
| LS–PFMT extra sessions–SNRI–TVT | 2727 | 82 | 16.06 | –0.13 | Dominated | 2 | 2 | 2 | 2 | 3 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2805 | 160 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |

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**TABLE 69** *Sensitivity analysis associated with recurrence of tension-free vaginal tape surgery*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (Hilton 2008[214])*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***Long-term cure rate of TVT increased to 81%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1526 | | 16.27 | | | 63 | 61 | 60 | 60 | 60 |
| LS–PFMT extra sessions–SNRI–TVT | 1618 | 93 | 16.12 | –0.14 | Dominated | 6 | 6 | 5 | 5 | 5 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1653 | 127 | 16.08 | –0.18 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–PFMT basic–TVT | 1684 | 159 | 16.15 | –0.12 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1745 | 219 | 15.95 | –0.32 | Dominated | 4 | 3 | 3 | 3 | 4 |
| LS–TVT | 1778 | 252 | 16.20 | –0.07 | Dominated | 27 | 29 | 30 | 31 | 31 |
| ***Long-term cure rate of TVT reduced to 65% in first year and 61% in the second year*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1826 | | 16.09 | | | 79 | 78 | 79 | 79 | 78 |
| LS–PFMT extra sessions–SNRI–TVT | 1888 | 62 | 15.97 | –0.12 | Dominated | 12 | 12 | 12 | 12 | 12 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1913 | 88 | 15.93 | –0.16 | Dominated | 8 | 8 | 8 | 8 | 8 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1983 | 158 | 15.81 | –0.28 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 2207 | 382 | 15.83 | –0.26 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–TVT | 2540 | 714 | 15.73 | –0.36 | Dominated | 1 | 1 | 1 | 2 | 2 |

**Mortality and success rate of TVT surgery**

These results did not change to any extent when the mortality risk of surgery was reduced to zero or the success rate of TVT surgery was increased by 5%. The results of this analysis are shown in Appendices 26–27.

#### *Changes to the structure of the model*

**Probability of containment after failure or recurrence for non-surgical treatment**

The likelihood that the strategies would be considered cost-effective in cure rate base case did not largely change, although the costs for the strategy associated with no surgical treatments were increased, and the outcomes (QALYs) were decreased when the proportion of women using containment products increased (*Table 70*).

**Probability of containment after failure or recurrence for first surgical treatment**

For the model based on cure rates, the likelihood that the different strategies would be considered cost-effective did not change when the probability of using containment products after failure or recurrence was applied, although costs for each given strategy increased and the outcomes (QALYs) decreased when the proportion of women using containment products increased (*Table 71*).

**Adding strategies that use VCs and ES**

As indicated in Model framework, strategies using VC and ES were to be considered in sensitivity analyses. The results of the deterministic analysis are reported in *Table 72*. The strategy that employed lifestyle changes and PFMT basic followed by ES followed by TVT surgery (LS–PFMT basic–ES–TVT) was dominated (more costly and less effective than another strategy). The strategy that employed lifestyle changes and PFMT basic followed by VCs followed by TVT surgery (LS–PFMT basic–VC–TVT) was dominated. The addition of strategies involving VCs and ES had a small probability of being considered cost-effective (less than 12%) and did not greatly influence the results.

#### *Other sensitivity analyses*

Changes to starting ages, time horizon, quality of life and discount rates all had no substantial effect on the results. As the starting age was increased the costs and outcomes for each strategy were reduced because of the increase in mortality as age increased. As the time horizon reduced there was less opportunity for women who had undergone the relatively costly surgery to accrue much benefit. Reducing the discount rate meant that the sustained benefits of surgery were given more weight in the analysis as were the costs of using containment products. Therefore, the LS–TVT strategy increased in its likelihood of being cost-effective. The results of these sensitivity analyses are reported in Appendix 26.

## Results based upon improvement rates

### Deterministic results

In these analyses the costs were lower and the QALYs were higher than those reported in analyses based on cure rates (*Table 73*). The strategy that used lifestyle changes and PFMT basic followed by PFMT with extra sessions followed by TVT surgery (LS–PFMT basic–PFMT extra sessions–TVT) was the least costly (£1795) and the strategy that had lifestyle and PFMT with extra sessions followed by TVT surgery (LS–PFMT extra sessions–TVT) was the most effective (16.37 QALYs). The strategy that had lifestyle changes followed by TVT surgery (LS–TVT) was the most costly (£2425) and the least effective (16.2 QALYs).

### Probabilistic results

Probabilistic analysis was performed comparing all these strategies. As illustrated in *Figure 43*, the strategy that used lifestyle and PFMT with extra sessions followed by TVT surgery (LS–PFMT extra sessions–TVT) has more than a 50% probability of being considered cost-effective when society's willingness to pay for an additional QALY is more than £10,000. The other strategies have a less than 20% chance of being considered cost-effective, as society's willingness to pay more for additional QALYs increases. The strategy that had the least probability of being considered cost-effective was the one that used lifestyle changes followed by TVT surgery.

### Sensitivity analyses

#### *Changes to the effectiveness and cost of PFMT basic and PFMT extra sessions*

**Change in the long-term recurrence rates of PFMT basic and PFMT extra sessions**

When the long-term cure rates of PFMT with extra sessions were the same as PFMT basic, then the strategy that had the highest probability of being cost-effective changed from lifestyle and PFMT

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***TABLE 70*** *Sensitivity analysis associated with changes to the probability of containment after failure or recurrence for non-surgical treatment*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (the probability of containment after failure or recurrence for non-surgical treatments is 0%)*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***Probability of containment after failure or recurrence for non-surgical treatments is 30%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1917 | | 15.85 | | | 59 | 58 | 57 | 57 | 57 |
| LS–PFMT extra sessions–SNRI–TVT | 1992 | 75 | 15.72 | –0.13 | Dominated | 12 | 12 | 12 | 12 | 12 |
| LS–PFMT basic–PFMT extra sessions–TVT | 2018 | 101 | 15.69 | –0.16 | Dominated | 14 | 14 | 14 | 14 | 15 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 2094 | 177 | 15.57 | –0.28 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–TVT | 2249 | 332 | 15.67 | –0.18 | Dominated | 10 | 11 | 11 | 11 | 11 |
| LS–PFMT basic–TVT | 2263 | 346 | 15.57 | –0.28 | Dominated | 4 | 5 | 5 | 5 | 5 |
| ***Probability of containment after failure or recurrence for non-surgical treatments is 60%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 2190 | | 15.50 | | | 52 | 51 | 51 | 51 | 51 |
| LS–PFMT extra sessions–SNRI–TVT | 2259 | 68 | 15.39 | –0.12 | Dominated | 20 | 20 | 19 | 19 | 19 |
| LS–PFMT basic–PFMT extra sessions–TVT | 2279 | 89 | 15.36 | –0.14 | Dominated | 16 | 16 | 17 | 17 | 17 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 2346 | 156 | 15.25 | –0.26 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 2525 | 335 | 15.27 | –0.24 | Dominated | 8 | 9 | 9 | 9 | 9 |
| LS–PFMT basic–TVT | 2639 | 449 | 15.12 | –0.39 | Dominated | 2 | 2 | 3 | 3 | 3 |

***TABLE 71*** *Sensitivity analysis associated with changes to the probability of containment after failure or recurrence of the first surgical treatment*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALYs (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (the probability of containment after failure or recurrence for first surgical treatments is 0%)*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***Probability of containment after failure or recurrence for first surgical treatments is 30%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1680 | | 16.13 | | | 77 | 76 | 75 | 75 | 75 |
| LS–PFMT extra sessions–SNRI–TVT | 1761 | 82 | 16.00 | –0.13 | Dominated | 9 | 9 | 9 | 9 | 9 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1794 | 114 | 15.97 | –0.17 | Dominated | 5 | 5 | 5 | 5 | 5 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1878 | 199 | 15.84 | –0.29 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1937 | 258 | 15.93 | –0.21 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–TVT | 2046 | 367 | 15.94 | –0.19 | Dominated | 9 | 10 | 10 | 10 | 10 |

| Strategy | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALYs (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | Incremental cost per QALY (£) | 10,000 | 20,000 | 30,000 | 40,000 | 50,000 |
| ***Probability of containment after failure or recurrence for first surgical treatments is 60%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1712 | | 16.07 | | | 74 | 74 | 73 | 73 | 73 |
| LS–PFMT extra sessions–SNRI–TVT | 1791 | 79 | 15.94 | –0.13 | Dominated | 13 | 12 | 13 | 13 | 13 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1822 | 111 | 15.91 | –0.16 | Dominated | 6 | 6 | 6 | 6 | 6 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1905 | 193 | 15.78 | –0.29 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–PFMT basic–TVT | 1993 | 281 | 15.83 | –0.24 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–TVT | 2127 | 415 | 15.80 | –0.27 | Dominated | 5 | 6 | 6 | 6 | 6 |
| ***Probability of containment after failure or recurrence for first surgical treatments is 100%*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1755 | | 15.98 | | | 73 | 72 | 73 | 72 | 72 |
| LS–PFMT extra sessions–SNRI–TVT | 1830 | 75 | 15.86 | –0.12 | Dominated | 15 | 15 | 15 | 15 | 15 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1860 | 106 | 15.83 | –0.15 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic –PFMT extra sessions–SNRI –TVT | 1940 | 185 | 15.71 | –0.27 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic–TVT | 2067 | 312 | 15.70 | –0.29 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–TVT | 2234 | 479 | 15.62 | –0.37 | Dominated | 2 | 3 | 3 | 3 | 3 |

***TABLE 72*** *Sensitivity analysis associated with strategies including vaginal cone and electrical stimulation*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (six strategies)*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 74 | 72 | 71 | 71 | 71 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 15 | 18 | 18 | 19 | 19 |
| ***Base case adding two strategies including VC and ES*** | | | | | | | | | | |
| LS–PFMT extra sessions–TVT | 1644 | | 16.20 | | | 77 | 76 | 75 | 75 | 75 |
| LS–PFMT extra sessions–SNRI–TVT | 1727 | 82 | 16.06 | –0.13 | Dominated | 6 | 6 | 6 | 6 | 6 |
| LS–PFMT basic–VC–TVT | 1739 | 95 | 15.93 | –0.27 | Dominated | 1 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1758 | 113 | 16.02 | –0.17 | Dominated | 2 | 2 | 2 | 2 | 2 |
| LS–PFMT basic–PFMT extra session–SNRI–TVT | 1842 | 197 | 15.89 | –0.30 | Dominated | 0 | 0 | 0 | 0 | 0 |
| LS–PFMT basic–TVT | 1886 | 242 | 16.03 | –0.17 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–TVT | 1973 | 328 | 16.08 | –0.12 | Dominated | 13 | 15 | 15 | 16 | 16 |
| LS–PFMT basic–ES–TVT | 2159 | 514 | 15.88 | –0.32 | Dominated | 0 | 0 | 0 | 0 | 0 |

***TABLE 73*** *Base-case results using on the improvement rates of the mixed-treatment model*

| Strategy | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | ICER |
|---|---|---|---|---|---|
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | £2147 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated |
| ***Results without dominated and extendedly dominated options*** | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | £2147 |

with extra sessions followed by TVT surgery (LS–PFMT extra sessions–TVT) to lifestyle and PFMT basic followed by TVT surgery (LS–PFMT basic–TVT) (*Table 74*). Similarly, reducing the cure rates of both PFMT basic and PFMT with extra sessions also meant that lifestyle and PFMT basic followed by TVT surgery (LS–PFMT basic–TVT) was most likely to be cost-effective.

### Changes to the ORs of PFMT basic and PFMT extra sessions compared with no treatment

The results of the sensitivity analysis performed using different point estimates in clinical effectiveness for improvement rates of PFMT extra sessions and PFMT basic are reported in *Table 75*. When the OR of PFMT with extra sessions compared with no treatment falls, strategies involving this treatment are less likely to be considered cost-effective. The strategy that increased more in terms of the likelihood of being cost-effective was lifestyle changes and PFMT basic followed by TVT surgery (LS–PFMT basic–TVT).

### Changes to the cost of PFMT with extra sessions

As indicated in Resource utilisation and cost estimation, the cost of PFMT with extra sessions may be underestimated. When the cost of PFMT with extra sessions increases, the strategies containing this treatment became less likely to be considered cost-effective (*Table 76*). When the cost of PFMT increased beyond £200 there was an increasing chance that lifestyle changes and PFMT basic followed by TVT surgery (LS–PFMT basic–TVT) would be considered cost-effective.

## *Changes to the effectiveness of surgery*

### Change in the recurrence rates of TVT

As indicated in Estimation of model probabilities, the long-term recurrence rates of incontinence after TVT surgery were estimated from the trial by Ward and colleagues.[213] There is some uncertainty attached to this estimate and it is probable that this value could be either an over- or underestimate. As long-term cure rates of TVT surgery decreased, the costs associated with long-term TVT surgery for each strategy were increased because the long-term recurrence of TVT surgery was also increased leading to a decrease in long-term benefits. *Table 77* describes the results of the sensitivity analyses for changes in the long-term cure rates for TVT surgery. When the probability was increased to 81%, the likelihood that lifestyle changes and PFMT with extra sessions followed by TVT (LS–PFMT extra sessions–TVT) was cost-effective fell to approximately 60%. The main gainer was the strategy of lifestyle changes followed by TVT (LS–TVT), which had a 30% chance of being considered cost-effective over the range of values considered. When the probability was reduced to 65%, the likelihood that the strategy lifestyle changes and PFMT with extra sessions followed by TVT (LS–PFMT extra sessions-TVT) was considered to be cost-effective is increased to 80% and that of lifestyle changes followed by TVT is reduced to 1% (*Table 78*).

### Mortality and success rate of TVT

The results did not change to any extent when the mortality risk was reduced to zero or the success rate of TVT was increased to 5%. The results of these analyses are shown in Appendix 27.

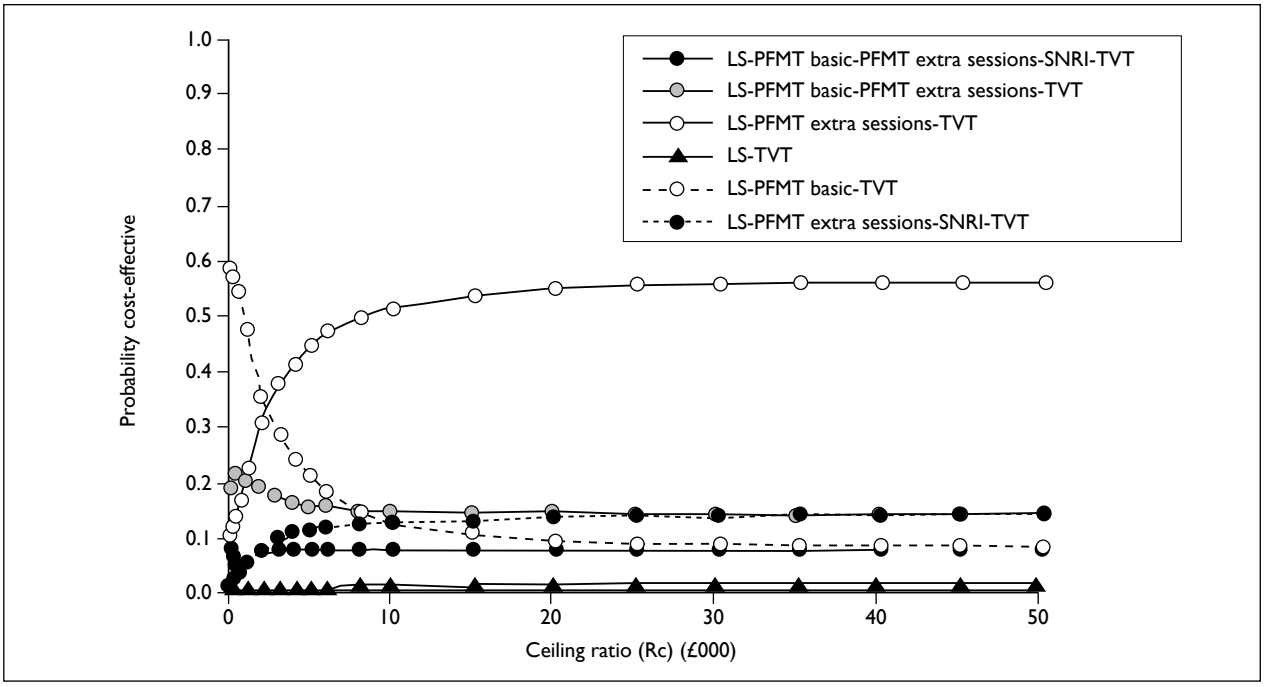


***FIGURE 43*** *Cost-effectiveness acceptability curves determined by society's willingness to pay for a quality-adjusted life-year for the six strategies.*

### *Changes to the structure of the model*

**Probability of containment after failure or recurrence for non-surgical treatment**

The likelihood that the strategies would be considered cost-effective in the improvement model hardly changed when the probability that women might use containment products rather than progress to the next active treatment was increased to 30% and 60% (*Table 78*).

**Probability of containment after failure or recurrence for first surgical treatment**

When women might use containment products rather than resort to a second operation (if one was necessary) the likelihood of the strategy lifestyle changes and basic PFMT followed by PFMT with extra sessions followed by tension-free tape (LS-PFMT basic-PFMT extra sessions-TVT) would be considered cost-effective reduced (*Table 79*).

**Adding strategies using VCs and ES**

For the sensitivity analysis the only difference was that the likelihood of the strategy involving the use of VCs (LS–PFMT basic–VC–TVT) was more likely to be considered cost-effective instead of the lifestyle changes and basic PFMT followed by TVT (LS–PFMT basic–TVT) (*Table 80*).

### *Other sensitivity analysis*

Changes to starting ages, quality of life and discount rates had no substantial effect on the results. As the starting age was increased, the costs and outcomes for each strategy were reduced because of the increase in mortality as age increased. However, as the time horizon was reduced in the analysis using the improvement rates, the non-dominated strategy of lifestyle-PFMT basic-PFMT with extra sessions followed by TVT (LS–PFMT basic–PFMT extra sessions–TVT) had a slightly increased likelihood of being considered cost-effective. Reducing the discount rate meant that the sustained benefits of surgery were given more weight in the analysis as were the costs of containment products. The results of these sensitivity analyses are reported in Appendix 27.

## Summary of results

The economic model presented in this chapter considered some of the management strategies that have the potential to be, or are currently being, used in managing women with SUI. These strategies included the following interventions: lifestyle changes, physical therapies, medical therapies and surgery. The effectiveness data for non-surgical treatments came from the results of mixed-treatment model. This was because the data

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**TABLE 74** *Sensitivity analyses associated with recurrence of pelvic floor muscle training (PFMT) with extra sessions and PFMT basic*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Strategy | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | Incremental cost per QALY (£) | 10,000 | 20,000 | 30,000 | 40,000 | 50,000 |
| ***Base case [cure rates of PFMT basic and PFMT with extra sessions at 5 and 15 years in the Lagro–Janssen (1998)[210] and Bø (2005)[208] studies]*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 8 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 64 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 1973 | 294 | 16.08 | –0.23 | Dominated | 1 | 1 | 1 | 1 | 1 |
| ***Long-term cure rates of PFMT with extra sessions were the same as the that of PFMT basic*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1870 | | 16.29 | | | 11 | 10 | 10 | 10 | 10 |
| LS–PFMT basic–TVT | 1873 | 3 | 16.34 | 0.06 | 53 | 56 | 54 | 52 | 51 | 50 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1885 | 11 | 16.2 | –0.14 | Dominated | 7 | 7 | 7 | 7 | 7 |
| LS–PFMT extra sessions–TVT | 2035 | 162 | 16.34 | 0 | Dominated | 15 | 16 | 16 | 17 | 17 |
| LS–PFMT extra sessions–SNRI–TVT | 2071 | 198 | 16.23 | –0.12 | Dominated | 9 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 552 | 16.20 | –0.14 | Dominated | 2 | 3 | 5 | 5 | 6 |

*continued*

***TABLE 74*** *Sensitivity analyses associated with recurrence of pelvic floor muscle training (PFMT) with extra sessions and PFMT basic (continued)*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Long-term cure rate of PFMT with extra sessions and PFMT basic is reduced by 20%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1918 | | 16.26 | | | 13 | 12 | 12 | 12 | 11 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1936 | 18 | 16.18 | –0.09 | Dominated | 7 | 6 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1939 | 21 | 16.32 | 0.06 | 376 | 54 | 50 | 49 | 48 | 47 |
| LS–PFMT extra sessions–TVT | 2101 | 162 | 16.32 | 0 | Dominated | 15 | 15 | 16 | 17 | 17 |
| LS–PFMT extra sessions–SNRI–TVT | 2142 | 203 | 16.19 | –0.13 | Dominated | 7 | 8 | 8 | 8 | 8 |
| LS–TVT | 2425 | 486 | 16.20 | –0.12 | Dominated | 5 | 8 | 9 | 10 | 10 |
| ***Cure rate of PFMT with extra sessions and PFMT basic is reduced by 60%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 2081 | | 16.19 | | | 11 | 10 | 10 | 10 | 10 |
| LS–PFMT basic–TVT | 2098 | 17 | 16.25 | 0.06 | 278 | 55 | 50 | 47 | 46 | 45 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2112 | 14 | 16.09 | –0.17 | Dominated | 3 | 3 | 3 | 3 | 3 |
| LS–PFMT extra sessions–TVT | 2260 | 162 | 16.25 | 0 | Dominated | 10 | 12 | 13 | 14 | 14 |
| LS–PFMT extra sessions–SNRI–TVT | 2313 | 215 | 16.11 | –0.14 | Dominated | 4 | 4 | 4 | 4 | 4 |
| LS–TVT | 2425 | 327 | 16.20 | –0.05 | Dominated | 17 | 21 | 23 | 23 | 24 |

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**TABLE 75** *Sensitivity analyses associated with changes to the odds ratio of pelvic floor muscle training with extra sessions compared with no treatment*

| | Deterministic result | | | | | Probability cost–effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (OR of PFMT with extra sessions compared with no treatment is 25.4)*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 8 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 64 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 3 |
| ***OR of PFMT with extra sessions compared with no treatment is 10*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 7 | 6 | 6 | 6 | 6 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 6 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 7 | 6 | 6 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 65 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 11 | 12 | 12 | 12 | 12 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 1 | 1 | 2 | 2 |
| ***OR of PFMT with extra sessions compared with no treatment is 3*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1858 | | 16.29 | | | 10 | 9 | 9 | 8 | 8 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1872 | 14 | 16.21 | –0.08 | Dominated | 6 | 6 | 5 | 5 | 5 |
| LS–PFMT basic–TVT | 1873 | 15 | 16.34 | 0.06 | 268 | 53 | 47 | 46 | 45 | 44 |
| LS–PFMT extra sessions–TVT | 2068 | 195 | 16.32 | –0.02 | Dominated | 24 | 29 | 30 | 32 | 32 |
| LS–PFMT extra sessions–SNRI–TVT | 2102 | 229 | 16.21 | –0.14 | Dominated | 5 | 5 | 5 | 5 | 5 |
| LS–TVT | 2425 | 552 | 16.20 | –0.14 | Dominated | 2 | 4 | 5 | 5 | 5 |

***TABLE 76*** *Sensitivity analysis associated with changes to the cost of pelvic floor muscle training with extra sessions strategy*

| | Deterministic result | | | | | Probability cost–effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Strategy | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | Incremental cost per QALY (£) | 10,000 | 20,000 | 30,000 | 40,000 | 50,000 |
| ***Base case (cost of PFMT with extra sessions is based on 12 visits per cycle)*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 8 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 64 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 3 |
| ***Cost of PFMT with extra sessions is increased by 200*** | | | | | | | | | | |
| LS–PFMT basic–TVT | 1873 | | 16.34 | | | 9 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1939 | 66 | 16.31 | –0.04 | Dominated | 10 | 8 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1948 | 75 | 16.24 | –0.11 | Dominated | 7 | 6 | 6 | 6 | 6 |
| LS–PFMT extra sessions–TVT | 2138 | 265 | 16.37 | 0.03 | 8510 | 63 | 67 | 67 | 67 | 68 |
| LS–PFMT extra sessions–SNRI–TVT | 2165 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 11 |
| LS–TVT | 2425 | 287 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 2 |

| Strategy | Deterministic result | | | | | Probability cost–effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | Incremental cost per QALY (£) | 10,000 | 20,000 | 30,000 | 40,000 | 50,000 |
| ***Cost of PFMT with extra sessions is increased by 400*** | | | | | | | | | | |
| LS–PFMT basic–TVT | 1873 | | 16.34 | | | 54 | 31 | 20 | 14 | 11 |
| LS–PFMT basic–PFMT extra sessions–TVT | 2084 | 211 | 16.31 | –0.04 | Dominated | 8 | 7 | 7 | 7 | 6 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2092 | 219 | 16.24 | –0.11 | Dominated | 6 | 6 | 6 | 6 | 6 |
| LS–PFMT extra sessions–TVT | 2338 | 465 | 16.37 | 0.03 | 14,932 | 23 | 42 | 53 | 59 | 62 |
| LS–PFMT extra sessions–SNRI–TVT | 2365 | 27 | 16.27 | –0.10 | Dominated | 9 | 11 | 12 | 12 | 12 |
| LS–TVT | 2425 | 87 | 16.20 | –0.17 | Dominated | 1 | 3 | 3 | 3 | 3 |
| ***Cost of PFMT with extra sessions is increased by 1000*** | | | | | | | | | | |
| LS–PFMT basic–TVT | 1873 | | 16.34 | | | 77 | 54 | 42 | 31 | 24 |
| LS–TVT | 2425 | 552 | 16.20 | –0.14 | Dominated | 3 | 4 | 4 | 4 | 4 |
| LS–PFMT basic–PFMT extra sessions–TVT | 2517 | 644 | 16.31 | –0.04 | Dominated | 4 | 5 | 6 | 6 | 6 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 2526 | 652 | 16.24 | –0.11 | Dominated | 3 | 5 | 5 | 5 | 5 |
| LS–PFMT extra sessions–TVT | 2938 | 1065 | 16.37 | 0.03 | 34,199 | 8 | 23 | 34 | 43 | 50 |
| LS–PFMT extra sessions–SNRI–TVT | 2965 | 27 | 16.27 | –0.10 | Dominated | 6 | 9 | 10 | 11 | 11 |

***TABLE 77*** *Sensitivity analysis associated with recurrence of tension-free vaginal tape surgery*

| | Deterministic result | | | | | Probability cost-effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (Hilton 2008[214])*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 8 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 64 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 3 |
| ***Long–term cure rate of TVT increased to 81%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1767 | | 16.32 | | | 5 | 3 | 3 | 3 | 3 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1780 | 13 | 16.25 | –0.07 | Dominated | 3 | 3 | 3 | 3 | 3 |
| LS–PFMT basic–TVT | 1808 | 41 | 16.38 | 0.06 | 698 | 14 | 10 | 9 | 8 | 8 |
| LS–PFMT extra sessions–TVT | 1884 | 76 | 16.40 | 0.02 | 3103 | 59 | 62 | 62 | 62 | 61 |
| LS–PFMT extra sessions–SNRI–TVT | 1919 | 34 | 16.30 | –0.11 | Dominated | 13 | 13 | 13 | 13 | 13 |
| LS–TVT | 2260 | 375 | 16.31 | –0.09 | Dominated | 6 | 9 | 10 | 11 | 11 |
| ***Long–term cure rate of TVT reduced to 65% in first year and 61% in the second year*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1831 | | 16.29 | | | 20 | 16 | 15 | 14 | 14 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1833 | 3 | 16.22 | –0.07 | Dominated | 9 | 8 | 8 | 8 | 8 |
| LS–PFMT basic–TVT | 1963 | 132 | 16.29 | <0.01 | Extendedly dominated | 6 | 5 | 5 | 5 | 5 |
| LS–PFMT extra sessions–TVT | 2012 | 182 | 16.33 | 0.04 | 4356 | 55 | 59 | 61 | 62 | 62 |
| LS–PFMT extra sessions–SNRI–TVT | 2029 | 17 | 16.24 | –0.10 | Dominated | 11 | 11 | 11 | 11 | 11 |
| LS–TVT | 2921 | 908 | 15.85 | –0.48 | Dominated | 0 | 0 | 0 | 0 | 0 |

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**TABLE 78** *Sensitivity analysis associated with probability of containment after failure or recurrence for non-surgical treatment*

| Strategy | Deterministic result | | | | | Probability cost–effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | Incremental cost per QALY (£) | 10,000 | 20,000 | 30,000 | 40,000 | 50,000 |
| ***Base case (the probability of containment after failure or recurrence for non-surgical treatments is 0%)*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 8 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 64 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 3 |
| ***Probability of containment after failure or recurrence for non-surgical treatments is 30%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1850 | | 16.07 | | | 19 | 18 | 17 | 17 | 17 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1855 | 5 | 16.11 | 0.04 | 113 | 40 | 38 | 38 | 37 | 37 |
| LS–PFMT basic–TVT | 2027 | 172 | 16.01 | –0.11 | Dominated | 9 | 10 | 9 | 9 | 10 |
| LS–PFMT extra sessions–TVT | 2064 | 208 | 16.08 | –0.03 | Dominated | 23 | 25 | 25 | 26 | 26 |
| LS–PFMT extra sessions–SNRI–TVT | 2074 | 218 | 16.01 | –0.11 | Dominated | 9 | 9 | 10 | 10 | 10 |
| LS–TVT | 2425 | 570 | 15.85 | –0.27 | Dominated | 0 | 0 | 1 | 1 | 1 |
| ***Probability of containment after failure or recurrence for non-surgical treatments is 60%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1898 | | 15.90 | | | 37 | 36 | 35 | 35 | 35 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1916 | 18 | 15.92 | 0.02 | 991 | 42 | 41 | 40 | 40 | 40 |
| LS–PFMT basic–TVT | 2181 | 265 | 15.67 | –0.25 | Dominated | 2 | 3 | 3 | 3 | 3 |
| LS–PFMT extra sessions–TVT | 2182 | 266 | 15.74 | –0.18 | Dominated | 14 | 15 | 16 | 16 | 16 |
| LS–PFMT extra sessions–SNRI–TVT | 2189 | 273 | 15.79 | –0.13 | Dominated | 5 | 6 | 6 | 6 | 6 |
| LS–TVT | 2425 | 509 | 15.50 | –0.42 | Dominated | 0 | 0 | 0 | 0 | 0 |

***TABLE 79*** *Sensitivity analysis associated with probability of containment after failure or recurrence for first surgical treatment*

| | Deterministic result | | | | | Probability cost–effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (the probability of containment after failure or recurrence for first surgical treatments is 0%)*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 8 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 64 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 3 |
| ***Probability of containment after failure or recurrence for first surgical treatments is 30%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1793 | | 16.29 | | | 14 | 11 | 11 | 10 | 10 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1801 | 8 | 16.23 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1877 | 84 | 16.31 | 0.02 | Extendedly dominated | 11 | 9 | 8 | 8 | 8 |
| LS–PFMT extra sessions–TVT | 1940 | 147 | 16.35 | 0.05 | 2744 | 58 | 62 | 63 | 64 | 64 |
| LS–PFMT extra sessions–SNRI–TVT | 1967 | 26 | 16.25 | –0.10 | Dominated | 10 | 11 | 11 | 11 | 12 |
| LS–TVT | 2460 | 520 | 16.07 | –0.28 | Dominated | 0 | 0 | 0 | 0 | 0 |

| Strategy | Deterministic result | | | | | Probability cost–effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Cost (£) | Incremental cost (£) | QALYs | Incremental QALYs | Incremental cost per QALY (£) | 10,000 | 20,000 | 30,000 | 40,000 | 50,000 |
| ***Probability of containment after failure or recurrence for first surgical treatments is 60%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1792 | | 16.28 | | | 20 | 17 | 16 | 16 | 16 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1799 | 8 | 16.21 | –0.07 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–PFMT basic–TVT | 1881 | 89 | 16.28 | 0 | Dominated | 12 | 9 | 8 | 8 | 7 |
| LS–PFMT extra sessions–TVT | 1943 | 151 | 16.32 | 0.04 | 3731 | 49 | 54 | 56 | 56 | 57 |
| LS–PFMT extra sessions–SNRI–TVT | 1968 | 25 | 16.22 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2495 | 553 | 15.94 | –0.38 | Dominated | 0 | 0 | 0 | 0 | 0 |
| ***Probability of containment after failure or recurrence for first surgical treatments is 100%*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1789 | | 16.26 | | | 27 | 25 | 24 | 24 | 24 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1797 | 8 | 16.20 | –0.06 | Dominated | 13 | 11 | 11 | 11 | 11 |
| LS–PFMT basic–TVT | 1886 | 96 | 16.23 | –0.03 | Dominated | 9 | 7 | 7 | 7 | 7 |
| LS–PFMT extra sessions–TVT | 1945 | 156 | 16.28 | 0.02 | 6811 | 42 | 46 | 47 | 47 | 47 |
| LS–PFMT extra sessions–SNRI–TVT | 1970 | 24 | 16.19 | –0.09 | Dominated | 10 | 11 | 11 | 12 | 12 |
| LS–TVT | 2542 | 597 | 15.77 | –0.52 | Dominated | 0 | 0 | 0 | 0 | 0 |

***TABLE 80*** *Sensitivity analysis associated with strategies including vaginal cone and electrical stimulation*

| | Deterministic result | | | | | Probability cost–effective for different threshold values for society's willingness to pay for a QALY (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Strategy** | **Cost (£)** | **Incremental cost (£)** | **QALYs** | **Incremental QALYs** | **Incremental cost per QALY (£)** | **10,000** | **20,000** | **30,000** | **40,000** | **50,000** |
| ***Base case (six strategies)*** | | | | | | | | | | |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | | 16.31 | | | 8 | 7 | 7 | 7 | 7 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 8 | 16.24 | –0.07 | Dominated | 7 | 7 | 6 | 6 | 6 |
| LS–PFMT basic–TVT | 1873 | 78 | 16.34 | 0.04 | Extendedly dominated | 10 | 7 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 143 | 16.37 | 0.07 | 2147 | 64 | 68 | 69 | 69 | 69 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 3 |
| ***Base case adding two strategies including VC and ES*** | | | | | | | | | | |
| LS–PFMT basic–VC–TVT | 1615 | | 16.31 | | | 11 | 8 | 6 | 6 | 5 |
| LS–PFMT basic–PFMT extra sessions–TVT | 1795 | 179 | 16.31 | <0.01 | Extendedly dominated | 1 | 1 | 1 | 2 | 2 |
| LS–PFMT basic–PFMT extra sessions–SNRI–TVT | 1803 | 188 | 16.24 | –0.07 | Dominated | 6 | 6 | 6 | 6 | 6 |
| LS–PFMT basic–ES–TVT | 1872 | 257 | 16.30 | –0.01 | Dominated | 1 | 1 | 1 | 1 | 1 |
| LS–PFMT basic–TVT | 1873 | 258 | 16.34 | 0.04 | Extendedly dominated | 9 | 6 | 6 | 6 | 5 |
| LS–PFMT extra sessions–TVT | 1938 | 323 | 16.37 | 0.07 | 4723 | 61 | 67 | 68 | 68 | 68 |
| LS–PFMT extra sessions–SNRI–TVT | 1965 | 27 | 16.27 | –0.10 | Dominated | 10 | 10 | 10 | 10 | 10 |
| LS–TVT | 2425 | 487 | 16.20 | –0.17 | Dominated | 1 | 2 | 2 | 2 | 3 |

of direct comparison were not adequate, as they were based on very few and very small studies.

There were no data on the clinical effectiveness of lifestyle modification interventions. It was therefore assumed in the model that all women have received lifestyle change advice in each strategy and then go to the next treatment. There were no reliable data on the long-term clinical effectiveness of PFMT, drug therapy and TVT surgery. Long-term recurrence rates for PFMT, drug therapy and TVT were estimated by parametric extrapolation methods of the limited evidence base. Furthermore, there was also no information associated with long-term clinical effectiveness of other non-surgical treatments.

The cost–utility analyses were conducted using EQ-5D scores to value health effects in the two base-case analyses. Broadly speaking, the results that were based on cure rates were similar to those based on improvement rates.

In the cure-rate base-case analysis there was only one non-dominated or non-extendedly dominated strategy (i.e. it provided more benefits than a less costly strategy or more benefits than could be provided should a combination of a less and more costly strategies be used):

- lifestyle changes and PFMT with extra sessions followed by TVT (LS–PFMT extra sessions–TVT).

In the analysis based on improvement rates there were two strategies that were not dominated or extendedly dominated:

- lifestyle changes and PFMT with extra sessions followed by TVT surgery (LS–PFMT extra sessions–TVT) and
- lifestyle changes and PFMT basic followed by PFMT with extra sessions then TVT surgery (LS–PFMT basic–PFMT extra sessions–TVT).

For the cure-rate base-case analysis, the strategy 'lifestyle changes and PFMT extra session followed by TVT (LS–PFMT extra sessions–TVT)' was the least costly (£1644) and the most effective (16.20 QALYs) strategy. For the improvement-rate base-case analysis, the strategy 'lifestyle changes and PFMT basic followed by PFMT with extra sessions followed by TVT surgery (LS–PFMT basic–PFMT extra sessions–TVT)' was the least costly (£1795) and provided 16.31 QALYs. For both base-case analyses the strategy of 'lifestyle changes followed by TVT surgery (LS–TVT)' (mean cost = £1793 for cure rates and £2524 for improvement rates) was the most costly.

In the cure-rate base case, the strategy of 'lifestyle changes and PFMT basic followed by PFMT with extra sessions followed by SNRI and then TVT surgery' was the least effective (providing 15.89 QALYs) strategy. In the improvement-rate base-case analysis the strategy that used 'lifestyle changes followed by TVT surgery' was the least effective.

Although the differences between strategies in terms of costs and effects in both base-case analyses appear not to be large, the important issue is whether society is willing to pay for any additional gain. Only two strategies have a likelihood of being considered to be cost-effective of greater than 50% when the threshold is £20,000–30,000 per QALY: LS–PFMT extra session–TVT (cure rates) and LS–PFMT basic–PFMT extra sessions–TVT(improvement rates). All of the other strategies had between 0% and 20% likelihood of being considered cost-effective if society were willing to pay between £20,000 and £30,000 per QALY.

Results of probabilistic sensitivity analyses, performed to handle the uncertainty around the parameter estimates used within the model, were broadly consistent with the point estimates for both base-case analyses. The likelihood that different strategies might be considered cost-effective changed slightly in some sensitivity analyses. The results of the model were sensitive to changes in the long-term cure rates. However, these changes did not alter the conclusions.

The results of the sensitivity analyses were broadly similar to those of the base cases when different values of quality of life were used to estimate QALYs and when other assumptions made within the model were changed. For example, when the proportion of patients that used containment products after failure or recurrence for non-surgical or surgical treatments were changed.

The modelling performed in this section provided and contributed to the evidence available for evaluating the cost-effectiveness of non-surgical interventions for the treatment of SUI in women. This work also provided information on the long-term costs of managing women with SUI.

The data that were used to estimate cost-effectiveness came from the MTC model. These data represented the best available evidence to date

on the relative effectiveness of the non-surgical treatments.

The lack of long-term data on the cure and recurrence rates of the interventions under consideration limits the analyses. Long-term performance was extrapolated from short-term data. Also assumptions had to be made about these parameters; for example, the recurrence rates of PFMT with extra sessions were assumed to be the same as the PFMT basic. Due to a lack of reliable data, it is unclear whether this assumption is valid or not.

There was also uncertainty around the costs estimates. It was very difficult to determine the 'standard' number of sessions that there were in basic PFMT. Therefore, it was assumed that basic PFMT consisted of six sessions. These assumptions were also applied to all therapies that had some form of PFMT. The other area where there was a lack of data was the quality-of-life estimates.

# Chapter 10
# Discussion

Stress incontinence is the most common type of urinary incontinence experienced by women. The treatment options can be classified as non-surgical and surgical. Non-surgical interventions, such as PFMT, may require long-term adherence to an exercise regimen to produce continued benefit but (apart from medical therapies) they have few or no adverse events. Surgical treatment, on the other hand, may have a higher rate of *cure* or *improvement* in symptoms but has a greater risk of complications.

The choice of treatment is influenced by patient preference, professional advice and the research evidence. It takes into account factors such as symptom severity, degree of interference with lifestyle, presence of related problems and degree of comorbidity. A woman may seek and receive several different treatments during the course of her lifetime, and, from a health service perspective, it is important to balance effectiveness, potential adverse events and costs of individual treatments and alternative care pathways. This study aimed to assess the clinical effectiveness and cost-effectiveness of alternative non-surgical treatments and treatment pathways for women with SUI.

## Main results

### Summary of results from the survey of factors important to women with SUI

Central to the estimation of both effectiveness and cost-effectiveness is that the outcome measures chosen reflect factors that are important to the women themselves. As reported in Chapter 4, members of The Bladder and Bowel Foundation (formerly members of InContact)[99] ($n = 188$ women) were prospectively surveyed with the aim of gathering information on outcomes of importance to them and 105 responses were received. Areas of importance to women who suffer from SUI were assessed using a PGI. In addition, the questionnaire included the King's Health Questionnaire and the EQ-5D. The survey identified 38 different areas of life affected by SUI. The five most frequently reported were: going out or socialising, personal hygiene, sleep, shopping and depression. Ideally, these areas would then be used to derive outcomes of relevance to women in primary studies and systematic reviews. However, these outcomes were rarely considered in primary studies. PGI scores and EQ-5D scores were positively correlated and these correlations were statistically significant. Nevertheless, the areas identified by the PGI did not map well to the EQ-5D. Correlations between the seven domains of the King's Health Questionnaire and PGI were all negative but only two were statistically significant: personal relationships and severity measures. These data suggest that the PGI may be capturing concerns of women who suffer from SUI which are not adequately captured by generic instruments such as the EQ-5D.

### Summary of results from the systematic review of effectiveness

The focus of the systematic reviews of effectiveness was on the rates of cure and cure or improvement (this latter outcome is referred to in the text as improvement), quality of life, and adverse events. The systematic review of clinical effectiveness identified 88 trials reporting data from 9721 women. The included studies covered five generic interventions (PFMT with or without BF, ES, VCs, BT and SNRI medications) with many variations and combinations of them. Data were available for 37 interventions and 68 direct head-to-head (pairwise) comparisons. The MTC included 14 treatments and took data from the 55 trials (6608 women) that reported data for these treatments. Cure data were available for 3560 women (38 trials) and improvement data were available for 6140 women (47 trials). In total, 41% and 61% of these data for cure and improvement, respectively, came from 10 trials comparing SNRI with placebo.

A summary of the treatment comparisons showing both the direct comparisons and the MTC results is given in *Table 81*. PFMT with or without BF appeared to be more effective than no treatment both in terms of *cure* and *improvement*. ES, SNRI, BT and PFMT plus ES had, on average, higher odds of cure and improvement compared with no treatment. VCs, and PFMT plus SNRI had higher

odds of improvement compared with no treatment. The direct, head-to-head comparisons were inconclusive about whether PFMT with or without BF was better than other treatments. For example, the ORs (point estimate) for improvement favoured PFMT (with or without BF) over other standalone treatments (ES, VCs, BT and SNRI), but the CIs were wide and included one (no difference).

The MTC results provided similar results to the direct comparisons. Because this comparison was able to draw upon both the direct and indirect comparative evidence, it was able to provide more precise estimates of relative effectiveness than provided by the direct pairwise comparisons.

Pelvic floor muscle training, when supervised, with extra sessions (more than two sessions or contacts with a health-care professional per month), was better than basic PFMT in terms of both cure and improvement, as shown by both direct evidence and the MTC model (see the final row of each section of *Table 81* and, for the MTC model only, see *Table 82*).

Both pelvic floor muscle training with extra sessions,and PFMT with BF were also more effective in terms of both cure and improvement compared with: no treatment; ES; VCs; or SNRI (*Table 82*). There was considerable uncertainty about whether either is better than BT.

Evidence about PFMT (with or without BF) combined with an adjunct treatment (e.g. ES, VCs) was generally inconclusive, largely due to a lack of available data. Adding BT to PFMT with BF appears to be more effective than PFMT with BF alone or BT alone, although interpretation requires caution, as this finding is based upon data from a single trial that considered a population who had both stress and urgency incontinence symptoms. The MTC results for these pairs of treatments were also inconclusive.

All of these results need to be considered cautiously. Importantly, the longevity of any treatment effects was unclear because of the small amount of data available and limited duration of follow-up.

## Summary of results from the economic model

Data from the MTCs were used to populate an economic model. The economic model presented in this report compared eight different management strategies. These were chosen because they were believed to be relevant to the NHS and they might potentially be cost-effective. The model compared cumulative costs and QALYs for a 40-year time horizon for two separate analyses; one based on *cure* rates and the other based on *improvement* rates.

In the model based on *cure* rates, the least costly strategy was lifestyle intervention, followed by PFMT with extra sessions (or PFMT plus BF) and then surgery if necessary, with a mean cost per woman treated of £1644. The most costly strategy was lifestyle changes followed by surgery with a mean cost per woman treated of £1973. In terms of QALYs, the least effective strategy was lifestyle changes followed by surgery (mean QALYs per woman treated = 16.1). The most effective was lifestyle changes followed by PFMT with extra sessions followed by surgery if necessary (mean QALYs per woman treated = 16.2). There were relatively modest differences between treatments in terms of both QALYs and costs. One interpretation of these results would be that any of these treatment strategies could be equally well provided by the NHS. Nevertheless, when the incremental cost-effectiveness was estimated then it was highly likely that lifestyle changes followed by PFMT with extra sessions followed by surgery if necessary would be cost-effective (there was an over 70% chance that this intervention would be considered cost-effective at a threshold value of £20,000 per QALY).

For the model based on *improvement* rates, the QALYs and costs for each treatment were greater than those for the model based on *cure* rates. This is because *improvement* rates were greater than *cure* rates but no quality-of-life data that were specific to improvement were available. Therefore, it was assumed that the utility associated with *improvement* was the same as the utility associated with *cure*. Costs were greater because it was assumed that women would incur some costs of containment products, even if their symptoms were improved. As a consequence, comparisons with the analysis made using *cure* rates should be interpreted cautiously.

In the model based on *improvement* rates, the least costly strategy was lifestyle changes, followed by PFMT basic, PFMT with extra sessions and then surgery (mean cost per woman treated = £1795), and the most costly was lifestyle changes followed by surgery with a mean cost per woman treated of £2425. In terms of QALYs, the least effective

***TABLE 81*** *Treatment comparisons from direct- and mixed-treatment methods*

| Intervention | | Direct comparison | | | MTC |
|---|---|---|---|---|---|
| **1** | **2** | **Number of trials** | **Number of people** | **Est (95% CrI)** | **Est (95% CrI)** |
| ***Cure*** | | | | | |
| PFMT | NT | 8 | 605 | 5.41 (1.64 to 17.82) | 4.56 (1.95 to 12.4) |
| PFMT + BF | NT | 2 | 110 | 21.54 (3.65 to 126.98) | 9.65 (3.37 to 33.3) |
| ES | NT | 6 | 288 | 1.10 (0.41 to 2.94) | 1.63 (0.506 to 5.54) |
| SNRI | NT | 3 | 1292 | 1.46 (1.00 to 2.14) | 1.42 (0.377 to 5.35) |
| BT | NT | 1 | 123 | 4.03 (0.80 to 20.23) | 4.87 (1.05 to 26.1) |
| PFMT + ES | NT | 2 | 155 | 1.76 (0.27 to 11.54) | 4.59 (1.20 to 22.4) |
| PFMT | ES | 5 | 124 | 2.65 (0.82 to 8.60) | 2.82 (0.911 to 9.3) |
| PFMT | VC | 3 | 245 | 0.61 (0.09 to 3.95) | 0.963 (0.274 to 3.51) |
| PFMT + BF | VC | 1 | 46 | 0.86 (0.25 to 2.93) | 2.03 (0.528 to 8.53) |
| PFMT | BT | 1 | 75 | 2.61 (0.98 to 6.96) | 0.935 (0.206 to 4. 28) |
| PFMT + BF | BT | 1 | 132 | 0.67 (0.25 to 1.76) | 1.98 (0.431 to 9.62) |
| ES | VC | 2 | 106 | 1.00 (0.26 to 3.91) | 0.341 (0.0782 to 1.48) |
| PFMT | PFMT + ES | 4 | 133 | 1.02 (0.29 to 3.55) | 0.998 (0.257 to 3.47) |
| PFMT | PFMT + VC | 1 | 46 | 0.44 (0.09 to 2.10) | 0.41 (0.0246 to 6.2) |
| PFMT + BF | PFMT + BF + BT | 1 | 125 | 0.32 (0.13 to 0.79) | 0.542 (0.0614 to 4.95) |
| PFMT + ES | ES | 1 | 22 | 3.75 (0.33 to 43.31) | 2.82 (0.598 to 15.5) |
| PFMT + BF + BT | BT | 1 | 129 | 2.11 (0.92 to 4.82) | 3.64 (0.419 to 32.7) |
| PFMT | PFMT + BF | 8 | 370 | 0.48 (0.30 to 0.77) | 0.474 (0.2 to 1.07) |
| PFMT basic | PFMT extra | 3 | 118 | 0.11 (0.03 to 0.43) | 0.12 (0.0462 to 0.268) |

*continued*

***TABLE 81*** *Treatment comparisons from direct- and mixed-treatment methods (continued)*

| Intervention | | Direct comparison | | | MTC |
|---|---|---|---|---|---|
| 1 | 2 | Number of trials | Number of people | Est (95% CrI) | Est (95% CrI) |
| ***Improvement*** | | | | | |
| PFMT | NT | 11 | 689 | 11.75 (3.49 to 39.55) | 8.97 (4.4 to 20.8) |
| PFMT + BF | NT | 2 | 110 | 24.20 (2.02 to 290.58) | 21.7 (7.24 to 75.2) |
| ES | NT | 7 | 369 | 3.93 (1.43 to 10.80) | 4.75 (2.02 to 11.9) |
| VC | NT | 2 | 212 | 5.43 (0.07 to 396.77) | 6.99 (2.63 to 20.7) |
| SNRI | NT | 10 | 3672 | 2.02 (1.67 to 2.44) | 2.24 (1.09 to 4.68) |
| BT | NT | 1 | 123 | 9.60 (4.22 to 21.87) | 11.3 (1.92 to 70.1) |
| PFMT + ES | NT | 2 | 108 | 8.69 (1.87 to 40.32) | 13.1 (2.91 to 67.5) |
| PFMT + SNRI | NT | 1 | 96 | 3.28 (1.41 to 7.64) | 5.63 (0.784 to 43) |
| PFMT | ES | 6 | 190 | 2.18 (0.76 to 6.28) | 1.9 (0.81 to 4.67) |
| PFMT | VC | 5 | 331 | 1.01 (0.52 to 1.95) | 1.29 (0.527 to 3.18) |
| PFMT + BF | VC | 1 | 46 | 1.14 (0.34 to 3.85) | 3.11 (0.948 to 10.7) |
| PFMT + BF | BT | 1 | 129 | 1.71 (0.79 to 3.70) | 1.92 (0.336 to 12.1) |
| PFMT | SNRI | 1 | 99 | 1.60 (0.71 to 3.60) | 4.01 (1.53 to 12) |
| ES | VC | 3 | 141 | 1.30 (0.59 to 2.84) | 0.675 (0.235 to 1.9) |
| PFMT | PFMT + ES | 3 | 160 | 0.84 (0.34 to 2.07) | 0.686 (0.153 to 3.12) |
| PFMT + BF | PFMT + BF + ES | 2 | 102 | 0.86 (0.36 to 2.08) | 0.935 (0.208 to 4.29) |
| PFMT | PFMT + VC | 1 | 46 | 0.84 (0.26 to 2.68) | 0.509 (0.07 to 3.34) |
| PFMT + BF | PFMT + BF + BT | 1 | 124 | 0.35 (0.13 to 0.97) | 0.352 (0.0332 to 3.67) |
| PFMT | PFMT + SNRI | 1 | 100 | 0.78 (0.34 to 1.82) | 1.59 (0.214 to 12.9) |
| PFMT + ES | ES | 1 | 22 | 4.67 (0.77 to 28.47) | 2.77 (0.554 to 14.4) |
| PFMT + VC | VC | 1 | 34 | 5.00 (0.52 to 48.46) | 2.52 (0.358 to 20.2) |

***TABLE 81*** *Treatment comparisons from direct- and mixed-treatment methods (continued)*

| Intervention | | Direct comparison | | | MTC |
|---|---|---|---|---|---|
| 1 | 2 | Number of trials | Number of people | Est (95% CrI) | Est (95% CrI) |
| PFMT + BF + BT | BT | 1 | 127 | 4.90 (1.84 to 13.10) | 5.5 (0.551 to 60.8) |
| PFMT + SNRI | SNRI | 1 | 101 | 2.04 (0.90 to 4.64) | 2.52 (0.337 to 20) |
| PFMT | PFMT + BF | 7 | 296 | 0.41 (0.18 to 0.97) | 0.414 (0.143 to 1.15) |
| PFMT basic | PFMT extra | 2 | 74 | 0.05 (0.01 to 0.28) | 0.174 (0.0617 to 0.473) |

Est, point estimate; PFMT basic, PFMT with up to two sessions per month; PFMT extra, PFMT with extra sessions (more than two per month).
Note: All mixed-treatment comparison results are taken from the models with PFMT combined as one treatment, except those in bold text, which are from those with PFMT split into basic and extra sessions.

strategy was lifestyle changes followed by surgery (mean QALYs per woman treated = 16.2). The most effective was lifestyle changes followed by PFMT with extra sessions followed by surgery if necessary (mean QALYs per woman treated = 16.37). Which treatment strategy was most likely to be cost-effective depended upon society's willingness to pay for a QALY. Below a threshold of £30,000 per QALY, lifestyle changes followed by PFMT basic and then surgery was the intervention most likely to be considered cost-effective. Above that a threshold of £30,000 per QALY, lifestyle changes followed by PFMT with extra sessions followed by surgery if necessary was most likely to be considered cost-effective. This strategy had a 55% likelihood of being considered cost-effective when society's willingness to pay for a QALY was between £10,000 and £30,000.

The role of drug therapy appears limited, as strategies involving drug management were unlikely to be considered cost-effective. This is primarily due to the non-adherence to SNRI treatment caused by the side effects of the drugs, which limited their effectiveness. Furthermore, the strategy involving surgery without the use of non-surgical treatments was not likely to be cost-effective.

When success was defined in terms of *cure* or *improvement*, the results were insensitive to the introduction of strategies involving VCs or ES. It was also found that the interpretation of the cost-effectiveness results did not greatly change when the model was adapted to allow women to exercise preference not to seek surgery or repeat surgery, should cure or sufficient improvement not be achieved.

These data suggest that adopting an intervention such as PFMT with extra sessions (or potentially other more intensive forms of PFMT, such as PFMT with BF) would be more efficient than PFMT basic. This is important as PFMT basic is perhaps closest to the form of PFMT most common in the NHS. Therefore, although PFMT basic does appear to improve the symptoms of women with SUI, consideration should be given to whether it is practical and acceptable to both women and the NHS to provide some form of more intensive PFMT (either alone or with an adjunct, such as BF training).

The results were most sensitive to changes in the effectiveness of PFMT with extra sessions. Should the chance of PFMT with extra sessions achieving *cure* or *improvement* reduce, or should longer-term recurrence rates increase, then the likelihood that lifestyle changes followed by PFMT with extra sessions followed by surgery is cost-effective would fall. For the model based on *cure* rates, lifestyle changes followed by PFMT with extra sessions followed by surgery would no longer be the most cost-effective strategy when long-term *cure* rates were reduced by more than 60%. For the model based on *improvement* rates, lifestyle changes followed by PFMT with extra sessions followed by surgery would no longer the most cost-effective

***TABLE 82*** *Odds ratios for comparisons between PFMT with extra sessions and PFMT plus BF with other treatments (mixed-treatment comparison models)*

| Intervention | | Cure, median (95% CrI) | Improvement, median (95% CrI) |
|---|---|---|---|
| **1** | **2** | | |
| ***PFMT with extra sessions*** | | | |
| PFMT extra | NT | 10.7 (5.03 to 26.2) | 25.7 (10.3 to 73.1) |
| PFMT extra | PFMT basic | 8.36 (3.74 to 21.7) | 5.75 (2.11 to 16.2) |
| PFMT extra | PFMT + BF | 0.867 (0.45 to 1.69) | 1.01 (0.32 to 3.16) |
| PFMT extra | ES | 7.43 (2.72 to 22.3) | 4.68 (1.75 to 13.2) |
| PFMT extra | VC | 3.02 (1.04 to 9.53) | 3.79 (1.32 to 11.5) |
| PFMT extra | SNRI80 | 7.44 (2.44 to 27.8) | 12 (3.92 to 42.4) |
| PFMT extra | BT | 1.41 (0.481 to 4.48) | 2.13 (0.34 to 14.5) |
| PFMT extra | PFMT + ES | 3.51 (1.12 to 10.2) | 1.24 (0.27 to 5.79) |
| PFMT extra | PFMT + ES + BF | 1.17 (0.07 to 20.5) | 1.19 (0.23 to 6.3) |
| PFMT extra | PFMT + VC | 3.45 (0.31 to 35.6) | 2.11 (0.26 to 16) |
| PFMT extra | PFMT + VC + BF | 1.87 (0.04 to 46.2) | 9.66 (0.62 to 158) |
| PFMT extra | PFMT + BT + BF | 0.422 (0.09 to 2.14) | 0.369 (0.03 to 4.4) |
| PFMT extra | PFMT + drug | – – | 5.82 (0.73 to 50.7) |
| ***PFMT plus BF*** | | | |
| PFMT + BF | NT | 12.3 (5.35 to 32.7) | 25.4 (8.68 to 86.9) |
| PFMT + BF | PFMT basic | 9.63 (4.12 to 25.9) | 5.68 (1.88 to 18.3) |
| PFMT + BF | PFMT extra | 1.15 (0.59 to 2.22) | 0.99 (0.32 to 3.11) |
| PFMT + BF | ES | 8.55 (2.88 to 27.6) | 4.63 (1.37 to 16.9) |
| PFMT + BF | VC | 3.47 (1.19 to 11) | 3.75 (1.17 to 12.5) |
| PFMT + BF | SNRI80 | 8.58 (2.64 to 33.4) | 11.8 (3.37 to 48.4) |
| PFMT + BF | BT | 1.62 (0.54 to 5.18) | 2.11 (0.38 to 12.5) |
| PFMT + BF | PFMT + ES | 4.05 (1.15 to 12.7) | 1.23 (0.21 to 7.51) |
| PFMT + BF | PFMT + ES + BF | 1.34 (0.07 to 24) | 1.18 (0.27 to 5.21) |
| PFMT + BF | PFMT + VC | 3.96 (0.35 to 41.2) | 2.09 (0.25 to 16.7) |
| PFMT + BF | PFMT + VC + BF | 2.14 (0.05 to 53.7) | 9.54 (0.57 to 170) |
| PFMT + BF | PFMT + BT + BF | 0.49 (0.11 to 2.28) | 0.37 (0.04 to 3.61) |
| PFMT + BF | PFMT + drug | – – | 5.75 (0.67 to 54.2) |

Note: This table is extracted from *Tables 85* and *86* reported in Appendix 23.

strategy when long-term improvement rates of PFMT with extra sessions were the same as PFMT basic. The long-term success rates of PFMT with extra sessions were based upon data from Bø and colleagues,[115,159] who used a combination of group and individual sessions with women, as well as longer-term provision of training. It is unclear, however, what factors determined the outcomes they observed (e.g. was the motivation of the women atypical, was it the intensity of the intervention or some other factor?) or whether the results of this study could be replicated in routine NHS practice.

The results were also sensitive to changes in the cost of PFMT with extra sessions. Lifestyle changes followed by PFMT with extra sessions followed by surgery would no longer be cost-effective when the cost of PFMT with extra sessions was increased by nearly £1000 per woman treated in the model based on *cure* rates, and £400 per woman treated when it was in the model based on *improvement* rates.

Overall, the results of the economic evaluation suggests that further research to develop and test a more intensive PFMT intervention that is acceptable to women and feasible for the NHS is warranted.

## Strengths, assumptions, limitations and uncertainties

Numerous previous studies have considered the relative effectiveness of non-surgical treatments for SUI in women.[50,56,60,64,68,71,83–85,87,88,106,201,224–228] What our study has added is the systematic review and overview of the treatments relevant to the NHS, where evidence on the relative effectiveness has been derived using more advanced methods of meta-analysis than have been used previously. These methods have allowed us to provide clearer evidence about which treatments work and how well they work than was hitherto available. The statistical approach of MTC allowed indirect evidence to supplement direct head-to-head comparisons of treatments. This made the comparison of treatments much easier than trying to interpret the data from the 68 direct head-to-head (pairwise) comparisons.

Despite extensive searching and the identification of a large number of studies, few data were available for most comparisons. Over time this may be rectified, and, indeed, an updated search conducted up to June 2009 identified additional 12 articles that appear to meet our inclusion criteria (these studies are listed in Appendix 28).

Of the studies that were identified, nearly one-half of the participants in the included trials (46%, 4554/9803) came from the 12 trials that included a SNRI as one of their trial arms. Given this, a pragmatic decision was made to include studies where women with urgency urinary incontinence symptoms also formed part of the study population (population types 2 and 3).

Generally, these studies were less likely to show large effect sizes than studies that only included women with SUI alone. The studies with mixed populations, however, tended to have a larger sample, but involved fewer supervisory sessions than studies of women with only SUI. Both of these factors may also have affected the estimated size of effect.

Even for the relatively simple clinical outcomes, such as *cure* or *improvement,* the lack of consensus on the most appropriate method for assessing incontinence presented a particular problem for evidence synthesis. Ideally, the success of a treatment should be gauged on the ability of women to lead a normal social life. Using this definition usually means that the woman herself reports a satisfactory resolution (or near resolution) of her symptoms. Unfortunately, patient-reported measures were not always available. Moreover, available data (including proxy measures based on the quantification of symptoms derived from diaries or pad tests) did not differentiate those who are sufficiently better (and do not want further treatment) from those who are better but do want further treatment.

A further challenge for evidence synthesis that is related to the lack of consistency between studies and the limited reporting of studies was that intervention protocols were complex and varied considerably across studies. For example, PFMT differed widely in terms of the precise nature of the exercises, how patients were instructed, and the frequency and duration of therapy (Appendix 12). Generally, such data were poorly reported, with the exercise protocol not consistently described using the same criteria. In an attempt to explore the impact of intensity of therapy, PFMT was defined solely by the frequency of supervisory clinic sessions or contacts with a health-care professional. Similarly, the complex nature of the intervention protocols also meant that it was difficult to decipher which aspect of the intervention actually worked. For example, the addition of BF training to PFMT appeared beneficial in enhancing the effect of PFMT. This may have occurred because women made greater use of PFMT and increased their adherence to the training programme. Introducing a BF device may also intensify the nature or the quantity of supervision provided by the health-care professional, which, in itself, may be beneficial for women. What the research does highlight is the importance of intensity of therapy on effectiveness and cost-effectiveness, and the need for the evidence-based development of more intensive regimens that can be taken forward to rigorous evaluation in adequately powered RCTs.

When assessing the effectiveness of treatment emphasis was given to using the data collected at the end of the supervised treatment phase. It was expected that these data would represent the point where the treatments would show their maximum effect. Long-term data beyond the supervised treatment phase were sparse but the evidence gathered for the economic evaluation suggests that the effectiveness was not maintained.

This may be due to poor adherence to a muscle training programme or whether the effects of training can be sustained into the longer term. The results of the economic evaluation are sensitive to changes in long-term performance of non-surgical interventions. Improvements in the long-term performance will improve the cost-effectiveness of non-surgical treatments.

Although the meta-analyses have limitations, one of the strengths of this study is that it has used these rigorously assembled data within an economic evaluation. This economic evaluation compared treatment strategies relevant to the NHS and hitherto no such analysis existed. Indeed, no economic evaluations were identified which compared all the relevant treatments.

Modelling the cost-effectiveness of non-surgical treatments was challenging because of the number of potential management strategies that might be relevant and also the lack of data available. As described in Chapter 9, considerable efforts were made to identify relevant data, and extensive sensitivity analyses were used to explore the impact of uncertainties. Useful information to help guide practice has been produced but it should be remembered that, apart from drug therapy, few data were available for any of the treatments, and very few data on long-term performance were available for any therapy. Therefore, the results of this study should be treated cautiously.

All of the strategies considered within the economic model included lifestyle advice (e.g. reduce weight, restrict caffeine intake, etc.). It was assumed that, although advice would be given, it would be ineffective. A recent trial has shown that weight reduction (lifestyle change) in obese women may reduce the symptoms of incontinence and further work on lifestyle interventions may be worthwhile.

Within the economic evaluation the effectiveness of treatments were measured in QALYs, which were derived from EQ-5D values obtained from the literature (and in a sensitivity analysis from a survey conducted as part of this study). The EQ-5D has been recommended as the method of valuing health states by NICE,[105] but it may not be sensitive enough to capture the concerns of women. Any failure to accurately measure the benefits of treatment may lead to erroneous conclusions about cost-effectiveness.

A further limitation of the economic model was that there were no quality-of-life data to differentiate between cure and improvement. It might be expected that the quality of life of women whose symptoms had improved but who were not cured would be less than women who were cured. Alternatively, changes in the frequency of incontinence may fail to translate into benefits of importance to women. Ideally, further research should be conducted on the quality of life of women whose symptoms are improved and who no longer seek further treatment.

Within all of the economic analyses, the preferences of women for the process of care have not been considered. Women are likely to have preferences about who provides the care, where the care is provided, and what risks and costs they face themselves. These factors are not captured by measures such as the EQ-5D. Therefore, research to elicit the preferences of women for the different outcomes and processes of treatment in a form that is suitable for incorporation into an economic evaluation is likely to be worthwhile. Such data would be complementary to existing data and could help to highlight areas in which the preferences of women for outcomes of importance to them would lead to different policy decisions.

The economic model has focused on costs to the NHS. It has been assumed that certain costs, such as those for VCs and containment products, may be incurred by the NHS. In practice, women may buy the cones and may well incur the costs of containment management themselves. Other costs that may fall on the women have not been included. These include the other costs of managing symptoms, such as laundry costs, and the time and travel costs related to accessing care. It might be expected that the more effective treatments would reduce the costs of managing symptoms borne by the women and their families. However, the more effective treatments may also require substantially more time commitment (and travel costs to access care) from the women. The net effect of these two factors is uncertain.

A further limitation with respect to costs is that the handling of facility costs and hospital management costs has not been wholly consistent. For example, for some interventions, such as the use of physiotherapy, the cost has been used upon the staff and equipment used to provide a session but has not included an element to cover the facility and management costs. However, for other interventions, for example the cost of surgery, these are based on nationally available figures that do include an element to cover facility costs and

hospital management costs. The net impact of this is to make PFMT interventions more likely to be cost-effective compared with surgery. However, as the sensitivity analysis has illustrated, increases in the cost of PFMT would need to be substantial to change the overall results and it is implausible that this would actually be the case.

Nevertheless, despite the limitations of the evidence base, there is evidence from a number of trials that PFMT plus BF and PFMT with extra sessions was effective. Furthermore, strategies involving these treatments are likely to be considered cost-effective at threshold values that society might be willing to pay for a QALY.

# Chapter 11
# Conclusions

## Implications for the NHS

- The available data suggest that non-surgical treatments for SUI in women are effective and could potentially be cost-effective, but a judgement is required as to whether the benefits are worth the cost.
- There is no evidence that PFMT basic (which is similar to the form of PFMT provided by the NHS)[43] is any better than no treatment when success is measured in terms of *cure,* although it is better than no treatment when success is measured in terms of *improvement*.
- There is clear evidence from a number of trials that 'PFMT plus BF' and 'PFMT with extra sessions' were effective compared with no treatment.
- Both 'PFMT plus BF' and 'PFMT with extra sessions' are more effective (for both *cure* and *improvement*) than PFMT basic.
- Evidence from a small number of trials suggests that other non-surgical treatments may also be effective (PFMT plus BT and BF; PFMT plus ES and BF; PFMT plus VCs and BF). There is, however, insufficient evidence to recommend their routine use by the NHS.
- A strategy by which women can progress to surgery almost immediately is unlikely to be cost-effective, primarily because of the cost of surgery.
- Treatment with SNRI drugs are, on average, effective (measured in terms of *cure* or *improvement*), but the frequency of side effects mean that women do not tend to use this therapy for long. Therefore, strategies involving SNRI are unlikely to be cost-effective.
- As no treatment or treatment strategy is perfect, women should be offered support to help them articulate what it is that they hope to achieve from therapy.
- The differences between the treatment strategies considered (measured in QALYs) were relatively modest and, although some strategies were found to be more likely to be cost-effective, the evidence base was limited.
- The feasibility of the potentially cost-effective more intensive forms of PFMT is questionable, as there may not be sufficient trained therapists to provide this care at present. For the use of these therapies to increase, staff would need to be recruited, trained and retained. Recent surveys about the provision of care by the NHS by the Continence Foundation (Judith Wardle, formerly of the Continence Foundation, March 2009, personal communication) found that less costly therapists were being substituted for the higher-grade continence nurse specialists. Given the potential demand for care, non-specialist care providers are likely to be necessary, in addition to care provided by specialist therapists, but they will need appropriate training.
- Opportunities for self-management by the women should be encouraged, as women can purchase VCs themselves or they could undertake PFMT without formal supervision. Therapies are most likely to be effective and cost-effective when women receive training so that they can perform the exercises correctly.
- Continuing and ongoing support for women with SUI may be required beyond current programmes, as long-term performance is central to estimates of long-term effectiveness.
- Conversely, providing therapies when there is no sustained follow-up may not be a good use of scarce practitioner time or resources.

## Implications for women

Non-surgical treatment for SUI can provide either cure or improvement in symptoms. A non-surgical treatment might not totally resolve symptoms but may lead to sufficient improvement so that a woman considers that further treatment is not worthwhile. Although the woman may not desire further treatment, it should be noted that symptoms may still be bothersome and may require the use of containment products. The cost of using containment products and extra laundry will still fall on women and their families.

For some women, non-surgical treatments can delay or prevent the need for surgery. This may be particularly important for those women who have no desire to undergo surgery and may be prepared to accept severe incontinence rather than face surgery. The recourse to surgery early

in a treatment pathway might be preferred by some women who are unable to use non-surgical treatments or who are unwilling to devote the sustained time and effort required to obtain and maintain an improvement in symptoms. However, over the longer term better outcomes might be achieved if the women try out a non-surgical treatment first.

Some of the therapies do not necessarily need involvement of the health service. Women can purchase VCs themselves, or they could undertake PFMT without formal supervision. These treatments can be effective, but whether this is worthwhile depends upon the ability of the woman to perform the therapy correctly. Therefore, women should consider whether some formal instruction by suitably trained health-care professionals would be helpful to ensure that they are performing correct contractions.

The long-term success of the treatments such as PFMT declines over time. One potential reason for why this happens is that women do not continue to perform the exercises in the long term. This requires a behaviour change that women might find difficult to initiate and maintain. Without making and maintaining this change, it is likely that symptoms will return and further treatments, including surgery, might be required.

## Further research

Evidence has been provided to show that several of the non-surgical treatments for SUI can be effective, at least in the short term, and are potentially cost-effective. The evidence, however, is based upon a number of small trials, and, for many comparisons, only single trials.

- Further definitive evidence from large well-designed studies of the most promising regimens (in terms of likely effectiveness, cost-effectiveness and feasibility within the health service) is required to provide a definitive answer.
- Any further research, be it from a trial, on long-term outcomes, benefit assessment, or costs, should be incorporated into an updated economic evaluation, as and when it becomes available.
- Such trials should consider the long-term effectiveness of more intensive versions of PFMT (e.g. PFMT with BF training) in typical standard health-care setting and an economic modelling exercise that will place the results of the trial into the context of other relevant research and extrapolate from the trial results.
- The effectiveness and cost-effectiveness will depend upon the long-term effective of treatments, which, in turn, may depend upon whether any training programme is adhered to and sustained into the longer term. Research in how this might be achieved in a way that is feasible for both the NHS and women is required.
- Further work to understand what outcomes are of importance to women and the strength of preference of women for these outcomes is required.
- Understanding the preferences of women for different ways that care could be provided, and the trade-offs between different process and outcome measures, would be useful. Women may also have preferences about the process of care as well as the outcome of care. Ideally, such data should be suitable for incorporation into a subsequent economic evaluation.
- The impact of costs (both in terms of out of pocket expenses and time) that fall upon women and their families should be explored further. Specifically, information is needed about the trade-off between the costs of managing symptoms (use of self-purchased containment products, laundry costs, etc.) and the time and travel costs of treatment.
- If an effective and efficient follow-up regimen can be developed, then the incentives/disincentives faced by NHS providers may need to be reconsidered. For example, within England, performance current monitoring goals might lead to a focus on 'first contacts' at the expense of follow-up care.

## Summary of conclusions

More intensive forms of PFMT ('PFMT with extra sessions' and 'PFMT with BF') are effective and potentially worthwhile uses of NHS resources. Nevertheless, the data came from a few small trials and further information from large well-designed studies is required to establish whether these interventions are effective, cost-effective and feasible for the NHS to provide.

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## Contribution of authors

Robert Pickard led the drafting of the background chapter and was assisted in this by Jenni Hislop. Jenni Hislop also assisted Mari Imamura in the completion of the systematic review of effectiveness. Mary Kilonzo led the drafting of the chapter outlining the decision problem and led the economic evaluation, on which she worked closely with Shihua Zhu. Laura Ternent designed, conducted and led the survey of members of the Bladder and Bowel Foundation. She was assisted in this by Brian Buckley and Cathryn Glazener. David Jenkinson led the work on mixed-treatment comparisons and drew upon the advice of Jonathan Cook and comments of Mari Imamura and Cathryn Glazener. Sheila Wallace conducted the literature searches, drafted sections of the report related to this work and provided reference management for the whole project. Paul Abrams, Christine Bain, Brian Buckley, Linda Cardozo, June Cody, Sharon Eustice, Adrian Grant, Jean Hay-Smith, Ghulam Nabi, James N'Dow, Robert Pickard and Judith Wardle all provided advice in their own areas of expertise and provided critical comments throughout the project. Luke Vale was involved in all elements of the project and, along with Mari Imamura, provided project management. All authors assisted in preparing the manuscript, reading and commenting on drafts, and reading the final draft.

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## Feedback

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***We look forward to hearing from you.***

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