Acupuncture for women with refractive Overactive Bladder Syndrome

Marinus Cloete MBChB (UFS) FCOG (SA)

A dissertation submitted to the Faculty of Health Sciences of the University of Cape Town in fulfilment of the requirements for the degree of Master of Medicine (Obstetrics and Gynaecology) Part III.

Date of submission: December 2010

Supervisor: Dr. Stephen Jeffery
Urogynaecology Unit Groote Schuur Hospital, Cape Town

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Declaration

I, Marinus Cloete, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole document or any portion of the contents in any manner whatsoever.

Signature……

Date……

Declaration by supervisors

The research which Dr Marinus Cloete has undertaken and the presentation of this dissertation was supervised by Dr Stephen Jeffery. This study was carried out while Dr Cloete was a registrar in the Department of Obstetrics and Gynaecology at the University of Cape Town.

I am satisfied that this was Dr Cloete's original work and that this dissertation should be submitted in fulfilment of the requirements for the degree of Master of Medicine (Obstetrics and Gynaecology) Part III.

Supervisor: Dr S Jeffery

Signature:…… Date:…….

Acknowledgements

Dr Stephen Jeffery, Head of the Urogynaecology unit of Groote Schuur Hospital, for guiding me, supervising this study and giving generously of his time.

Mariette Pitlo and Lindsay Wallace, Physiotherapists at the Female Continence Clinic. Without them this study would not have been possible.

Dr Sedick Isaac for his patience and guidance with the statistical analysis.

All the patients from the Female Continence Clinic who eagerly participated in the study.

ABSTRACT

Background

Overactive Bladder Syndrome (OAB) represents a health condition of increasing public and medical recognition. The burden on the individual patient and the potential economic impact is staggering.

Public Health care in SA is economically under resourced. Treatment modalities for OAB in these settings are limited to bladder training and oral immediate-release oxybutynin. Long term effectiveness and tolerance is unsatisfactory in some patients. There is currently no alternative therapy available to them.

Objectives

To evaluate the efficacy of acupuncture in refractive OAB. The primary aim was to evaluate the effect on frequency, nocturia and urge urinary incontinence. The secondary aim was to evaluate the effect of the response on self-perceived quality-of-life.

Patients and methods

The study was conducted at a specialized urogynaecology unit in a resource limited setting. In a self-controlled time cohort study, 20 consecutive women with OAB who were refractive to standard treatment, were recruited. Participants received weekly acupuncture treatments for four weeks. Three-day bladder diaries and the King's Health Questionnaire (KHQ) were completed at 3 intervals: at baseline; at week 6; and at 3 months.

Results

There was a 22% (p=0.002) and 23% (p=0.002) decrease in frequency, a 38% (p=0.004) and a 31% (p=0.015) decrease in nocturia and a 20% (p=0.002) and a 32% (p=0.0003) decrease in incontinence from baseline to week 6 and to 3 months respectively.

Both the general domains of the KHQ showed significant improvement by 3 months (P=0.002 and 0.009 respectively).

All seven lifestyle domains showed significant improvement at week 6 and again at 3 months. The most significant decrease was seen in Emotional Limitations (p<0.001).

The only domain that showed a marginal significant decrease from week 6 to 3 months was Social Limitation (p=0.49).

Conclusion

In this study of women with refractive OAB, acupuncture produced significant symptomatic and quality-of-life improvement in all outcomes measured.

ABBREVIATIONS

OAB	Overactive Bladder Syndrome
ICS	International Continence Society
UI	Urinary Incontinence
UUI	Urgency Urinary Incontinence
SUI	Stress Urinary Incontinence
BMI	Body Mass Index
QoL	quality-of-life
FCC	Female Continence Clinic
GSH	Groote Schuur Hospital
frequency	refers to urinary frequency
urgency	refers to urinary urgency
HRT	Hormone replacement therapy
PTNS	Posterior Tibial Nerve Stimulation

CHAPTER 1
Introduction

1.1 Background

Overactive Bladder Syndrome (OAB) represents a health condition of increasing public and medical recognition. Current treatment options for patients who are diagnosed with OAB in resource limited settings in South Africa are limited to bladder retraining and oxybutynin. Our anecdotal experience at a specialised urogynaecological unit is that these modalities are often associated with unsatisfactory cure rates. A recent retrospective chart based audit on 84 patients with urgency urinary incontinence (UUI) attending the Female Continence Clinic at Groote Schuur Hospital in Cape Town found that only 23% considered their symptoms to have improved with the standard treatment (1). We have no further therapy to offer these patients.

When considering its distressing impact, it is not difficult to appreciate that these troublesome symptoms may represent a continuous, daily burden on any individual's functioning. There is a growing demand for OAB research to provide physicians with new treatment modalities to improve the quality of care in patients with this disorder.

Acupuncture for bladder dysfunction has been used in traditional Chinese medicine for many years. Recent scientific studies have shed some light on the possible mechanism of this intervention. This has subsequently led to acupuncture trials for OAB with noticeable results. Acupuncture is safe and well tolerated with few side effects. Considering that there is no alternative treatment available in our unit, acupuncture for patients with refractive OAB was investigated.

1.2 Terminology

The overactive bladder was identified as a condition by the International Continence Society (ICS) in 1988 when it was introduced, as a diagnostic entity, to incorporate a range of associated clinical symptoms including urge incontinence, urinary frequency,

urgency, and nocturia (2). The exact definition has been a point of debate for several years.

To enable better communication and understanding among clinicians, researchers and the public, the ICS adopted broader, symptom-based definition in 2001 by encompassing a "syndrome of symptoms". This consensus definition defines OAB as urinary urgency, with or without urge incontinence, usually with urinary frequency and nocturia, in the absence of pathologic or metabolic factors that would explain these symptoms (3).

Urgency has now become the cornerstone symptom of OAB (4). It is defined as the complaint of a sudden compelling desire to pass urine, which is difficult to defer. Urge urinary incontinence (UUI), also referred to as "OAB-wet", is the complaint of involuntary leakage accompanied by or immediately preceded by urgency. A patient who considers that he/she voids too often by day has increased daytime frequency and nocturia is the complaint that the individual has to wake at night more than once to void. These ICS-definitions adequately described bladder symptoms within the OAB population when assessed by the level of symptom bother (5).

A subset of patients with overactive bladder symptoms experience urgency, frequency, and nocturia, but do not have urge incontinence, a condition referred to as "OAB-dry."

For the purpose of this study, refractive OAB was defined by symptoms not satisfactorily relieved by standard first-line treatment given at our specialised unit.

1.3 Prevalence of OAB in women

Until recently, prevalence data for OAB were lacking. Differences in definition and assessment of symptoms made it difficult to compare data across studies. The new definition proposed by the ICS attempted to eliminate this problem by standardising terminology. Since then, the definitions have been accepted internationally and study participants with OAB can be identified by using clinically validated symptom-based criteria.

The methodology used for collecting data can also make comparison challenging. Some data is collected using postal questionnaires while other investigators conduct personal or telephonic interviews. In instances where postal surveys are used, varying response rates may introduce bias to the data. Incontinent women may ignore questionnaires, deny having UI or they may respond in greater numbers because they are drawn to the subject. Interview responses on the other hand may be more susceptible to social bias.

Crude prevalence studies from the United States and Europe are abundant, but these population surveys focused on UI in general. Three recent surveys represent a significant advance in our understanding of the prevalence of specifically OAB symptoms and their impact. This data, from the United States and Europe, has confirmed the clinical suspicion that OAB is a highly prevalent disorder.

.

Two of the three large population-based studies have been conducted before the new definition of OAB was introduced.

In the European survey of 16 776 men and women aged 40 years and older, Milsom et al. (6) reported OAB symptoms in 16.6% of respondents. This survey was conducted by telephone interviews and, in Spain, by face-to-face interviews (due to the lower proportion of households having a telephone). Frequency (85%) was the most commonly reported symptom, followed by urgency (54%) and urge incontinence (36%). Of these patients, 79% had experienced symptoms for at least a year with 49% experiencing symptoms for more than three years. By extrapolating the results, the investigators estimated that a total of 22.18 million individuals in France, Italy, Spain, Sweden, Germany and the United Kingdom are burdened by OAB.

A similar prevalence was found in the USA. The National Overactive Bladder Evaluation Program (7) surveyed over 17,000 households using a clinically validated computer-assisted telephone interview questionnaire. This survey was validated and had a sensitivity of 61% and specificity of 91% for OAB. Of the women who were eligible and completed the survey 16.9% reported symptoms. Of these patients, 9.3%

were incontinent. Applied to the US population as a whole, this translates into approximately 33.3 million affected adults.

The third study, known as the EPIC study (8), is the largest multinational, population based, cross-sectional survey to estimate the prevalence of lower urinary tract symptoms using current ICS definitions. A total of 58 139 adults aged 18 years or older were contacted in Canada, Germany, Italy, Sweden and the UK and 19 165 participated in the survey. The prevalence of OAB in women was 12.8%.

The geographical diversity of these surveys calls into question whether the population surveyed significantly impacts on the reported prevalence of OAB. There is no epidemiological evidence to support a difference in prevalence rates between countries. A slightly higher prevalence was reported in Spain in Milson's survey. This may reflect the method of data collection. The survey was conducted by direct interview in which respondents may have felt more able to discuss their bladder control problems.

The prevalence rate in developed areas seems to correlate with the limited data available on those in developing areas. In Korea, for example, the prevalence of OAB was 14.3% (9).

There is, however, very little data available on the epidemiology of urinary incontinence on the African continent. A Medline search using keywords "incontinence", "Africa" followed by a sequential Medline search using "incontinence" and each of the 56 African countries revealed scanty data on incontinence overall with only a handful of poor quality studies reporting basic epidemiological data such as prevalence. None of these studies were conducted in South Africa.

Africa has unique problems and challenges. We suspect that women in Africa believe that there is no effective treatment for incontinence available and might see incontinence as a normal process of aging. Racial and cultural differences in help-seeking behaviour can influence people's initial response to acknowledging a lack of

bladder control. For long it has been suspected that black South African women rarely develop stress incontinence (10), but little is known regarding urge incontinence.

1.4 Incidence and Natural History of OAB in women

Despite recent advances in the standardisation of definitions and diagnostic criteria for OAB and the understanding of the epidemiology and risk factors, very few studies have reported on the incidence and natural history of OAB.

An important prospective study by Wennberg et al. (11) looked at the progression of OAB in the same women over 16 years. Frequency increased by 3% ($P<0.001$) and nocturia by 20% ($P<0.05$) from 1991 to 2007. The incidence of OAB was 20% and the corresponding remission rate was 43%. A limitation to this study is that it is not clear whether the level of remission reflects active treatment or whether it is part of the natural course of incontinence.

In 2009 Garnett et al. (12) assessed the long-term natural history of OAB symptoms. In their study they reviewed the original urodynamic traces of women who were referred to a urogynaecological unit with OAB symptoms at least 10 years earlier. All patients with a confirmed diagnosis of OAB were offered a repeat urodynamic and symptomatic assessment. OAB symptoms were persistent in 88% of the study population. Similarly Aitchison et al. (13) reported 88% of patients with urge incontinence to be unchanged at 5-year follow-up.

Nygaard et al. (14) interviewed and then re-interviewed 2025 women older than 65 years at three and 6-year intervals. The incidence and remission rates for OAB-wet without treatment intervention were 29% and 22% respectively.

OAB seems to be a dynamic condition and it is highly likely that symptoms continue in the long term.

1.5 Risk Factors for OAB in women

Various risk factors for the development of OAB have been identified through epidemiologic research.

OAB is likely to become a more significant clinical problem with age. In the EPINCONT study (15), a large Norwegian survey of over 27 000 people, the risk factors for UI were analysed separately in strata of different types. They found that the lowest prevalence was observed in the younger age groups (12% for women <30 years), the highest was observed among the eldest (40% for women >90 years). However, there was also a peak around mid-age with a prevalence of 30% among women 50–54 years of age. Epidemiological studies have implicated oestrogen deficiency in the aetiology of lower urinary tract symptoms occurring following the menopause. Estrogen and progesterone receptors have been found throughout the lower urinary tract (16), and many of the tissues involved in female continence have been found to be oestrogen-sensitive. Urge urinary incontinence is more prevalent after the menopause (17). The peak prevalence of stress urinary incontinence occurs around the time of the menopause but declines following the menopause (18) . Seventy percent of incontinent postmenopausal women relate the onset of their incontinence to the time of their menopause (19).

In the NOBLE study (7), the likelihood of OAB-wet increased markedly between the ages of 35 and 44 years, with a further increase after age 55 years. Although older age seems to be associated with OAB, it is not only the elderly who suffer from it. It is well documented that the OAB-prevalence is also significant in a younger population. In the EPIC study (8), 43% of respondents were aged 40–64 years. Van der Vaart et al. (20) reported a prevalence of 11.9% for OAB-dry and 15.3% for OAB-wet in a female population aged 20-45 years.

Most studies have shown obesity to be commonly associated with incontinence and the prevalence of OAB-wet is seen to increase with an increasing body mass index (BMI). In the NOBLE study (7), the prevalence of OAB-wet in participants with a BMI more than 30 was 2.2 times higher than those among participants with BMI's less than 24. Liberman et al. (21) found that 42.1% of respondents who experienced incontinence were in the top third of the BMI range. In the Heart and Estrogen/Progestin Replacement Study (HERS) (22), increasing BMI was found to be a significant predictor of incontinence. This study published an evaluation of the effects of hormone therapy on the risk of stress and urge urinary incontinence, a

secondary endpoint in this cardiac prevention trial. Self-reported incontinence was documented at 4 months after randomization and then yearly over the study period. During the 4 years of treatment, 64% of the women randomly assigned to hormone therapy compared with 49% of those assigned to placebo reported weekly incontinence. This higher risk was evident at 4 months and persisted throughout treatment. This effect appears to be independent of age. Four years of treatment with HRT caused an excess risk of 12% for weekly urge incontinence episodes and 16% for weekly stress incontinence. It was suggested by the authors that the association of hormone therapy and incontinence might be due to the progestogen component of this regimen.

Between 1993 and 1998, the Women's Health Initiative (WHI) study group performed a multicenter, double-blind, randomized trial of menopausal women. In 23 296 study subjects aged between 50 and 79 years, urinary symptoms were reviewed at baseline and after 1 year (23). The incidence of urinary symptoms was reported via a standardized and validated questionnaire. Measurements of severity included self-reported frequency, and associated limitations in daily activities and 'degree of bother'. Women were randomly assigned to receive either HRT or placebo. For those who reported no urinary symptoms at baseline, combined HRT was associated with an increased incidence of any urinary incontinence at 1 year. For those women who had initially reported urinary incontinence upon enrolment, there was a significant increase in the risk of worsening symptoms in the combined HRT group. Of those who had reported some degree of urinary incontinence at baseline, there was also a significant risk of worsened symptoms with oestrogen treatment. The HERS and WHI trial were primarily designed to evaluate other outcomes. The urinary tract measures were limited to self-reported, subjective descriptions of incontinence symptoms without more reproducible, objective outcomes. However, self-reported symptoms are important in reflecting the experience of patients and are useful in assessing the overall benefits of such a treatment.

During the 1990s, the Hormones and Urogenital Therapy (HUT) Committee produced a meta-analysis report to clarify the confusion over oestrogen use for the treatment of urinary symptoms (24). On identifying 166 articles, 23 met the entry criteria. Of these, six were controlled clinical trials and 17 uncontrolled series. Meta-analysis

found an overall significant beneficial effect of oestrogen on subjective symptom improvement for all subjects and for subjects with urodynamic stress incontinence alone. Placebo groups also reported subjective improvement of 10–56%. There were, however, no objective data and the studies included heterogeneous groups and considerably varying diagnostic criteria, therapeutic interventions and outcome assessments.

In a case-control study by Parazzini (25), over a 1000 women with OAB were consecutively observed in first level gynaecological centres in Italy. They found an increased risk of all types of urinary incontinence in women who had undergone hysterectomies, but they did not find any association among vaginal delivery, menopausal status, age at menopause and risk of urinary incontinence. In the HERS hormone replacement did not affect the frequency of SUI or UUI.

Data from the EPINCONT study (26) further demonstrated that former and current smoking was associated with incontinence, but only for those who smoked more than 20 cigarettes per day. Severe incontinence was weakly associated with smoking regardless of number of cigarettes.

1.6 The Impact of OAB

OAB presents a distinct entity of unpredictable and troublesome symptoms. Many individuals find the condition and its associated symptoms personally and socially devastating. It is not only episodes of incontinence that affect well-being - frequency and urgency also have considerable detrimental effects on daily activities. Patients with OAB use a variety of behavioural modification and coping skills to reduce the impact of their symptoms. These include toilet-seeking, restriction of fluid intake, dietary restrictions, limitation of physical activity, and in severe cases, limitation of social activities. A cycle of anxiety and distress regarding possible urine loss and embarrassment leads to a great psychological burden and various degrees of social isolation.

OAB compromises patients' emotional well being. In the EPIC study, Irwin et al. (8) found that of a group of patients with OAB, 32% reported that having these

symptoms made them feel depressed, and 28% reported feeling very stressed. In the NOBLE study, Stewart et al (7) observed that OAB-patients had clinically and statistically higher depression scores, poorer sleep quality and lower levels of overall quality-of-life (QoL).

OAB compromises patients' working lives. Irwin et al (27) found that more than 21% of the population was worried about interrupting meetings because of frequent trips to the toilet, and 3% of the population changed jobs or were fired because of their bladder control problems. UUI was also a factor in the patients' employment decisions. OAB may as such impair a woman's ability to function normally in the workplace and can result in job loss.

Coyne et al. (28) matched 1434 OAB cases of the EPIC with designated controls. Participants with OAB reported significantly less work productivity and sexual satisfaction, higher rates of depressive symptoms and lower levels of overall health.

OAB further results in significant costs to the patient and public healthcare. In the last year, two important studies demonstrated the considerable economic impact of OAB. The prevalence data derived from the EPIC study were combined with healthcare resource-use data to derive current direct and indirect annual cost of illness estimates for OAB in Canada, Germany, Italy, Spain, Sweden and the UK (29). The estimated total cost for patients with OAB in these countries is €9.7 billion. New data from the United States suggest that the economic burden of OAB is about five fold higher than older, non-comprehensive estimates (30). Total national costs of $65.9 billion are estimated.

1.7 Pathophysiology of OAB

In spite of recent advances, the pathophysiology of OAB remains poorly understood. Researchers have been left to use hypothetical reasoning to translate scientific observations to the clinical setting. What is becoming increasingly clear is that the control of bladder functioning is far more complex than previously believed.

Traditionally the etiology of "overactivity" has been understood as neurological or myogenic in basis.

Neurogenic detrusor overactivity is caused either by the sensitization of the normally silent peripheral afferent nerves to the bladder, or by damage to the central inhibitory pathways that normally inhibit the voiding reflex (31). This can then trigger primitive voiding reflexes as seen in patients with multiple sclerosis, cerebrovascular events and Parkinson's disease. There the end product is a disorder of the surrounding nerve supply.

The myogenic basis of detrusor overactivity is thought to involve changes in the detrusor muscle itself, due to factors such as acidosis, hypoxia and structural changes, resulting in altered detrusor contraction (32). There the end product is abnormal properties of smooth muscle.

New theories have recently been described. The role of the urothelium in regulating bladder function has led to the hypothesis of a mechanosensory basis for OAB. The urothelium seems to be involved in sensory mechanisms and can release chemical mediators (33). Localisation of afferent nerves next to the urothelium suggests that urothelial cells could be targets for neurotransmitters released from bladder nerves or that chemicals released by urothelial cells could alter afferent nerve excitability. There must be a balance between the two mechanisms. In pathological conditions, the balance becomes modified causing a shift that leads to overactivity.

The autonomous bladder theory (34), which is also a relatively new hypothesis, suggests that the detrusor is modular. Each module is supplied by the myovesical plexus and there can be synchronisation of activity between modules. A network of interstitial cells is located beneath the urothelium. As gap junctions provide pathways for direct cell-to-cell communication, the interstitial cellular network may operate as a functional syncytium, integrating signals and responses in the bladder wall (35). 'Miscommunication' can lead to overactivity.

Oestrogen deficiency at the menopause is known to affect the collagen content of skin, and the use of oestrogen treatment has been shown to increase collagen content,

dermal thickness and elasticity of skin in postmenopausal women (36). Estrogens are also known to have an effect on the synthesis of collagen and the metabolism of collagen in the lower genital tract (37). Exogenous oestrogen affects the remodelling of collagen in urogenital tissues, changing the quality and quantity of collagen in postmenopausal women (38). Studies have indicated that exogenous oestrogen results in a reduction of total collagen concentration in the periurethral tissues, a decrease in the cross-linking of collagen and an increase in levels of collagen turnover markers in both continent and incontinent women (39). The increased bladder resting tension and contractility, combined with weaker supportive structure around the urethra, may alter the pressure balance in favour of leakage. Animal models have indicated that oestrogen significantly decreases the amount of collagen fibers, increases the amount of muscle fibers in the detrusor muscle and therefore decreases the collagen/smooth muscle ratio in the detrusor muscle and in the urethral muscle layer (40).

Oestrogen given in pharmacological doses can have a significant hypertropic effect on bladder smooth muscle, resulting in increased contractile function. Other physiological effects of oestrogen include an increase in periurethral vascularity (41). The vascular network of the urethra plays an important role in the maintenance of urinary continence, accounting for one-third of urethral pressure (41). Estrogens influence central neurologic control of micturition, although their exact role is not fully understood.

1.8 Conservative Management

Current therapies for OAB are limited. The focus of much ongoing research is on the improvement of the management for bladder control problems.

1.8.1 Bladder Training

This forms the foundation of OAB treatment. A combination of patient education, scheduled voiding and urge-suppression techniques aim to restore bladder control. Patients are encouraged to gradually extend the time between voids and in doing so, to increase bladder capacity. Urge inhibition can be achieved by practicing manoeuvres designed to inhibit the micturition reflex. Instead of rushing to the toilet,

which increases intra-abdominal pressure and exposes patients to visual cues that can trigger incontinence, patients are encouraged to pause, sit down if possible, relax, and contract pelvic floor muscles repeatedly to diminish urgency and prevent urine loss. When urgency subsides, they can proceed to the toilet at a normal pace. The rationale for the use of bladder training is that it inhibits involuntary bladder contractions. The mode of action remains unclear. It is unknown whether it incorporates other aspects of the physiology and mechanisms of urinary continence or if it induces unspecified psychological pathways. In the process of patients being made aware of the situations that lead to incontinence, patterns of daily activity may change. These can include physical and/or psychological changes and are unique to each individual. It can take months to achieve but may help patients who are physically and mentally able to make these changes.

In a review of this technique by Fantl (42), more than 50% of women in a community dwelling population with urinary incontinence showed a 50–75% reduction in symptoms.

Several randomised, controlled trials, largely involving middle-aged women and women under 75 years of age who had urge or mixed urge–stress incontinence, suggest that cognitively intact, motivated patients respond positively to bladder training (43, 44). Data from a Cochrane review for 172 women from three trials comparing bladder training to no bladder training favoured bladder training, but confidence intervals were wide and no statistically significant differences were found for primary outcome variables (45). Clinical experience suggests that any effects of bladder training tend to wane over time. The length of follow up in most trials was too limited to assess this.

From a practical point of view, behavioural therapy programs may be difficult to apply in many practices as they are time consuming. It does not help to tell patients to lengthen voiding intervals by simply ‘holding on’. Patients must be educated, trained in the acquired techniques and must be highly motivated.

1.8.2 Pelvic Floor Exercise

Patients are taught how to identify and exercise pelvic floor muscles. This can help in aborting detrusor contractions and can be as important as bladder training. It is thought that pelvic floor muscle exercises create a reflex inhibition of the bladder in addition to the provision of enhanced periurethral support.

Nygaard et al (46) reported a significant decrease in the mean number of incontinent episodes per day in a sample of 71 women with detrusor instability after a 3-month course of pelvic floor muscle exercises. 44% percent of all enrolees had at least 50% improvement in the number of incontinent episodes per day. This increased to 56% of enrolees who completed the treatment course. Six months after completing the course of exercises approximately one third of all enrolees reported that they continued to note good or excellent improvement and desired no further treatment.

In a Cochrane review two comparisons of bladder training with pelvic floor muscle training plus biofeedback included 164 women: none of the differences in the primary outcomes achieved statistical significance (45).

1.8.3 Biofeedback

This was first described more than 25 years ago (47). Patients are retrained within a closed feedback loop by making unconscious physiologic processes available as a visual or auditory stimulus. Improvement of at least 50% is common. It is time consuming and therefore seldom used as therapy today.

1.8.4 Electrical stimulation

This therapy has evolved over the past 40 years. Although the mechanism of action of electrical stimulation remains unproven in humans, most experts believe that non-implanted electrical stimulation works by stimulating the pudendal nerve afferent nerves and that it affects striated muscle (48). It is also believed that neuromodulating therapy affects the neural signalling that controls continence.

In a review of the literature by Brubaker, good evidence for the use of electrical stimulators to reduce at least 50% of symptoms of OAB was presented (49). No economic analyses of this therapy are available, but its financial and technical limitations are well acknowledged.

A neuromodulation device for posterior tibial nerve stimulation (PTNS) was released in the USA and UK for treatment of OAB. It is based on the work done in the 1980s using an acupuncture needle placed in the posterior tibial nerve and passing an electric current through it (50). This creates a feedback loop that neuromodulates bladder innervation. Although this treatment has no side effects and has success rates of between 60 – 80%, it requires multiple visits (weekly over 12 weeks) and a significant time commitment. Several other investigators have since reported compelling results with the use of PTNS for the treatment of OAB, some of which have provided highly favourable comparisons to pharmacotherapy (51, 52).

The Study of Urgent PC vs Sham Effectiveness in Treatment of Overactive Bladder Symptoms (SUmiT) was a multicenter, double-blind, randomized, controlled trial comparing the efficacy of percutaneous tibial nerve stimulation to sham therapy (53) . This is the first neuromodulation study to use a published validated sham component. A total of 220 adults with overactive bladder symptoms were randomized to 12 weeks of treatment with weekly percutaneous tibial nerve stimulation or sham therapy. Overactive bladder and quality of life questionnaires as well as 3-day voiding diaries were completed at baseline and at 13 weeks. Subject global response assessments were completed at week 13. The 13-week subject global response assessment for overall bladder symptoms demonstrated that percutaneous tibial nerve stimulation subjects achieved statistically significant improvement in bladder symptoms with 54.5% reporting moderately or markedly improved responses compared to 20.9% of sham subjects from baseline ($p > 0.001$). All individual global response assessment subset symptom components demonstrated statistically significant improvement from baseline to 13 weeks for percutaneous tibial nerve stimulation compared to sham. Voiding diary parameters after 12 weeks of therapy showed percutaneous tibial nerve stimulation subjects had statistically significant improvements in frequency, night time voids, voids with moderate to severe urgency

and urinary urge incontinence episodes compared to sham. No serious device related adverse events or malfunctions were reported.

The trial provides level I evidence that percutaneous tibial nerve stimulation therapy is safe and effective in treating overactive bladder symptoms.

The neuromodulator devices are expensive and their use is limited in the public health sector in South Africa.

1.9 Medical Management

Many classes of drugs, often used as an adjunct to various non-pharmacological therapies, have been studied for the treatment of OAB. The most commonly used medications to treat OAB have anticholinergic properties. Anticholinergics are competitive inhibitors of acetylcholine. These agents block the muscarinic effects and thereby inhibit involuntary bladder contractions.

A Cochrane review favoured anticholinergic drugs compared with bladder training for symptomatic improvement of OAB (54). A combination of anticholinergics with bladder training was most effective.

Several drugs, with different doses, formulations, and routes of administration are available in clinical use, but because of high costs, the use of these preparations in resource scarce environments is limited to immediate-release oral oxybutynin.

Oxybutynin has anticholinergic effects and acts mainly on the muscarin-3 (M3) subtype receptors. These receptors are responsible for the contractile properties of the bladder.

Given in the immediate-release oral formulation, oxybutynin has led to a clinically significant improvement, defined as a reduction in incontinence episodes by more than 50 percent, in approximately 60 to 80 percent of study subjects. (55.56). As such it is an effective drug, but patient compliance is poor because of its side effect profile and many patients discontinue treatment. Unfortunately, salivary glands share an M3

receptor, and therefore dry mouth is a major side effect and the most common reason patients discontinue its use. Dry mouth is reported in up to two thirds of subjects (57).

Although dry mouth is most common, other bothersome side-effects including constipation, gastroesophageal reflux, blurry vision, urinary retention and cognitive impairment can occur. A starting dose of 2.5 mg daily is standard. This daily dose can be increased by 2.5 mg until there is a satisfactory response in symptoms or the adverse effects become too troublesome. The effective dose is found by titrating the medication to relieve the symptoms barring the limit of side effects on dosing. Reducing the dose might help to relieve the side effects and should be attempted before discontinuation. A maximum dose is 15mg daily.

CHAPTER 2
Acupuncture for OAB

2.1 Available Evidence for acupuncture for OAB

In a recent randomised, controlled trial, Emmons et al (58) compared treatment acupuncture with a placebo acupuncture for OAB. A total of 74 women completed all aspects of the study and were analyzed. The treatment arm involved classic acupuncture in bladder specific points given weekly over four weeks, whereas the placebo arm included acupuncture in relaxation points. Although there was a reduction in the number of incontinence episodes in the treatment group compared to in the placebo group (59% vs. 40%), this difference was statistically insignificant. There were, however, statistically significant reductions in urinary frequency (14% vs. 4%, $p<0.03$) and urgency (30% vs. 3%, $p<0.016$) in the treatment group. In this group, maximum cystometric capacity increased by 12% compared to 4% in the control group, which was marginally statistically significant ($p< 0.049$). Most considerably, the quality of life, as assessed by the incontinence impact questionnaire score, showed an improvement in the treatment group (52% vs. 23%, $p<0.004$). Therefore, in this study, acupuncture had a significant short-term effect on OAB symptoms, similar in scope to the improvement offered by drug therapy and physical or behavioural therapy.

In another interesting study, Kelleher et al (59) compared the efficacy of acupuncture to conventional anticholinergic drug therapy (oxybutynin) in the management of irritative bladder symptoms. The 39 patients in the study had not received any other treatment before study inclusion. Twenty patients received six weekly acupuncture treatments and 19 patients received daily oral oxybutynin. Both groups were reviewed weekly. Although urgency and frequency were significantly improved by both methods of treatment (60% and 67%; 26% and 18%; $p<0.005$), nocturia was significantly improved only by acupuncture (25%; $p<0.05$). There was no significant improvement in urge incontinence in either group. Unsurprisingly, the frequency of side effects was much higher in the group treated with anticholinergics. Both groups experienced reduced levels of anxiety due to improvement in their bladder symptoms.

Three months following the last treatment, 8 of the 20 patients in the acupuncture group were symptom free versus 7 of the 19 patients in the oxybutynin group. This trial demonstrated that acupuncture was as effective as anticholinergic therapy in the management of irritative bladder symptoms, but without the adverse effects often associated with the drug therapy.

Chang (60) allocated 52 women (age 17 to 52) with frequency and urgency to one of two groups. The first group received treatment acupuncture at the points used for urinary symptoms. The second group received acupuncture at the points used for gastrointestinal disease. All the participants underwent urodynamic measurements before and after acupuncture. Of the patients in the first group, 84% reported symptomatic improvement whereas only 23% of the patients receiving acupuncture at the gastro-intestinal points reported an improvement. It is not clear how this improvement was calculated and no statistical analysis was done. Presentation of these data makes it difficult to determine a specific result. The maximum cystometric capacity increased in 89% ($p<0.01$) and the peak urinary flow rate decreased in 77% of participants ($p<0.02$) after acupuncture at the bladder points. The investigators concluded that in the group receiving acupuncture at bladder points, detrusor activity was suppressed. Of note is that 54% of the patients had temporary improvement and required second and third treatments.

There have been a number of non-controlled observational trials demonstrating the efficacy of acupuncture on bladder symptoms. Philip et al (61) successfully used acupuncture to treat patients with idiopathic detrusor overactivity. In their open non-controlled study, 20 patients (aged 19 to 69) completed weekly acupuncture treatments for 10 to 12 weeks. 63% percent of their cohort became continent. The most marked finding was that in the group that showed the most dramatic improvement, frequency was completely abolished. In the subgroup with diurnal symptoms, there was significant symptomatic improvement in 10 out of 13 patients (77%). Urodynamic changes were, however, disappointing with few objective changes and no improvement in the pattern of the filling curves. They concluded that acupuncture is at least as effective as other non invasive treatments for diurnal symptoms of idiopathic detrusor overactivity, with the added advantage of no side effects and with excellent patient tolerance. Unfortunately this study was poorly

designed and was open to bias during the follow-up assessment. A critical limitation of this study was that there was no statistical analysis done.

Acupuncture also appears to improve enuresis in children. A report from Minni (62) described the effect of acupuncture in 22 children (age 5 to 12) with enuresis. All the children had acupuncture treatment once a week for 8-10 weeks. Clinically, a gradual elimination of enuresis was observed in 11 cases and an improvement in the other seven children. The authors concluded that acupuncture was effective in suppressing uninhibited bladder contractions in enuresis. It is well established that there is a significant spontaneous remission rate for childhood enuresis. This limits the findings of the study as results may not be applicable to adults. It is a small study and no statistical evidence for findings was given.

In a small open clinical follow-up study by Bergstrom et al (63) significant improvement for 25 older women with urge- or mixed-type urine incontinence was documented after a series of twelve acupuncture treatments. Patients were followed-up one and 3 months after treatment. Patients were found to only improve after the 8th treatment. The nocturia mean was significantly reduced at follow-ups (from 1.57 to 0.97, p=0.004–0.009). The frequency mean did not show any significant changes. Urge and UI were both significantly reduced from baseline to three months after the treatment. QoL scores also improved significantly. At three months follow-up, there was a tendency for the improvement to decline, but this was not significant. The small sample size limits the validity of this study.

The use of acupuncture for the treatment of detrusor overactivity in patients with chronic spinal cord injuries was investigated by Honjo et al. (64). A total of 13 patients were treated. In this small study, incontinence disappeared in two and decreased by up to 50% in a further six patients.

2.2 Possible Mechanism of Action

Acupuncture has been used widely in the treatment of diseases in China for thousands of years. Its true mechanism of action, however, remains obscure. According to

traditional Chinese medicine, acupuncture is based on the theory that there are energy channels called meridians that run throughout the body and that disease results from blockages of this "life energy". Acupuncture is used as one method of releasing these blockages. Given the western, biomedical model, acupuncture is difficult to comprehend as there is no evidence to support the existence of these meridians. As acupuncture has become increasingly more accepted in the Western World, scientists have looked for westernised explanations to describe why it works and there is an intriguing and growing body of research on the topic. In the bladder, specifically, different physiological mechanisms might be at work.

It is accepted that acupuncture partially works through the endorphinergic system (65, 66). Endorphins are increased by acupuncture (67, 68). Enkephalins are endogenous ligands for endorphin receptors and have been demonstrated in lower urinary tract smooth muscle and in ganglia of the urinary bladder (69). Urinary bladder motility is depressed by enkephalins via activity on vesical ganglia (70). In animal studies it has been shown that the pontine micturition centre is under tonic inhibition from enkephalins (71) and that enkephalins injected intracerebroventricularly increase the threshold for micturition (72). Thus stimulation of the endorphinergic system seems to have an inhibitory effect on the pontine micturition centre and thus might help with bladder control.

Acupuncture is a form of somatic sensory stimulation. In anaesthetised animals, Sato has shown that somatic afferent stimulation on the perineal area inhibits micturition contractions of the urinary bladder (73).

Researchers at the University of Southampton and University College London have recently shown that the impact of acupuncture goes beyond the acknowledged placebo effect caused by the patient's own expectation of feeling benefit of treatment (74). Positron Emission Tomography scans were performed to explore the cerebral consequences in patients in three different arms of the study: real acupuncture, placebo acupuncture and skin prick only. They found that the insula ipsilateral to the site of needling was activated to a greater extent during real acupuncture than during the placebo intervention. Real acupuncture also caused greater activation than skin prick in the right dorsolateral prefrontal cortex, anterior cingulate cortex, and

midbrain. These results suggest that real acupuncture has a specific physiological effect.

2.3 Issues with design of acupuncture studies

Many studies reporting different measures to improve irritative bladder symptoms are criticised for the significant placebo effect found in them. Little is understood about the complexities of the interaction between acupuncture, placebo, patient, and practitioner. This relative ignorance may be responsible for the confusing results of acupuncture trials and the lack of clarity emerging from systematic reviews.

In placebo controlled trials of conventional treatment methods, approximately one third of patients experience a placebo response. Trials investigating the role of acupuncture in the treatment of OAB are no different. They present major methodological problems, particularly as we understand so little about the underlying biological mechanisms.

The design of an appropriate placebo control group is also a major challenge. In trials of new drugs, double blinding is the accepted standard. However, since acupuncture is a procedure rather than a pill, it is difficult to design studies in which both the acupuncturist and patient are blinded as to the treatment being given. The same problem arises in double-blinding of virtually all surgical procedures. One proposed solution to blinding patients has been the development of 'sham acupuncture'. Needling is performed superficially or at non-acupuncture sites. Controversy remains over whether sham acupuncture may function as a true placebo (75).

'Sham needling' is not an inert equivalent for the treatment it mimics as it may be have a real effect similar to that of acupuncture. It is more than a placebo and does seem to have a therapeutic effect that negates its use as a real placebo. It could be seen as an active intervention in its own right - an intervention that is complex with multiple components and synergistic interaction (76).

The debate for a true placebo for acupuncture is ongoing. Only with more rigorous scientific research will the role of the placebo effect be further elucidated.

2.4 Objectives of the study

The objective of the study was to investigate acupuncture as a treatment modality to improve the symptoms of patients with refractive OAB.

- The primary aim was to evaluate the effect on frequency, nocturia and UUI.

- The secondary aim was to evaluate the effect on self-perceived QoL.

CHAPTER 3
Patients and Methods

3.1 Study design

Twenty consecutive patients who regard their symptoms of OAB as not satisfactorily relieved by standard treatment were invited to participate and all agreed. The patients functioned as their own controls over a period of time. Each patient's pre-treatment evaluation was compared to post-treatment evaluation at different points. All patients have received conventional treatments prior to recruitment. Fixed treatment regimes were not changed during the study.

3.2 Study setting

Recruitment took place at the Female Continence Clinic (FCC) at Groote Schuur Hospital (GSH) in Cape Town. GSH is one of the major teaching hospitals of the Associated Academic Hospitals' group and is an integral component of the Health Service of the Provincial Administration of the Western Cape, South Africa. The University of Cape Town is associated with Groote Schuur Hospital. The FCC is a tertiary level clinic which receives referrals from general practitioners, primary care clinics, district hospitals and secondary level hospitals in its catchment area.

The patient population consists mainly of individuals of middle to low socio-economic status.

3.3 Subject selection

The participants were women with OAB that is refractive to standard treatment given at our specialised unit. Standard treatment involves concurrent behavioural and pharmacology treatment. Potential participants were identified by consultants and registrars from the Department of Gynaecology and Department of Urology who staff the clinic and were recruited by the Principle Investigator.

Inclusion criteria

1. Aged ≥18 years.
2. Refractive OAB.
3. Able to give informed consent.

Exclusion criteria

Patients known with conditions that can cause similar symptoms as OAB was excluded. Treatment naïve patients and patients with mainly stress incontinence were also excluded.

1. Mixed Incontinence with Stress Incontinence as dominant symptom.
2. Urinary tract infection.
3. Urinary tract obstruction.
4. Interstitial cystitis.
5. Urinary Tract Fistula.
6. Urethral diverticulum.
7. Urogenital tumours.
8. Cerebrovascular lesions, dementia, Parkinson's disease and multiple sclerosis.
9. Pregnancy or recent birth.
10. Acupuncture treatments for any other condition.
11. Needle phobia.
12. Newly diagnosed patients with OAB that have not completed at least three months of pharmacological treatment.
13. Newly diagnosed patients with OAB that have not completed at least three months of behavioural therapy.

3.4 Acupuncture Treatment

Acupuncture was performed weekly for four weeks (see time line below). Disposable stainless steel needles that were 0.22 mm wide and are 50-mm long were used for the procedures. The acupuncture was performed by experienced physiotherapists and supervised by a consultant urogynaecologist who is board-certified in medical acupuncture. The following acupuncture points were used:

- Bilateral Sanyinjiao, Sp6; 4 cun[1] superior to the tip of the medial malleollus.

- Bilateral Weiyang, BL 39; at the lateral end of the popliteal crease, medial to the tendon of biceps femoris.

- Bilateral Pangguangshu, BL 28; in the depression, 1.5 cun[1] lateral to the midline between the lower medial border of the posterior superior iliac spine and the sacrum.

- Midline Guan Yuan, CV4; on the saggital line, two cun[1] superior to the crest of the pubic symphysis.

[1] The cun is a measurement relative to the patient's body that is used to find acupuncture points. One cun is equal to the space between the distal interphalangeal joint and the proximal interphalangeal joint on the middle finger.

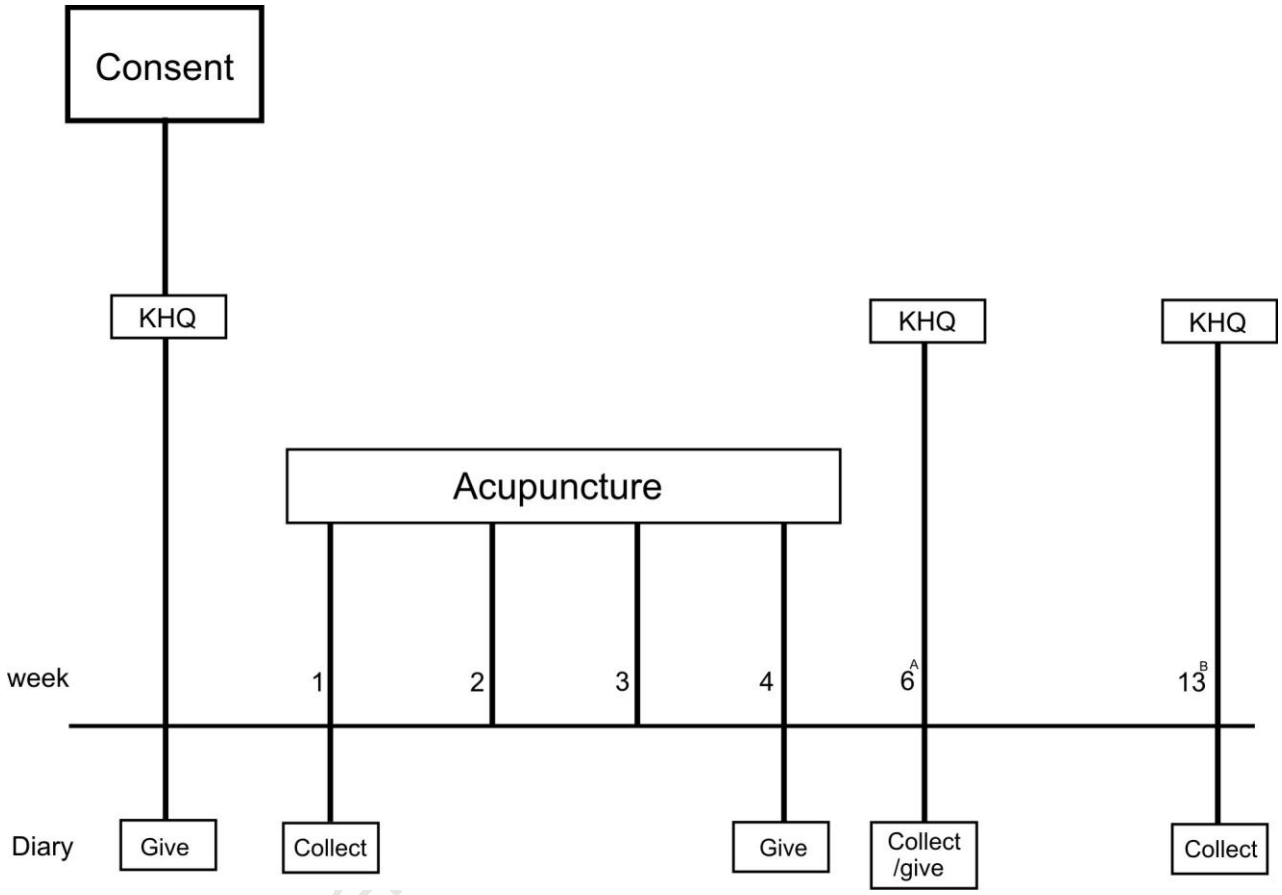
Traditionally these points have been used in the treatment of urinary problems.

An acupuncture point-finder was used to aid in identifying the acupuncture points. It comprises of a point finder electrode that is passed over a patient's skin, an electrode held by the patient and a balancing and sensitivity adjustment circuit electrically connected to the point finder and electrodes so as to produce an imbalance signal when the point finder electrode passes over an acupuncture point. An amplifier circuit is provided in connection with the balancing and sensitivity adjustment circuits that generate an audio signal. The point finder was only used during the first treatment. Thereafter the points were marked with long lasting dye.

Needles were inserted at the same 7 points during each of the weekly sessions and remained in place for 20 minutes.

3.5 Study Time Line

Figure 1: Illustration of the Study Time Line:



A: 'week 6' refers to 5 completed weeks after the first acupuncture

B: week 13 refers to 12 completed weeks after the first acupuncture and will be referred to as '3 months' in the study

3.6 Data Collection

3.6.1 Recruitment

Demographic data was gathered by completing the data collection sheet (Refer to appendix 1). Following this, each participant completed the King's Health Questionnaire (Refer to appendix 2) to assess baseline QoL.

3.6.2 Measurements

The bladder diary

Participants kept three-day bladder diaries (Refer to appendix 3) at three different times during the study: prior to treatment, at week 6 and at 3 months (Refer to time line). These data collecting points are similar than that of the Emmons trial (58). Participants recorded the frequency of day and night time voiding and incontinence episodes over three day periods. Bladder diaries are commonly used for assessment of treatment outcome in both clinical practice and research studies (62, 63).

The King's Health Questionnaire

Each participant's QoL was assessed at three different times during the study: prior to treatment, week 6 and 3 months (Refer to time line). The King's Health Questionnaire was used for this purpose. This is a condition-specific health-related quality-of-life instrument for the assessment of patients with lower urinary tract conditions including OAB. The questionnaire was designed at a tertiary referral urogynaecology unit at King's College Hospital, London, following six different pilot studies (64). The questionnaire was shown to be reliable both by test-retest analysis and by measurement of its internal consistency. The questionnaire was found to be a valid and reliable instrument for the assessment of QoL in women with urinary incontinence (65).

The questionnaire translates into two general domains - General Health and Incontinence Impact - and seven lifestyle domains comprising of Role Limitation, Physical Limitation, Social Limitation, Personal Limitation, Emotional Limitation, Sleep Limitation and Severity Scoring. Scores range from 0 to 100; where 100 is the worst possible condition and 0 means that there is no influence on daily living. A decrease in the score therefore means improvement in QoL.

3.7 Statistical Analysis

Demographic data was entered into Microsoft Excel and analysed using SPSS Statistics 18 (SPSS Corporation Chicago, Illinois, USA).

Data from the bladder dairies and the KHQ was collected at successive time intervals and analysed. Fisher's Least Significant Difference (LSD) procedure was used. The null hypothesis was tested with Analysis of Variance (ANOVA). Pairwise comparisons of the self-control groups were done.

Statistical significance was defined at $p \leq 0.05$.

3.8 Ethics

Written consent was obtained in the patients' language of choice (Refer to appendix 4, appendix 5 and appendix 6). The consent form also contained information regarding the aim of the study, acupuncture treatment and time line.

Ethical approval was obtained from the Research Ethics Committee of the Faculty of Health Sciences of The University of Cape Town (REC REF: 009/2009).

All aspects of the study complied with the Declaration of Helsinki, Sixth revision, 59th Meeting, Seoul (66).

CHAPTER 4

Results

4.1 Patient Characteristics

A total of 20 women were recruited into the study. All invited patients agreed to participate. One participant did not complete the trial due to work commitments.

Table 1 shows the patient characteristics of the study group. The mean age of the 20 study participants was 51 years (Standard Deviation, 10.1) with only three patients included who were less than 40 years of age. The mean body mass index was 31 (Standard Deviation, 7.2).

Most women recruited into the study were of mixed race (80%). Most study participants (90%) had at least one year of secondary education. Of the participants 55% were in a stable relationship and 60% were sexually active. Eighty-five percent of the women recruited into the study had at least one vaginal delivery. The minority had instrumental deliveries and episiotomies.

Most of the women were postmenopausal (75%) and 25% had a history of previous or current hormone therapy use. Only 5% of participants were still on HRT. Thirty percent of the patients had a previous hysterectomy and only 5% had prolapse symptoms at presentation. 40% of patients had a previous anterior vaginal repair procedure. The minority of patients had stress-incontinence surgery and surgery for posterior compartment prolapse.

More than half of the study group were treated for hypertension (65%); half of these patients used diuretics.

Table 1: Patient Characteristics

Age, mean (standard deviation)	51	(10.064)
Body mass index, mean (standard deviation)	31	(7.240)
Race:		
Mixed Race	18	(90)
White	2	(10)
Education:		
At least secondary level	18	(90)
Interpersonal relationship		
In stable relationship	11	(55)
Habits:		
Smoking	8	(40)
Obstetric history:		
Vaginal delivery [1]	17	(85)
Instrumental delivery[2]	4	
Episiotomy	5	(25)
Gynaecological history:		
Postmenopausal	15	(75)
Previous hormone therapy use	5	(25)
Hysterectomy[3]	6	(30)
Prolapse symptoms	5	(25)
Medical history:		
Hypertension	13	(65)
Current diuretic use	7	(35)
Diabetes	5	(25)
Gynaecological surgical history:		
Anterior vaginal repair	8	(40)
Posterior vaginal repair	2	(10)
Stress incontinence surgery [4]	5	(25)
Special Investigations:		
Cystoscopy	10	(50)
Urodynamic Studies	15	(75)

1 one never pregnant, one only miscarriages, one only c-sections

2 three forceps deliveries, one vacuum extraction

3 two abdominal, four vaginal

4 details unknown

On 75% of participants urodynamic studies were performed. It is not clear why this was not done in the other 25% of participants.

Only 50% of patients had a cystoscopy. Therapies directed toward the uroepithelial dysfunction and neural up regulation associated with interstitial cystitis/painful bladder syndrome may be an important adjunct for patients who have failed or have had a partial response to anticholinergic therapy and behaviour modification.
Cystoscopy should therefore be indicated in patients with a history of refractive symptoms and recurrent urinary tract infection. Although some urogynaecology units suggest that all patients in whom symptoms of overactive bladder develop should undergo cystoscopy to rule out carcinoma in situ and other intravesical abnormalities, the cost effectiveness of this approach is uncertain.

Table 2 shows symptoms of OAB at initial presentation to FCC and at the time of study enrolment. Symptoms included urinary frequency, urinary urgency, urge incontinence and nocturia. The median time interval between onset of symptoms and study enrolment was six years (Inter Quartile range, 4-13 years). The frequency of symptoms were similar between initial presentation to FCC and study recruitment; urinary frequency, nocturia and urinary urgency were all present in the majority of patients at initial presentation (95%, 80% and 100%, respectively) and at study enrolment (100%, 90% and 100%, respectively).

Table 2: Overactive bladder symptoms at presentation and recruitment

Symptom	**Initial**	**Current**
Frequency	19 (95)	20 (100)
Nocturia	16 (80)	18 (90)
Urgency	20 (100)	20 (100)
Urge Incontinence	11 (55)	8 (40)

Table 3 reflects the conservative management strategies of patients at our unit prior to enrolment. At time of enrolment, 65% of patients were still practising pelvic floor exercises and 35% of patients were still receiving oxybutynin. The dose of oxybutynin varied according to therapeutic response and side effects. The majority of patients discontinued oxybutynin due to ineffectiveness and intolerance. In addition to standard treatments, four patients (20%) also received bladder installations. Notably, at recruitment, none of the participants were utilizing bladder training to control symptoms.

Table 3: Management strategies of patients with overactive bladder syndrome prior to enrolment.

	Median duration, years (Inter Quartile range) [1]	**Ongoing treatment,** number (percentage)
Pelvic floor exercises	1 (1-4)	13 (65%)
Bladder training	0.5 (0.3- 0.6)	0
Oxybutynin	3.5 (1.75-6)	7 (35%)

1 at time of enrolment

4.2 Bladder Diaries

4.2.1 Frequency

Table 4 represents the mean frequency over three days for the three different intervals. At recruitment it was 32. This decreased to 26 and 25 at week 6 and 3 months respectively.

Table 4: Frequency means

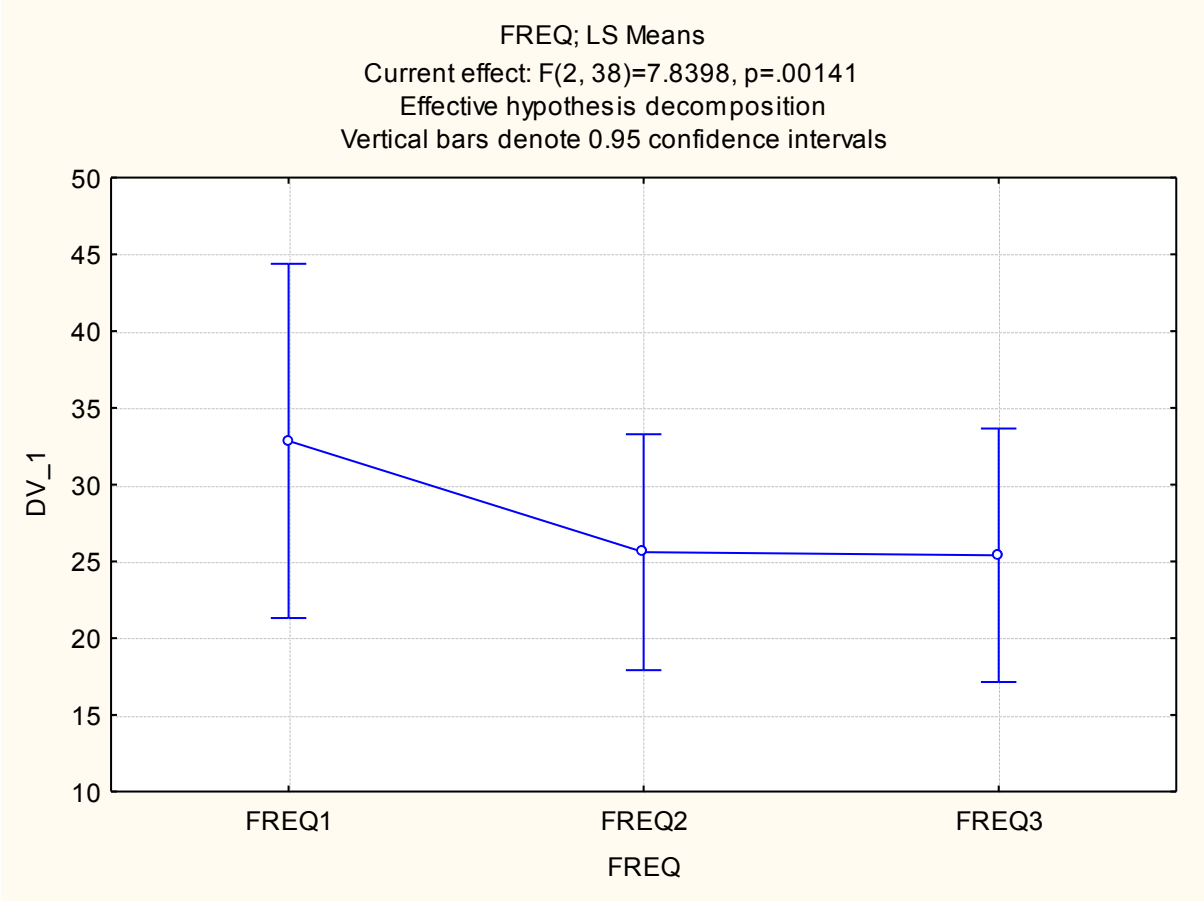
	Mean	Lower 95% CI	Upper 95% CI
FREQ1[1]	32	21	44
FREQ2[2]	26	18	33
FREQ3[3]	25	17	34

1 frequency at baseline

2 frequency at week 6

3 frequency at 3 months

Figure 2: Analysis of Variance for frequency means



There is a difference between the groups (p=0.001).

Table 5: Comparisons of frequency means using Fisher's Least Significant Difference

	FREQ	{1}	{2}	{3}
1	FREQ1		0.001680	0.001293
2	FREQ2	0.001680		0.926166
3	FREQ3	0.001293	0.926166	

There was a significant decrease in frequency from baseline to week 6 (p=0.002) and from baseline to 3 months (p=0.002). There was no difference between week 6 and 3 months (p=0.9).

4.2.2 Nocturia

Table 6 represents the mean number of nocturia over three days for the three different intervals. At recruitment it was 10. This decreased to 6 at week 6 and increased to 7 at 3 months.

Table 6: Nocturia means

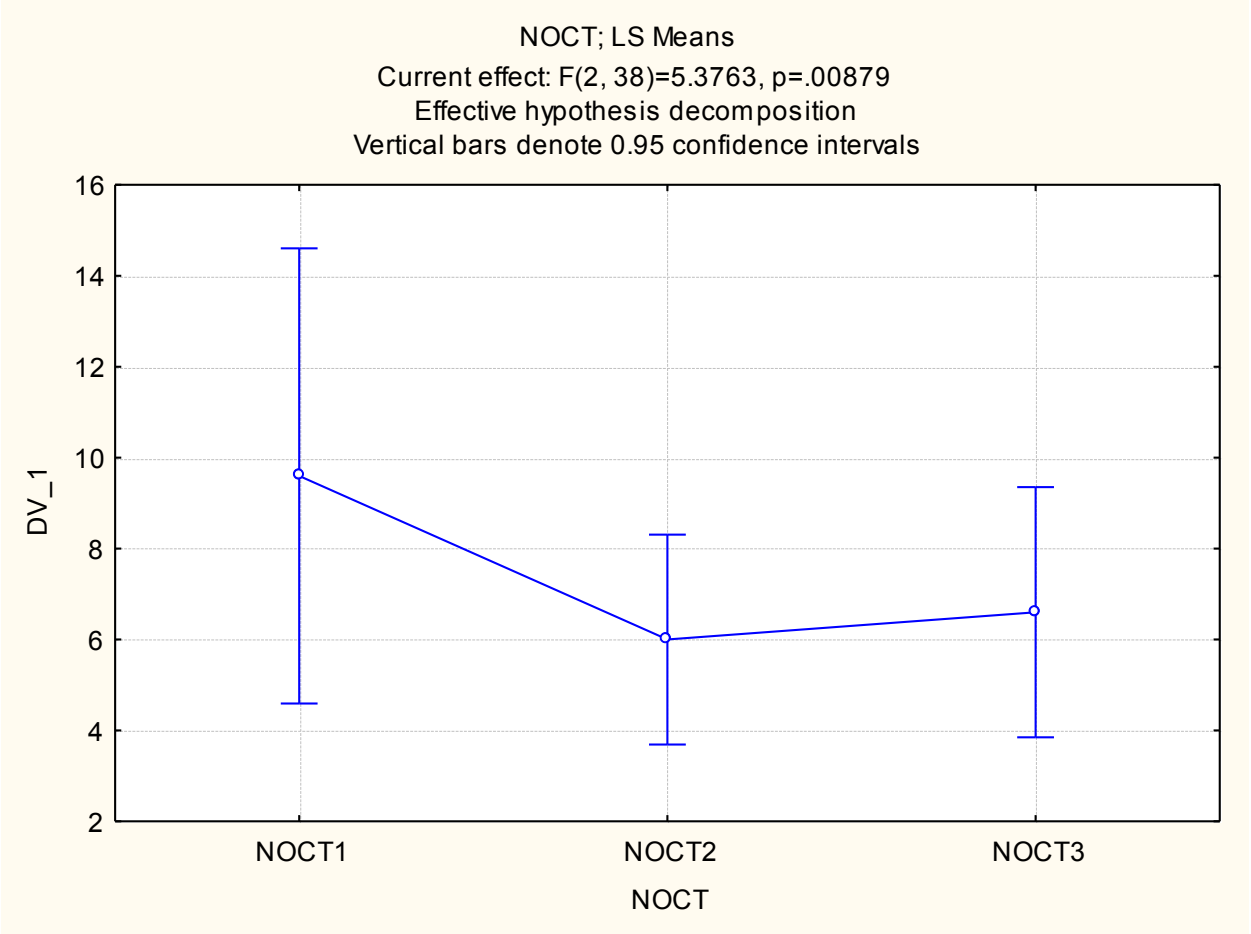
	Mean	Lower 95% CI	Upper 95% CI
NOCT1[1]	10	5	15
NOCT2[2]	6	4	8
NOCT3[3]	7	4	9

1 nocturia at baseline

2 nocturia at week 6

3 nocturia at 3 months

Figure 3: Analysis of Variance for nocturia means



There is a difference between the groups (p=0.009).

Table 7: Comparisons of nocturia means using Fisher's Least Significant Difference

	NOCT	{1}	{2}	{3}
1	NOCT1		0.004044	0.014920
2	NOCT2	0.004044		0.612973
3	NOCT3	0.014920	0.612973	

There was a significant decrease in nocturia from baseline to week 6 (p=0.004) and from baseline to 3 months (0.015). There was no difference between week 6 and 3 months (p=0.6).

4.2.3 Incontinence

Table 8 represents the mean number of incontinence over three days for the three different intervals. At recruitment this was 9. This decreased to 7 and 6 at week 6 and 3 months respectively.

Table 8: Incontinence means

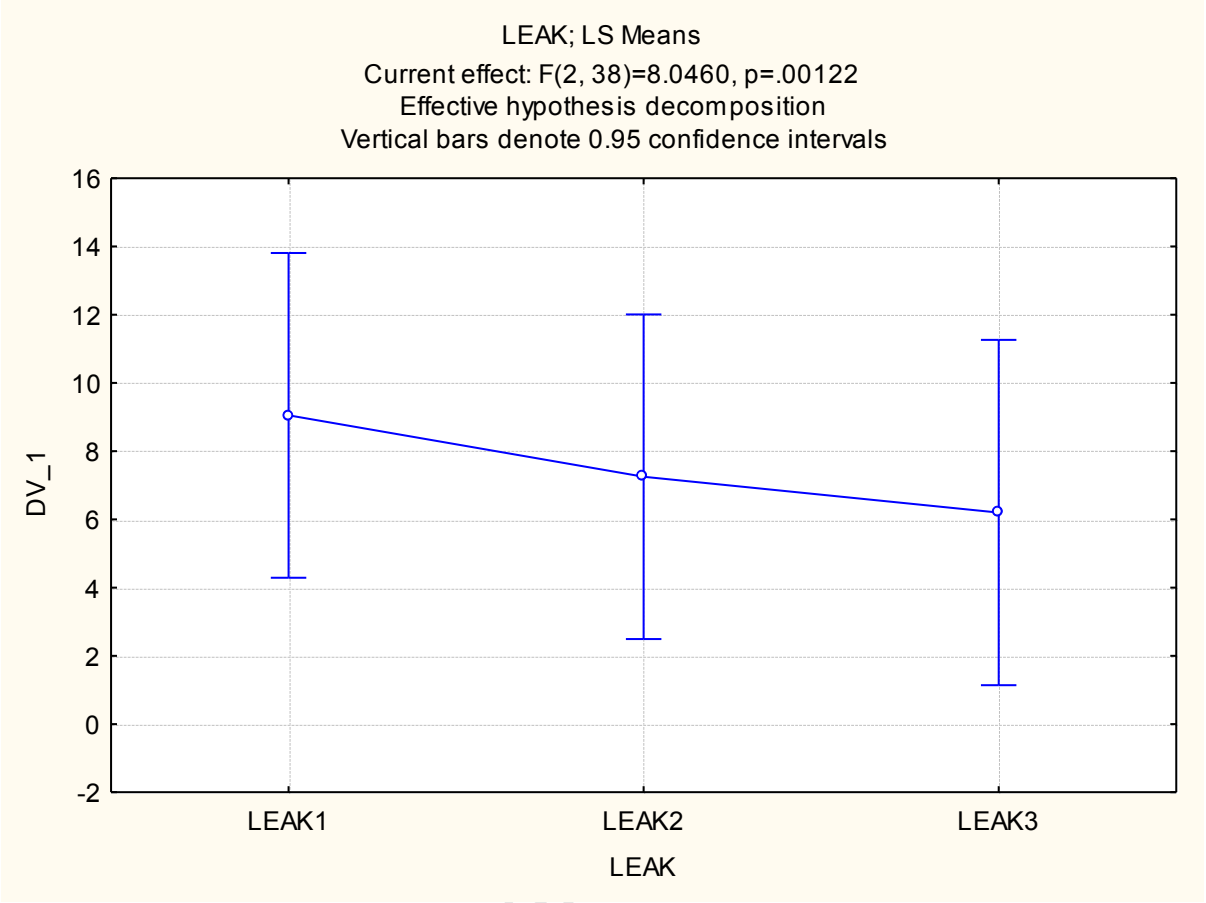
	Mean	Lower 95% CI	Upper 95% CI
LEAK1[1]	9	4	14
LEAK2[2]	7	3	12
LEAK3[3]	6	1	11

1 incontinence at baseline

2 incontinence at week 6

3 incontinence at 3 months

Figure 4: Analysis of Variance for incontinence means



There is a difference between the groups (p=0.001).

Table 9: Comparisons of incontinence means using Fisher's Least Significant Difference

	LEAK	{1}	{2}	{3}
1	LEAK1		0.016658	0.000312
2	LEAK2	0.016658		0.152195
3	LEAK3	0.000312	0.152195	

There is a significant decrease in incontinence from baseline to week 6 (p=0.02) and from baseline to 3 months (p=0.0003). There is no further significant decrease from week 6 to 3 months (p=0.15).

4.3 The King's Health Questionnaire

4.3.1 KHQ: General Health

Table 10 represents the mean score in General Health as documented on the KHQ at baseline and week 6 and 3 months respectively. This score is calculated out of 100 where 0 represents no influence on QoL.

Table 10: General Health score means

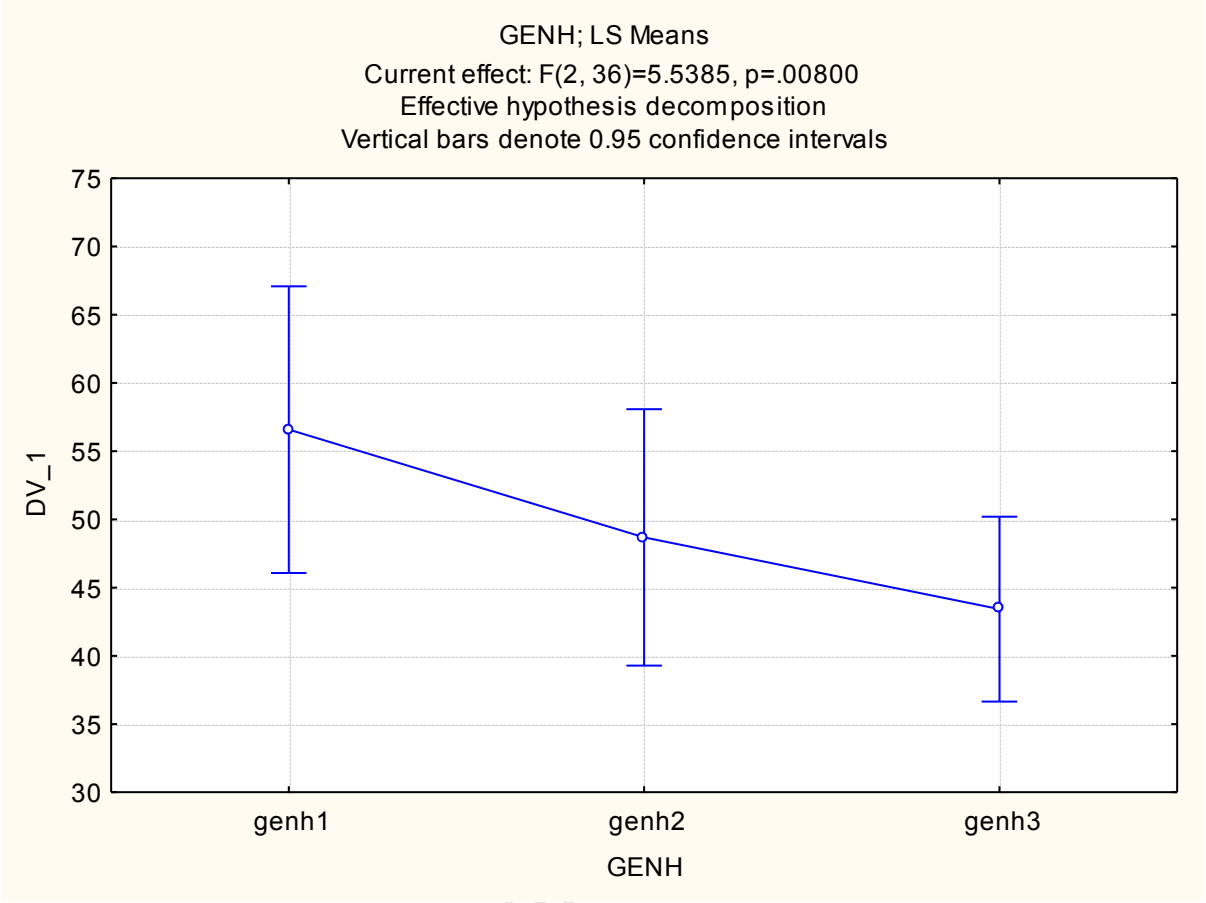
	Mean	Lower 95% CI	Upper 95% CI
genh1[1]	57	46	67
genh2[2]	49	39	58
genh3[3]	43	37	50

1 general health score at baseline

2 general health score at week 6

3 general health score at 3 months

Figure 5: Analysis of Variance for General Health score means



There is a difference between the groups (p=0.008).

Table 11: Comparisons of General Health score means using Fisher's Least Significant Difference

	GENH	{1}	{2}	{3}
1	genh1		0.054951	0.002150
2	genh2	0.054951		0.194345
3	genh3	0.002150	0.194345	

There was a marginal improvement in general health scores from baseline to week 6 (p=0.05), but a significant improvement from baseline to 3 months (0.002).There was no difference between week 6 and 3 months (p=0.2).

4.3.2 KHQ: Incontinence Impact

Table 12 represents the mean score in Incontinence Impact as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 12: Incontinence Impact scores means

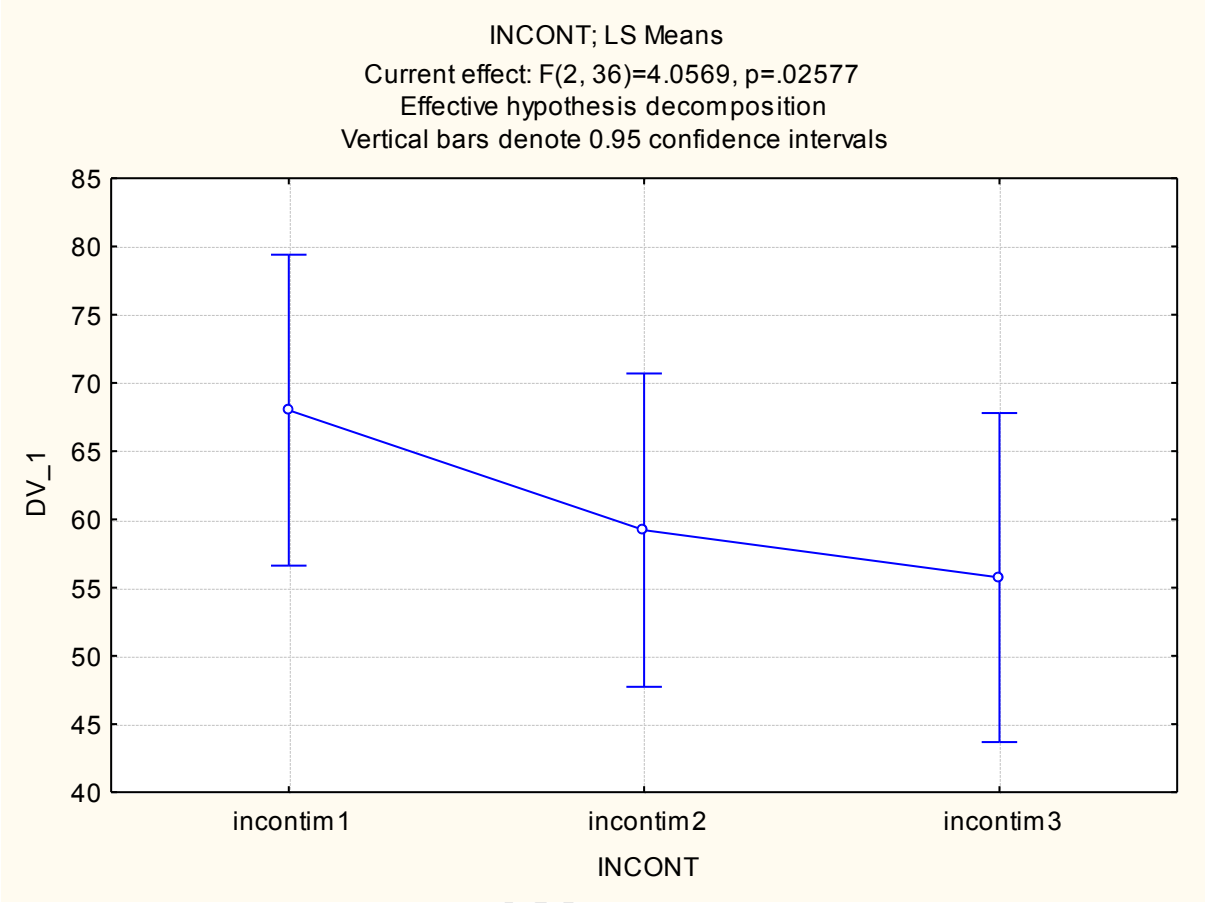
	Mean	Lower 95% CI	Upper 95% CI
incontim1[1]	68	57	79
incontim2[2]	59	48	71
incontim3[3]	56	44	68

1 incontinence impact score at baseline

2 incontinence impact score at week 6

3 incontinence impact score at 3 months

Figure 6: Analysis of Variance for Incontinence Impact score means



There is a difference between the groups (p=0.026).

Table 13: Comparisons of Incontinence Impact score means using Fisher's Least Significant Difference

	INCONT	{1}	{2}	{3}
1	incontim1		0.055326	0.008960
2	incontim2	0.055326		0.438910
3	incontim3	0.008960	0.438910	

There is no difference between incontinence impact at baseline and at week 6 (p=0.055). There is a significant improvement in impact scores from baseline to 3 months (p=0.009) and no difference between week 6 and 3 months (p=0.4).

4.3.3 KHQ: Role limitation

Table 14 represents the mean score in Role Limitation as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 14: Role Limitation score means

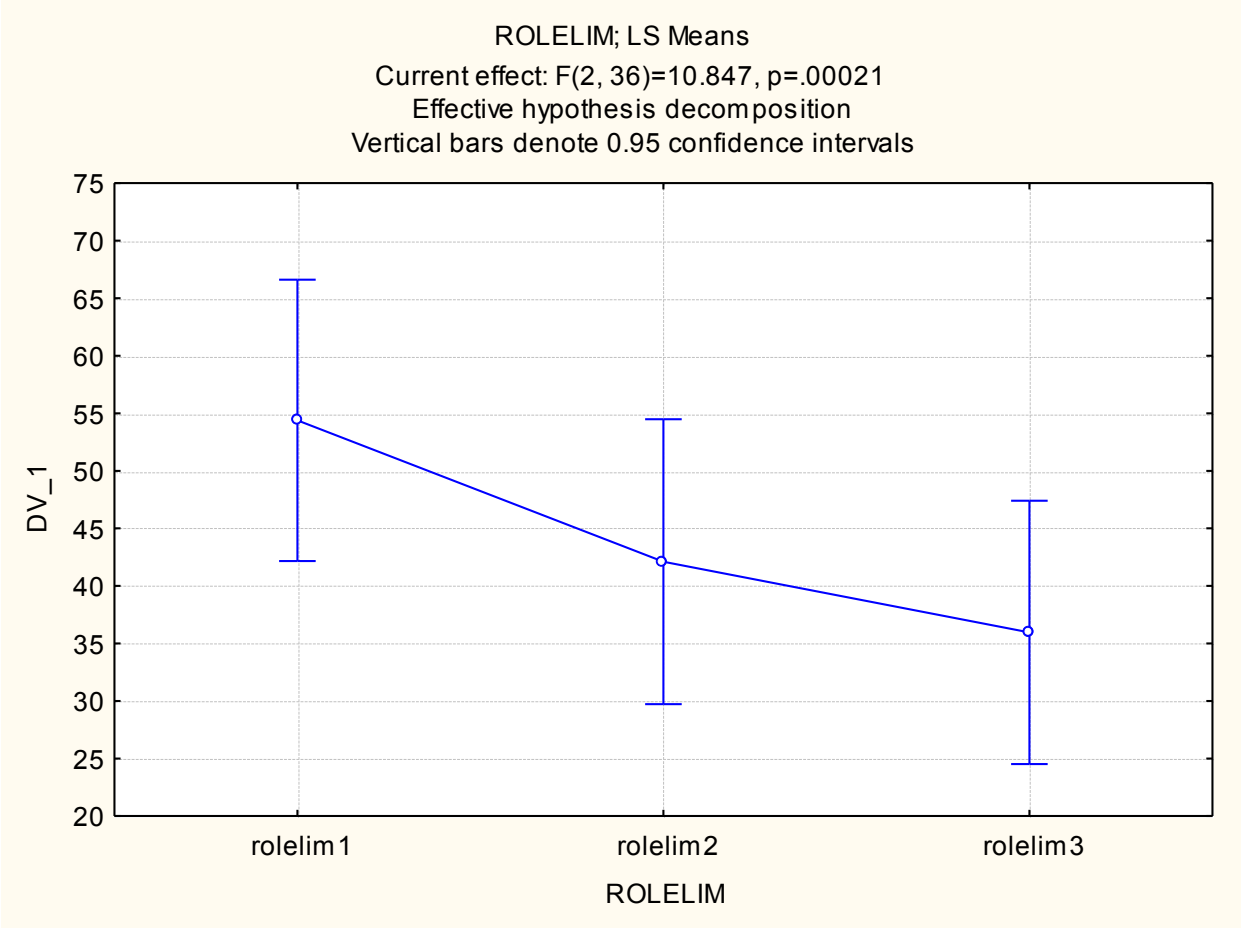
	Mean	Lower 95% CI	Upper 95% CI
rolelim1[1]	54	42	67
rolelim2[2]	42	30	54
rolelim3[3]	36	25	47

1 role limitation score at baseline

2 role limitation score at week 6

3 role limitation score at 3 months

Figure 7: Analysis of Variance for Role Limitation score means



There is a difference between the groups (p=0.0002).

Table 15: Comparisons of Role Limitation score means using Fisher's Least Significant Difference

	ROLELIM	{1}	{2}	{3}
1	rolelim1		0.004294	0.000055
2	rolelim2	0.004294		0.135864
3	rolelim3	0.000055	0.135864	

There was a significant improvement in role limitation scores from baseline to week 6 (p=0.004) and from baseline to 3 months (0.00005). There was no difference between week 6 and 3 months (p=0.1).

4.3.4 KHQ: Physical Limitation

Table 16 represents the mean score in Physical Limitation as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 16: Physical Limitation score means

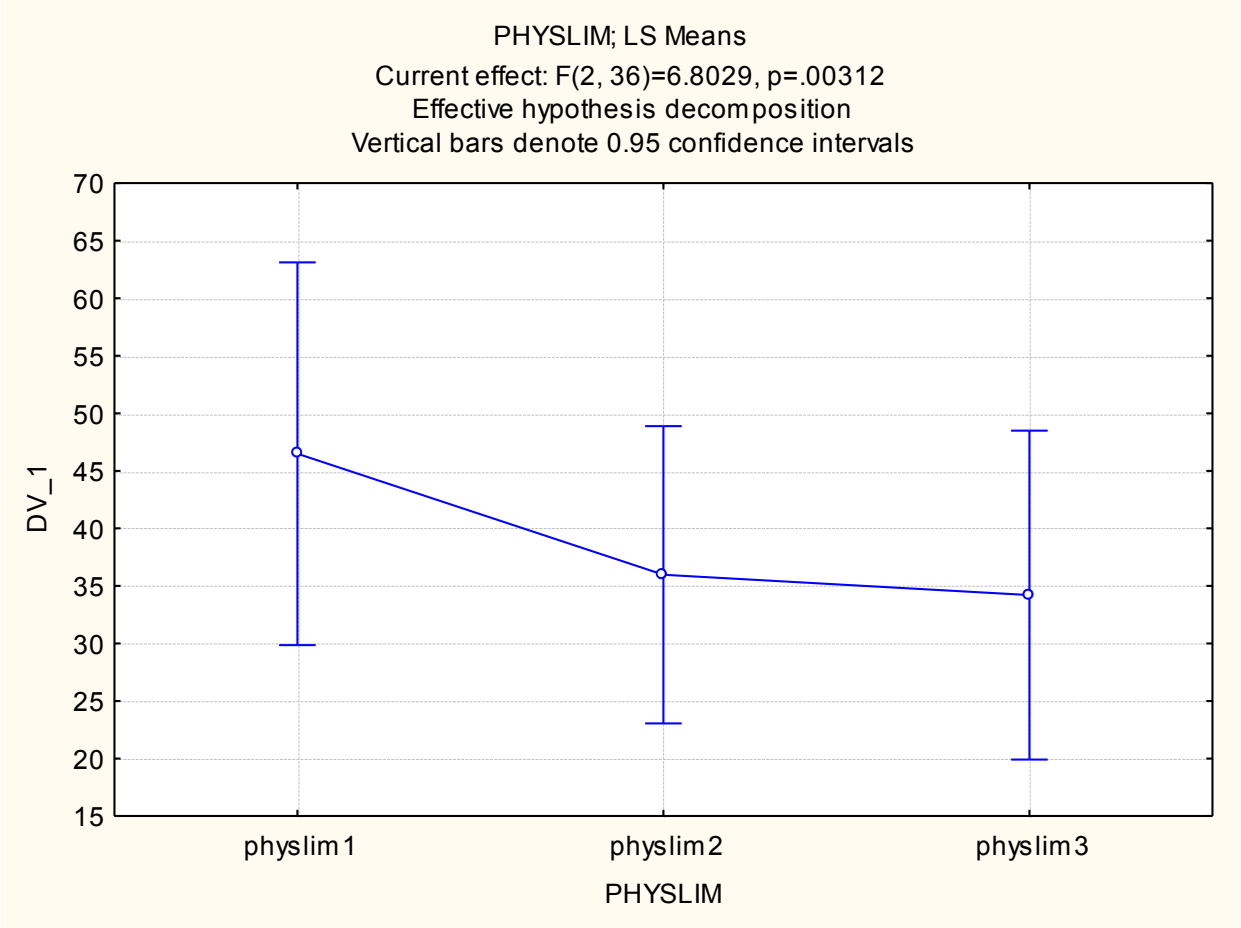
	Mean	Lower 95% CI	Upper 95% CI
physlim1[1]	46	30	63
physlim2[2]	36	23	49
physlim3[3]	34	20	48

1 physical limitation score at baseline

2 physical limitation score at week 6

3 physical limitation score at 3 months

Figure 8: Analysis of Variance for Physical Limitation score means



There is a difference between the groups (p=0.003).

Table 17: Comparisons of Physical Limitation score means using Fisher's Least Significant Difference

	PHYSLIM	{1}	{2}	{3}
1	physlim1		0.005984	0.001612
2	physlim2	0.005984		0.627405
3	physlim3	0.001612	0.627405	

There was a significant improvement in physical limitation scores from baseline to week 6 (p=0.006) and from baseline to 3 months (0.002). There was no difference between week 6 and 3 months (p=0.6).

4.3.5 KHQ: Social Limitation

Table 18 represents the mean score in Social Limitation as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 18: Social Limitation score means

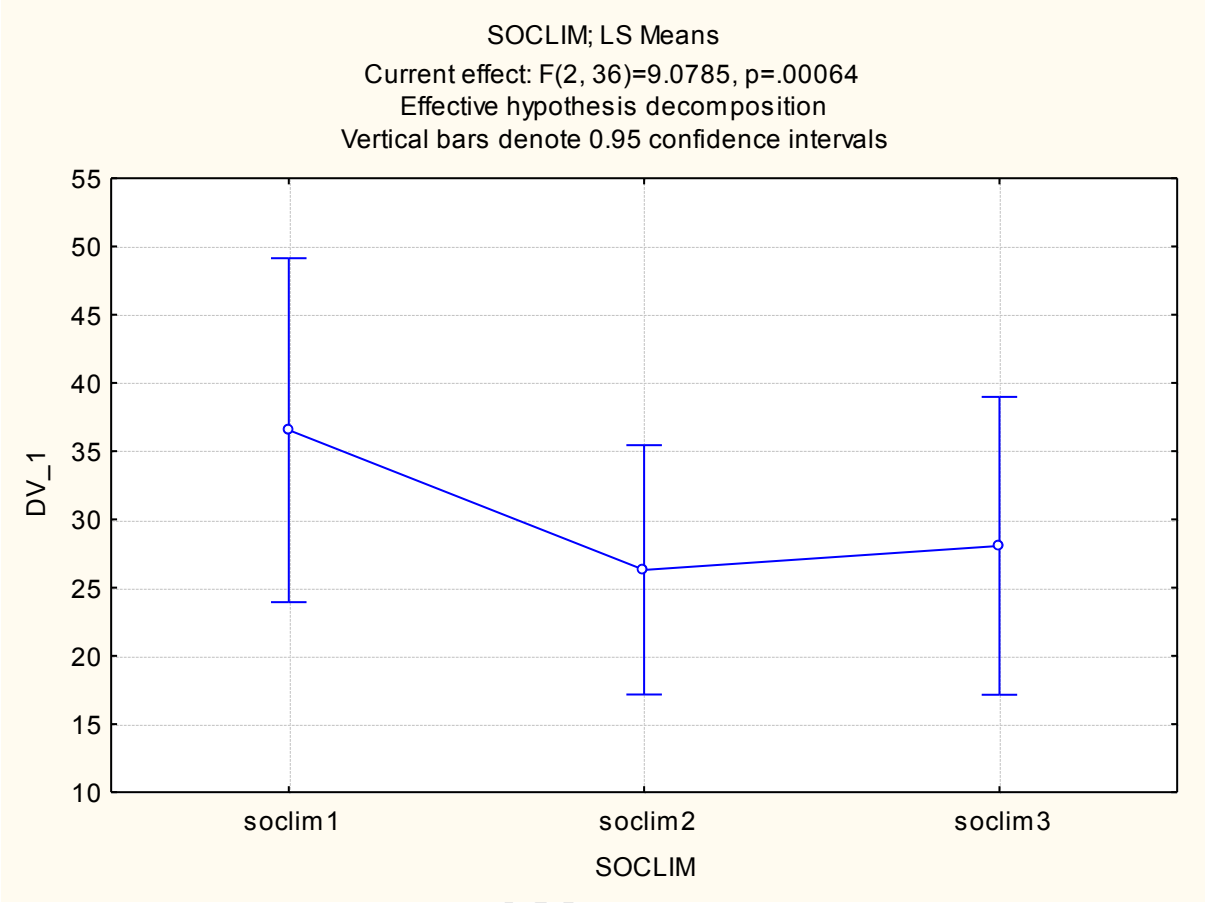
	Mean	Lower 95% CI	Upper 95% CI
soclim1[1]	36	24	49
soclim2[2]	26	17	35
soclim3[3]	28	17	39

1 social limitation score at baseline

2 social limitation score at week 6

3 social limitation score at 3 months

Figure 9: Analysis of Variance for Social Limitation score means



There is a difference between the groups (p=0.0006).

Table 19: Comparisons of Social Limitation score means using Fisher's Least Significant Difference

	SOCLIM	{1}	{2}	{3}
1	soclim1		0.000316	0.002184
2	soclim2	0.000316		0.498452
3	soclim3	0.002184	0.498452	

There was a significant improvement in social limitation scores from baseline to week 6 (p=0.0003) and from baseline to 3 months (0.002). There was not a statistically significant improvement between week 6 and 3 months (p=0.49).

4.3.6 KHQ: Personal Limitation

Table 20 represents the mean score in Personal Limitation as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 20: Personal Limitation score means

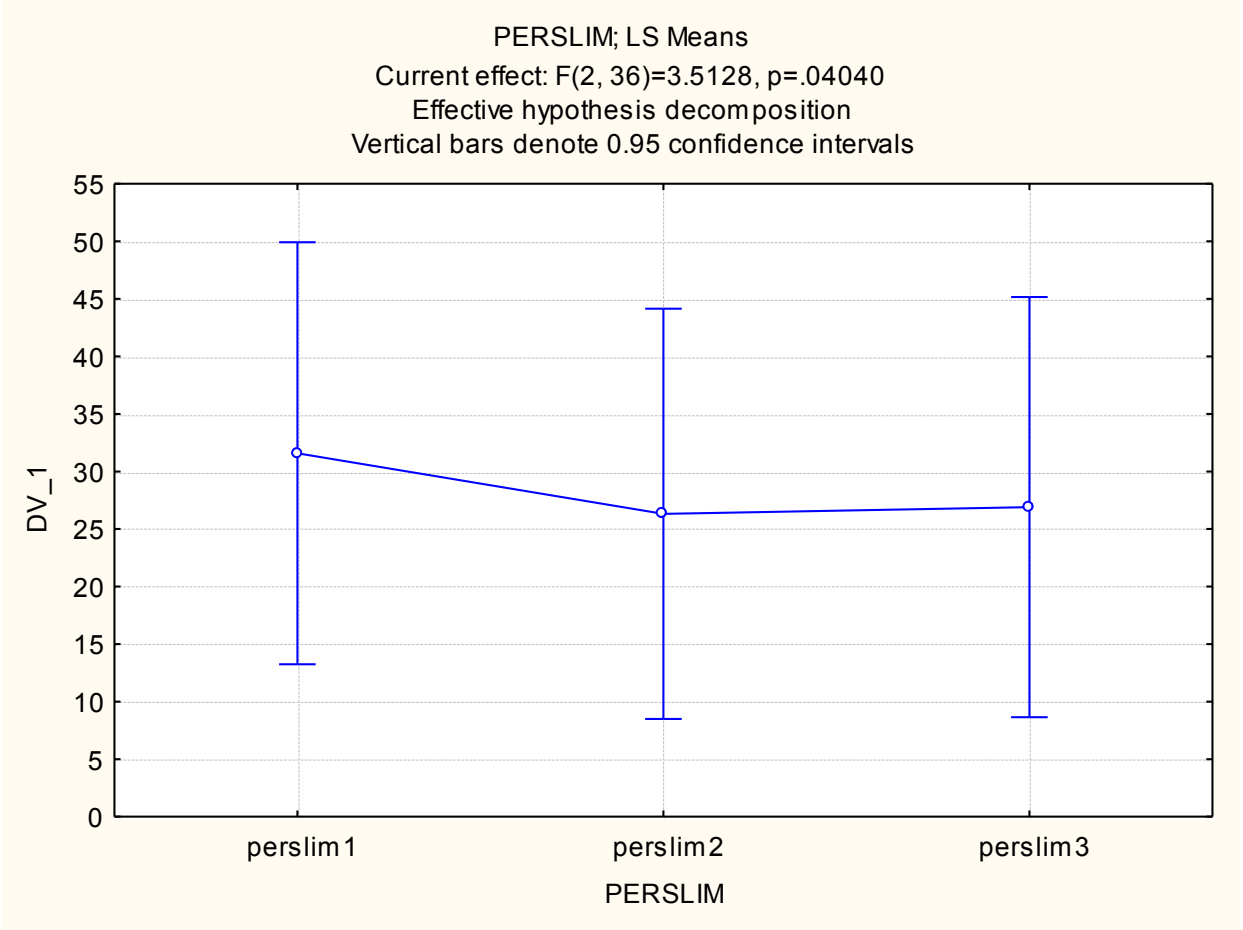
	Mean	Lower 95% CI	Upper 95% CI
perslim1[1]	32	13	50
perslim2[2]	26	8	44
perslim3[3]	27	9	45

1 personal limitation score at baseline

2 personal limitation score at week 6

3 personal limitation score at 3 months

Figure 10: Analysis of Variance for Personal Limitation score means



There is a difference between the groups (p=0.04).

Table 21: Comparisons of Personal Limitation score means using Fisher's Least Significant Difference

	PERSLIM	{1}	{2}	{3}
1	perslim1		0.020845	0.038278
2	perslim2	0.020845		0.791657
3	perslim3	0.038278	0.791657	

There was a significant improvement in personal limitation scores from baseline to week 6 (p=0.02) and from baseline to 3 months (0.04). There was no difference between week 6 and 3 months (p=0.8).

4.3.7 KHQ: Emotional Limitation

Table 22 represents the mean score in Emotional Limitation as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 22: Emotional Limitation score means

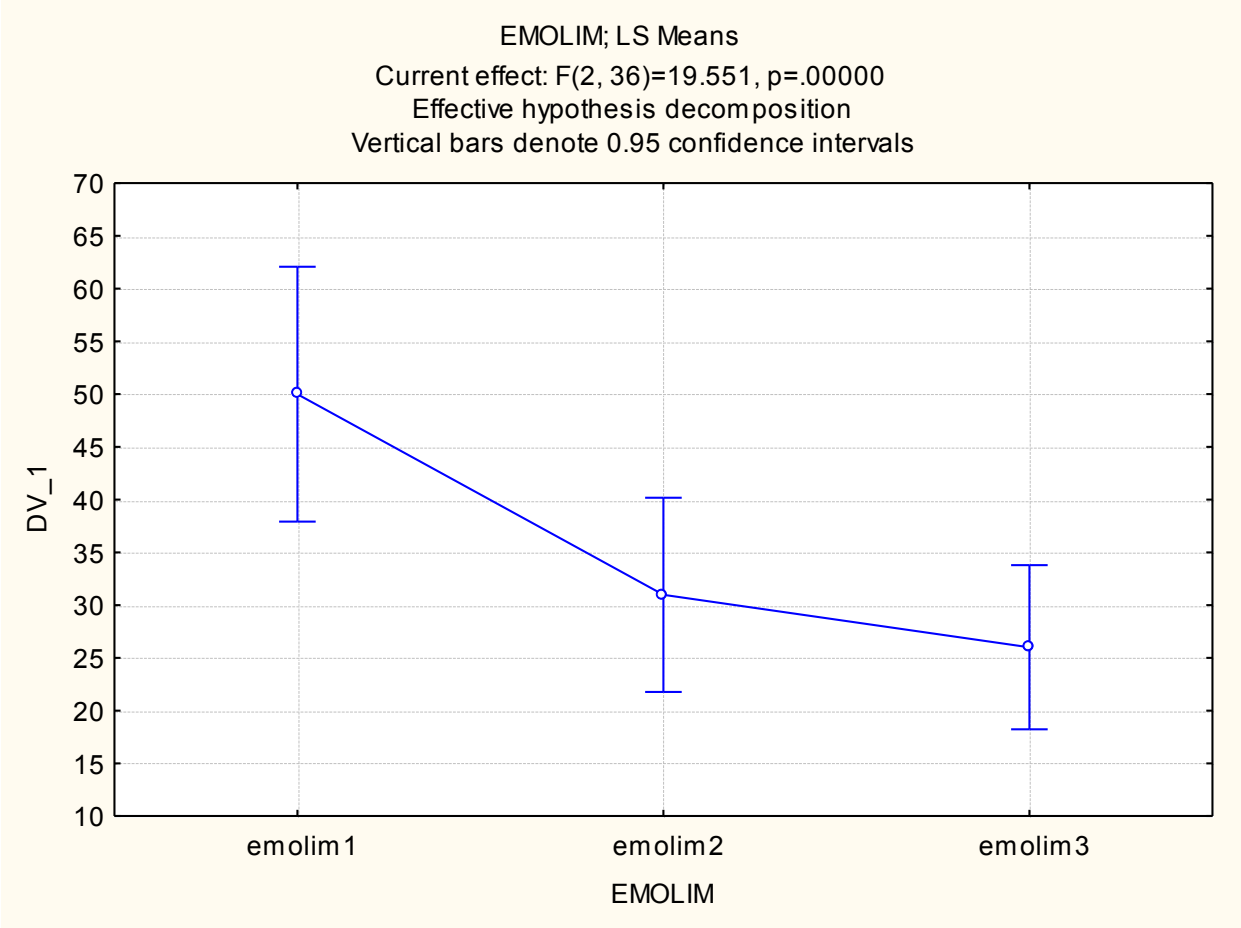
	Mean	Lower 95% CI	Upper 95% CI
emolim1[1]	50	38	62
emolim2[2]	31	22	40
emolim3[3]	26	18	34

1 emotional limitation score at baseline

2 emotional limitation score at week 6

3 emotional limitation score at 3 months

Figure 11: Analysis of Variance for Emotional Limitation score means



There is a difference between the groups (p=0.00000).

Table 23: Comparisons of Emotional Limitation score means using Fisher's Least Significant Difference

	EMOLIM	{1}	{2}	{3}
1	emolim1		0.000038	0.000001
2	emolim2	0.000038		0.227850
3	emolim3	0.000001	0.227850	

There was a significant improvement in emotional limitation scores from baseline to week 6 (p=0.00004) and from baseline to 3 months (0.000001). There was no difference between week 6 and 3 months (p=0.2).

4.3.8 KHQ: Sleep Limitation

Table 24 represents the mean score in Sleep Limitation as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 24: Sleep Limitation score means

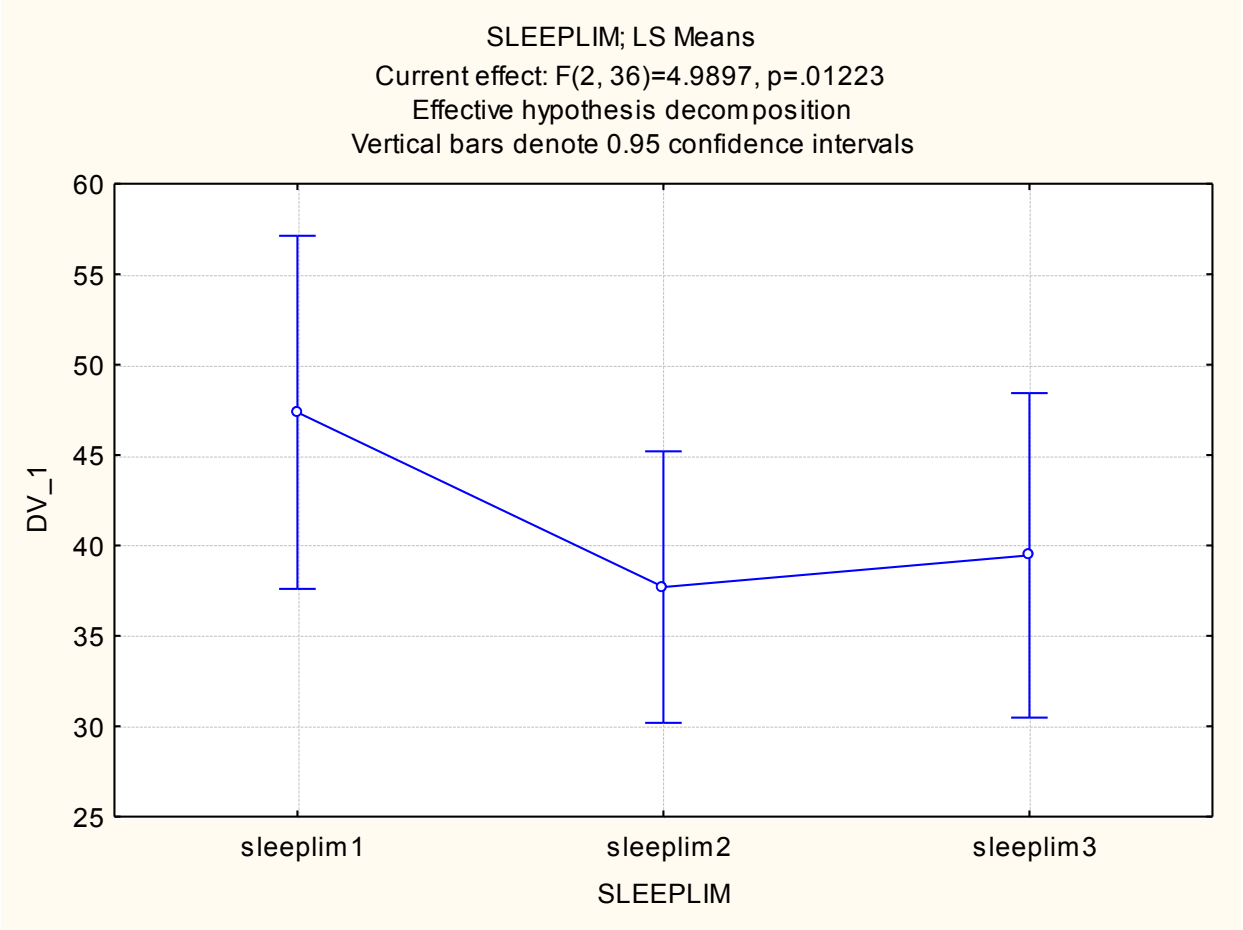
	Mean	Lower 95% CI	Upper 95% CI
sleeplim1[1]	47	38	57
sleeplim2[2]	38	30	45
sleeplim3[3]	39	30	48

1 sleep limitation score at baseline

2 sleep limitation score at week 6

3 sleep limitation score at 3 months

Figure 12: Analysis of Variance for Sleep Limitation score means



There is a difference between the groups (p=0.012).

Table 25: Comparisons of Sleep Limitation score means using Fisher's Least Significant Difference

	SLEEPLIM	{1}	{2}	{3}
1	sleeplim1		0.005347	0.020356
2	sleeplim2	0.005347		0.594078
3	sleeplim3	0.020356	0.594078	

There was a significant improvement in sleep limitation scores from baseline to week 6 (p=0.005) and from baseline to 3 months (0.02). There was no difference between week 6 and 3 months (p=0.6).

4.3.9 KHQ: Severity Scoring

Table 26 represents the mean Severity Scoring as documented on the KHQ at baseline and week 6 and 3 months respectively.

Table 26: Severity Scoring means

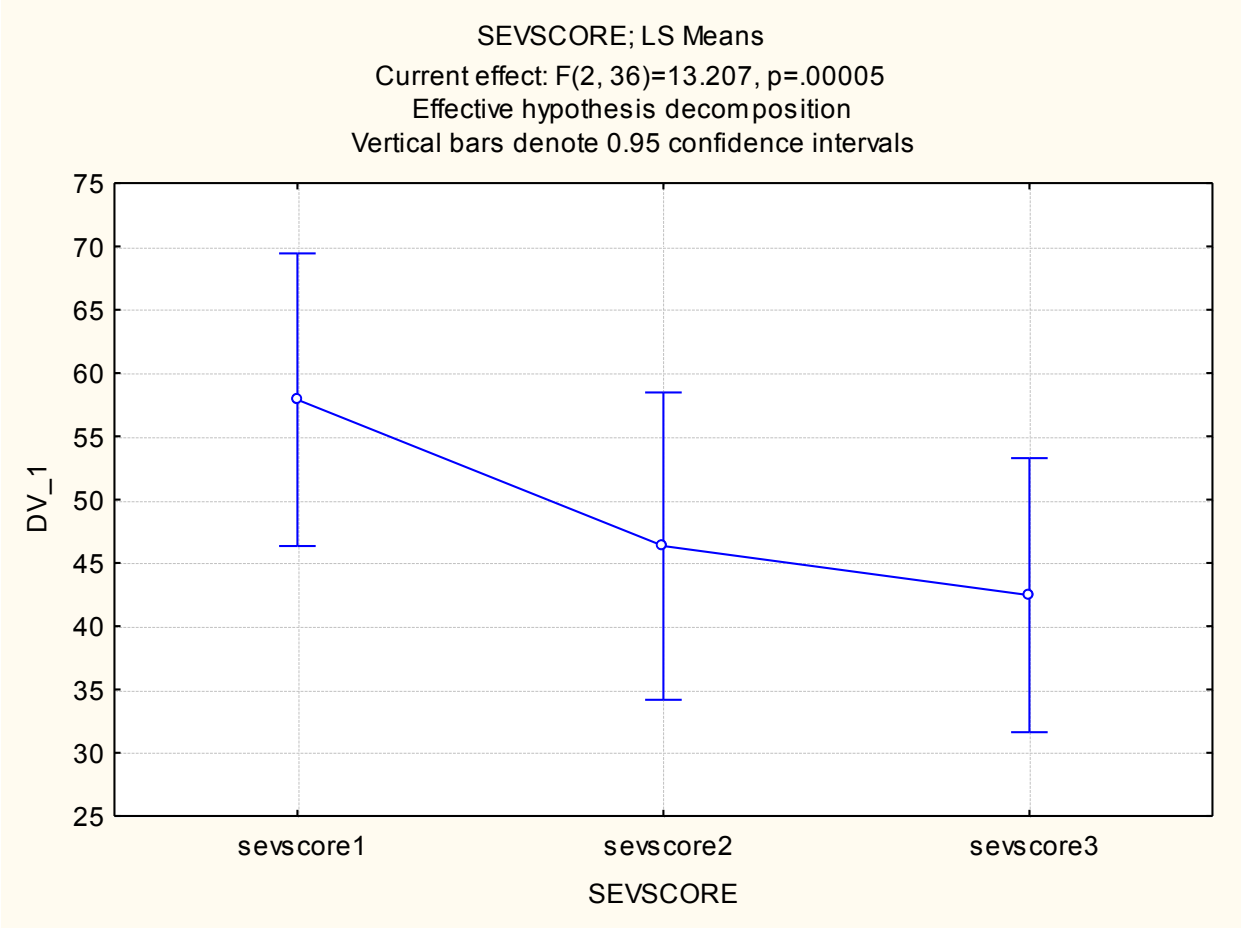
	Mean	Lower 95% CI	Upper 95% CI
sevscore1[1]	58	46	69
sevscore2[2]	46	34	58
sevscore3[3]	42	32	53

1 severity scoring at baseline

2 severity scoring at week 6

3 severity scoring at 3 months

Figure 13: Analysis of Variance for Severity Scoring means



There is a difference between the groups (p=0.00005).

Table 27: Comparisons of Severity Score means using Fisher's Least Significant Difference

	SEVSCORE	sevscore1	sevscore2	sevscore3
1	Sevscore1		0.000718	0.000018
2	Sevscore2	0.000718		0.222696
3	Sevscore3	0.000018	0.222696	

There was a significant improvement in severity scores from baseline to week 6 (p=0.0007) and from baseline to 3 months (0.00002). There was no difference between week 6 and 3 months (p=0.2).

CHAPTER 5
Discussion

In this study of women with refractive OAB, acupuncture produced significant symptomatic and quality-of-life improvement in all outcomes measured.

5.1 Key findings from the Bladder Diaries

Bladder diaries were used in our study to evaluate the effectiveness of acupuncture in reduction of frequency, nocturia and urine incontinence caused by refractive OAB. We observed a reduction in all symptoms.

- There was a 22% (p=0.002) and 23% (p=0.002) decrease in frequency from baseline to week 6 and to 3 months respectively.
- There was a 38% (p=0.004) and a 31% (p=0.015) decrease in nocturia from baseline to week 6 and to 3 months respectively.
- There was a 20% (p=0.002) and a 32% (p=0.0003) decrease in incontinence from baseline to week 6 and to 3 months respectively.

The clinical significance of improvement in bladder control and symptoms of OAB is still undecided in urogynaecological circles. For that reason the QoL of patients must be evaluated to gage the level of clinical significance.

5.2 Key findings from the Kings' Health Questionnaire

Questionnaires were used in our study to evaluate the effectiveness of acupuncture in improving the self-perceived QoL of the participants. We observed an improvement.

- Both the general domains, General Health and Incontinence Impact, showed significant improvement by 3 months (P=0.002 and 0.009 respectively).

- All seven lifestyle domains showed significant improvement at week 6 and again at 3 months. Most significantly was a decrease in Emotional Limitations (p=0.00004 at week 6 and p=0.000001 at 3 months).

The significance in overall improvement of QoL indicate that the improvement seen in bladder control could also be clinically significant.

5.3 Discussion of the Participant Characteristics

The complexity of this cohort is clearly displayed in their characteristics.

The mean age of the 20 study participants was 51 years (Standard Deviation, 10.1). In a 2010-comparison by Helfand et al (82) of over seven million people with the diagnosis of OAB, as recorded by 85 health care plans in America, the overall prevalence of OAB increased as a function of age: 4.9% of all patients were 45–54 years of age, 6.7% of patients were 55–64 years of age, and 9.6% of patients were >65 years of age. OAB seems to become a more significant clinical problem with age, but most of our participants were in the younger category. We suspect that many elderly patients in our population believe that urine incontinence is a normal part of aging and might not discuss this symptom with their health care workers.

The mean body mass index was 31 (Standard Deviation, 7.2). It has long been recognized that obesity is a risk factor for all types of UI and this trend was also seen in our participants.

In our study, 85% of the women had at least one vaginal delivery. Evidence suggests that the risk of OAB is not increased by vaginal births (15, 25). Interestingly, in a prospective study of 344 women, van Brummen et al (83) found that bothersome UUI was more prevalent after a Caesarean Section than a vaginal delivery.

The black population seems to be unrepresented at the FCC and this is reflected in our study as none was recruited. As discussed in the introduction, we suspect that this reflects cultural difference in help-seeking behaviour.

A recent investigation by Coyne et al (84) found a similar impact of OAB on sexual health as in our study. Although few of the participants in our study (10%) reported incontinence during sexual intercourse on completion of the KHQ (see appendix 2), the majority expressed a fear of this and blamed OAB for decreased sexual desire.

Treatment of OAB seems to fail in achieving the anticipated response in some patients treated at our unit. It is difficult to explain. This is probably due to a combination of factors. It is possible that some patients are not as motivated as others in persisting with behavioural techniques. It is also possible that some patients are more sensitive to side effects of the anticholinergic medication used, Most of the patients in our study seemed eager to improve their bladder control, but 35% stopped performing pelvic floor exercises and none were practising bladder training. This is still considered to be the cornerstone of treatment for OAB. Many studies have documented this decline in the active involvement of OAB management from patients suffering from it (42-45).

5.4 Comparison with other studies

In a recent randomised-controlled trial, Emmons et al (58) compared treatment acupuncture with a placebo acupuncture for OAB. The treatment arm involved the same bladder specific acupuncture points at the same intervals compared to in our study. Participant in their study had only one follow-up at 2-4 weeks after the treatment. We compared our results at week 6 (two weeks after treatment) with their results. Frequency decreased more in our study compare to theirs, 22% versus 14%, but incontinence improved much more in their study, 59% versus 20%. We suspect this reflects the notable difference in the populations. In our study, participants represented a complex group of patients that were refractive to treatment. In their study, participants were treatment naive. Similarly they found a significant improvement in QoL (p=0.004), but different questionnaires were used so domains cannot be compared directly.

Kelleher et al (59) compared the efficacy of acupuncture to oxybutynin in the management of OAB. Different acupuncture points were used and participants in the acupuncture arm received two more treatments than the patients in our study. The

results seem to be similar to ours. In comparison, frequency improved with 22% in our study versus 26% in theirs, nocturia improved with 31% versus 25%. Interestingly there was no improvement in UI in their study.

The methodology of other acupuncture studies for irritative bladder symptoms (60-64) differ to such an extent that we cannot compare the data.

5.5 Practical Points

Acupuncture is time consuming for the patient and for the health care provider. Patients would have to be motivated to return for repeated treatments and a dedicated team of urogynaecologists and physiotherapist would be needed to feasibly employ it in a busy clinic. Advantages of acupuncture are that the needles are cheap and the intervention safe (85) and does not impact on nursing staff duties.

5.6 Strength of the study

To the best of our knowledge this is the first report of the use of acupuncture as a treatment for OAB in a cohort that is refractive to treatment given at a specialised unit in a resource limited setting.

5.7 Limitation of the study

We acknowledge the possibility that the patient's own expectation of benefiting from the treatment may contribute to a significant placebo effect in our study. One can argue that in our study, the type of patient recruited may be less susceptible to placebo effect as they did not respond to previous therapy. Nevertheless, there remains a certain limitation.

We acknowledge that our study is also limited by the availability of a good placebo for acupuncture (refer to discussion 2.3 of issues with study design of acupuncture studies).

Our study is limited by the small number of participants.

In other larger scale studies QoL questionnaires were completed by the patients without assistance. In our study participants needed guidance and therefore all questionnaires were completed with the assistance of a medical doctor. Criticism against this way of data collection might be that it intrudes social bias. As the assistance was given to all of the participants by the same experienced doctor, we hope to have limited this.

In our study ICS definitions were used (3). OAB as a symptom complex is defined from the individual's perspective and not based on urodynamic studies. Still we acknowledge that urodynamic studies could have added to the findings of our study.

5.8 Implications for future research

Western perception of complementary medicine must not constrain the performance of clinical research in this field. In our study, acupuncture had a significant short-term effect on OAB. These results need to be confirmed with a larger sample randomised-controlled trial comparing acupuncture to a relevant placebo. Trials should be extended to see whether the effect is sustained beyond three months. To date there has not been a well constructed longitudinal long-term follow up study of patients that received acupuncture for OAB.

Responders should be evaluated against non responders in an attempt to characterise these groups.

Very little data is available for patients with OAB in South Africa. As discussed in the introduction, there are no South-African prevalence studies presumably because of challenges arising from misconceptions of the condition in the general population. These studies must be undertaken.

There is a need for a validated, standardised South African questionnaire for urinary incontinence to ensure consistency in future research in our country. These questionnaires should be able to evaluate urge. The relation between ‘objective’

improvement and ‘subjective’ benefit is a complex issue and should be addressed in ongoing research.

The use of an internationally accepted definition must be emphasised. An interesting project would be to evaluate South African gynaecologists’ concept of OAB and the definitions that they use.

More studies are required to fully understand the association between diuretic use and OAB, particularly its impact on health-related QoL.

Patients seem to be erratic in their practice of bladder training. There are no trials to address the value of later reinforcement of this technique. This strategy might have an important impact on refractive OAB.

5.9 Implications for practice

In our study, acupuncture for women with refractive OAB was effective in reducing symptoms and improved QoL. Care must be taken in extending these findings to all patients with OAB. The study assessed women with refractive OAB to standard treatment in a resource limited setting. Before implementing the treatment into practise more research is needed.

CHAPTER 6

Conclusion

OAB is under the spotlight. We now recognize the tremendous number of patients with this problem. The burden on the individual patient and the potential economic impact is staggering.

Health care in South Africa is economically under resourced. Treatment modalities for OAB are limited to bladder training and oral immediate release oxybutynin. Some patients fail to respond. There is currently no alternative therapy available to them.

In this study of women with refractive OAB, acupuncture produced significant symptomatic and QoL improvement in all outcomes measured.

Acupuncture as a low risk intervention is safe and well tolerated by patients. Even without substantial grade I evidence, there is support for the possible benefit of acupuncture in OAB. This avenue should be explored further.

REFERENCES:

1. Asire-Bediako A, Pillay C. An audit of management of female incontinence at the Female Continence Clinic at Groote Schuur Hospital, Cape Town. Research Day Department of Obstetrics and Gynaecology University of Cape Town, 2008.

2. Abrams P, Blaivas JG, Stanton S, Andersen JT. The standardisation of terminology of lower urinary tract function. Scand J Urol Nephrol (suppl) 1988; 114:5-19.

3. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn 2002; 21: 167–178.

4. Brubaker L. Urgency: the cornerstone symptom of overactive bladder. Urology 2004; 64 (suppl 6a): 12–16.

5. Irwin DE, Abrams P, Milsom I, Kopp Z, Reilly K. Understanding the elements of overactive bladder: questions raised by the EPIC study. BJU Int 2008; 101: 1381-7.

6. Milsom I, Abrams P, Cardozo L, Roberts RG, Thüroff J, Wein AJ et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. BJU Int 2001; 87:760–6.

7. Stewart WF, Van Rooyen JB, Cundiff G, Abrams P, Herzog AR, Corey R et al. Prevalence and burden of overactive bladder in the United States. World J Urol 2003; 20: 327–36.

8. Irwin DE, Milsom I, Hunskaar S, Reilly K, Kopp Z, Herschorn S et al. Population-based survey of urinary incontinence, overactive bladder, and other

lower urinary tract symptoms in five countries: results of the EPIC study. Eur Urol 2006; 50: 1306–1314.

9. Lee YS, Lee KS, Jung JH. Prevalence of overactive bladder, urinary incontinence, and lower urinary tract symptoms: results of Korean EPIC study. World J Urol 2011; 29: 185-190

10. Knobel J. Stress incontinence in the black female. S Afr J Obstet Gynaecol 1975; 49: 430–32.

11. Wennberg A, Molander U, Fall M, Edlund C, Peeker R, Milsom I et al. A longitudinal population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in women. Eur Urol 2009; 55:783-91.

12. Garnett S, Swithinbank L, Ellis-Jones J, Abrams P. The long-term natural history of overactive bladder symptoms due to idiopathic detrusor overactivity in women. BJU Int 2009; 104: 948-53.

13. Aitchison M, Carter R, Paterson P et al. Is the treatment of urgency incontinence a placebo response? Results of a five-year follow-up. Br J Urol 1989; 64: 478-80.

14. Nygaard IE, Lemke JH. Urinary incontinence in rural older women: prevalence, incidence, and remission. J Am Geriatr Soc 1996; 44: 1049-54

15. Hannestad YS, Rortveit G, Sandvik H, Hunskaar S. A community-based epidemiological survey of female urinary incontinence: The Norwegian EPINCONT study. J Clin Epidemiol 2000; 53:1150 –7.

16. Losif CS, Batra S, Ek A, Astedt B. Estrogen receptors in the human female lower urinary tract. Am J Obstet Gynecol 1981;141:817–2.

17. Thomas TM, Plymat KR, Blannin J, Meade TW. Prevalence of urinary incontinence. BMJ 1980; 281:1243–5.

18. Kondo A, Kato K, Saito M, Otani T. Prevalence of incontinence in females in comparison with stress and urge incontinence. Neurourol Urodynam 1990;9:330–1.

19. Losif CS, Bekassy Z. Prevalence of genitourinary symptoms in the late menopause. Acta Obstet Gynecol Scand 1984;63:257–6.

20. Van der Vaart CH, de Leeuw JRJ, Roovers JPWR. The effect of urinary incontinence and overactive bladder symptoms on quality of life in young women. Br J Urol Int 2002; 90:544-9.

21. Liberman JN, Hunt TL, Stewart WF, Wein A, Zhou Z, Herzog AR et al. Health-related quality of life among adults with symptoms of overactive bladder: results from a U.S. community-based survey. Urology 2001; 57:1044-50.

22. Grady D, Brown JS, Vittinghoff E, Applegate W, Varner E, Snyder T; HERS Research Group. Postmenopausal hormones and incontinence: the heart and estrogen/ progestin replacement study. Obstet Gynecol 2001; 97:116– 120.

23. Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin on urinary incontinence. JAMA 2005;293:935– 48.

24. Fantl JA, Cardozo L, McClish DK. Estrogen therapy in the management of urinary incontinence in postmenopausal women: a metaanalysis. First report of the Hormones and Urogenital Therapy Committee. Obstet Gynecol 1994;83:12–18.

25. Parazzini F, Chiaffarino F, Lavezzari M, Giambanco V; VIVA Study Group. Risk factors for stress, urge or mixed urinary incontinence in Italy. BJOG 2003; Oct; 110:927-3.

26. Hannestad YS, Rortveit G, Daltveit AK, Hunskaar S. Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. Br J Obstet Gynaecol 2003;110:247-54.

27. Irwin DE, Milsom I, Kopp Z, Abrams P, Cardozo L. Impact of overactive bladder symptoms on employment, social interactions and emotional well being in six European countries. BJU Int 2006; 97:96–100.

28. Coyne SK, Sexton CC, Irwin DE, Kopp ZS, Con J. Kelleher CJ, Milsom I. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: results from the EPIC study. BJU Int 2008; 101:1388-95.

29. Irwin DE, Mungapen L, Milsom I, Kopp Z, Reeves P, Kelleher C. The economic impact of overactive bladder syndrome in six Western countries. BJU Int 2009; 103:202-9.

30. Ganz ML, Smalarz AM, Krupski TL, Anger JT, Hu JC, Wittrup-Jensen KU, Pashos CL. Economic Costs of Overactive Bladder in the United States. Urology 2010; 75:526-532.

31. De Groat WC. A neurologic basis for the overactive bladder. Urology 1997; 50 (6A Suppl):36–52.

32. Brading AF. A myogenic basis for the overactive bladder. Urology 1997; 50 (6A Suppl):57–67.

33. Birder LA, de Groat WC. Mechanisms of Disease: involvement of the urothelium in bladder dysfunction. Nat Clin Pract Urol 2007; 4:46-54.

34. Drake MJ, Mills IW, Gillespie JI. Model of peripheral autonomous modules and a myovesical plexus in normal and overactive bladder function. Lancet 2001; 358:401–403.

35. Sui GP, Rothery S, Dupont E, Fry CH, Severs NJ. Gap junctions and connexin expression in human suburothelial interstitial cells. BJU Int 2002; 90:118-29.

36. Brincat MP, Baron YM, Galea R. Estrogens and the skin. Climacteric 2005;8:110–23.

37. Robinson D, Cardozo L. The role of estrogens in female lower urinary tract dysfunction. Urology 2003;62:45–51.

38. Waetjen LE, Dwyer PL. Estrogen therapy and urinary incontinence: what is the evidence and what do we tell our patients? Int Urogynecol J 2006;17:541–5.

39. Keane DP, Sims TJ, Abrams P, Bailey AJ. Analysis of collagen status in premenopausal nulliparous women with genuine stress in continence. Br J Obstet Gynaecol 1997;104:994–8.

40. Sartori MG, Gira˜o MJ, de Jesus Simo˜ es M, Sartori JP, Baracat EC, Rodrigues de Lima G. Quantitative evaluation of collagen and muscle fibers in the lower urinary tract of castrated and under-hormone replacement female rats. Clin Exp Obstet Gynecol 2001;28:92–6.

41. Aikawa K, Sugino T, Matsumoto S, Chichester P, Whitbeck C, Levin RM. The effect of ovariectomy and estradiol on rabbit bladder smooth muscle contraction and morphology. J Urol 2003;170:634–7

42. Fantl JA. Behavioral intervention for community- dwelling individuals with urinary incontinence. Urology 1998; 51(suppl 2A): 30–34.

43. Burgio KL, Goode PS, Locher JL, et al. Behavioural training with and without biofeedback in the treatment of urge incontinence in older women: a randomized controlled trial. JAMA 2002; 288:2293-2299.

44. Burgio KL, Locher JL, Goode PS, et al. Behavioural vs. drug treatment for urge urinary incontinence in older women: a randomized controlled trial. JAMA 1998; 280:1995-2000.

45. Wallace SA, Roe B, Williams K, Palmer M (2004) Bladder training for urinary incontinence in adults. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD001308.

46. Nygaard IE, Kreder KJ, Lepic MM, Fountain KA, Rhomberg AT. Efficacy of pelvic floor muscle exercises in woman with stress urge, and mixed urinary incontinence. Am J Obstet Gynecol 1996; 174:120–125.

47. Cardozo LD, Stanton SL, Hafner J, Allan V. Biofeedback in the treatment of detrusor instability. Br J Urol 1978; 50: 250–254.

48. Trontel JV, Janko M, Godec C. Proceedings: Electrical Stimulation for urinary incontinence: a neurophysiological study. Urol Int 1974; 29: 213–220.

49. Brubaker L. Electrical stimulation in overactive bladder. Urology 2000; 55(5A Suppl):17-23.

50. Kohli, N. and Rosenblatt, P. Neuromodulation techniques for the treatment of overactive bladder. Clin Obstet and Gynae 2002; 45: 218 – 232.

51. Peters KM, MacDiarmid SA, Wooldridge LS. Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine:

results from the Overactive Bladder Innovative Therapy Trial. J Urol 2009; 182: 1055.

52. Govier FE, Litwiller S, Nitti V. Percutaneous afferent neuromodulation for the refractory overactive bladder: results of a multicenter study. J Urol 2001; 165: 1193.

53. Peters KM, Carrico DJ, Perez-Marrero RA, Khan AU, Wooldridge LS, Davis GL, Macdiarmid SA. Randomized trial of percutaneous tibial nerve stimulation versus Sham efficacy in the treatment of overactive bladder syndrome: results from the SUmiT trial. J Urol. 2010 Apr;183(4):1438-43.

54. Alhasso AA, McKinlay J, Patrick K, Stewart L. Anticholinergic drugs versus non-drug active therapies for overactive bladder syndrome in adults. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD003193.

55. Chapple CR, Khullar V, Gabriel Z, Muston D, Bitoun CE, Weinstein D. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol. 2008; 54:543-62.

56. Nabi G, Cody JD, Ellis G, Herbison P, Hay-Smith J. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. Cochrane Database Syst Rev 2006;18:CD003781.

57. Versi E, Appell R, Mobley D, Patton W, Saltzstein D and The Ditropan XL Study Group, Dry mouth with conventional and controlled-release oxybutynin in urinary incontinence, Obstet Gynecol 2000; 95:718–721.

58. Emmons SL, Otto L. Acupuncture for overactive bladder: a randomized controlled trial. Obstet Gynecol 2005; 106:138-43.

59. Kelleher C.J, Filshie J, Burthon G. Acupuncture and the treatment of irritative bladder symtoms. Acupunct. Med 1994; 12:9–12.

60. Chang, P. Urodynamic studies in acupuncture for women with frequency, urgency and dyuria. J.Urology, 1988; 140: 563 – 556.

61. Philip T, Shah PJR, Worth PHL. Acupuncture in the treatment of bladder instability. Br. J. Urol 1988; 6:490–493.

62. Minni B, Capozza N, Creti G, De Gennaro M, Caione P, Bischko J. Bladder instability and enuresis treated by acupuncture and electro-therapeutics: early urodynamic observations. Acupunct Electrother Res. 1990; 15:19-25.

63. Bergstrom K, Carlsson CP, Lindholm C, Widengren R. Improvement of urge- and mixed-type incontinence after acupuncture treatment among elderly women—a pilot study. J Auton Nerv Syst 2000;79:173–80.

64. Honjo H, Naya Y, Ukimura O, Kojima M, Miki T. Acupuncture on Clinical Symptoms and Urodynamic Measurements in Spinal-Cord- Injured Patients with Detrusor Hyperreflexia. Urol Int 2000; 65:190-195 .

65. Pomeranz B, Chiu D. Naloxone blockade of acupuncture analgesia: endorphin implicated. Life Sci 1976; 1:1757-62.

66. Mayer DJ, Price DD. Endorphin release as mechanism of acupuncture analgesia. Pain. 1981 ;11:273-80.

67. Sjölund B, Terenius L, Eriksson M. Increased cerebrospinal fluid levels of endorphins after electro-acupuncture. Acta Physiol Scand 1977; 100:382-4.

68. Carlsson C. Acupuncture mechanisms for clinically relevant long-term effects--reconsideration and a hypothesis. Acupunct Med. 2002; 20:82-99.

69. Alm P, Alumets J, Hakanson R, Owman C. Enkephalin-immuno-reactive nerve fibres in the feline genitor-urinary tract. Histochemistry 1981; 72: 351-355.

70. Klarskov P. Enkephalin Inhibits Presynaptically the Contractility of Urinary Tract Smooth Muscle. Br J Urol. 1987; 59: 31-35.

71. Jubelin B, Galeano C, Ladouceur D, Lemaire S, Elhilali MM. Effect of enkephalin on the micturition cycle of the cat. Life Sci 1984; 21:2015-27.

72. Hisamitsu T, de Groat WC. The inhibitory effect of opioid peptides and morphine applied intrathecally and intracerebroventricularly on the micturition reflex in the cat. Brain Res. 1984; 23:51-65.

73. Sato A, Sato Y, Suzuki A. Mechanism of the reflex inhibition of micturition contractions of the urinary bladder elicited by acupuncture-like stimulation in anesthetized rats. Neurosci Res 1992 ;15:189-98.

74. Pariente J, White P, Frackowiak RS, Lewith G. Expectancy and belief modulate the neuronal sbustrates of pain treated by acupuncture. Neuroimage 2005 May 1;25(4):1161-7.

75. White AR, Filshie J, Cummings TM. Clinical trials of acupuncture: consensus recommendations for optimal treatment, sham controls and blinding. Complement Ther Med 2001; 9:237–245.

76. Madsen MV, Gøtzsche PC, Hróbjartsson A. Acupuncture treatment for pain: systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture group. BMJ 2009; 338: a3115.

77. Wyman, JF, Choi, SC, Harkins, SW, et al. The urinary diary in evaluation of incontinent women: A test-retest analysis. Obstet Gynecol 1988; 71:812.

78. Brown JS, McNaughton KS, Wyman JF, Burgio KL, Harkaway R, Bergner D, et al. Measurement characteristics of a voiding diary for use by men and women with overactive bladder. Urology 2003;61:802–9.

79. Kelleher CJ, Cardozo LD, Khullar V, Salvatore S. A new questionnaire to assess the quality of life of urinary incontinent women. Br J Obstet Gynaecol. 1997; 104: 1374-9.

80. Kelleher CJ, Pleil AM, Reese PR, Burgess SM, Brodish PH. How much is enough and who says so? BJOG. 2004; 111:605-12.

81. Declaration of Helsinki (adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964 and amended Tokyo 1975, Venice 1983, Hong Kong 1989, South Africa 1996, Edinburgh 2000 and Seoul 2008). The World Medical Association, Inc., Femey-Voltaire, France.

82. Helfand BT, Evans RM, McVary KT. A Comparison of the Frequencies of Medical Therapies for Overactive Bladder in Men and Women: Analysis of More Than 7.2 Million Aging Patients. Eur Urol 2010; 57: 586-591.

83. Van Brummen HJ, Bruinse HW, van de Pol G, Heintz AP, van der Vaart CH. Bothersome lower urinary tract symptoms 1 year after first delivery: prevalence and the effect of childbirth. BJU Int 2006; 98 :89-95.

84. Coyne KS, Margolis MK, Jumadilova Z, Bavendam T, Mueller E, Rogers R. Overactive bladder and women's sexual health: what is the impact? J Sex Med 2007; 4:656-66.

85. Lao L, Hamilton GR, Fu J, Berman BM. Is acupuncture safe? A systematic review of case reports. Altern Ther Health Med 2003; 9: 72–83.

Appendix 1: Data collection

Study number _____
Age _____
Weight_____Height_____BMI_____

1. Demographics		
1 A	Race : Coloured= 1, White= 2, Black= 3, Indian= 4, other=5	
1 B	Marital status: Married=1, single=2, divorced=3, Living with partner=4, widow=5	
1 C	Education: < secondary level= 1, secondary level=2, tertiary level= 3	
2. Habits		
2 A	Smoking:	
2 A 1	Yes=1, No=2	
2 A 2	If yes: Pack year history	
2 B	Alcohol: Yes=1, No=2, if yes: unit/ weeks	

3 Obstetric History		
3 A	Gravity	
3 B	Parity	
3 C	Number of vaginal births	
3 D 3 E 3 F	If yes: Forceps delivery Yes=1, No=2 Vacuum Extraction Yes=1, No=2 Episiotomy Yes=1, No=2	
3 G	Number of C/sections	

4 Gynaecological History		
4 A	Post menopausal : Yes=1, No=2	
4 B	If yes: Age of menopause	
4 C	HRT use Previous=1, current=2, never=3	
4 D	If previous of current: Type of HRT Oestrogen only=1 Oestrogen and progesterone=2	
4 E	If previous or current: Duration of HRT treatment	
4 F	Hysterectomy Yes=1, No=2	
4 G	Prolapse symptoms: Yes=1, No=2	

5. Medical history		
5 A	Hypertension Yes=1, No=2	
5 B	If yes: on diuretic? Yes=1, No=2 If yes, type and dose	
5 C	Other class anti-hypertensions	
5 D	Diabetes Yes=1, No=2	
5 E	If diabetes, insulin dependant? Yes=1, No=2	
5 F	Oral antihypoglycemics	
5 G	Neurological disorders: Yes=1, No=2	
5 G	Psychological disorders: Yes=1, No=2	
5 G	other	

6. Surgical history		
6 A	Hysterectomy Yes=1, No=2	
6 B	If yes Abdominal=1 Vaginal=2	
6 C	Anterior vaginal repair Yes=1, No=2 If yes, details	
6 D	Posterior vaginal repair Yes=1, No=2 If yes, details	
6 E	Stress in continence surgery Yes=1, No=2 If yes, details	
6 G	Cystoscopy Yes=1, No=2 If yes, details	
6 E	Other	

7. History of OAB	
7 A	Initial presenting symptoms: Yes=1, No =2
7 A 1	Frequency
7 A 2	Nocturia
7 A 3	Urgency
7 A 4	Urge incontinence
7 A 5	Stress incontinence
7 A 6	Voiding dysfunction (straining, post micturation dribbling, incomplete emptying)
7 A 7	Bladder pain
7B	Duration of symptoms
7C	Was urodynamic studies performed Yes=1, No=2
7D	If yes, was OAB demonstrated? Yes=1, No=2
7 E	Current Symptoms: Yes=1, No=2
7 E 1	Frequency
7 E 2	Nocturia
7 E 3	Urgency
7 E 4	Urge incontinence
7 E 5	Stress in continence
7 E 6	Voiding dysfunction (straining, post micturation dribbling, incomplete emptying)
7 E 7	Bladder pain

8. Non pharmacological management	
8 A	Pelvic floor exercises:
8 A 1	Date initiated
8 A 2	Date stopped
8 A 3	Duration of exercises performed
8 A 4	Improvement documented Yes=1, No=2
8 B	Bladder retraining:

8 B 1	Date initiated	
8 B 2	Date stopped	
8 B 3	Duration of training	
8 B 4	Improvement documented Yes=1, No=2	
8 C	Bladder instalation: Yes=1, No=2	

9 Pharmacological treatment		
9A1	Oxybutynin : Previous=1, current=2, never=3	
9A 2	Duration of use	
9A 3	Maximum dose used	
9A 4	If stopped: Final Reason stopped No improvement=1, Side effects=2, Both=3 If 2 ,specify	
9A 5	Other :	

10. Acupuncture History		
10 A	Previous acupuncture Yes=1, No=2	
10 B	If yes, specify	

11. Urine dipstic		
	Normal Yes=1, No=2 If no, specify	

Appendix 2: King's Health Questionnaire

KING'S HEALTH QUESTIONNAIRE

Study number	
Today's date:	

How would you describe your health at present?

Please tick one answer.

Very good	○
Good	○
Fair	○
Poor	○
Very poor	○

How much do you think your bladder problem affects your life?

Not at all	○
A little	○
Moderately	○
A lot	○

Office use

5

4

Please turn the page.

We would like to know what your bladder problems are and how much they affect you. From the list below, choose ONLY THOSE PROBLEMS that you have at present. LEAVE OUT those that do not apply to you.

How much do they affect you?	A little	Moderately	A lot
To choose please tick ✓			
FREQUENCY: going to the toilet to often.	○	○	○
NOCTURIA: getting up at night to pass urine.	○	○	○
URGENCY: a strong and difficult to control desire to pass urine	○	○	○
URGE INCONTINENCE: urinary leakage associated with a strong desire to pass urine	○	○	○
STRESS INCONTINENCE: urinary leakage with physical activity eg coughing, sneezing, running	○	○	○
NOCTURNAL ENURESIS: wetting the bed at night	○	○	○
INTERCOURSE INCONTINENCE: urinary leakage with sexual incontinence	○	○	○
FREQUENT WATERWORKS INFECTION:	○	○	○
BLADDER PAIN:	○	○	○
Difficulty PASSING URINE:	○	○	○
OTHER SPECIFY:	○	○	○
Office Use	□ +	□ +	□

Please turn the page

Below are some daily activities that can be affected by your bladder problems.
How much does your bladder problem affect you?
We would like you to answer every question. Simply tick the circle that applies to you.

	Not at all	Slightly	Moderately	A lot
ROLE LIMITATIONS				
To what extent does your bladder problem affect your household tasks (eg cleaning, shopping, etc)	○	○	○	○
Does your bladder problem affect your job or your normal daily activities outside the home?	○	○	○	○
PHYSICAL / SOCIAL LIMITATIONS				
Does your bladder problem affect your physical activities (eg going for a walk, run, sport, gym, etc)	○	○	○	○
Does your bladder problem affect your ability to travel?	○	○	○	○
Does your bladder problem limit your social life?	○	○	○	○
Does your bladder problem limit your ability to see/visit friends?	○	○	○	○

PERSONAL RELATIONSHIPS	Not appli-cable				
Does your bladder problem affect your relationship with your partner?	○	○	○	○	○
Does your bladder problem affect your sex life?	○	○	○	○	○
Does your bladder problem affect your family life?	○	○	○	○	○
Office Use	☐☐	☐☐	☐☐	☐	☐☐

Please turn the page.

	Not at all	Slightly	Moderately	A lot
EMOTIONS				
Does your bladder problem make you feel depressed?	○	○	○	○
Does your bladder problem make you feel anxious or nervous?	○	○	○	○
Does your bladder problem make you feel bad about yourself?	○	○	○	○
SLEEP / ENERGY				
	Never	Sometimes	Often	All the time
Does your bladder problem affect your sleep?	○	○	○	○
Do you feel worn out / tired?	○	○	○	○
Do you do any of the following? If so how much?	Never	Sometimes	Often	All the time
Wear pads to keep dry?	○	○	○	○
Be careful how much fluid you drink?	○	○	○	○
Change your underclothes when they get wet?	○	○	○	○
Worry in case you smell?	○	○	○	○
Get embarrassed because of your bladder problem?	○	○	○	○
Office Use	□□□	□□	□	□□□

Thank you. Now kindly check that you have answered all the questions.

Appendix 3: Bladder Diary

				ACCIDENTS		
						
Time	**Drinks** What kind? / How much?		**Urine** How many times? / How much? (circle one)	**Accidental leaks** (circle one)	**Did you feel a strong urge to go?** (circle one)	**What were you doing at the time?** Sneezing, exercising, having sex, lifting, etc.
7-8 p.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
8-9 p.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
9-10 p.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
10-11 p.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
11-12 p.m. (midnight)			○ ◒ ●	💧 ◒ ●	Yes	No	
12-1 a.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
1-2 a.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
2-3 a.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
3-4 a.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
4-5 a.m.			○ ◒ ●	💧 ◒ ●	Yes	No	
5-6 a.m.			○ ◒ ●	💧 ◒ ●	Yes	No	

I used _____ pads. I used _____ diapers today (write number).

Questions to ask my health care team: _____

Appendix 4: Consent in English

University of Cape Town

Dr Steven Jeffery
Dr Marinus Cloete
Department of Gynaecology
Faculty of Health Sciences
University of Cape Town
Anzio Road
Observatory
7925

Acupuncture in women with overactive bladder syndrome

INFORMED CONSENT and INFORMATION FORM

Dear Patient

My name is _____

I wish to invite you to participate in a study that aims to find out how good acupuncture is in helping to treat Overactive bladder (OAB). We hope that this will help us to look better after people living with OAB, like you, in the future. The study is being run by the department of Gynaecology at the University of Cape Town and will be conducted at the Continence Clinic at Groote Schuur Hospital. Dr Steven Jeffery is the Principal Investigator and Dr Marinus Cloete is the Lead Investigator.

OAB is the sudden, intense desire to urinate and can be accompanied by unwanted urine leakage (referred to as "wetting accidents"). This happens because the bladder muscle squeezes too often or when you don't want it to. A person may be aware of the sensation to urinate but will be unable to stop leakage before reaching the toilet. OAB is also usually associated with wanting to urinate more than eight times in a day or twice a night.

We ask you to join in this study because we want to find out more about how to treat people with OAB. We as doctors can help patients with OAB to learn to control their bladders and we can prescribe medication to take. For most patients these treatments work, but for some it does not. So what is there more to do if you feel the treatment is not working? Doctors in America and in Europe have found that acupuncture can also work for OAB. We want to see if it will work for our patients for whom other treatments did not work.

Acupuncture is an ancient system of healing developed over thousands of years as part of the traditional medicine of China. The aim of the treatment is to restore the balance of energy in the body. This is done through the painless application of fine needles into strategic points on the body. Inserting these very fine needles just into the skin is very safe.
Upon insertion, you may feel a slight sting. Once the needle is inserted, there should be no pain. You should feel comfortable during the treatment. Some people, but they are very few, feel dizzy and nauseous. We will stop the treatment immediately if you wish so.
You will receive four acupuncture treatments every week for four weeks. Each time seven needles will be inserted into your skin; two on your knees, two on your thighs, two on your lower back and one under your navel. Every time new needles will be used. A treatment lasts twenty minutes. The medical staff inserting the needles is trained to do so. Sometimes during the study we will ask you to keep track of your wetting accidents and other bladder problems by writing them down in a diary.

It is very important that you come back for your follow-up appointments so that we can see if the acupuncture has helped you. We will ask you to come back three times: two weeks, one month and

three months after the treatment. Each time we will give you a paper with a few questions written on it that you must tick. This will take about 10 minutes to complete.

All the information that you give to us will be confidential. Your name will not be on the information and the information will not be copied into your clinic notes. All the information will be locked up.

It is possible that you might not benefit from acupuncture at all. We can not guarantee any improvement.

If you are still taking medication for OAB you must continue to take this during the treatment with acupuncture. We always recommend patients to continue with the bladder training.

This study is not funded and there will be no reimbursement for travelling to the clinic.

This study was approved by the Research Ethics Committee of the University of Cape Town. Their job is to ensure your safety and protect you during the study.

The University of Cape Town (UCT) undertakes that in the event of you suffering any significant deterioration in health or well being that is caused in your participation in the study it will provide immediate medical care. Any trial related injuries are covered by UCT's insurance.

The decision to participate is entirely your own.

IF YOU DECIDE NOT TO PARTICIPATE, YOUR TREATMENT WILL NOT BE DISADVANTAGED IN ANY WAY. In addition, at any point during the study you are free to withdraw without telling us why.

Since this is a research study, the results will not be made available to the participants. When the results of the study become available, names of the participating patients will not be included.

Do you have any questions? During the study you may contact either the Research Ethics Committee (021 406 6492) or Dr Marinus Cloete (0824957831) if you have further questions.

Consent to participate in the study:

I have read the above / the above has been read to me. I have had the opportunity to discuss the study with Dr _____ and ask any questions.

I consent to take part in this study:

Name of person consenting _____

Signature/ fingerprint _____

Date _____

Name of person taking consent _____

Signature _____

Date _____

Name of Witness _____

Signature _____

Date _____

Appendix 5: Consent in Afrikaans

Universiteit van Kaapstad

Dr Steven Jeffery
Dr Marinus Cloete
Departement van Ginekologie
Fakulteit van Gesondheids Wetenskappe
Universiteit van Kaapstad
Anzio Road
Observatory
7925

Akupunktuur in vrouens met ooraktiewe blaas sindroom

INGELIGTE TOESTEMMING en INFORMASIE FORM

Geagte Pasient

Ek is _____

Ek wil u uitnooi om deel te neem in ‘n navorsings projek waarmee ons wil uitvind hoe goed is akupunktuur in die behandeling van ooraktiewe blaas (OAB). Ons hoop dat dit ons sal help om in die toekoms beter te kyk na pasiente met OAB. Die projek word gedoen deur die departement van Ginekologie van Universiteteit van Kaapstad by die Kontinensie Kliniek van Groote Schuur Hospitaal. Dr Stephen Jeffery is die Prinsipale Navorser en Dr Marinus Cloete is die Hoof Navorser.

OAB is die skielike, intense behoete om te urineer en kan lei tot ongewenste urine lek (verwys na as “nat ongelukkies”). Dit gebeur omdat die blaas spier the veel saamtrek of saamtrek wanneer jy dit nie wil he nie. ‘n Persoon mag bewus wees van die behoefte om te urineer maar sal nie urine lek kan keer voor hulle by die toilet uitkom nie. OAB is ook gewoonlik geassosieer met die behoefte om meer as agt keep op ‘n dag te urineer en meer as twee keer per nag.

Ons vra u om deel te neem aan die navorsings projek sodat ons meer kan leer oor hoe om mense met OAB te behandel. As dokters kan ons mense probeer help om hulle blase te beheer en medikasie voor te skryf, maar dit werk nie altyd nie. Dokters in Amerika en Europa het uitgevind dat akupunktuur help vir OAB. Ons wil kyk of dit vir ons patiente ook gaan help sodat ons hulle beter kan behandel.

Akupunktuur is ‘n eeu oue sisteem van heeling wat ontwikkel is oor duisende jare as deel van tradisionele Chinese medisyne. Die doel van die behandeling is om die energie balans in die liggaam te herstel, deur die pynlose plaasing van fyn naaldjies op strategiese plekke in die liggaam. Dit is baie veilig om hierdie fyn naaldjies net onder die vel in te druk. Wanneer dit ingedruk word kan u ‘n ligte prik voel, maar wanneer die naaldjie in is sal u geen pyn voel nie. U moet gemaklik voel gedurende die behandeling. Party mense, hulle is by verre in die minderheid, voel bietjie duislig en naar.
U sal vier akupunktuur behandelings oor ‘n tydperk van vier weke ondergaan. Met elke behandeling sal sewe naaldjies onder u vel geplaas word; twee op u knee, twee op u bobene, twee op u laer rug en een onder u naeltjie. Met elke behandeling word nuwe naalde gebruik. ‘n Behandeling duur twintig minute. Al die mediese personeel wat die naaldjies inplaas is opgelei daarin.

Op seker intervalle gedurende die projek sal ons u vra om tred te hou van u ongelukkies en ander blaas porbleme deur dit neer te skryf in ‘n boekie.

Dit is baie belangrik dat u sal terugkom vir u opvolg besoeke sodat ons kan sien of die akupuntuur u gehelp het of nie. Ons sal u vra om drie keer terug te kom: twee weke, een maand en drie maande na die behandeling. Ons sal u elke keer vra om ‘n vraelys uit te vul deur antwoorde te merk. Dit sal omtrent 10 minute nee mom die lys te voltooi.

Die projek sal gemoniteer word deur die Navorsings Raad van die Universiteit van Kaapstad. Hulle is daar om u veiligheid te verseker gedurende die projek. Die Universiteit van Kaapstad (UK) onderneem om mediese behandeling te voorsien sou u gesondheid aansienlik deur die studie geaffekteer word. Enige ernstige beserings wat deur die studie veroorsaak is sal deur die UK se versekering gedek word.

Die besluit om deel te neem moet geheel en al u eie wees.

SOU U BESLUIT OM NIE DEEL TE NEEM NIE, SAL U BEHANDELING IN GEEN WYSE DAAR ONDER LEI NIE. Verder mag U enige tyd gedurende die projek besluit om te ontrek sonder om te se hoekom.

Aangesien dit ‘n navorsings projek is kan ons nie vir u die uitslae van die vraelyste gee nie. Die antwoorde op die vraelyste bly bewaar deur die Hoof Navorser en u naam sal nooit daarop verskyn nie nie.

Het u enige vra? Gedurende die projek is u welkom om die Navorsings Raad (021-4066492) of Dr Marinus Cloete (0824957831) te skakel met verder vrae.

Toestemming om deel te neem in ‘n navorsings projek:

Ek het bogenoemde gelees/ dit is aan my voorgelees. Ek het die geleentheid gehad om dit te bespreek met Dr_____ en ek kon vrae vra.

Ek gee toestemming om deel te neem aan die navorsings projek:

Naam van persoon wat toestemming gee _____

Handtekening/ Vingerafdruk _____

Datum _____

Naam van persoon wat toestemming neem _____

Handtekening _____

Datum _____

Naam van Getuie _____

Handtekening _____

Datum _____

Appendix 6: Consent in Xhosa

uGqirha Steven Jeffery
uGqirha Marinus Cloete
Kwicandelo Lwezabafazi
KwiDyunivesi yaseKapa
Isitalato yi Anzio
eObservetory
7925

Unyango ngeenaliti kubafazi abanezinyi ezingalawulekiyo .

Isivumelwaqno nephepha lwencukanca.

Sigulane esithandekayo

Igama lam ngu……

Ndinqwenela ukukumema ukuba uthathe inxaxheba kwizifundo ngokufuna ukwazi ukuba. Unyango lwenaliti lubanceda njani abantu abanezinyi ezingalawulekiyo .Siyathemba ukuba ekwenzeni kwethu oluphando luyokusinceda ekuphandeni ngokungcono abantu abaphila nalenqxaki yesinyi esingalawulekiyo ekuhambeni kwexesha. Izifundo ezi ziqhutywa licandelo lwicandelo Lezabafazi kwi Dyunivesi yase Kapa kwaye ziyakubanjelwa kwiklinik kwisibhedlele sase Groote Schuur , uQqirha Steven Jeffery uyi nqununu aze u Marinus Cloete yena abeyinhloko koluphando .

Isinyi esingalawulekiyo kuikufuna ukuchama ngesaphume kwaye ingade uzichamele nokuzichamela. Kwenzaka okokuba izihlunu zesinyi ziyacunduselana ngokukhawuleza. Uye uzive ukuba ufuna ukuchama kodwa ungakwazi ukulawula umchamo xana uphumayo phambi kokuba ufike endlwini wangasese . Xana unessinyi esingalawulekiyo senza nakanjalo ukuba ufune ukuchama kakhulu amaxesha asibhozo ngemini okanye kabini ngobusuku.

Siyakucela ukuba uzokuthatha inxaxheba kwezizifundo kuba sifuna ukufumanisa ngokuphangaleleyo ukuba sinfgabanyanga kanjani abantu abanezinyi ezingalawulekiyo. Thina singoogqirha singabanceda abantu abanalenqxaki ukuba bafunde ukulawula izinyi zabo kwaye siyabanika namayeza abawathathe kodwa oku akusoloko kusebenza .
Oogqirha bas melika(America)naseYurophu (Europe) bafumanise ukuba unyango lwenaliti luyanceda nalo kwingxaki zesiinyi esingangalawulekiyo. Sifuna ukubona ulunyango luzokusebenza na kwizigulana zethu ukwenzela ukuba sibenako ukubanika unyango olunqcono.

Unyango ngenaliti luhlobo lakudala kakhulu olunyango siluthathe etshayina(China). Injongo zolunyangpo ku,kunqcna iminyango idlamkile ngokufaka inaliti kwindawo. Ezithile apha emzimbeni .Ukufakwa kwe naliti esikhumbeni somzimba akunabungozi kwaphela. Xa ezinaliti zifakwa emzimbeni uzokuva nje xa uhlatywayo xa sele ingene inaliti esikhumbeni awuva kwanto uzoba uzizolele nje .Abanye abanye abanye abantu baye bazive benesiyezi kwaye nathi bazokugabha kodwa babambalwa kakhulu abobantu. Uzakufumana unyango lwenaliti amaxesha amane (four)qho ngeveki iiveki ezine(four).Qho ngexesha lonyango ufumana iinaliti ezisixhenxe esikhumbeni okanye elofeleni lomzimba (skin)ziyakuba mbini emadolweni (knees)zibembini emathangeni(thighs)zibembini ngasemva esinqeni(back) ibenye phantsi kombono(navel).Ngawo onke amaxesha kusetyenziswa inaliti ezintsha. Unyango olu luthatha imizuzu engamashumi amabini (20 minits). Bonke abasebenzi abasebenza kolunyango baluqeqeqqshelwe.

Kuzakubakho amaxesha esizakuthi sikucele ukuba uqwalasele ingozi zokuzimanzisa kwakunye nezinye ingxaki othi uzifumane zesinyi ngokuthi uzibhale phantsi encwadini yakho.

Isivumelwano sokuthatha inxaxheba kwezisifundo:

Ndifunde okanye ndifundelwe ,kwaye ndinethuba lokuxoxa no
Gqirha ……kwaye dingabuza nowuphi na Umbuzo.

Ndiyavuma ukuthatha inxaxheba kwizifundo :
Igama lomntu ovumayo……
Sayina okanye beka ubhontsi……
Umhla….....

Igama lomntu othatha isivumelwano
……
Sayina ……
Umhla……

Igama lenqina……..
Sayina…….
Umhla……