

THE PREDICTIVE VALUE OF EPAQ IN THE URODYNAMIC DIAGNOSES IN WOMEN

by

SHANTEELA ASMAHRA McCOOTY

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College of Medical and Dental Sciences

University of Birmingham

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ABSTRACT

Urinary incontinence (UI) is a common, debilitating condition investigated by urodynamics (UDS). UDS is invasive and not 100% accurate and thus less invasive methods such as the electronic Personal Assessment Questionnaire (ePAQ) require further investigation. This thesis involved a systematic review assessing 11 studies reporting on the clinical uses of ePAQ and demonstrated its reliability in assessing quality of life (QoL) but there were no studies found which had assessed predictive ability. The quality and accuracy of UDS traces performed as part of a large diagnostic accuracy study were assessed and recommendations made for improvement in the quality performance. Finally a prospective, consecutive study involving 390 women assessed the ability of ePAQ to predict a diagnosis of DO on UDS in women with overactive bladder (OAB) and of urodynamic stress incontinence (USI) on UDS in women who have stress urinary incontinence (SUI) and demonstrated fair predictive ability. There was a positive relationship between OAB and SUI scores and a positive UDS diagnosis. Further research is required to assess whether ePAQ can be used in a predictive model with other predictors e.g. symptoms and examination findings to better predict disease and treatment outcomes.

DEDICATION

This thesis is dedicated to my two daughters, Nyela and Amera who have inspired me. They are the reason why I have continued to pursue my dreams and I hope that my aspirations will show them that with hard work, determination and love, all things are possible.

Audrey Brown, sadly you never got the opportunity to read my thesis but you too inspired me throughout my nursing career thus far and I will be forever grateful for your words of wisdom and encouragement, R.I.P.

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LIST OF ABBREVIATIONS

AUC	Area Under Curve
BCTU	Birmingham Clinical Trials Unit
BWNFT	Birmingham Women's NHS Foundation Trust
EMBASE	Excerpta Medica Database
ePAQ-PF	Electronic Personal Assessment Questionnaire- Pelvic Floor
BUS	Bladder Ultrasound
CI	Confidence Interval
CINAHL	Cumulative Index for Nursing and Allied Health
CNS	Central Nervous System
DO	Detrusor Overactivity
GUP	Good Urodynamic Practice
ICS	International Continence Society
IUGA	International Urogynaecology Association
LR	Likelihood Ratio
LUT(S)	Lower Urinary Tract Symptom(s)
MEDLINE	Medical Literature Analysis and Retrieval System Online
MUI	Mixed Urinary Incontinence
NHS	National Health Service
NICE	National Institute for health and care Excellence
NPV	Negative Predictive Value
OAB	Overactive Bladder
PFMT	Pelvic floor muscle training
PPV	Positive predictive value
POP	Pelvic Organ Prolapse

POP-Q	Pelvic Organ Prolapse Quantification System
PTNS	Percutaneous Tibial Nerve Stimulation
QC	Quality Control
QoL	Quality of Life
QUADAS	Quality Assessment of Diagnostic Accuracy Studies
ROC	Receiver Operating Characteristic
SNS	Sacral Nerve Stimulation
SOP	Standard Operating Procedure
STARD	Standards for Reporting of Diagnostic Accuracy
SUI	Stress Urinary Incontinence
TVT	Tension Free Vaginal Tape
UDS	Urodynamics
UI	Urinary Incontinence
UUI	Urgency Urinary Incontinence
UK	United Kingdom
USI	Urodynamic Stress Incontinence
UTI	Urinary Tract Infection
VD	Voiding Dysfunction

CHAPTER 1: INTRODUCTION

Background

Urinary incontinence is a condition that can adversely affect the physical, psychological and social well-being of the affected individual, as well their friends and family¹. This can have a substantial impairment on quality of life (QoL), particularly in regards to emotional symptoms, general well-being and sexual health ^{2, 3}.

The International Continence Society (ICS) define urinary incontinence (UI) as “the complaint of any involuntary leakage of urine” ⁴. UI is a common symptom that can affect both sexes; although, women are more commonly affected. This can occur in women of all ages, with many factors potentially predisposing UI (see Table 1).

Often self-esteem is lowered and due to the fear/embarrassment of this condition and seeking treatment, the emotional and health related quality of life (HRQOL) may become more of an issue to the sufferer ⁵. There are also significant financial implications, which include the costs of pads, prescription costs and time off work ^{6, 7}.

It is important to try and establish the cause of UI in order to initiate treatments and care pathways for the affected individual. However, UI may occur due to a number of abnormalities of the lower urinary tract (LUT) and/or illnesses, thus the aetiology in most cases is unknown, resulting in difficulties with the management of the condition.

Table 1: Potential risk factors for urinary incontinence

Diabetes insipidus	Excessive drinking
Diabetes mellitus	High caffeine and alcohol intake
Obesity (Body Mass Index >30)	Age
Previous pelvic surgery	Post-menopausal urogenital atrophy; urinary infections
Pelvic mass (e.g. fibroids)	Psychological issues
Pregnancy and vaginal delivery	Neurological disease
Parity	Complex medical history- combined conditions e.g. congestive cardiac failure, endocrine and renal impairment
Drugs (e.g. diuretics, cardiac drugs)	Toilet habit (e.g. prolonged voiding times)

Lower Urinary Tract

The lower urinary tract comprises of the bladder and urethra, which serves as a functional unit in the storage and voiding phase of the micturition cycle. The pelvic floor supports these two structures. Lower urinary tract symptoms (LUTS) are divided into three groups; storage, voiding and post micturition symptoms, these symptoms can vary in severity ⁸. Table 2 shows an adaptation of the groups of LUTS that also incorporates OAB and sensory symptoms.

Table 2: Symptoms of the Lower Urinary Tract

Storage	Voiding	Post micturition	Sensory
Frequency	Poor flow	Needing to revisit the toilet soon after voiding	Increased bladder sensation (earlier desire to void),
Urgency	Hesitancy	Post voiding dribble	reduced bladder sensation- desire to void occurs later than previously experienced
Nocturia	Intermittent flow	Feeling of incomplete emptying of bladder	Bladder pain
Urgency urinary incontinence	Straining	-	dysuria
-	Terminal dribble	-	-

Bladder Anatomy and Physiology

The urinary bladder is a flexible organ composed of three layers: transitional epithelium, a layer of smooth muscle (the detrusor muscle) and an adventitial layer of connective tissue on the outside. Neurological control of micturition or urination involves the central nervous system (CNS). This determines whether the bladder is

used to store or expel urine. Normally the bladder will fill over a period of 2-4 hours, as it fills the individual becomes increasingly aware of the need to pass urine. Changes at any level of this complex hierarchy can cause bladder dysfunction, resulting in symptoms. Neurological, anatomical and psychological changes can affect the processes that are involved in controlling micturition ⁹.

Overactive Bladder

Overactive bladder (OAB) is defined as “a symptom complex of urinary urgency (an intense, sudden desire to void), with or without incontinence, increased urinary frequency or nocturia in the absence of infection or other proven pathology” ¹⁰.

OAB is a storage symptom with an estimated 10-20% of the adult population being affected by it; millions of people worldwide have this condition and it increases with age ^{11, 12}. In a large, population-based epiLUTS study, the prevalence of OAB was found to be 12.8% ^{12, 13}. Various demographics were collected during the study and they found that LUTS increased with age and were highly prevalent amongst men and women aged >40years. With an increasing ageing population and advances in healthcare, the burden of OAB is likely to increase over the next few decades.

Affected women tend to implement ‘coping mechanisms’ in order to reduce the impact of their symptoms upon their daily living. Fluid restriction, avoiding going too far away from a toilet and emptying the bladder ‘*just in case*’ (before leaving home) are examples of coping mechanisms ¹⁴. People typically seek help 6-12 months after their first onset of symptoms ¹⁵. The true scope of this problem may be unknown due to under-reporting arising from the social embarrassment that is associated with this problem ¹⁶. It has been reported that urgency urinary incontinence (UUI) is more

bothersome than stress urinary incontinence (SUI) (involuntary leakage of urine caused by physical exertion). This is recognised as a predictive factor for depression and anxiety ¹⁷. Mixed urinary incontinence (MUI) is defined as a “complaint of involuntary loss of urine associated with urgency and also effort or physical exertion or on sneezing or coughing” ¹⁰. Although the term MUI incorporates mixed symptoms, it does not inform the clinician as to which symptom is the most bothersome to the patient.

Pathology of overactive bladder

There are a number of risk factors that can potentially contribute to the worsening of OAB symptoms, including urinary tract infection, calculi, inflammation, obstruction and oestrogen deficiency ¹⁸.

There are four main hypotheses that attempt to explain the pathophysiological basis for OAB. These are the neurogenic, myogenic, afferent hypotheses, and the peripheral autonomy (integrative) theory.

Neurogenic theory

Changes in the central nervous system pathways, leading to an imbalance that increases bladder excitation. Inhibition is reduced and there is an increased afferent input¹⁹.

Myogenic theory

Partial denervation of the detrusor causes an alteration in the properties of the smooth muscle. This may lead to an increase in spontaneous excitability and resulting in untimely bladder contractions, leading to urgency ²⁰.

Afferent Theory

Afferent mechanisms have been highlighted as potential factors involved in the sensory basis of the OAB diagnosis ¹⁹. C-fibres are generally quiescent during normal voiding, but they may be critical for symptom generation in pathologic conditions (Sun and Chung, 2009) ²¹. For example, changes in the CNS pathways, denervation of the detrusor muscle and alterations in functional cells in the bladder wall may lead to OAB.

It has been concluded by several authors that the c-fibres form a new afferent pathway and establish the mechanism of bladder pain and detrusor overactivity^{22, 23}.

Peripheral (Integrative) theory

Drake et al (2001) ²¹ proposed that the bladder is modular; an increased bladder sensation can occur due to exaggerated localised modular contraction. Detrusor overactivity is caused by an enhanced modular activity like alterations in the normal properties, or interactions of various functional cells in the bladder wall ²⁴.

Current practice in management of Urinary Incontinence

The initial clinical assessment of any woman who is being investigated for UI should include her UI being categorised. The National Institute for Health Care Excellence

(NICE) clinical guidelines on urinary incontinence (CG 171, 2013) state that the woman's UI should be categorised as stress urinary incontinence (SUI), mixed urinary incontinence (MUI) or urgency urinary incontinence (UUI) and overactive bladder (OAB) to prioritise the treatment of the predominant symptom.

Clinical History

A thorough consultation (clinical history) will help to establish the type of UI experienced and its effects on the individual. History taking should be focused on the main symptoms of OAB: nocturia, urgency, frequency and urgency incontinence ¹⁵. Information should be collected on the duration, type and severity of symptoms as well as the impact these symptoms have on quality of life (QoL). Further information should be obtained about any co-existing medical, surgical and /or gynaecological conditions and also factors such as diet, oral fluid intake and medications.

Bladder diaries

These are useful tools in the investigation of LUTS and also to assess treatment response ²⁵. Completion of bladder diaries allows evaluation of fluid intake, fluid output and volumes voided as well as number of incontinence episodes (day and night), twenty-four hour urine production and provoking factors such as activities (skipping, jogging, coughing) ²⁵.

Physical examination

A vaginal examination is carried out if a woman complains of a "bulge" or "something coming down through the vagina". This is to rule out pelvic organ prolapse (POP) and

vaginal atrophy. Treatment options can then be explored for women with symptomatic POP (NICE CG171, 2013).

Investigations

Whilst OAB is a symptomatic or clinical diagnosis, an assessment that excludes any underlying cause for LUT dysfunction like urinalysis for urinary tract infection should be performed.

A urine dipstick test should be undertaken in all women who present with UI at their first clinical consultation. As there are other factors that may contribute to their symptoms (Table 1), the presence of blood, glucose, leucocytes and nitrates as well as protein should be detected.

The NICE guidance on urinary incontinence (CG171, 2003) state that if a woman has symptoms of a UTI and their urine tests positive for leucocytes and nitrates, a midstream urine specimen should be taken women for culture and sensitivity of antibiotics. They should then be prescribed a course of antibiotics (pending culture results).

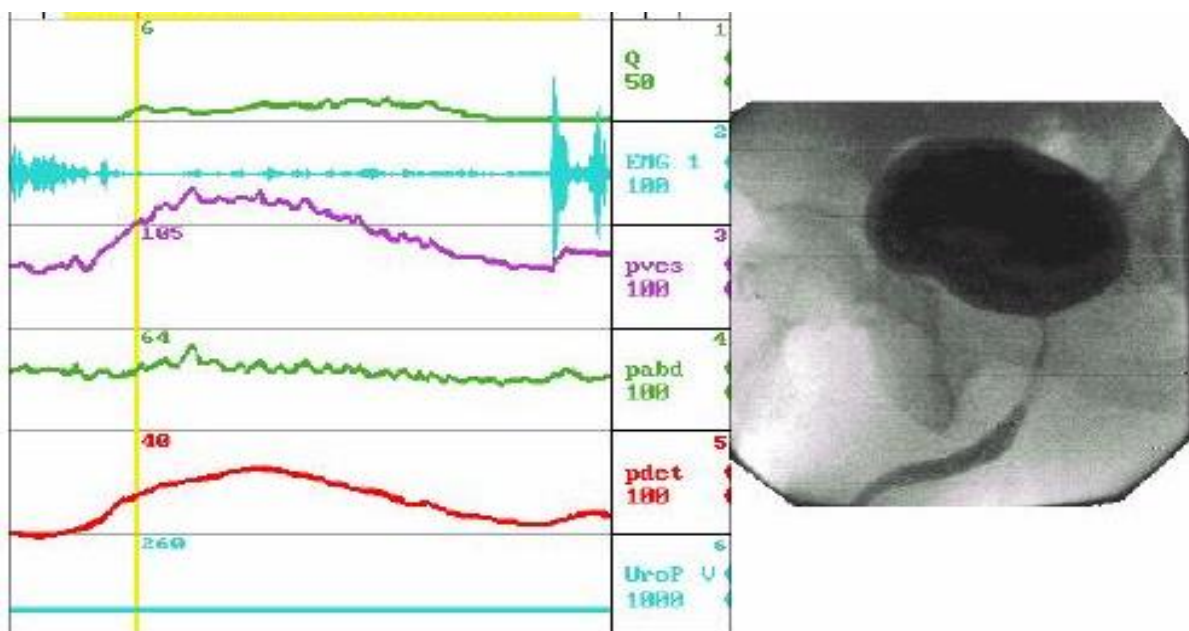
Questionnaires are increasingly used in health care in order to measure health-related QoL on an objective scale. These are either generic or specific to a particular condition. Generic questionnaires measure general concepts such as general coping strategies whilst the condition-specific questionnaires measure the differences between individuals with the same condition. However, the generic scoring systems are insensitive when dealing with a specific condition such as OAB ¹⁵.

Therefore, there may be a poor correlation in the differences between the patients and the grading of responses to treatment. Indeed, disease specific questionnaires are more appropriate in urogynaecology and in other clinical areas (such as clinics for women suffering with heavy menstrual bleeding). In order for a questionnaire to be considered a good, validated tool, adequate psychometric qualities must be demonstrated ²⁶. NICE have a number of recommended symptom scoring and quality of life questionnaires; which are incontinence-specific when therapies are being evaluated (Appendix 1).

Urodynamics

Urodynamics (UDS) is a diagnostic assessment of the lower urinary tract. It comprises of a series of interactive tests that look at the function of the bladder and urethra during both the filling and voiding phase with the aims of reproducing the patient's symptoms and secondly to provide a pathophysiological explanation for the patient's symptoms ²⁷.

Figure 1: Urodynamics trace (left) and video urodynamics (right)



UDS consists of uroflowmetry, filling cystometry and pressure flow or voiding (cystometry) ²⁸. Uroflowmetry measures the flow rate during the voiding stage, the test involves the patient passing urine into a special toilet that measures urine flow rate. Multichannel cystometry evaluates the pressure and volume relationship in the bladder at both the filling and voiding stages. The detrusor pressure is calculated by subtracting the abdominal pressure (obtained from the catheter transducer inserted into either the rectum or vagina) from the intravesical pressure measured by bladder line. During filling cystometry, the patient is asked to report any symptoms experienced like first desire, normal desire, strong desire to void, pain, urgency, incontinence etc. At the end of the test, the filling catheter is removed, and whilst the bladder and rectal catheter remain in situ, various provocation manoeuvres such as jumping, coughing, and running water are carried out. The objective is to try and identify provoked detrusor overactivity (DO) or urodynamic stress incontinence (USI). The patient is then instructed to void with the transducers *in situ*; this is to record

opening and maximum detrusor pressures, as well as the voiding pattern. This process is known as the voiding cystometry phase of urodynamics (UDS).

In a bladder that is normally compliant, large volumes of urine can be accommodated without any significant rise in the detrusor pressure, however if the elasticity of the bladder is reduced and the pressure rises whilst being filled, the bladder is deemed to have low compliance.

Urinary symptoms can arise due to neurological disease in the brain, the suprasacral spinal cord, the sacral spinal cord or the peripheral nervous system. Damage within each of these areas tends to produce characteristic patterns of bladder and sphincter dysfunction (NICE CG148, 2012) ²⁹.

Medical conditions including Parkinson's disease, stroke, multiple sclerosis, spinal cord injuries and tumours of the central nervous system can cause a neurogenic bladder. Neurogenic detrusor overactivity (DO) can occur when there is evidence of DO in a patient has a neurological disorder.

Urodynamics (UDS) is ideally performed in the sitting or standing position ^{28, 30}. The aim of the test is to reproduce patient's symptoms. Multiple diagnoses can be given following UDS tests: detrusor overactivity (DO), urodynamic stress incontinence (USI), a combination of DO and USI, voiding dysfunction (VD) and a 'stable/normal' bladder.

- DO - defined as the occurrence of involuntary detrusor contractions during filling cystometry. These contractions may occur spontaneously or as a result

of provocation, they produce a wave form on the cystometrogram and vary in amplitude and duration ¹⁰.

- USI - is defined by the ICS/IUGA (2010) as the finding of involuntary leakage during cystometry; this is associated with increased intra-abdominal pressure, in the absence of a detrusor contraction.

UDS is often described as the 'gold standard' for evaluating LUTS ³¹. However, some studies have shown that UDS can be inaccurate and does not always correlate to the patient's symptoms ³²⁻³⁴. For instance, a proportion of women who have OAB symptoms do not have a clinical diagnosis of DO following UDS. One reason for this may be because UDS does not mimic the 'normal physiology' of the bladder. Although UDS may not be necessary for the routine management of all patients, objective data are provided from the procedure, which may guide medical and surgical treatment ³⁵.

UDS is a costly procedure at approximately £212 per person and is also an invasive diagnostic test that has an associated risk of urinary tract infections ³⁶.

UDS is indicated prior to implementing surgical treatments, following failure of conservative management and medical treatments. NICE (CG171, 2012) recommends invasive treatments like Botulinum toxin A or neuromodulation in patients who have failed conservative therapies and have Detrusor Overactivity (DO).

Ambulatory UDS is an extended version of the laboratory UDS, whereby this is often performed over a four-hour period. This test may be offered if the patient symptoms

have not been reproduced by the standard UDS. This test may be more sensitive in detecting the rate of DO than the conventional UDS ³⁷.

The advantages of ambulatory UDS are that the patient is given a lot more time to present and report their symptoms. The situation where the patient may usually leak is often without the presence of any clinicians. A diary is kept throughout the duration of the test and specific buttons are pressed on the machine to indicate the symptoms experienced, i.e. leaking, walking or experiencing urgency.

Options for treatment

Behavioural modification can be implemented whilst using bladder diaries and factors such as caffeine reduction and bladder retraining should also be initiated ^{38, 39}.

Currently, physiotherapy treatment options for UUI include pelvic floor muscle training (PFMT) or pelvic floor exercises. This treatment is the most common used for women with SUI, although it is sometimes used for women who present with MUI or UUI.

A trial of supervised PFMT (at least 3 months duration) should be offered to women with SUI (NICE CG171, 2012).

It is known that the detrusor muscle contraction can be inhibited by a pelvic floor contraction, induced by electrical stimulation ⁴⁰. Inhibition involves an automatic increase in tone for the pelvic floor muscle and urethral striated muscle; therefore, voluntary pelvic floor contractions may provide some benefit to those who have UUI (by controlling these symptoms) ⁴¹.

Whilst conservative measures are desired as first line treatment, an integral part of OAB management includes drug therapy for most symptomatic women.

Antimuscarinic/anticholinergic medication is the mainstay of treatment; however, side effects associated with these result in difficulties with compliance. The NICE guidelines (CG171) advise that following the failure of conservative treatment, a trial of anticholinergics should be offered.

An anticholinergic is a substance that blocks the neurotransmitter acetylcholine in the central and peripheral nervous system. Anticholinergic drugs inhibit the parasympathetic nerve impulses; they selectively block the binding of the neurotransmitter acetylcholine to its receptor in the nerve cells. The rationale for using anticholinergic drugs in the treatment of overactive bladder syndrome is to block the parasympathetic acetylcholine pathway and thus abolish or reduce the intensity of detrusor muscle contraction.⁴²

Electronic personal assessment questionnaire (ePAQ) is one such questionnaire which is being used in a lot of urogynaecology departments throughout the country to assess the pelvic floor specific QoL (detailed in chapter 2). We wanted to study the evidence on diagnostic, prognostic and other utilities of ePAQ. We also wanted to assess whether this instrument could be used to reduce the need for invasive tests like urodynamics.

ELECTRONIC PERSONAL ASSESSMENT QUESTIONNAIRE (ePAQ)

The electronic Personal Assessment Questionnaire-Pelvic Floor (ePAQ-PF) was developed by the Sheffield Teaching Hospitals NHS Trust in 2002. The concept behind the development of this questionnaire was due to the perceived need to reduce the use of paper questionnaires and use computer interviewing ⁴⁰. It was thought that this would improve communication and patient assessment, particularly in regard to the sensitive issue of pelvic floor disorders.

In this thesis, unless otherwise stated; 'ePAQ' should be understood to mean ePAQ-PF.

The ePAQ has undergone rigorous psychometric testing and test-retest reliability and is known as a validated and robust tool for measuring QoL in relation to pelvic floor dysfunction ⁴⁰. The completion of paper questionnaires can become a burden to the patient and might be onerous to collate for a clinician ⁴³. In contrast, computerised questionnaires have been known to achieve higher response rates in terms of completion and participants have also found these easier to complete ⁴⁴.

There are 132 items in this questionnaire to provide a detailed assessment into pelvic floor symptoms and health-related QoL ⁴⁵. The ePAQ is a self-administered, interactive, computer-based questionnaire that comprises of four dimensions; measuring urinary, bowel, vaginal and sexual symptoms, looking at their related impact and effect on QoL. In the four dimensions there are either four or five scored domains, each one comprising three to seven items. A scoring algorithm is used and each item has a scoring system between 0 and 3 (0 indicates best and 3 worst health

status). A scale of 0-100 is produced at the end of the questionnaire indicating the best health (0) and the worst health status (100). Each page of the ePAQ will include a question about how often the symptoms occur and its effect on the individual's QoL. The results from the questionnaire do not show the answers to any of the questions. Following completion, a report is generated and symptoms scores are categorised by the specific groups of the pelvic floor function.

Currently, ePAQ is used to improve clinical consultation and assess treatment/ QoL outcomes in patients who complain of pelvic floor symptoms. Figure 2 shows an example of the report produced after a completed questionnaire.

The last two items in the questionnaire seek consent for use of patient data. In relation to service evaluation, the first asks: *“Are you willing to allow confidential use of your answers in order to evaluate the care you receive?”* (Yes/No). The second relates to evaluation of the questionnaire and asks: *“Are you willing to allow confidential use of your answers to check how this questionnaire is working?”* (Yes/No).

Figure 2 Picture of a completed ePAQ

ePAQ electronic Personal Assessment Questionnaire

Bladder & urinary symptoms		Score (0 - 100)	Impact
Pain	33	<div><div></div></div>	<div><div></div></div>
Voiding	25	<div><div></div></div>	<div><div></div></div>
Overactive bladder	17	<div><div></div></div>	<div><div></div></div>
Stress incontinence	20	<div><div></div></div>	<div><div></div></div>
Quality of life	11	<div><div></div></div>	
Bowel symptoms		Score (0 - 100)	Impact
Irritable bowel	47	<div><div></div></div>	<div><div></div></div>
Constipation	44	<div><div></div></div>	<div><div></div></div>
Evacuation	43	<div><div></div></div>	<div><div></div></div>
Continence	5	<div><div></div></div>	<div><div></div></div>
Quality of life	11	<div><div></div></div>	
Vaginal symptoms and prolapse		Score (0 - 100)	Impact
Pain & sensation		Dimension skipped	
Capacity		Dimension skipped	
Prolapse		Dimension skipped	
Quality of life		Dimension skipped	
Sex life		Score (0 - 100)	Impact
Urinary		Dimension skipped	
Bowel		Dimension skipped	
Vaginal		Dimension skipped	
Dyspareunia		Dimension skipped	
General sex life		Dimension skipped	

Potential uses of ePAQ as a predictive tool in LUTS

The bladder has been described as an unreliable witness ⁴⁶. UDS is considered to be the gold standard diagnostic test for investigating lower urinary tract symptoms (LUTS). The UDS can discriminate between a person with the disease (i.e. DO or USI) and a person without the disease (i.e. stable bladder) to give the post-test probability of a disease. However, it is invasive, expensive and can give a risk of urinary tract infection (UTI). Rosier (2013) states that the invasiveness of UDS remains a drawback; raising the threshold for its use ⁴⁷. There is widely available evidence on the clinical relevance of UDS, however, it is somewhat fragmented (Rosier, 2013). There are variations within clinical practice, the need for continuous quality control and also the correlation between patient symptoms and the results of the UDS investigation. Schafer et al (2002) ²⁷ identify that there are limitations with the UDS equipment and also the lack of a consensus in relation to the right method of measurement including, the signal processing, documentation and interpretation. The clinical utility of any diagnostic tool can be judged by whether the test is reproducible, can confirm the diagnosis and if the clinical outcome of treatment is better than having used the tool³⁰. With UDS being invasive and time consuming, alternative methods have been sought out in order to diagnose detrusor overactivity⁴⁸.

Until and unless there is another method that proves to be more reliable, the UDS will remain the gold standard investigation. There is thus a need to consider other less invasive tools that may allow us as clinicians to identify a sub-group of women with

LUTS that are more likely to have pathology (i.e. either DO or USI) and thus most benefit from the invasive test i.e. UDS.

The ePAQ is a non-invasive, reliable and relatively easy to use tool^{40, 53, 54} and we hypothesize, its urinary domain may have sufficient predictive value to reduce the need for invasive UDS. To date, there have been no data on the diagnostic value of ePAQ in accurately predicting the urodynamic diagnoses of women who have OAB symptoms.

Aims and objectives

It is hypothesised that women who have higher scores on ePAQ for OAB or SUI will have a higher likelihood of DO or USI respectively diagnosed at the time of UDS. We aimed to explore whether ePAQ has good diagnostic accuracy for detrusor overactivity and urodynamic stress incontinence which might enable us to reduce the need to perform UDS.

Objectives:

This thesis has the following objectives:

1. To perform a systematic review of the literature to assess the utility of the ePAQ-PF in clinical practice for women with lower urinary tract symptoms.
2. To perform quality assurance of the gold standard test of Urodynamics.
3. To assess the ability of the electronic personal assessment questionnaire (ePAQ) to predict a urodynamic diagnosis of detrusor overactivity (DO) in women with OAB and urodynamic stress incontinence (USI) in women who have SUI.

CHAPTER 2: SYSTEMATIC REVIEW OF ELECTRONIC PERSONAL ASSESSMENT QUESTIONNAIRE TO ASSESS CLINICAL UTILITY IN WOMEN WITH LOWER URINARY TRACT SYMPTOMS

Introduction

The ePAQ system provides a validated approach to the assessment of pelvic floor symptoms. It is used to assess responsiveness to therapies and assess quality of life in women. It provides a detailed software analysis from a set of user-friendly questions. When patient responds with assent to an item about a particular symptom, an impact question relating to the 'bothersomeness' of that symptom is automatically presented. These questions relating to 'bother' are only displayed if the patient states they have an issue with that symptom. The patient's most bothersome symptoms are highlighted and presented as a graph and also numerically (Figure 2). The overview of their ePAQ report can then be used to aid the clinical consultation, by questioning the patient on her symptoms identified on her report.

Systematic reviews are considered a key element of evidence-based healthcare ⁴⁹. We wanted establish the evidence base for using ePAQ in clinical practice. In particular, we wished to assess whether any previous research had been performed to assess its predictive ability for UDS diagnoses. A scoping search conducted in

2013 did not find any evidence on diagnostic accuracy of ePAQ and UDS diagnoses and thus this systematic review was then extended to assess the literature on all clinical utilities of the ePAQ.

Methods

Four part question

Population: women with pelvic floor symptoms

Intervention: electronic pelvic floor assessment questionnaire

Comparison: none

Outcomes: effectiveness, diagnosis, prognosis, qualitative data

Study design: prospective or retrospective cohort studies, case series

Literature Search

The following databases were used: The Cumulative Index to Nursing and Allied Health (CINAHL), Cochrane database, Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica Database (EMBASE), National Library for Health, Meta Register of controlled trials and Google Scholar (from ePAQ inception 2004-October 2013). Various relevant key words, word variations and Medical Subject Headings (MeSH) were used without language restrictions. The key words used in the search were: ePAQ, electronic Personal Assessment Questionnaire, electronic Pelvic Floor Assessment Questionnaire, quality of life questionnaire, overactive bladder, urinary incontinence and prolapse. In order to explore any relevant literature that related to the research question a combination of Boolean operators 'OR' and 'AND' were utilised to bring the key words and topics

together. The CINAHL, Cochrane and EMBASE databases provided a number of results in relation to questionnaires (Appendix 2).

Study selection and data extraction

Two review authors (PM- Consultant in Urogynaecology and SM- a urogynaecology research nurse) scrutinised the electronic searches consisting of studies where ePAQ had been used as a form of measuring QoL and selected potentially relevant manuscripts on the basis of the title and abstract. Full manuscripts of the potentially relevant studies were obtained. A final decision on inclusion or exclusion of the manuscripts was made following review of the full manuscripts (Figure 3). Included studies had to fulfil the criteria as described in the clinical question above. A list of excluded manuscripts and the rationale for exclusion can be found in Appendix 3. The required information from the primary studies was extracted and details about the participants, study, and outcomes were noted.

The selected studies were then assessed for methodological quality using the Newcastle Ottawa Scale ⁵⁰. This scale was chosen as it has undergone reliability and validity assessment. One of its strengths is that it is a convenient and fairly simple tool to use for the quality assessment of non-randomised studies. Our clinical question considered a study design which consisted of a selection of cohort studies. The Newcastle Ottawa Scale has a star rating system used to indicate the quality of a study. Quality was defined as the confidence that the study design, conduct and analysis minimised bias in the estimation of test accuracy. The risk of bias was regarded as low if a study obtained four stars for selection, three stars for

ascertainment of exposure and two stars for comparability⁵⁰. A medium risk of bias was regarded as studies with two or more stars for selection, one for comparability and two for exposure. Any study that scored one or zero stars for selection, exposure or comparability was considered to have a high risk of bias. Following the initial literature search, relevant articles (which fulfilled the 4 part clinical question) were selected. We looked at the rationale for each study, the methods and materials used to obtain the data and the results of each study. We then grouped the similar themes from each study and tabulated them in accordance to the following: predicting prognosis, treatment response, test-retest reliability and qualitative purposes.

Results

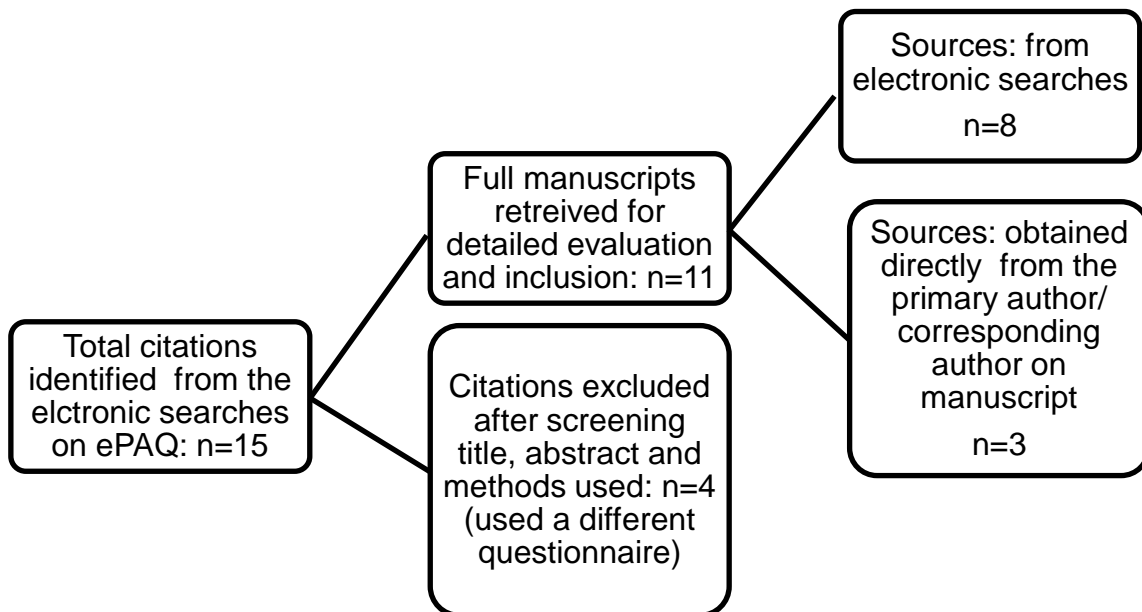
A total of 15 publications were identified in the electronic search and 11 studies were included in this review (Figure 3).

The studies included in the systematic review were tabulated into various categories: predicting prognosis, treatment response, test-retest reliability and qualitative/miscellaneous studies (see Tables 3a-3d). The methodology, findings and the strengths/limitations have been listed.

The qualitative studies included semi-structured interviews and cross-sectional surveys being conducted on women who were seen in a urogynaecology unit and had completed an ePAQ. Prospective cohort studies using ePAQ for women who had undergone surgery included women who completed the ePAQ pre and postoperatively. The majority of the study population were of Caucasian origin and the mean age groups varied from 29.7 years to 60.5 years.

The sample population in the various studies ranged from 34 to 4,506 women. The studies were conducted for a few months up to three years.

Figure 3: Selection process for studies included in the electronic Personal Assessment Questionnaire systematic review



**Table 3a: Details of studies included in the systematic review on electronic Personal Assessment Questionnaire-
pelvic floor: predicting prognosis.**

Author, Year	Title	Sample	Methodology	Findings	Strengths/limitations
Jha et al (2009) ⁵¹	Factors influencing outcome following the tension-free vaginal tape (TVT).	100 women who were undergoing TVT and had completed ePAQ pre-operatively and 3 months post-operatively were included in this study. (January 2006-May 2007)	A prospective observational study which aimed to evaluate factors which may influence the outcome with TVT. Linear regression was used for analysis.	85% had urodynamic stress incontinence (USI). Women who had more severe symptoms preoperatively had a greater improvement in SUI. All dimensions on the urinary domain of ePAQ had improved following a TVT.	Pre-operative data regarding bladder test diagnoses was provided, indicating the rationale for treatment. This is the first study looking at the effect of severity of pre-existing symptoms (stress urinary incontinence) Additional factors which have a potential to influence outcome of surgery were not included-examples of this include previous continence surgery and also parity.

Elenskaia et al (2012) ⁵²	Pelvic organ support, symptoms and quality of life during pregnancy: a prospective study.	>18years old and had a singleton pregnancy (with no complications) The aim was to evaluate changes in pelvic organ support and pelvic floor symptoms during their first pregnancy. The hypothesis was that pregnancy is associated with worsening changes of the pelvic floor and its function.	182 Women who attended their first visit to clinic at 20 weeks. 150 (82.4%) women attended the 36-week visit. Of these, 147 (80.8%) completed ePAQ and 148 (81.3%) had an assessment of their pelvic support using the POP-Q system.	The mean age = 29.7 years. There were no significant changes in POP-Q between the two visits. There were no changes in vaginal symptoms. There were increased symptoms and bothers associated with voiding and stress urinary incontinence during pregnancy. Constipation had improved (p=0.02). None of the pelvic floor symptoms had an impact on QoL.	Data was unable to be provided from the first trimester of pregnancy. The electronic format of ePAQ was not used for this study. This may have influenced the disclosure of specific information.
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**Table 3b: Details of studies included in the systematic review on electronic Personal Assessment Questionnaire-
pelvic floor: treatment response.**

Author, Year	Title	Sample	Methodology	Findings	Strengths/limitations
Jones et al (2009) ⁵³	Responsiveness of the electronic Personal Assessment Questionnaire- Pelvic Floor (ePAQ-PF).	54 women having a tension-free vaginal tape (TVT) for stress urinary incontinence and 47 undergoing prolapse surgery	ePAQ was completed at baseline and 3 months post- operatively The responsiveness of the questionnaire was evaluated using effect sizes, standardised response means, responsiveness statistic and minimally importance	The mean age of the women in TVT group was 49.9years (range 35.8 to 70.3) and 60.5 years for the prolapse group (range 35.1 to 79.2).70.4% of women who had a TVT felt “much better” post-op. 61.7% of women with prolapse repair felt “much better” post-op A comparison of mean scores from baseline to follow-up (for the TVT group) in all domains showed an overall improvement, except for the bowel domains (IBS, constipation, evacuation and continence). An improvement in all domains of ePAQ for baseline and follow up (prolapse	A small sample size, the time scale of the study was not mentioned- difficult to know whether the dataset and length of study may have influenced the outcome measure. Health changes identified through the completion of this questionnaire, pre and post intervention.

			difference.	group) showed an improvement in all domains, except the bowel domains for constipation and evacuation.	
Dua et al (2012) ^{a54}	The effect of prolapse repair on sexual function in women.	474 women who had undergone prolapse surgery between 2008 - 2010.	Prospective study on women who were undergoing prolapse repair. The ePAQ had been completed at pre and 3 months' postoperative intervals. The sex (vaginal and dyspareunia)	474 women underwent prolapse surgery. 393 had completed ePAQ and had given consent for their data to be used. 271 women were sexually active prior to surgery and 197 had completed a pre and post questionnaire. Significant improvements had been recorded by the women who had and anterior repair or anterior repair	Largest prospective study that evaluates sexual function outcomes following vaginal prolapse surgery. The main outcomes measured were clearly identified through focusing on a specific domain of the questionnaire. The study highlights how effective this questionnaire is in assessing change in QoL,

			domains were the main focus of this study.	and vaginal hysterectomy. Women who had a posterior repair had some improvement in sexual function post-operatively.	following surgery for vaginal symptoms.
Dua et al (2012) ^{b50}	The effect of posterior colporrhaphy on anorectal function.	Prospective, observational study on 60 Caucasian women who were undergoing posterior colporrhaphy. The effect that this type of prolapse procedure has on bowel symptoms was the main objective of the study (January and	Women who were seen in a tertiary referral urogynaecology centre, completed ePAQ at their initial assessment and 3-6 months post-operatively. Pre and post-operatively bowel scores were compared using student t-test.	The mean age = 58.3 years (+/-11.8 years) and the mean Body Mass Index (BMI) was 28.05 (+/-5.2). 57% had IBS, 62% reported bowel continence problems, 81% had evacuatory problems and 47% constipation 59/60 women had grade 2 or more prolapse on POPQ.27% had Posterior repair with perineorrhaphy and 73% had just a posterior vaginal repair42% of women had improved bowel evacuation. 37% had improvements in	This is the first study to report on the overall bowel-related quality of life. Women from ethnic minority backgrounds were not included in this study, result findings may have differed. Follow up was conducted between 3 and 6 months, results may have differed over a longer period of time. This study was observational and related to one specific centre.

		October 2010)		continence and 61% had seen an improvement with bowel related QoL. Bowel evacuation and continence improved 3-6 months post-operatively.	
Jadav et al (2013) ⁵⁵	Does sacral nerve stimulation improve global pelvic function?	43 patients with faecal incontinence were included.	Women with faecal incontinence completed ePAQ pre and post treatment. All women had sacral neuromodulation for faecal incontinence. The data was analysed for a period of five years.	<p>The mean age = 56.5 years.</p> <p>The median follow up was 6.8 months.</p> <p>All women had urinary symptoms. 81.4% had vaginal symptoms and 85.7% had described some sexual dysfunction.</p> <p>There was a significant improvement in faecal incontinence and bowel related QoL.</p> <p>58.1% reported a global health improvement, mainly in the bowel domain.</p>	<p>ePAQ has been used to confirm improvement in pelvic floor function relating to the 4 domains on the questionnaire.</p> <p>9 patients were lost to follow up (no completed post-treatment ePAQ and despite efforts to obtain this data, they were excluded).</p>

**Table 3c: Details of studies included in the systematic review on electronic Personal Assessment Questionnaire-
pelvic floor: test-retest reliability.**

Author, Year	Title	Sample	Methodology	Findings	Strengths/limitations
Radley et al (2006) ⁵⁶	Computer interviewing: concept, development and psychometric testing of an ePAQ in primary and secondary care (June 2003 and January 2004).	432 women recruited - 204 in primary care and 228 in secondary care.	Cross-sectional study of women using ePAQ prior to appointment. Women untreated in primary care returned a week later to complete ePAQ. Psychometric testing conducted to assess whether this questionnaire could be used to evaluate pelvic floor	In primary care, the findings show that test- retest analysis was acceptable ($p < 0.001$) and alpha co-efficient > 0.7 . In secondary care, 14 domains with the four dimensions (urinary, bowel, vaginal and sexual symptoms) were consistent. 14 domains within the 4 dimensions (urinary, bowel, sexual and vaginal symptoms) had alpha values of > 0.7 . ePAQ was found to be a user-friendly tool which may enhance the questioning of women with pelvic floor disorders.	Questions can be omitted which may improve non- response rates The patient's willingness for their data to be used for audit is recorded. The costs of the computer software may be an issue amongst some NHS units.

			symptoms.		
Jones et al (2008) ⁵⁷	Electronic pelvic floor symptoms assessment: tests of data quality of ePAQ-PF.	599 women with pelvic floor disorders completed ePAQ.	A cross-sectional survey conducted in a urogynaecology unit where ePAQ is completed as part of routine clinical care and prior to clinical consultation.	The mean age of the women at time of completing the questionnaire was 52.6 years. Of the 599 completed questionnaires, 17 were excluded due to incomplete data. 3 (0.5%) women declined to answer urinary, bowel or vaginal dimensions and 90 (15.5%) women declined to answer the sexual dimension. 70.3% women had some bladder concerns; 45.9% had expressed bowel problems, 50.2% of the women had vaginal problems.	The study was set in a secondary care unit. Primary care women were not included and therefore it is not possible to state whether results may have been different. This study illustrates that ePAQ can be used as a tool to detect changes in pelvic floor disorders.

**Table 3d: Details of studies included in the systematic review on electronic Personal Assessment Questionnaire-
pelvic floor: qualitative/miscellaneous research.**

Author, Year	Title	Sample	Methodology	Findings	Strengths/limitations
Jha et al (2012) ⁵⁸	Incontinence during intercourse: myths unravelled.	480 women who attended a urogynaecology unit during the months of January 2006-July 2010.	Prospective study of women referred with urinary incontinence. They went on to have urodynamics and had completed an ePAQ. The aim of the study was establish the extent to which coital incontinence occurs, its impact on QoL and the correlation between the different urodynamics diagnosis and coital leakage	The mean age = 48.3 years. 58% of women had USI 19% of the women had Detrusor Overactivity. 130 women did not complete the sexual dimension of the questionnaire. 60% of women who had urinary incontinence also reported leaking with intercourse.	This is the largest study looking at sexual symptoms and urodynamic diagnoses whilst using ePAQ to assess its effects on sexual function. Demographic data in relation to ethnicity, parity, body mass index may have provided further information on this topic

Dua et al (2013) ^{a59}	Understanding women's experiences of electronic interviewing during the clinical episode in urogynaecology: a qualitative study.	Initially 34 women were approached but due to various reasons, 20 women who had completed ePAQ before and after pelvic floor intervention were included in the study.	Qualitative study conducted through the use of semi-structured interviews. The study was conducted between July 2009 and July 2010. A thematic approach was used to identify themes and categories.	All women were Caucasian with a mean age of 58 years. 8 themes were identified relating to the women's views on using the questionnaire benefit and the burden of completing this questionnaire. Women felt that their understanding into their own condition had actually improved following the completion of ePAQ; Communication with their clinician had improved as they felt more prepared for consultation. ePAQ was found to be generally acceptable and easy to use. Some women found the questionnaire to be a burden due to its multiple choice format.	A small sample size was used over a 1 year period. Only Caucasian women were interviewed, further interviews from women of ethnic minority backgrounds may have altered the results. The potential to enhance understanding and educate women about their symptoms highlighted in this study. Due to technical failure, one of the interviews was unable to be used as part of the final analysis.
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Dua et al (2013) ⁶²	The personal impact of pelvic floor symptoms and their relationship to age.	A total of 4,506 women who attended urogynaecology clinics had completed ePAQ-95% of these women (4,311) gave consent for their data to be used.	Symptom frequency and impact scores were categorised into mild, moderate and severe. These were then compared amongst the different age groups <35, 36-50, 51-65 and >65 years.	615 women were <35years (14.2%), 1,219 (28.2%) were aged between 36 and 50 years, 1,438 (33.3%) were 51-65 years and 1,047 (24.3) were >65 years at time of completing ePAQ. The mean impact scores for OAB, SU), voiding dysfunction and bladder pain were lower in older women. Severe urinary symptoms did not show any difference in the impact in different age groups. Older women had lower impact scores for vaginal and bowel dimensions. In the sexual dimension of ePAQ, older women were less bothered by all sexual symptoms.	This is the first study that has reported on individual symptoms and its relation to age A large sample size was obtained over a 3 year period. Previous surgical history and medical conditions were not included which may have Influenced the result findings. Women who are treated for pelvic floor symptoms in the community were not included. Results may differ from women in primary and secondary care.
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Predicting prognosis

There is the potential to use ePAQ when counselling women about surgical interventions (e.g. for continence or pelvic organ prolapse), outcomes and their perception of success (post operatively). Additional co-morbidities may influence how successful (or not) a patient perceives her treatment to be. For example, women with LUTS and pelvic floor symptoms may have higher expectations of improvement, following surgery.

A tension free vaginal tape (TVT) is a surgical procedure undertaken for the treatment of SUI. It involves inserting a synthetic polypropylene sling in the mid-urethral area to provide a hammock effect, relieving leaking associated with activities such as laughing and coughing. The ePAQ is often used pre and postoperatively in this sub-group of women and can be used to evaluate the subjective effect of the procedure.

Jha et al (2009)⁵¹ looked at factors that may influence the outcome with women having a TVT. They found that women with more severe symptoms preoperatively had a significantly greater improvement in SUI symptoms ($p < 0.001$) and QoL ($p = 0.016$). Women with more severe SUI may expect greater improvement, both in their incontinence and their health-related quality of life (HRQoL) following a TVT.

Other factors that may have influenced the outcome of a TVT was not explored. For example, data on any previous surgery for POP or continence was not provided.

This study illustrates how ePAQ data can be used when discussing treatment response.

Lower urinary tract and pelvic floor symptoms are also known to increase during pregnancy and pelvic floor symptoms can become worse ⁶⁰.

A prospective study aimed to evaluate the changes in pelvic floor symptoms and the effect of QoL during pregnancy ⁵². Both an objective assessment of pelvic organ support (using the Pelvic Organ Prolapse Quantification [POP-Q] system) and subjective evaluation of symptoms with the ePAQ were performed in the second trimester and then repeated at 36 weeks gestation. There were no significant changes in POP-Q points or stage between the two visits except for a significant increase in genital hiatus ($p=0.0001$) and perineal body length ($p=0.0001$). The vaginal symptoms did not show any changes. Symptoms and bother with voiding difficulties and stress urinary incontinence increased during pregnancy. Constipation ($p=0.02$) and evacuation subdomains improved significantly ($p=0.009$). In the sexual domain, the only subdomain that worsened significantly ($p=0.03$) was “sex and vaginal symptoms”. None of the pelvic floor symptoms impacted the QOL.

There is a possibility that specific information was not disclosed as a paper copy of ePAQ was used as opposed to the electronic format.

Treatment response

The ePAQ is responsive to health status change following surgery and is suitable to be used as an outcome measure in urogynaecology. A study conducted by Jones et al (2009) ⁵³ aimed to evaluate how responsive the ePAQ was in women who were undergoing TVT for stress urinary incontinence (SUI) or prolapse surgery.

The results showed that at baseline the women who were undergoing a TVT scored high for the SUI domain and similarly, the women who were having prolapse surgery

also scored high in the prolapse domain. The scores reduced dramatically in these domains postoperatively. In the TVT group, the largest effect sizes were seen in the urinary domains for SUI, QoL and OAB. In the prolapse group, the largest effect sizes were seen in the vaginal domains for prolapse and quality of life. This indicates how useful used as comparison of their symptoms (pre and post-operatively).

Sexual function in a woman can become affected due to underlying pelvic floor disorders such as a pelvic organ prolapse (POP). There are different forms of surgery depending on the type of POP (posterior repair, anterior repair, anterior repair with a vaginal hysterectomy and a combined posterior and anterior repair). Women undergoing prolapse repair between 2008 and 2010 were asked to complete an ePAQ for the assessment of their symptoms.¹²³ sexually active women had completed the questionnaire both pre and 3-6 month postoperatively. The results highlighted that vaginal surgery can improve pain with intercourse and sexual function related QoL in those undergoing an anterior repair or anterior repair and vaginal hysterectomy⁵⁴. Women undergoing a combined procedure had the least improvement in sexual function but the women who had a posterior repair (in isolation) had an improved sexual function, although pain during intercourse was still an issue. Overall, the completion of an ePAQ is helpful when discussing treatment response.

In another study by Dua et al (2012)⁵⁵, 60 women undergoing posterior colporrhaphy had completed an ePAQ. A significant improvement was seen in bowel evacuation (42%), continence (37%) and bowel-related QoL (61%) scores. IBS score improved by 28%, but this did not reach significance. There was no significant change noted in constipation (0.5%). This study has illustrated the importance of assessing symptoms as a pre-operative ePAQ may prove valuable when discussing surgery and its potential impact on various symptoms with women.

Many women undergoing sacral neuromodulation for faecal incontinence have coexisting pelvic floor dysfunction. Women with faecal incontinence underwent assessment using the ePAQ (Pre- and post-stimulator). It was found that ePAQ scores improved significantly more in the bowel continence domain than in other domains following Sacral Nerve Stimulation (SNS) treatment ($P < 0.005$).

Improvement related to QoL in urinary symptoms and overall bowel function was also significant ($P < 0.005$). A global health improvement was reported in 58.1%, mainly in bowel evacuation ($P < 0.01$) and in vaginal pain and sensation ($P < 0.05$). This was a small study of 43 women with analysis of the data taking place over a 4.5-year period. The study has demonstrated global improvement in pelvic floor function in bowel, urinary, vaginal and sexual dimensions in women following SNS for faecal incontinence.

Test-retest reliability

Radley et al (2006)⁵⁷ conducted a qualitative study that considered how women perceived the completion of the ePAQ with the primary care setting. This data

suggested that after completing an ePAQ, women felt more prepared for their clinical consultation. Communication had improved and women felt the questionnaire was generally acceptable and easy to use ($P < 0.001$)⁵⁶. In contrast, some women had reported it was too long and restrictive with its multiple choice format⁶¹.

Jones et al (2008)⁵⁸ performed a large study on women within the secondary care setting. This study looked at the data quality of completing ePAQ and found that the majority of the respondents had urinary symptoms (70.3%). There was a good response rate (596/599 completed ePAQ). As women were only recruited from secondary care, we do not have any data to compare (secondary vs. primary) from this cohort of patients.

Overall these two studies proved that ePAQ was reliable and a good tool to detect change for women with pelvic floor disorders.

Qualitative / miscellaneous data

Omotosho and Rogers (2009) identify that patients may be reluctant to ask about sexual concerns while seeking health care. One study found that women who had completed ePAQ had answered most questions in three out of the four dimensions; the sexual dimension of the questionnaire had the highest 'declined to answer' (130/480 respondents)⁵⁹. This may indicate that the higher rates of completed data were due to the option of omitting specific sections i.e. the sexual dimensions.

Women of all ages may present with pelvic floor symptoms, how they are affected will be influenced by underlying factors. The 'bother' or impact of pelvic floor symptoms may vary between different age groups⁶¹. This is a useful consideration when counselling patients regarding the risk benefit ratio of various treatment options as this can change depending on the age and 'impact' of the condition.

Quality of the studies

The quality of the included studies was variable. The number of patients varied and most of the studies did not comment about the demographics of the non-responders. The quality assessment for the included studies is detailed in Table 4.

Table 4: Quality of studies included in the electronic Personal Assessment Questionnaire systematic review

(One star for fulfilling each quality item within the selection and outcome categories and a maximum of two stars can be given for comparability, N/A not applicable)

Author, date	Representativeness of the sample	Sample size	Non respondents	Ascertainment of risk factor	Comparable groups	Outcome assessment	Statistical test
Dua et al (2013) ⁵⁹	**	*	X	*	**	**	*
Dua et al (2013) ⁵⁹	*	*	*	*	X	*	*
Jones et al (2009) ⁵³	*	*	X	**	*	*	*
Jha et al (2009) ⁵¹	**	**	X	**	*	*	*
Dua et al (2011) ⁵⁴	*	**	X	**	*	*	*
Dua et al	*	*	*	**	*	*	*

(2012) ⁵⁰							
Jadav et al (2013) ⁵⁵	*	*	*	**	*	*	*
Jha et al (2012) ⁵⁸	*	*	*	*	X		*
Elenskaia et al (2012) ⁵²	*	**	X	*	X	*	*
Radley et al (2006) ⁵⁶	*	*	*	**	*	*	*
Jones et al 2008 ⁵⁸	*	**	*	N/A	X	*	*

Representativeness of the sample/ sample size

There were limitations of using the Newcastle Ottawa scale when assessing the representation of the cohort in respect to the community. It was difficult to ascertain whether the results of a particular study would be more at risk of bias if the study was performed on a smaller cohort of patients. There may be an increased risk of bias if the cohorts of patients. Follow up of patients may vary from centre to centre or dependent upon the patients' health. Therefore it may be difficult to compare similar groups of patients if their follow up appointment time and duration differed. Targeted patients may appear to be biased when performing a study and therefore the generalisability of results can be compromised.

Non-respondents were recorded and reasons listed for some of the studies.

Non respondents/ascertainment of risk factor

Although the studies had demonstrated a selected population group, 5 out of the 11 studies had no statement regarding non-respondents. This somewhat limited that particular part of the study assessment. In contrast, all studies had ascertained any risk factors by using secure patient data and a validated tool.

Comparable groups/ outcome assessment

In one study, there was no description of the sampling strategy (Jadhav et al, 2013). Jha et al (2012) ⁵⁸ demonstrated that a large proportion of women did not complete the sexual dimension of their ePAQ but comparability between respondents and non-respondent's characteristics was satisfactory.

The results from the ePAQ completed pre and post intervention were used as an outcome measure of success.

Discussion

The use of ePAQ in pre and post-operative assessment ^{46,48,50}, treatment of LUTS and its utility in evaluation of pelvic floor related QoL has been established. The initial validation that was carried out in primary and secondary care had established the basic psychometric properties of the ePAQ ⁴⁰. This systematic review ⁶⁷ highlighted the lack of evidence regarding the predictive ability of ePAQ for urodynamic diagnoses in women with LUTS.

A further study conducted within secondary care with a total of 599 women with pelvic floor disorders had looked into further tests of data quality. This study took into account the secondary factor analysis, internal consistency, descriptive statistics as well as the levels of missing data ^{51, 54}. Internal consistency and reproducibility have been identified as two important aspects of reliability ⁶².

Results from the first study had established that the ePAQ was suitable for measuring symptoms, 'bother' and quality of life in women who have pelvic floor disorders ⁴⁰.

Women who have recurrent pelvic floor disorders or present with a complex history (i.e. have underlying symptoms in all the ePAQ domains) require a valid measure of their health and impact on QoL. In this instance, the ePAQ can provide value and an insight into the 'bother' of each symptom, (to what extent it is an irritation or a nuisance). These data are potentially important to collect for clinicians who will be

required to produce patient related outcome measures data to justify continuing support for their services.

The ePAQ offers potential to improve efficiency and effective triage in health care ⁶³; (Quality, Innovation, Productivity and Prevention, 2013). A significant advantage of this electronic method is improved response rates⁴³, in addition to its eco-friendly (paper-saving) nature. The ePAQ was also associated with high satisfaction levels and lower levels of embarrassment than discussion with a health professional⁶⁴.

If consent is obtained from participants to use their data for research purposes, there is a potential to create a huge data resource.

If women are using the urogynaecology service for the first time, they may be more likely to accept the ePAQ as the norm for data collection in this service. The relative anonymity created by the use of the ePAQ may enable sensitive and potentially embarrassing questions to be answered with greater ease.

The fact that ePAQ can be completed remotely in patient's own home, with the results being made available to clinicians for review, may enable further reduction in new-to follow up ratios of outpatient visits by only inviting women with on-going problems for further clinic review, as well as triaging patients to nurse-led or consultant-led clinics. Patients whose ePAQ responses suggest symptoms are much improved (confirmed by telephone) would not need to attend an outpatient clinic.

Limitations of ePAQ

The ePAQ has its limitations as one could argue that the number of questions asked on the ePAQ is time consuming. The length of the questionnaire is important, it has been reported that a long questionnaire may prove burdensome to patients (Omatosho and Rogers, 2009). However, the initial evaluation of the ePAQ identified an average completion time of 20 minutes.

Although the omission of a particular domain will not provide the clinician with some information, the ePAQ can still be used as a focus point in the assessment of the other domains. This allows for any issues to be explored in greater detail and also allows a reduction in the time spent answering irrelevant questions. For example, women who present to the clinic with urinary symptoms may choose to omit the bowel domain of ePAQ. The clinician may still question the patient's bowel habits as this may be relevant to the treatment offered.

In some NHS trusts ePAQ is not yet used extensively for various reasons including the cost implications as there is a reasonable cost involved in purchasing an ePAQ license. Additionally, in order to ensure good value for money a number of considerations must be taken into account: Investment from the hospital in hardware (PCs/Tablets), availability of network points or wireless networks and time available for staff to guide patients who struggle to complete the questionnaire. There is also the option to produce an ePAQ voucher for patients to enable them to complete the questionnaire at home.

There are no alternatives for women who do not have access to a computer or are illiterate. Family members or friends may read the questions out for those who are

illiterate, but this presents the possibility that questions will not be answered openly due to the nature and sensitivity of issues.

The ePAQ is available only in English, so some women who do not understand English or lack computer skills may not be able to complete it. Reluctance to change is another area where the use of the ePAQ may be limited and pose a potential difficulty, for example, some individuals may prefer to use paper questionnaires. Demographic details such as ethnicity, parity and body mass index are not included in the questionnaire, which may be seen as a limitation. The majority of the studies in this review included Caucasian populations. There is a lack of research regarding ethnic minority populations and the consequences of urinary incontinence (psychological, physical and social). Evidence from previous literature has already illustrated the importance of ascertaining the needs for incontinence care among ethnic minority groups⁶⁵. Therefore, collecting some details like ethnicity, parity, beliefs could generate further evidence in these subgroups and help improve the management of UI amongst ethnic minority groups.

We acknowledge that this systematic review may have weaknesses and we were unable to synthesise data as the primary studies were different. There was also a paucity of data and therefore we were somewhat limited with how we could draw conclusions from any common themes. The majority of the studies (9/11) also came from one recruiting centre which can potentially affect generalisability.

Since the systematic review, we have conducted another study using the ePAQ to illustrate improvement in OAB and bowel scores in patients who have anticholinergic or Mirabegron therapy⁶⁶. We found that there was a statistically significant improvement in the symptom score for OAB (p value <0.0005) and all of the bowel

domains (p value <0.0005) in women who had anticholinergic therapy. We concluded that ePAQ score on anticholinergic therapy appears to suggest that there is improvement in symptoms of OAB as well the bowels. Further research with a large cohort and complete data collection would provide more robust results.

Conclusion

In conclusion, the evidence gathered from the studies demonstrates that ePAQ is a useful tool in the assessment of QoL in relation to pelvic floor symptoms. It also enhances the facilitation of communication for both patient and clinicians and although reported to be a burden to complete the questionnaire, most women found it acceptable. In future studies, ethnicity and response rate could be studied in order to take into account any changing ethnicity trends amongst the British population. It is plausible that different religious and ethnic groups might have different views on the questionnaires that might affect completion rates. Previous studies have already highlighted the lack of information on such groups, hence further multicentre studies on ethnicity and acceptability will enable to increase the generalisability of the findings. Further research is required to assess the added value of ePAQ (along with bladder diaries, urine dipstick) in evaluation of OAB and the cost-effectiveness of this questionnaire for all the clinical utilities described in this chapter.

CHAPTER 3: URODYNAMICS & QUALITY ASSURANCE

Background

The precision and accuracy of the UDS procedure is vital in order to achieve the correct diagnosis, giving informed consent and also planning of the patient treatment pathway.

Quality control (QC) is defined as an aggregate of activities (such as design analysis and inspection for defects) designed to ensure adequate quality⁶⁷. QC is deemed a crucial element of the Good Urodynamic Practice (GUP) guidelines, which were developed following poor QC observed during review of UDS traces from multi-centre trials by the International Continence Society (ICS) in 2002²⁸.

The three main elements comprising of good urodynamic practice²⁸ have been identified as:

- A clear indication for and appropriate selection of, relevant test measurements and procedures,
- Precise measurements with data quality control
- Complete documentation and an accurate analysis and critical reporting of results.

Sullivan et al (2012)⁶⁰ state that the pressure or flow problems that easily occur during the UDS test can be sought and corrected. Invasive treatments i.e. surgery is influenced based upon UDS findings, therefore, it is paramount that QC is not compromised and accuracy is maintained throughout the test.

It is of utmost importance that clinicians performing the UDS test are familiar with the equipment that is used during the procedure ⁶⁸. UDS is a skilled procedure, which requires training in setting up the UDS equipment, calibration of the machine, interpreting the pressure/flow recordings and counselling patients. One of the difficulties often encountered during UDS is the ability to identify artefacts and interpret the results ⁶⁹.

A key aspect of maintaining the accuracy of UDS is to ensure that the initial resting pressures are correct and also recognised ⁷⁰. Previous studies have shown that reliability parameters can be poor despite standardised test-retest situations ⁷¹. UDS can be further compromised by inconsistencies in clinical practices. Variations in the UDS procedure may vary from site to site and may be dependent upon the equipment and experience/training of the staff ⁷². Consistency and quality control is therefore paramount in UDS testing, particularly as the diagnoses/results may inform management decisions including invasive treatments such as surgery ²⁸.

As a previous research nurse working on the Bladder Ultrasound Study (BUS), a diagnostic accuracy study of transvaginal bladder wall ultrasound in Detrusor Overactivity, my role involved conducting the UDS test and discussing options in relation to the management of women who had OAB symptoms⁷³.

Standard Operating Procedures (SOP) are written instructions that document how to perform a specific activity. These are written to help ensure that the quality and consistency of the activity is maintained. In our trust we use the departmental SOP; the BUS study SOP for performing UDS was based on the same. This was provided

so that all of the trained clinicians within the urogynaecology department should have been able to perform this test in a consistent and standardised manner.

Amongst NHS trusts that perform UDS, variations will exist regarding the equipment, catheters and filling rate of the test. This also applies to large multi-centre trials where it is possible that variations will exist due to differences in equipment and the training of staff ⁷⁴. Nager et al (2007) ⁷² found that a significant number of staff had inadequate training in UDS and little clinical involvement in the care of patients undergoing this procedure. A survey carried out by Siriam et al (2002) ⁷⁵ revealed that clinicians were reluctant to standardise UDS practice. However, it has been identified that clinical trials using outcomes of UDS studies require additional standardised procedures to ensure that inter-site variability is limited ⁶³. We wanted to explore whether clinicians involved in recruitment to the BUS study were adequately performing this test using the recommended study SOP (Appendix 4).

We aimed to audit the quality of UDS traces submitted to the Birmingham Clinical Trials Unit (BCTU) at the University of Birmingham (UoB), collected as part of the BUS study.

We also wanted to assess whether or not recommended changes in UDS practice had been implemented following an initial audit among the recruiting centres for the BUS study.

Methods

The BUS study protocol required all patients to have UDS and ultrasound scans of their bladder walls performed by two independent observers. The UDS studies were undertaken between May 2011 and May 2012 on women who had consented and were eligible to take part, and included 302 participants from 12 different centres across the UK.

UDS traces were submitted to the BCTU at the UoB as part of the BUS study protocol. An assessment of compliance with good urodynamic practice was performed by checking the adherence to the GUP guidelines. The reliability of initial diagnosis at the time of UDS being undertaken was assessed in accordance to the BUS study SOP manual.

Confidentiality of these results was maintained by entering the data into a Microsoft Excel spreadsheet which was then stored on an encrypted memory stick.

An assessment of compliance with the UDS SOP for the BUS study and with GUP guidelines was performed on 64 (20%) of the first 302 UDS traces. The UDS traces were supplied by each of the recruiting centres and randomly selected by the BUS study trial co-ordinator. This was deemed to be adequate by the BUS study data monitoring committee. A consultant in urogynaecology and a urogynaecology research nurse from the lead centre (BWNFT), both of who perform UDS studies; assessed the traces independently. They were blinded to the centre and the urodynamicist and recorded the following: Position of filling cystometry, filling rate, the presence of a cough per minute to assess adequacy of subtraction, presence of cough both pre and post void, the concurrence with the diagnosis given and also

whether there was adequate zeroing of the pressure transducers prior to commencing UDS.

There are a number of potential diagnoses and these include detrusor overactivity, urodynamic stress incontinence, mixed urinary incontinence, voiding dysfunction, a stable bladder or low compliance.

The results of this audit and reminders about following the SOP were shared with the collaborators via the newsletters and by emails to individual centres. We also discussed this at the BUS Study training days held 3 months and 15 months into the study. Following these interventions, a re-audit was performed on 60 urodynamic traces between June-December 2012 to assess the adherence.

Results

The initial audit found that all 64 traces had been performed using standard laboratory UDS studies.

Compliance with good urodynamic practice

Table 5 summarises the quality control criteria used to assess adherence to the recommended standard operating procedures (SOP) for BUS study which was based on GUP.

Only 4 of the 64 traces had inadequate zeroing pressures before commencing the filling cystometry. The recommended position of sitting was documented in 52 traces,

10 were in supine and standing position, and one was in supine position.

For the remaining 1 woman, the filling pump had broken resulting in a gravity fill and the position of filling was not documented.

Filling cystometry rate

In 34 of the 64 traces, the recommended filling cystometry rate of 100ml per minute was followed; in three of the traces, the pump was slowed to 50ml per minute in the later part of the test. For 29 traces, cystometry filling was performed at a rate less than 10ml per minute. The pump was slowed down to try and obtain a clinical diagnosis if the woman had urgency without detrusor contractions or expressed a feeling of urge to void. The reasons for reducing the filling rate were documented in the UDS report. In one case, the woman's bladder was filled at a rate of 30ml per minute because of the presence of detrusor contractions throughout the test.

Cough pre and post void

Patients should cough immediately before and after voiding to allow pressure transmission to be assessed. Compliance with the cough test pre void occurred in 77% (n=49/64) of traces. Cough pre void was absent in 14% (n=9/64) of traces. In 6% (n=4/64) of traces it was difficult to interpret whether the cough signal command had been initiated. In 3% (n=2/64) of traces, it was evident that the pressure catheter had fallen out before voiding, therefore the cough test would not provide accurate results. Compliance with the cough test post void occurred in 36% (n=23/64) of traces. Cough post void was absent in 25% (n=16/64) of traces. In 22% (n=14/64) of traces the rectal pressure catheter had fallen out, as indicated by a sharp decrease in

pressure, and in 175 (n=11/64) of traces it was difficult to identify whether both catheters (vesical and rectal) had fallen out.

Each cough test had appropriate signals in the traces and any artefacts that were noted were rectified early on.

Presence of one cough per minute

The minimum recommendation for quality control for a cough signal, as defined by the ICS ²⁸, is one cough per minute or every 50ml filled volume. Coughs per minute were evident in 78% (n=50/64) of traces, and absent in 22% (n=14/64).

Reliability of initial diagnosis

There was reviewer agreement with initial diagnoses at the time of the test in 91% (n=58/64) of traces. A total of 6% (n=4/64) of traces were considered to be of poor quality, resulting in a disagreement between the recruiting centre and the reviewers and 3% (n=2/64) of traces were given a different diagnosis following assessment by the reviewers'.

The four traces of poor quality had originally been given a different diagnosis by the recruiting centre. However, the traces supplied were extremely difficult to interpret as the recording was of a poor quality. This resulted in a lack of interpretation and a diagnosis was unable to be reached. The recruiting centre was asked to send another copy of the UDS trace but the quality was the same as the previous one. In the two traces where the diagnosis had been changed, an initial diagnosis was disputed by the two auditors. There was evidence from the traces that calibration of the pressure transducers was not satisfactory at the start of the UDS procedure.

Artefacts had then been identified which had been mistakenly used to confirm a diagnosis. The discrepancies were then fed back to the recruiting centre and advice given regarding further investigations.

Changes between the two audits

A second audit of a further 60 UDS traces was conducted between June 2012-December 2012 using the same criteria as the first audit following feedback to practitioners. Statistical comparisons between the two audits were performed using the Fisher Exact Test to generate P Values. **Table 5** summarises the quality control criteria used to assess the adherence to good urodynamic practice. The comparison between the audit and re-audit compliance is also illustrated in this table.

Table 5: Comparison between initial quality control criteria and adherence to Urodynamics-audit and re-audit of UDS traces

Recommended actions in standard operating procedures	Audit May 2011-May 2012 n= 64 (%)	Re-audit June 2012-December 2012 n= 60 (%)	P-Values
Adequate baseline pressures	60 (93.7)	57 (95)	1
Filling in sitting position	52 (81.2)	38 (63.3)	0.029
Recommended Cystometry filling rate 100mL/minute	34 (53.1)	43 (71.6)	0.042
Cough pre-void	49 (76.5)	60 (100)	<0.001
Cough post-void	23 (35.9)	45 (75)	<0.001
Cough per minute	50 (78.1)	58 (96.6)	0.002
Agreement between diagnoses	58 (90.6)	57 (95)	0.493

There was no significant comparison in the adequacy of baseline zeroing pressures, this was evident when checking the traces ($p=1$). However, any artefacts that had been identified at the start of the test and a reason for this had been documented. The GUP guidelines ²⁷ state that the initial recorded subtraction pressures should be 0-6cm/H₂O in 80% of cases. It is possible that some clinical examiners do not 'zero' to the surrounding atmospheric pressure preceding the cystometry, but 'zero' to the intra-corporeal vesical and abdominal pressure at the start of the investigation. This 'zero' is therefore the pressure that is registered in each of the pressure lines before the start of the filling phase of the study.

There was a significant reduction in the adherence of the recommended filling position ($p=0.029$). There was a reported significant increase in the number of patients who had their filling cystometry at the recommended filling rate of 100mls/min ($p=0.042$) and in the cough signals throughout the UDS procedure ($p<0.001$ and $p=0.002$). These significant improvements demonstrate a positive change in UDS practice as a direct result of reinforcing the importance of adhering to guidelines of clinical practice and procedures.

The initial urodynamic diagnoses given by the recruiting centres had been re-confirmed by the two assessors. However, there were no statistical comparisons to be made between the audit and re-audit ($p=.493$).

An overall increase in compliance and adherence may have ultimately influenced the quality of the traces supplied.

Discussion

The results of this audit show that urodynamic training and reiteration of guidelines and the SOP had a positive impact on most points related to performing UDS.

Training and education provided through the use of emails, newsletters and study days significantly raised the compliance with most of the criteria assessed using the GUP guidelines except for the filling position.

High quality recordings allow for a detailed interpretation to be made and a management plan to be implemented. Artefacts on any UDS trace can cause a discrepancy if not rectified. This can have significant implications on the management of the patient following the UDS procedure. The strengths of this audit are that there was anonymisation of the centre and urodynamicist, clear standards and the audit loop was completed. A selection of UDS traces was readily available and the findings from both audits were shared amongst the recruiting centres.

It is plausible that there are a number of factors that could have caused the filling position to decline following re-audit and this is potentially due to protocol violations related to performing UDS per their usual practice.

Hayek et al (2008) found that the patient's position is a significant variable during UDS and concluded that between 33% and 100% of patients in the supine position would have a failed diagnosis of DO.

There are potential limitations from this audit; we had only used a random selection of traces as opposed to auditing the entire BUS Study UDS traces. However, there is a possibility that if another QC audit on UDS traces had been conducted on other

National Health Service (NHS) trusts not involved in the BUS study, similar results may have been found.

A re-audit could be improved by conducting phone interviews, teleconferences and questionnaires via an email where the UDS clinicians discussed their clinical practice and rationale.

Recommendations for UDS in clinical practice

In order to ensure that high quality standards are achieved and maintained, it is essential to do regular evaluation of UDS practice and audits within departments. Standardisation in UDS is paramount if results are to be reliable; implications can result in major discrepancies between the UDS diagnoses, the patient pathway following the procedure and future care surgical or conservative treatment options. There may be barriers to achieving this due to infrastructure, varying equipment, staff attitudes and the experience in performing UDS. Therefore, improvement in compliance with GUP guidelines could be incorporated by all centres using a standardised checklist for performance that the clinicians could use to complete and record the UDS results.

Recommendations for use in UDS in research studies

Assessments, multi-disciplinary team meetings and formal training can limit the variations between urodynamic centres. In large multi-centre trials, it is possible that there will be variations in the urodynamic procedures which include the equipment and training of staff and hence clinical trials using UDS as outcomes require additional standardised procedures⁶³. Indeed this is also true for any study when

evaluating the intervention or when using it as a primary outcome. Multi-centre urodynamic studies require a continuous QC process. Currently, urodynamic training in the United Kingdom is varied and ranges from a certificate course to individual study days. All centres need to share the same course content in order to achieve standardisation.

CHAPTER 4: PREDICTIVE VALUE OF THE ePAQ IN DETRUSOR OVERACTIVITY AND URODYNAMIC STRESS INCONTINENCE

Background

The systematic review detailed in Chapter 2 ⁷⁶ identified studies which demonstrated that the ePAQ was easy to use and generally acceptable ⁵⁴. The completion of an ePAQ may potentially enhance the clinical consultation in regards to the types of questions asked by the clinician or the patient themselves. There is a need to find if there is any value added by ePAQ scores to the existing clinical assessment (examination, urine dipstick, cough stress test) in reducing the need for invasive tests like UDS.

Patients are experts in the experience of their symptoms and their impact on QoL. There is evidence in the literature that patients who have higher scores on disease specific QoL questionnaires have overall lower QoL ⁷⁷. In our systematic review ⁶⁷ we did not find any studies on the diagnostic or predictive value of ePAQ in various urodynamic diagnoses. The priority is to establish benefit for patient health by trying to reduce the need for diagnostic evaluations where appropriate and by using a non-invasive approach. There is a potential to reduce the cost of clinical activity/consultation time by using the ePAQ and focusing more on the specific areas of concern.

The objective of this study was to see if we could reduce the need for urodynamics by analysing whether the OAB or SUI scores of the urinary domain of the ePAQ –PF correlate well with UDS diagnoses. We hypothesised that women who have higher scores on ePAQ-PF for OAB or SUI will have a higher likelihood of DO or USI respectively.

Methods

This was a prospective cohort study that ran alongside the BUS study⁶⁴ where consecutive women who had been referred to the urodynamics clinic with a variety of LUTS were included if they fulfilled the following inclusion criteria:

- Presence of overactive bladder +/- stress urinary incontinence symptoms
- Age 18 years or over
- Comprehend and read English
- Completed both the tests of UDS and ePAQ

The exclusion criteria were:

- UDS performed in the last 6 months
- Did not speak, read or understand English
- Urine dipstick positive to leucocytes or nitrites
- Were on anticholinergics/antimuscarinics at the time of UDS
- They did not consent to use of their ePAQ data
- Previous Continence or POP surgery, within the last 6 months

Although this study was performed alongside the Bus study, not all patients from one study belonged to the other (ePAQ) study.

Performance of index test

The patients were encouraged to complete the ePAQ questionnaire as part of their routine clinical assessment in our centre. The details of this questionnaire are given in chapter 2. A designated 'ePAQ' room with three workstations and touch screen computers are dedicated for the completion of this questionnaire. ePAQ vouchers can also be generated in our clinics for our patients to complete at home. This is particularly useful if time constraints result in patients being unable to complete it whilst in clinic. Provided the woman had completed the urinary dimension, most importantly the OAB and SUI dimensions, the ePAQ results were printed off; the scores for OAB, SUI and voiding recorded onto the database. The scores from the OAB and SUI dimensions were then used to predict whether the patient will have DO or USI. For example, if a patient scored 60 for the OAB dimension and 40 for the SUI dimension we would predict that she would be diagnosed with DO, as OAB is the significant score.

Performance of reference standard

Reference standard is a test that confirms or refutes the presence or absence of a disease beyond reasonable doubt ⁴⁹. UDS was the 'gold' or reference standard in this study. UDS was carried out by healthcare professionals (nurses or doctors) in accordance to the GUP guidelines ²⁸. Women attended the clinic with a full bladder. Uroflowmetry was performed with the woman voiding in privacy on a flowmeter. Filling cystometry was performed with the woman in sitting position at 100mls/minute rate, followed by provocation measures and then voiding cystometry. All qualified

clinicians in our UDS clinic have attended a certified course in UDS and have at least 3 years' experience in conducting this procedure.

The clinician who performed the UDS would record the findings and diagnosis on the UDS report and inside the patient's notes. Where results were equivocal or inconclusive, ambulatory UDS was offered. The clinician performing this was blinded to the results of the ePAQ. Where ambulatory UDS was to be performed, it was intended that these results would be used as the final diagnosis on the database. Quality assurance checks were also performed on the index test of UDS ⁶⁹.

Design

The study was designed to meet the requirements of the QUADAS-2 tool (Quality Assessment of Diagnostic Accuracy Studies) ⁷⁸ (Appendix 5) and STARD (Standards for reporting of Diagnostic Accuracy) (Appendix 6).

Selection bias was regarded as 'low'/ reduced risk by recruiting all consecutive, eligible women into the study. Methodological bias was minimised by ensuring that the index tests and reference standard were performed independently (blinded to each other). Being blinded to the other results ensured that there was no previous knowledge on the diagnosis of the reference standard. Standard protocols for index and reference standard testing were drawn up and quality assurance checks were made on a sample of traces and a pre-specified statistical plan was followed. There is the potential risk of bias during the completion of ePAQ if the UDS was performed first (if distress was caused by undergoing the UDS procedure). The BUS study

found that acceptability of less invasive procedure (ultrasound) vs. UDS was more favourable ⁶⁴. Thus in this study all participants complete the ePAQ prior to UDS.

Ethics and Regulatory approvals

The necessary approvals required to undertake any study were sought prior to the commencement of the study. The University of Birmingham (UoB) and the Research and Development (R&D) department at the BWNFT advised that formal ethical approval was not required (Appendix 7). This decision was made as both the reference standard and index test are used and the data collected as part of routine clinical practice within our department. In addition, there is an individual disclaimer at the end of the ePAQ seeking permission to use the data for research purposes and evaluation. This study was therefore considered a service evaluation project.

Data collection

Results of the index test and reference standard were collected on the same day, these (ePAQ scores and UDS diagnosis) were entered onto a Microsoft excel spreadsheet (an encrypted trust safe stick was used for storage of this data). Patient identifiable details such as the woman's name and address were omitted for patient confidentiality. An Access database was developed to enable data extraction from the excel spreadsheet for the ease of statistical analysis. Any inconclusive results whereby the OAB or SUI scores on ePAQ were screened as "negative" or data was missing were excluded from analysis to avoid any misclassification.

Sample size and statistical analysis

ePAQ may be useful if it has high sensitivity to detect conditions such as DO and hence negate the need for UDS. A proportion of the tests will return false positive results so the study was powered to have enough participants so that the lower limits of confidence intervals for both sensitivity and specificity exceed particular values.

The BUS study ⁶⁴ demonstrated that the prevalence of DO is around 60%.

Thus a sample size of 400 will provide 240 sets of data to estimate the sensitivity and 160 to estimate the specificity. This would allow estimation of sensitivities with 95% confidence intervals of width 10% for sensitivity values around 70-80% and 14% for specificity values around 70-80%. This level of precision will be adequate to assess the usefulness of the test. In addition, a sample size of 390 would provide 234 (60%) sets of data to estimate the sensitivity and 157 to estimate the specificity. An observed sensitivity of 80% would have a 95% confidence interval with a width of 10.65%. We thus aimed to recruit a sample size of 400.

Possible factors that may influence ePAQ scores and QoL were assessed for their effect on ePAQ score and displayed as Box and Whisker plots include age, previous continence surgery, previous use of medication for bladder symptoms, menopausal status and parity ^{79, 80}. For all patients the results of the ePAQ and UDS were summarised as 2x2 contingency tables with the OAB and SUI scores on ePAQ as a predictor of DO and USI, following the UDS diagnosis. These describe the relationship between the results of the index test and the reference standard at a given diagnostic threshold (point at which results are classified as positive or negative). The table includes the number of true positives (TP: those that have the

disease and test positive), false positives (FP: those that do not have the disease and test positive), false negatives (FN: those that do have the disease and test negative) and true negatives (TN: those that do not have the disease and test negative).

Test performance was then summarised with 95% confidence intervals where appropriate as:

1. Sensitivity [Sensitivity= proportion of true positives that are correctly classified as such-1=false negative rate],
2. Specificity [Specificity= proportion of true negatives correctly identified as such-1=false positive rate];
3. Predictive values: Positive predictive value (PPV) and negative predictive values (NPV) [PPV and NPV]. PPV is related to the probability that the subject has a positive test result and truly have the disease. NPV is the probability that the subject has a negative test result under the gold standard.
4. Likelihood ratios (LR) describe how many times more likely it is that a person with the target condition will receive a particular test result than a person without. Positive likelihood ratios greater than 10 or negative likelihood ratios less than 0.1 are sometimes judged to provide convincing diagnostic evidence ⁸¹.
5. The summary test performance (diagnostic odds ratio) was assessed by drawing receiver operating characteristic (ROC) curve which plot the sensitivity versus 1-specificity at the different thresholds, and summarised as the area under the curve (AUC).

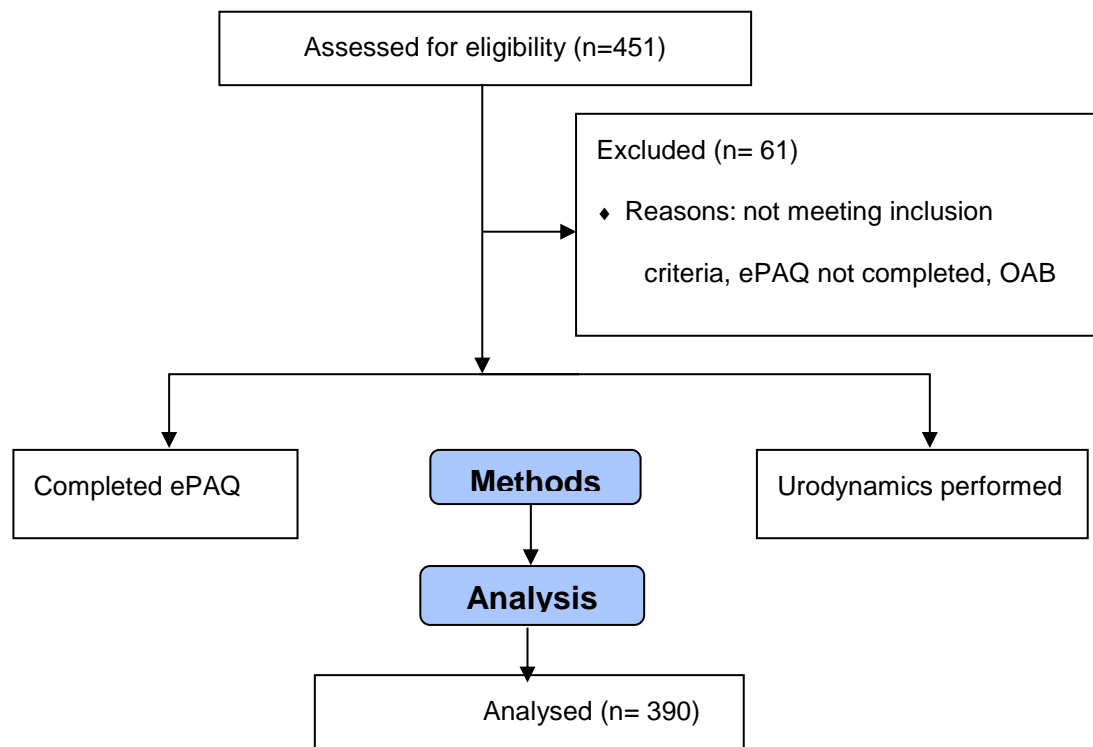
According to Zweig & Campbell (1993), ROC plots provide a pure index of accuracy, and are considered the gold standard in the statistical evaluation of a diagnostic test. The closer the curve is to the upper left hand corner the better the diagnostic performance⁸². The AUC ranges from 0 to 1, with 0.5 indicating a poor test where the accuracy is equivalent to chance. The AUC results were considered excellent for AUC values between 0.9-1, good for AUC values between 0.8-0.9, fair for AUC values between 0.7-0.8, poor for AUC values between 0.6-0.7 and failed for AUC values between 0.5-0.6^{83, 84}. Statistical analysis was performed using SPSS version 22. Numbers and percentages were used for specific categories such as occurrence or episodes. Accuracy was expressed in relation to sensitivity and specificity and the data were described as mean and standard deviation for the numeric parametric variables collected as part of the results. A significant level was set as 0.05. Mann-Whitney and Fisher Exact tests were used to calculate the P-Values generated for the analyses of the ePAQ study.

Results

Participants

During the 18-month study period of May 2013-November 2014, there were 451 women who were eligible to take part. Exclusion of data with inconclusive index test results (n=61), gave a sample of 390 women who had a complete index test (ePAQ) and reference standard result (UDS). Figure 4 demonstrates the participant flow.

Figure 4: Participant study flow diagram



Characteristics of the population

The study population consisted of a variety of women who presented with LUTS, deriving from different ethnic backgrounds and age groups (Table 6).

The mean age of these women was 53.4 years, with a standard deviation (SD) of 14.6 and ranging between 21-92 years. The majority (n=294; 75%) of the women were White Caucasian and had two children (n=157; 40.3%). There were 30 (7.6%) women in the study population who were nulliparous and 330 (92.4) women were multiparous (Table 6).

Table 6: Characteristics of included participants (n=390)

Age (Years)	Mean (SD)	53.4 (14.6)
	Missing	0 (-)
Ethnicity	White	294 (75.38%)
	Asian	67 (17.17%)
	African or Afro-Caribbean	17 (4.35%)
	Mixed/other	7 (1.79%)
	Unknown/Missing	5 (1.28%)
Parity	0	30 (7.7%)
	1	43 (11.0%)
	2	157 (40.3%)
	3	85 (21.8%)
	4	33 (8.5%)
	5	21 (5.4%)
	6	9 (2.3%)
	7	4 (1.0%)
	8	4 (1.4%)
	9	3 (0.8%)
	11	1 (0.3%)
Post-menopausal (LMP>1year)	Yes	220 (56.4%)
	No	170 (43.5%)
Previous treatment with anti- muscarinics	Yes	198 (50.7%)
	No	184 (47.17%)
	Cannot remember	8 (2.05%)
Previous incontinence or prolapse surgery	Yes	11 (2.82%)
	No	379 (97.18%)

Women included in this study presented with symptoms of OAB, mixed urinary incontinence (MUI), stress urinary incontinence (SUI) and one reported a lack of bladder sensation post childbirth delivery (**Table 7**).

Table 7: Relationship of presenting symptoms (Indications for Urodynamics)

Presenting problems	Frequency/number (%)	Preceded by (UUI/SUI)/number (%)
Mixed urinary incontinence	228 (58.4%)	UUI= 193 (49.4%) SUI= 35 (8.9%)
Overactive bladder unresponsive to conservative management	161 (41.2%)	N/A
Pure stress urinary incontinence	0 (0%)	N/A
Lack of bladder sensation (post-delivery)	1 (0.25%)	N/A

Urodynamic findings

Of the 390 women, 262 (67.2%) of them were diagnosed with DO, of these 6 women had ambulatory UDS and had a final diagnosis of DO.

USI was confirmed in 21.5% of the women (n=84/390). Various other diagnoses included stable/normal bladder, low compliance and MUI (**Table 8**).

Table 8: Urodynamic diagnoses

Diagnosis	Frequency (n)	Percent (%)
DO	262	67.1
USI	84	21.6*
MUI (DO & USI)	32	8.21
Normal/stable bladder	4	1.03
Voiding dysfunction	4	1.03
Low compliance	4	1.03

The various symptoms varied (**Table 9**) and in the group who presented with MUI, we categorised it by their predominant symptom (Stress or Urge).

75/390 women had stress predominant MUI, of these 45 were diagnosed with USI and 23 had DO. 7/390 had MUI.

147/390 women complained of urge predominant MUI, of these 106 were diagnosed with DO and 27 had USI. 11/390 had m MUI.

166/390 women presented with OAB symptoms, 132 were diagnosed with DO, 11 had USI and 14 had a diagnosis of MUI.

Table 9: Presenting symptoms against final urodynamic diagnosis

Presenting Symptom (n)	Urodynamics Diagnosis	Number
SUI (n=0)	-	0
MUI- Stress predominant	Detrusor Overactivity	23
	Urodynamic Stress Incontinence	45
	Normal/Stable bladder	0
	Mixed Urinary Incontinence	7
	Low Compliance	0
	Voiding Dysfunction	0
MUI- Urge predominant	Detrusor Overactivity	106
	Urodynamic Stress Incontinence	27
	Normal/Stable bladder	1
	Mixed Urinary Incontinence	11
	Low Compliance	1
	Voiding Dysfunction	1
MUI- Equally bothersome (n=1)	Urodynamic Stress Incontinence	1
Overactive Bladder	Detrusor Overactivity	132
	Urodynamic Stress Incontinence	11
	Normal/Stable bladder	3
	Mixed Urinary Incontinence	14
	Low Compliance	3
	Voiding Dysfunction	3
Lack of sensation (n=1)	Detrusor Overactivity	1
		Total (n)=390

Analysis of OAB scores on ePAQ according to patient characteristics

The Mann Whitney test was used to generate p-values for the analysis of the ePAQ scores.

The OAB score was found to be significantly higher in those over the age of 65 years ($p=0.009$) (Figure 5). The median OAB scores for those under the age of 65 were 33 and 42 in those who were over 65.

In those with a parity greater than 2, the OAB score was significantly higher ($p<0.001$). The median values in those with less than two children were 33 and 42 in those who have more than two children (Figure 6).

There was a significantly higher OAB score in those who had previously used anticholinergics ($p<0.001$) (Figure 7).

The OAB scores were not significantly different in menopausal women ($p=0.16$) (Figure 8) or those who had previous continence surgery ($p=0.083$) (Figure 9).

We arbitrarily dichotomised to this age group (age 65) as we wanted to see if there was any difference in women once they retire (in regards to lifestyle choices). We wanted to see whether the ePAQ scores would differ in a woman over 65, who may (or may not) lead a less active life (Figure 5).

Figure 5: Box and Whisker plot comparing overactive bladder score and women aged <65 and >65 years

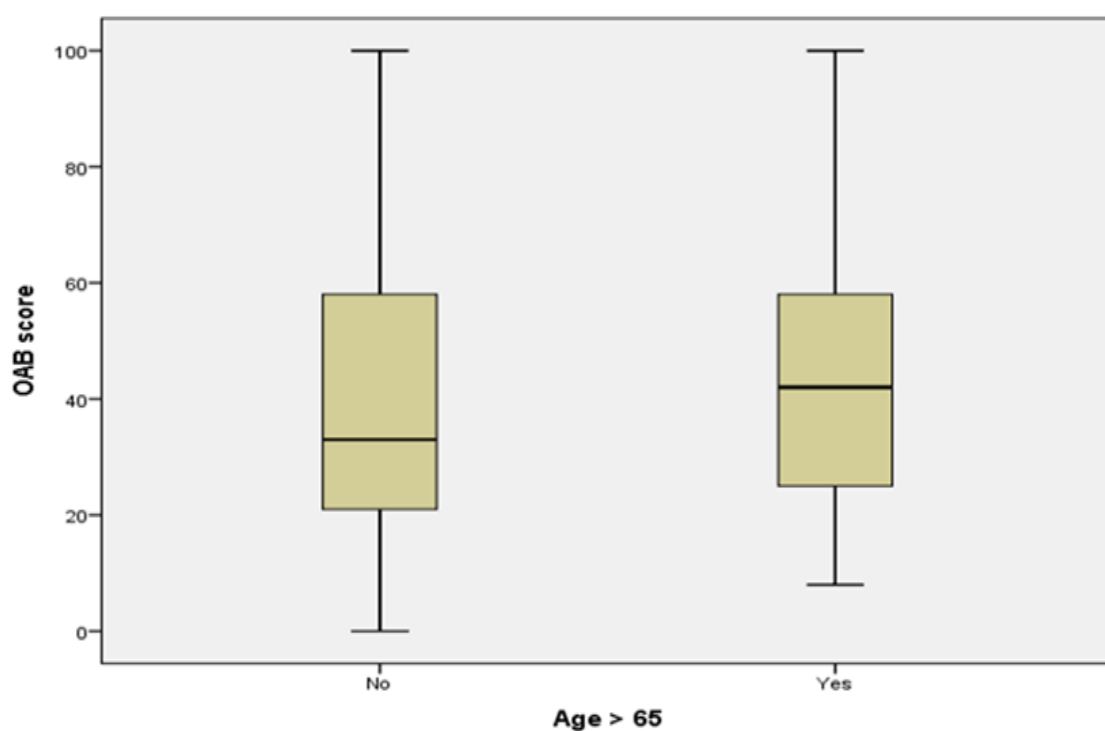
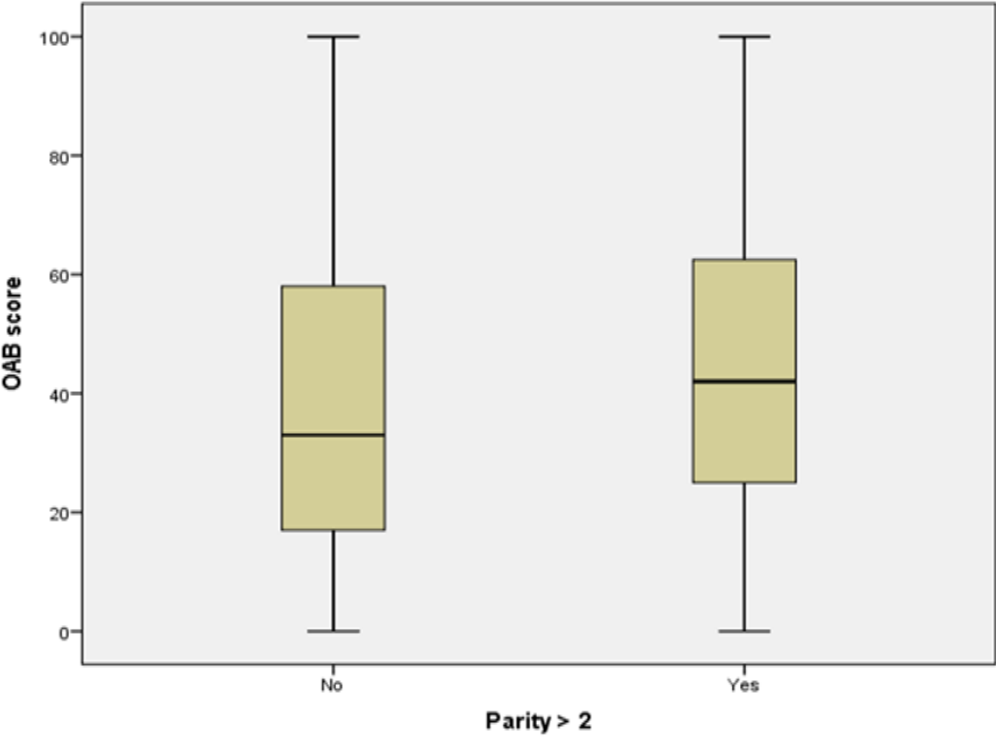
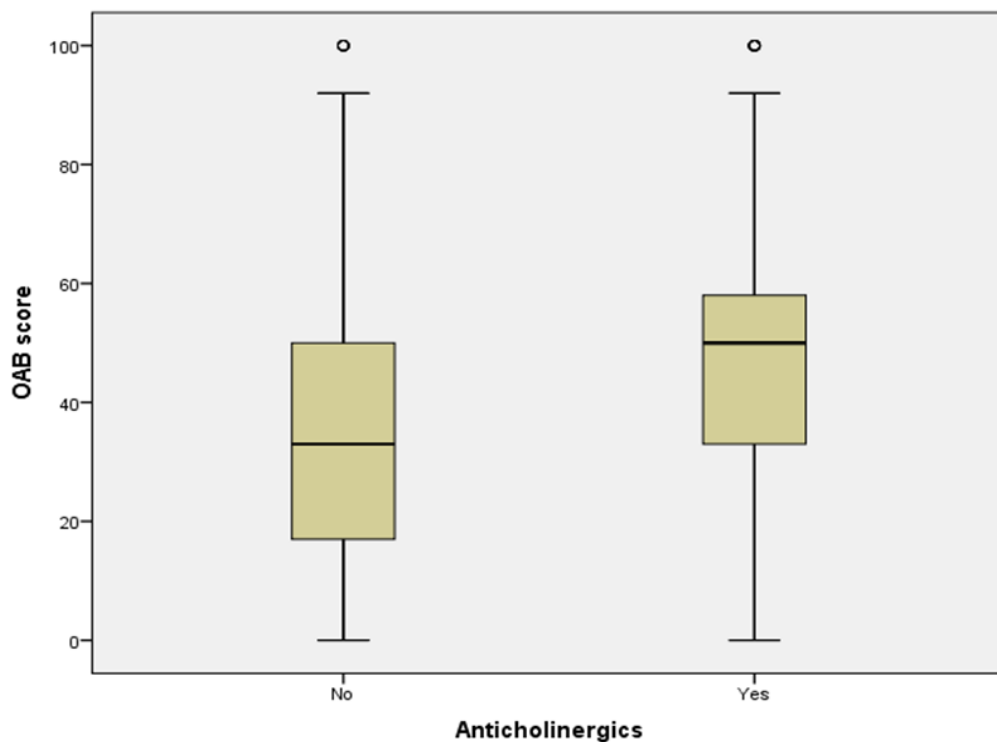


Figure 6: Box and whisker plot comparing overactive bladder score with women who had two or more children



Of the 390 women in the study, 198 women had tried at least one medication for OAB in the past, 184 hadn't previously taken any and 8 of the women could not remember whether they had taken any at all. The median values in those who had tried medication were 50 and in those who had not tried any medication for their bladder symptoms, it was 30 (Figure 7).

Figure 7: Box and whisker plot comparing overactive bladder scores in women who had previously tried/not used anticholinergics



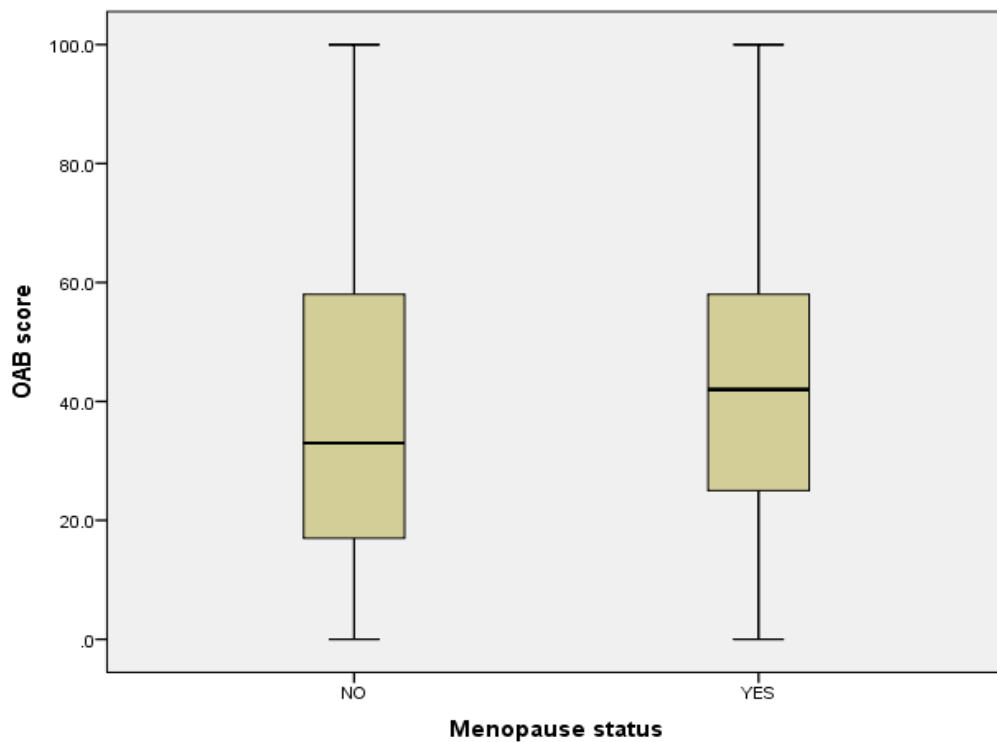
Menopausal state

Menopause was defined as the last menstrual period occurring 1 or more years ago.

There were 389 women with known menopausal state of which n=217 were menopausal (55.8%).

There was a non-significant difference in the reported OAB scores in menopausal women ($p=0.16$) (Figure 8). The median values in those who were menopausal were 40 and 33 in those who were pre-menopausal.

Figure 8: Box and whisker plot comparing overactive bladder score OAB score and menopausal state



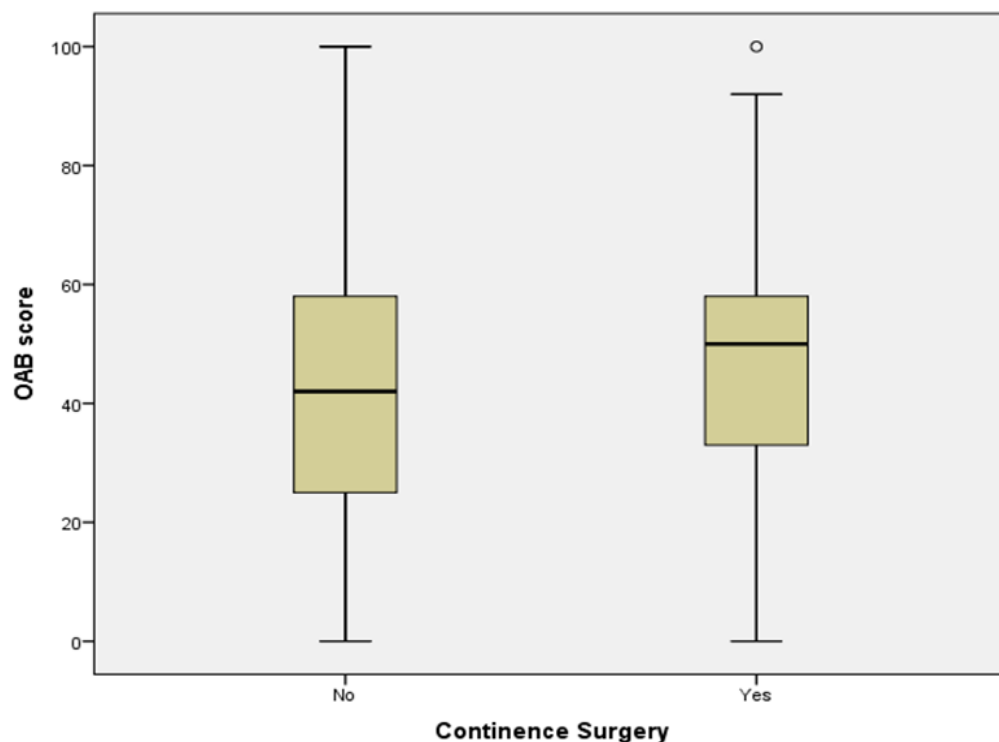
Continence surgery

Of the 390 women, 379 (97.18%) had never had surgery, whilst 11 (2.82%) had reported previous continence surgery. There was a significant difference in those who had previously undergone continence surgery as opposed to those who hadn't.

The median values in those who had never had any continence surgery was 42.0 and 50.0 in those who had previous continence surgery ($p = 0.083$) (Figure 9).

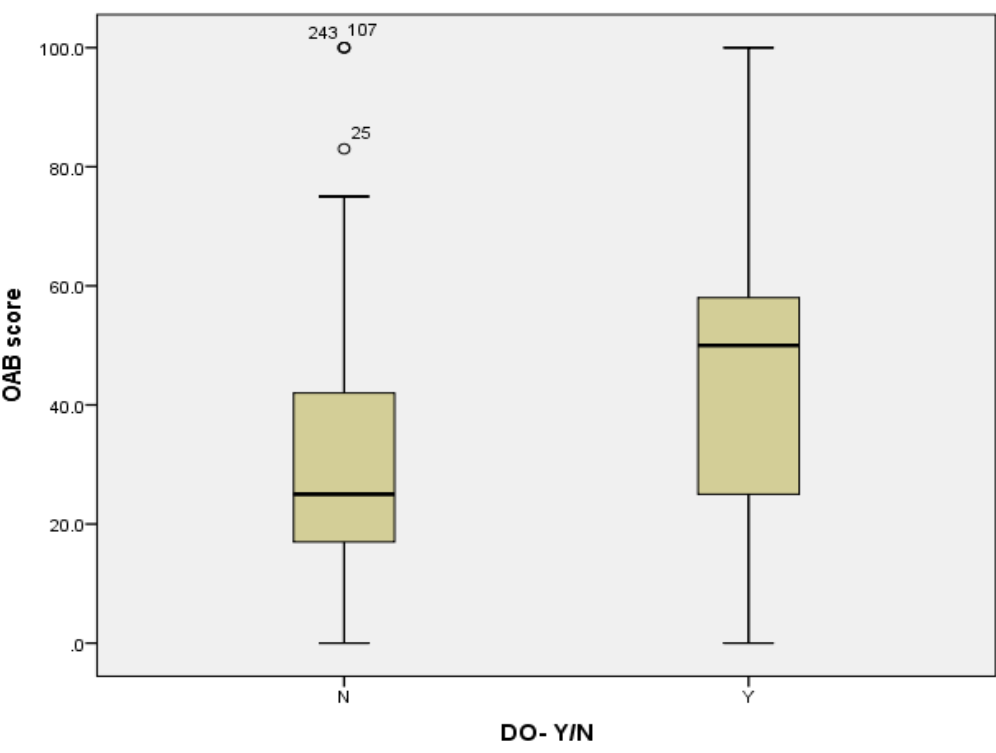
Sensitivity analysis on both the OAB and SUI score were not significantly different in those who had continence surgery.

Figure 9: Box and whisker plot comparing overactive bladder score and previous continence surgery/no surgery



There was a median OAB score of 50 in those who had a clinical observation of DO during the UDS investigation. The median score for those who were not diagnosed with DO was 20 (Figure 10).

Figure 10: Box and whisker plot comparing the electronic Personal Assessment Questionnaire overactive bladder score with the urodynamic observation of detrusor overactivity



Overactive bladder scores on ePAQ as a predictor of detrusor overactivity

To assess the predictive ability of the OAB score from ePAQ for urodynamic diagnosis varying cut-offs for the OAB score were assessed (**Table 10**).

A cut off point of 25 or above had a sensitivity of 85.1%, specificity of 38.3% and a correctly classified diagnosis in 69.7% of cases. The positive likelihood ratio (LR) was 1.3879.

Women, who scored 50 for OAB, had a sensitivity of 51.1 %, a specificity of 79.7% and were correctly diagnosed in 60.5 % of the cases. The positive LR in this score was 2.518.

Women, who were greatly affected by OAB and had scored 75 or above, had a sensitivity of 16.4%, a specificity of 95.3% and were correctly diagnosed in 42.3% of the cases. The positive LR in this group was 3.501.

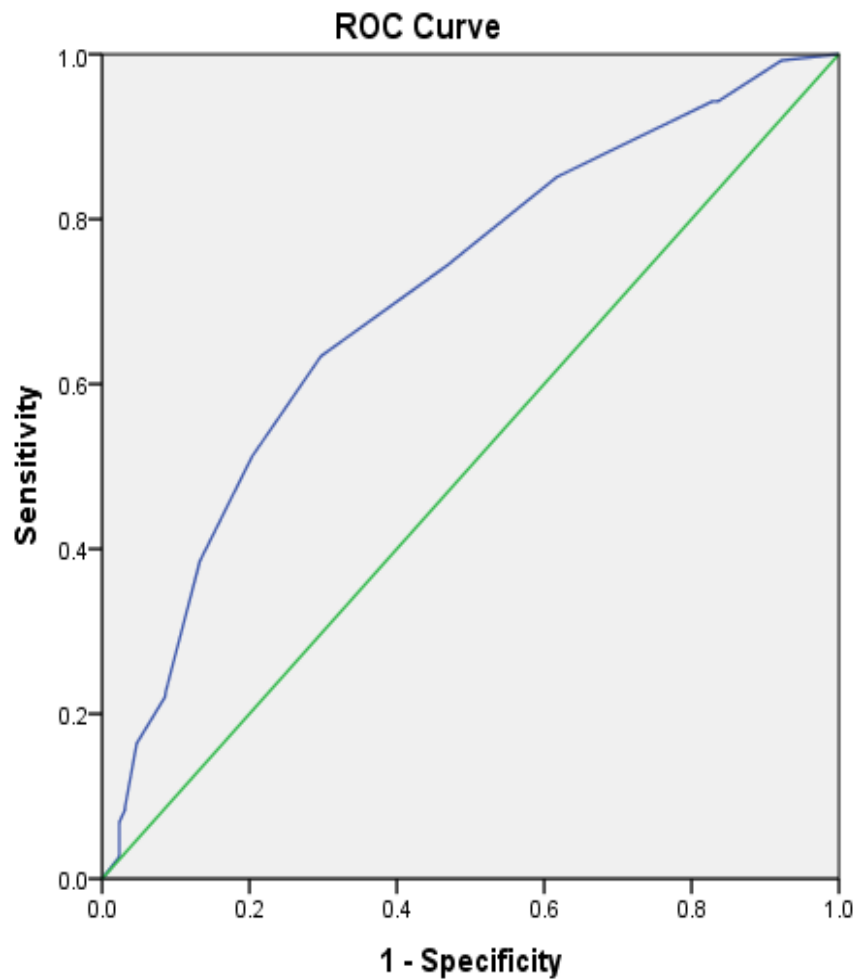
Thus as the OAB score on ePAQ increased so did the likelihood of DO on UDS up to a score of 75. Scores higher than this did not increase the likelihood of the diagnosis.

Table 10: Accuracy of the overactive bladder score on electronic Personal Assessment Questionnaire in predicting detrusor overactivity

Cutpoint of ePAQ score for OAB domain	Sensitivity	Specificity	Correctly classified	LR+	LR-	PPV	NPV
0	100.00%	0.0%	67.2%	1.0000	-	67.2	0.0
≥ 8	99.2%	7.8%	69.2%	1.076	0.098	68.8	3.8
≥ 14	94.3%	16.4%	68.7%	1.128	0.349	69.8	7.8
≥ 17	94.3%	17.2%	69.0%	1.138	0.333	70.0	8.2
≥ 25	85.1%	38.3%	69.7%	1.379	0.389	73.8	17.1
≥ 33	74.4%	53.1%	67.4%	1.588	0.481	76.5	22.9
≥ 42	63.4%	70.3%	65.6%	2.134	0.521	81.4	29.0
≥ 50	51.1%	79.7%	60.5%	2.518	0.613	83.8	32.5
≥ 58	38.5%	86.7%	54.4%	2.903	0.709	85.6	35.2
≥ 60	22.5%	91.4%	45.1%	2.620	0.848	84.3	36.7
≥ 67	22.1%	91.4%	44.9%	2.576	0.852	84.1	37.5
≥ 75	16.4%	95.3%	42.3%	3.501	0.877	87.8	39.5
≥ 80	8.8%	96.9%	37.7%	2.809	0.942	85.2	40.5
≥ 83	8.4%	96.9%	37.4%	2.687	0.946	84.6	40.9
≥ 92	6.9%	97.7%	36.7%	2.931	0.54	85.7	42.4
100	2.7%	97.7%	33.8%	1.140	0.997	70.0	43.6

The AUC for DO (including Ambulatory UDS) was 0.709 (95% confidence interval; 0.655-0.764) (Figure 11).

Figure 11: Receiver Operating Characteristic curve of overactive bladder electronic Personal Assessment Questionnaire score and detrusor overactivity on urodynamics

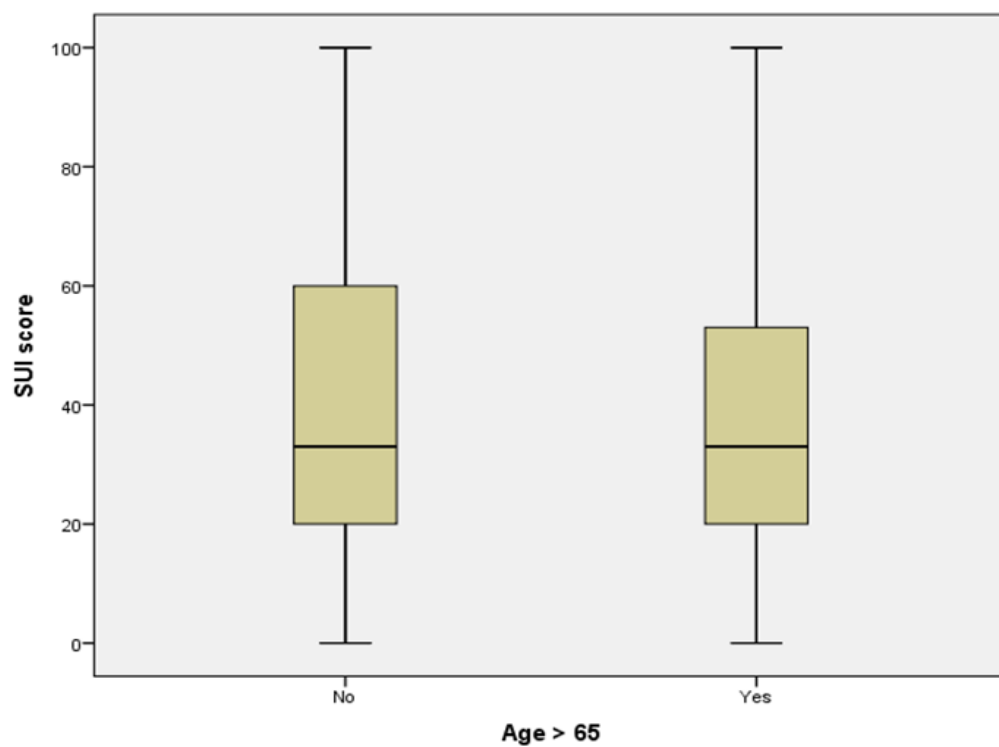


Diagonal segments are produced by ties.

Stress urinary incontinence scores on electronic Personal Assessment Questionnaire according to patient characteristics

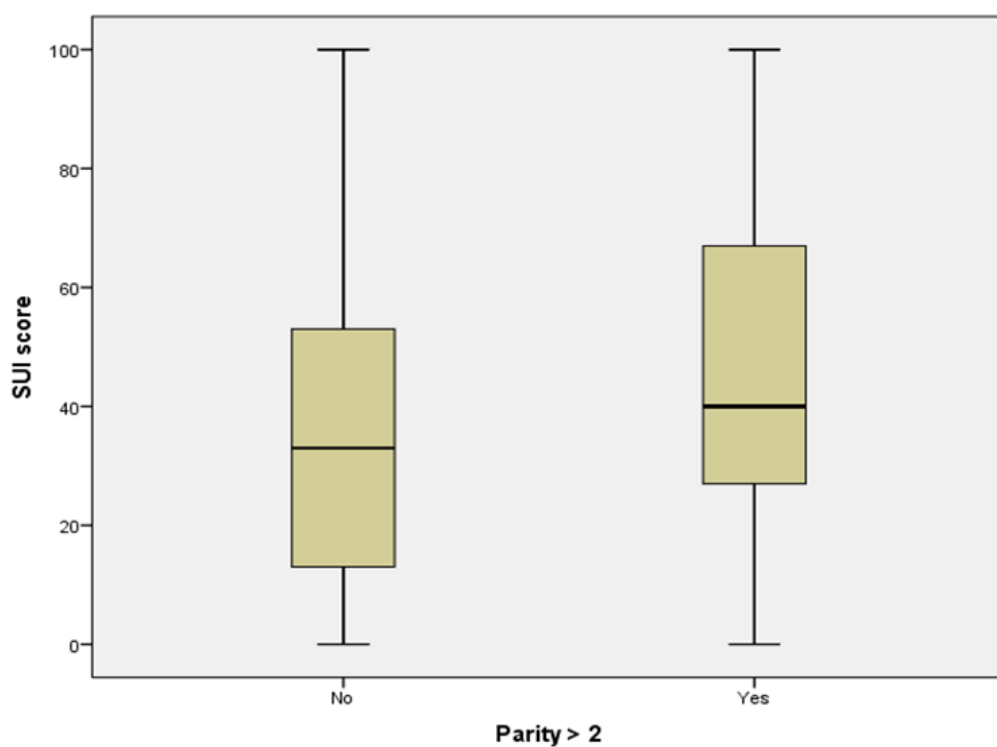
There was no statistical difference between the two age groups who had symptoms of SUI ($p=0.16$). The SUI scores on ePAQ had median values of 33.0 in the two stratified age groups (Figure 12).

Figure 12: Box and whisker plot comparing stress urinary incontinence score with age <65 and >65



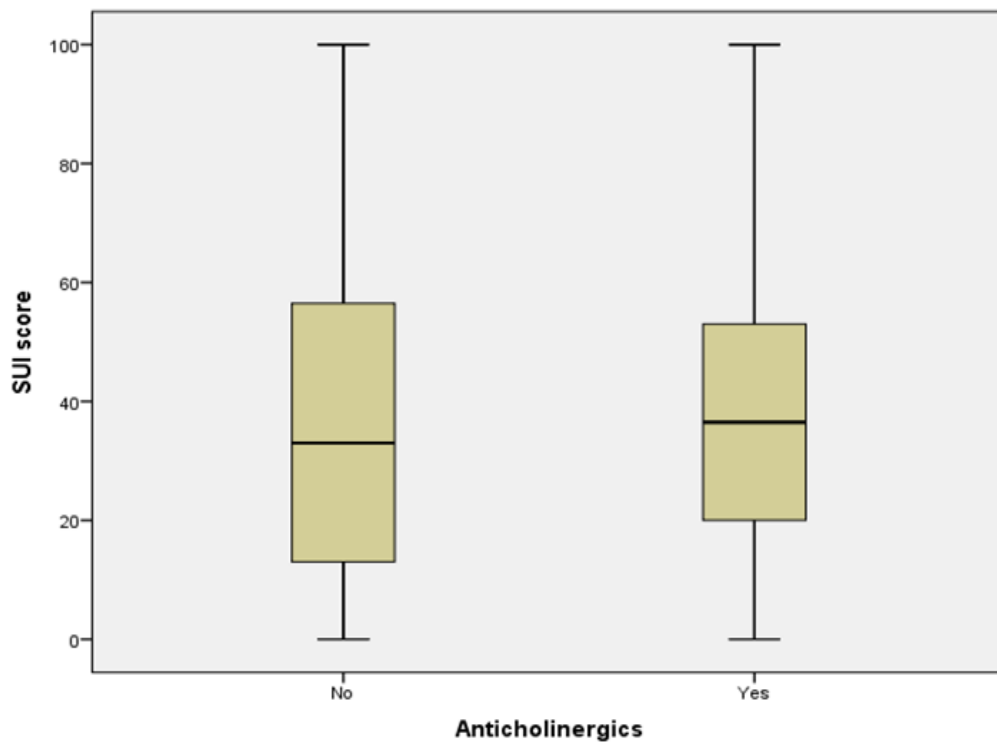
The SUI score was significantly higher in those with a parity greater than 2 ($p < 0.001$). The median values for those who had less than two children were 33 and 44 in those who had two or more children (Figure 13).

Figure 13: Box and whisker plot comparing stress urinary incontinence score in women who had two or more children



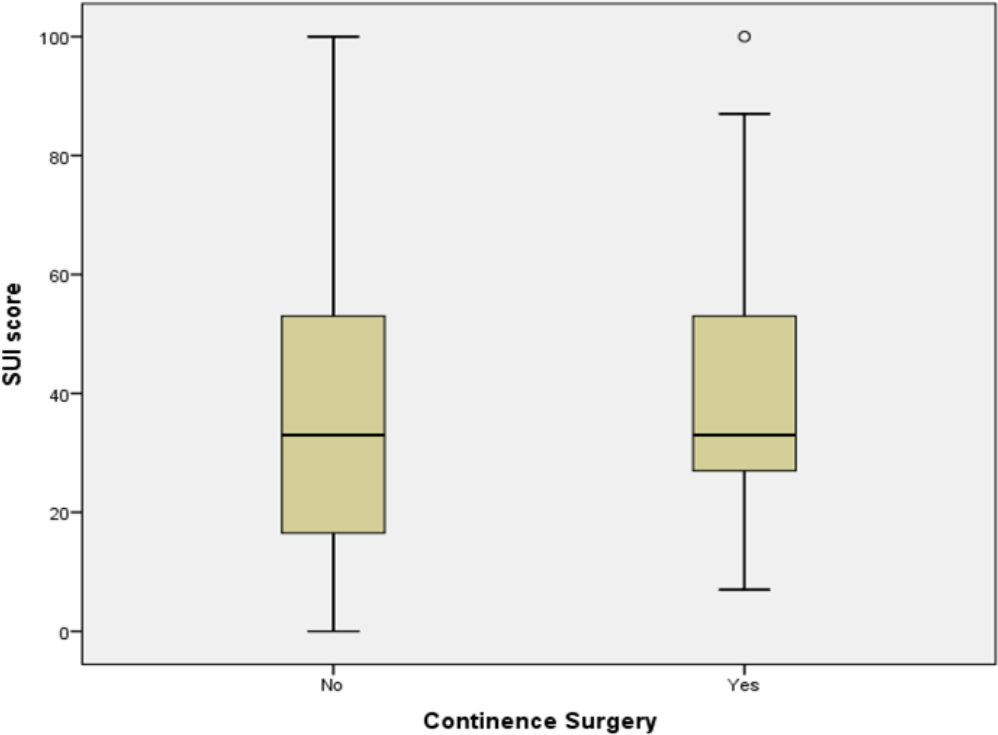
There was a small median difference between those who had tried anticholinergics (36.5) and those who hadn't tried them before (33) but this was not statistically significant (Figure 14). Anticholinergics made no impact on the score for SUI.

Figure 14: Box and whisker plot comparing stress urinary incontinence score in women who had previous/had not previously used anticholinergics



Both groups (surgery vs. non surgery) had a median score of 33.0 (Figure 15).

Figure 15: Box and whisker plot comparing SUI score and previous continence surgery vs. no surgery

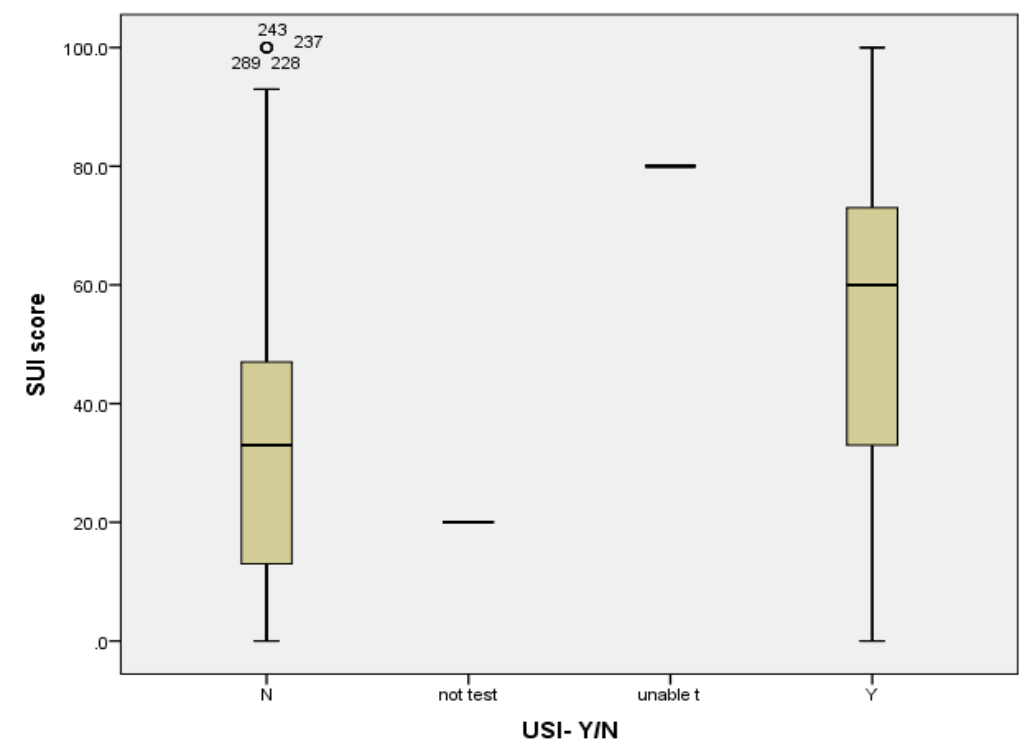


Menopausal status

Of the 390 women, 170 (43.5%) were pre-menopausal and 220 (56.4%) were post-menopausal. There was no significance between these two stratified groups when comparing their ePAQ scores for OAB and SUI (Chi ² 0.20 and the probability was $\chi^2 = 0.6566$ with a 95% confidence interval).

Women who scored high for SUI on ePAQ were more likely to have a clinical diagnosis of USI (Figure 16).

Figure 16: Box and Whisker plot comparing the electronic Personal Assessment Questionnaire stress urinary incontinence score with the urodynamic observation of urodynamic stress incontinence



Results for stress urinary incontinence scores on electronic Personal Assessment Questionnaire as a predictor of urodynamic stress incontinence

The analysis of the SUI scores was conducted using the same methods for the OAB scores. The various ePAQ scores and the sensitivity and specificity are given in Table 11.

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Table 11: Accuracy of the stress urinary incontinence score on electronic Personal Assessment Questionnaire in predicting urodynamic stress incontinence

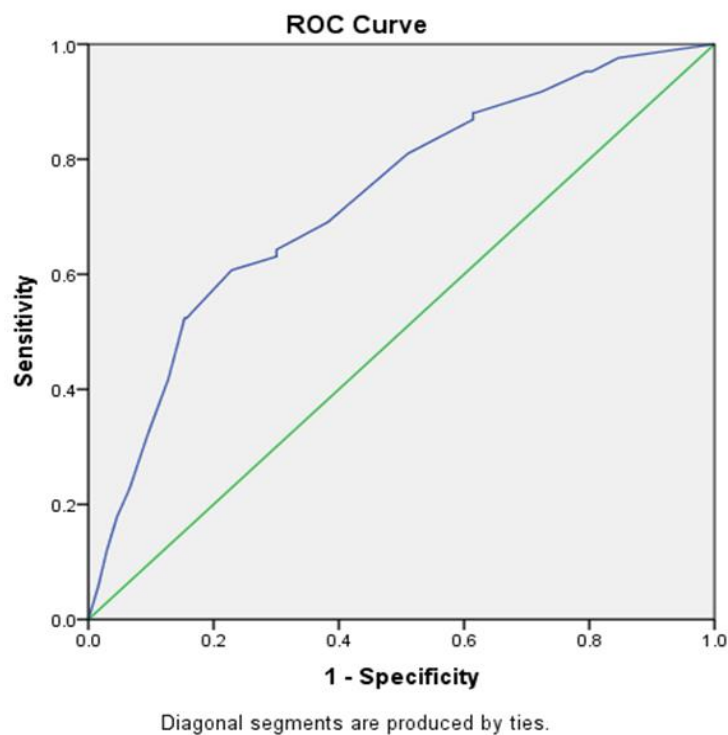
Score for SUI on ePAQ	Sensitivity	Specif icity	Correctly classified	LR+	LR-	PPV	NPV
0	100.0%	0.0%	21.5%	1.000	-	21.5	0.0
≥7	97.6%	15.4%	33.1%	1.153	0.155	24.0	37.9
≥8	95.2%	19.6%	35.9%	1.185	0.243	24.5	44.1
≥11	95.2%	19.9%	36.2%	1.190	0.239	24.6	45.5
≥13	95.2%	20.6%	36.7%	1.199	0.231	24.8	47.0
≥20	91.7%	27.8%	41.5%	1.269	0.300	25.8	57.0
≥22	88.1%	38.2%	49.0%	1.426	0.311	28.1	65.4
≥25	88.1%	38.6%	49.2%	1.434	0.309	28.2	66.7
≥27	86.9%	38.6%	49.0%	1.415	0.340	28.0	67.4
≥33	81.0%	49.0%	55.9%	1.588	0.389	30.4	74.6
≥40	69.0%	61.8%	63.3%	1.806	0.501	33.1	81.1
≥44	64.3%	69.9%	68.7%	2.138	0.511	37.0	84.3
≥50	63.1%	69.9%	68.5%	2.099	0.528	36.6	85.3
≥53	60.7%	77.1%	73.6%	2.654	0.509	42.1	88.4
≥56	52.4%	84.3%	77.4%	3.339	0.565	47.8	90.2
≥60	52.4%	84.6%	77.7%	3.410	0.563	48.4	91.5
≥67	41.7%	87.3%	77.4%	3.269	0.669	47.3	94.0
≥73	32.1%	90.5%	77.9%	3.392	0.750	48.2	96.2
≥80	22.6%	93.5%	78.2%	3.461	0.828	48.7	98.6
≥87	17.9%	95.4%	78.7%	3.903	0.861	51.7	101.2
≥93	11.9	97.1%	78.7%	4.048	0.908	52.6	103.1
≥100	6.0%	98.4%	78.5%	3.643	0.956	50.0	105.6

Women who had scored 8 or more for SUI had a sensitivity of 95.2%, specificity of 19.6% and USI was then correctly classified in 35.9% of the cases. The positive LR was 1.185. With a score of 25 or more, the sensitivity was 88.1% and the specificity was 38.6% and USI was then correctly classified as such in 49.2% of the cases, with a positive LR of 1.434. An SUI ePAQ score of 40 or more has a sensitivity of 69.0%, specificity of 61.8% and USI was then correctly classified in 63.3% of the cases, and the positive LR was 1.806.

Thus as the SUI score on ePAQ increased so did the likelihood of USI on UDS.

The AUC for USI was 0.731 (95% confidence interval 0.652-0.778) (Figure 17).

Figure 17: Receiver operating characteristic curve of stress urinary incontinence electronic Personal Assessment Questionnaire scores and urodynamic stress incontinence on Urodynamics



Discussion

Main findings

This study concluded that based on the ROC curves, OAB and SUI scores have a positive relationship with the urodynamic diagnosis. Thus, the higher the ePAQ score the more likely the patient is to have a positive UDS diagnosis.

Detrusor Overactivity (67.1%) was the predominant diagnosis observed during the UDS procedure. The detection rates of DO in women with OAB or urgency predominant MUI was 65.1%, indeed similar to other studies¹⁸. Where deemed necessary, ambulatory UDS was also offered and performed, we found that an additional 1.7% (7/390 women) were diagnosed with having DO.

Women presented to the urogynaecology clinic with a variety of symptoms, with the 58.4% of women complaining of MUI. There have been other reports in literature suggesting that MUI⁸⁵ or overactive bladder are the most prevalent type of UI in secondary care⁸⁶.

In the ePAQ study we had 91 women from ethnic minority groups which increase the generalisability of the findings. Cameron et al 2013⁸⁷ identify that race and ethnicity have shown variable effects on UI in women.

Factors identified in this analysis that may influence ePAQ scores for both OAB and SUI include age, previous continence surgery, previous use of medication for bladder symptoms, menopausal status and the parity.

A number of characteristics were collected during the study period including previous pregnancies and the number of children each women had (where applicable), the woman's menopausal status, previous use of medication for the bladder and also a history of surgical intervention for continence or pelvic organ prolapse.

Studies in the past have shown that pelvic floor symptoms have a different impact on women of different ages⁵⁹. Unfortunately, we did not collect the overall QoL scores for impact of the symptoms in relation to the age groups.

Minassian et al (2008)⁸⁸ have identified risk factors for UI like increased parity, higher body mass, increased weight, hysterectomy and in addition; a history of surgery.

Strengths and limitations

Although there are many studies that have utilised ePAQ-PF for treatment response and success⁶⁷ to the best of our knowledge, this is the first study to assess the predictive ability of ePAQ-PF in the urodynamic diagnoses. The study was prospective and recruited consecutive women presenting with LUTS from ethnically diverse groups and achieved its target sample size. The prevalence of DO in our study was similar to that reported in literature^{89, 90}. In our study, ambulatory UDS was offered to the appropriate women whose symptoms of UUI were not reproduced during the laboratory UDS studies. Ambulatory UDS may have a higher pick up rate of DO³⁷. The false positive and false negative rates were analysed and the potential influence of patient characteristics assessed. Quality control checks were done on some of the urodynamic traces to ensure that the gold standard test was robustly performed.

The robust design of this study increases confidence in the fact that the estimates of diagnostic accuracy are valid. All the criteria for a high-quality test accuracy evaluation have been met^{78, 91}. There is little data on ethnic minorities and UI⁶⁵, however almost 25% of our study population were of a black or minority ethnic group enhancing the generalisability of the results.

Limitations of the study are that we only looked at the scores relating to the OAB and SUI domains for the urinary component of the ePAQ. It is therefore plausible that the other domains such as pain, voiding and QoL may have provided further information and analysis to the overall diagnosis given. We did not audit all the urodynamic traces but the data monitoring committee for a bigger study ⁶⁴ felt that random sampling was adequate.

We could not assess the impact of inconclusive results as these were not formally assessed. Although there was data collected on various patient characteristics, it has been acknowledged that an assessment of these would need to be conducted to see whether they have any influence over the ePAQ scores. For example, logistic regression models would need to be performed to provide further clarification on whether specific characteristics may influence the overall predictive ability of ePAQ. This could include information such as the patient's mode of delivery i.e. (normal vaginal, caesarean section, instrumental delivery), body mass index, and the impact of medical or surgical treatment.

One area of concern in diagnostic accuracy research is misclassification made by the reference standard ⁹². UDS is known to be an imperfect gold standard test as a proportion of women, who have OAB symptoms, do not have a clinical diagnosis of DO following UDS ⁶⁹. UDS is also known to be less than 100% reproducible in previous studies of patients with overactive bladder and healthy volunteers ⁸¹. Errors in the reference standard typically lead to underestimation of sensitivity and specificity but misclassification rates would have to be extreme for no relationship to be observed at all ⁹³.

Having an imperfect gold standard (poor reproducibility of UDS) for the reference may have affected the test accuracy of our index test (the ePAQ). However, in the absence of another reliable diagnostic test for lower urinary tract dysfunction, clinicians have to utilise the UDS test which has been the accepted diagnostic test. The performance and interpretation of UDS in this ePAQ study was influenced by the results of our assessment of the quality assurance of UDS from the BUS study (Chapter 3) and thus performed under strict guidance with quality checking.

Future research

I intend to analyse the ePAQ data retrospectively to find out what was the cut off for OAB or SUI scores beyond which women ended up with surgery. This might help us counsel women on the possibility of needing invasive treatment in those with higher scores or higher impact on QoL earlier to improve patient compliance, satisfaction and may be reduce healthcare related costs.

Further research could assess the value added by ePAQ over and above the routine evaluation of OAB in clinical practice. Randomised controlled trials investigating treatments based on UDS vs. ePAQ OAB scores should be undertaken to determine the utility of UDS.

Finally, if multivariable logistic regression identifies several prognostic variables for UDS diagnoses then these could be incorporated in a prediction model for both UDS diagnosis and/or treatment need.

CHAPTER 5: DISCUSSION

Introduction

Millions of women worldwide are affected by urinary incontinence; many factors associated with this often leads to suffering and eventually, the individual seeking medical advice. Conservative treatment is ideal but in those who experience failure of this, UDS is often recommended. The UDS test is not 100% reproducible and has associated risks e.g. infection. The NICE guidelines (CG171) for urinary incontinence in women (2013) suggests a number of questionnaires which can be used to assess evaluation of treatment therapies⁹⁴ (Appendix 1). Electronic personal assessment questionnaire is a validated questionnaire which is used to assess the pelvic floor specific QoL (detailed in chapter 2) in our department. We wanted to study the evidence on diagnostic, prognostic and other utilities of ePAQ. We also wanted to assess whether this instrument could be used to reduce the need for invasive tests like urodynamics.

It is essential that the recognition and correction of abnormalities during the UDS procedure i.e. inadequate resting pressures are sought and remedial action taken. Quality control and regular audits of compliance to UDS procedures are required in order to ensure that high standards are performed. In addition, improvement can be sought and problems rectified if identified during an audit.

There were three specific objectives in this thesis which we have achieved:

1. A systematic review of the literature available to assess the use of the ePAQ in clinical practice for women with lower urinary tract symptoms has been performed.
2. Quality control of the urodynamic traces used in the study was performed.
3. Assessed the ability of the electronic Personal Assessment Questionnaire (ePAQ) to predict a diagnosis of DO on UDS in women with OAB and predict a diagnosis of USI in women who have SUI.

The main findings and conclusion for each of the above has been discussed in the preceding chapters (2-4). This final chapter reports on the key findings and limitations of the study.

Main findings

Evaluation of the index test (ePAQ)

Of the 11 studies discussed in the systematic review (Chapter 2) by McCooty & Latthe ⁷⁶, it is evident that the ePAQ has been established as a validated tool that can be used for women who have lower urinary tract and pelvic floor dysfunction.

The data obtained by completing the questionnaire are considered useful in terms of measuring symptoms, their impact 'bother', and health-related QoL. Data collected pre and post treatment are particularly useful in detecting how patients perceive the acceptability of their condition, the success of the treatment and improvement or deterioration in their health.

Various study designs and methodological factors were used amongst the studies and all population groups easily identified as having pelvic floor disorders or intervention for continence. The completion of an ePAQ appears to be generally more acceptable among women who complete this during their consultation visit as opposed to completing at their second appointment (follow up visit). It is optional, and therefore the choice to omit sensitive or potentially challenging issues may be seen as an advantage to the patient. The systematic review also found that older women were less concerned by sexual symptoms. This may potentially enhance the clinical consultation in regards to the types of questions asked by the clinician or the patient themselves.

Contrary to findings from previous studies demonstrating the usefulness of the ePAQ to assess women pre and post intervention, there were no studies found on the predictive ability of ePAQ and UDS diagnoses. Thus our focus and objective for the main study was to assess the ability of this tool in predicting the diagnosis of USI and DO in women who complaining of OAB and/or SUI.

Evaluation of the standard reference test (UDS) - quality control audit

The QC audit on UDS performed demonstrated a positive impact in most of the areas that were assessed. The audit and re-audit highlighted the importance of education and training in achieving compliance with GUP guidelines for UDS.

Re-iterating information and results can increase the level of adherence and maintain confidence in the professionals performing a test. The increase in compliance with

guidelines and SOPs has a benefit to those interpreting results and in this audit, reduced the variables that had been seen previously.

Ability of ePAQ to predict a diagnosis of detrusor overactivity and urodynamic stress incontinence

Based on the ROC curves, the ePAQ has fair ability to predict the urodynamic diagnoses of DO (0.709) and USI (0.731).

A less invasive way of assessing these women is desirable and it is hoped that one may find means of reducing the need for UDS.

ePAQ is widely used in the urogynaecology department at the BWNFT for the assessment of such women. This is often instructed to be carried out prior to clinical consultation. Our study found a small number of women had declined for their data to be used for research purposes, in this instance this group of women were immediately excluded from the study and any further analysis.

Strengths and limitations of this thesis

The ePAQ systematic review did not illustrate any studies in relation to predictive ability and therefore, no comparable data was available.

The studies reviewed were of variable quality. Common themes were identified and groups derived in accordance to the outcomes. There is a potential risk of bias as most studies were reported from one centre where ePAQ was developed.

The reference standard QC audit was performed as part of a multi-centre study, where 20% of the study population were randomly selected. It is therefore difficult to assess and identify how many of these traces were from our centre alone as the audit feedback was given to each centre. The UDS traces from our study would have been more compliant to the GUP guidelines and in accordance to our departmental SOP on UDS.

The design of this ePAQ test accuracy study increases confidence in the fact that the estimates of diagnostic accuracy are valid. All the criteria for a high-quality test accuracy evaluation were considered and met using the QUADAS- 2 tool and reported using the STARD tool.

A strong component of this ePAQ study is that a large number of patients (n=390) were included and the reasons for inconclusive data had been provided. This sample allowed for both analyses of the index and reference standard test. The women in the ePAQ study were from varying age groups, ethnicity and had various bladder symptoms. Doshani et al (2007) had previously found that little studies exist on the black and ethnic minority race ⁸⁰; our study population found that almost 25% were from a black or minority ethnic group.

Women were only included if they had accepted the disclaimer at the end of their completed ePAQ. There was the potential risk of bias during the completion of ePAQ if the UDS was performed first (if distress was caused by undergoing the UDS procedure).

The main limitation in this ePAQ study is that the total score for OAB and SUI had been utilised to draw the conclusions of the accuracy in predicting the diagnosis of DO and USI. There are individual questions that make up the overall score for both the USI and OAB domain. These were not looked at which may explain why for the OAB score there was some decrease in predictive utility at scores above 75.

Clinical implications

The ePAQ provides an additional instrument to clinical history in enhancing the confidence in providing a clinical diagnosis and relevant treatments. It also helps patients to be clearer in their mind as to whether their mixed urinary incontinence symptoms are stress or urge predominant and this will help to prioritise the relevant treatments. The ePAQ by itself is only a fair test in predicting urodynamic diagnoses and hence cannot replace this test. However, it can be used as an add on test to guide therapies based on patient 'bother' and also assess treatment response.

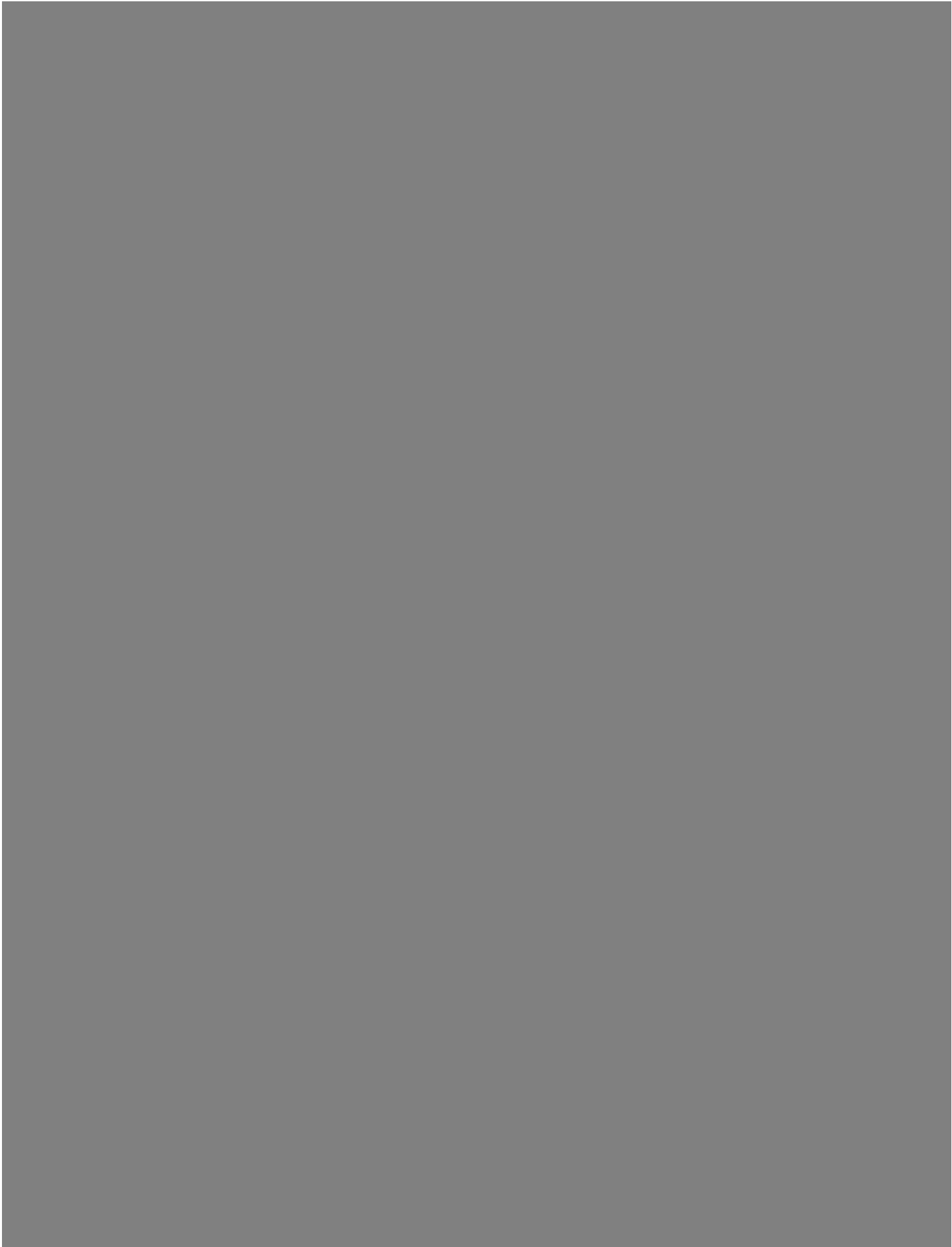
Implications for future research

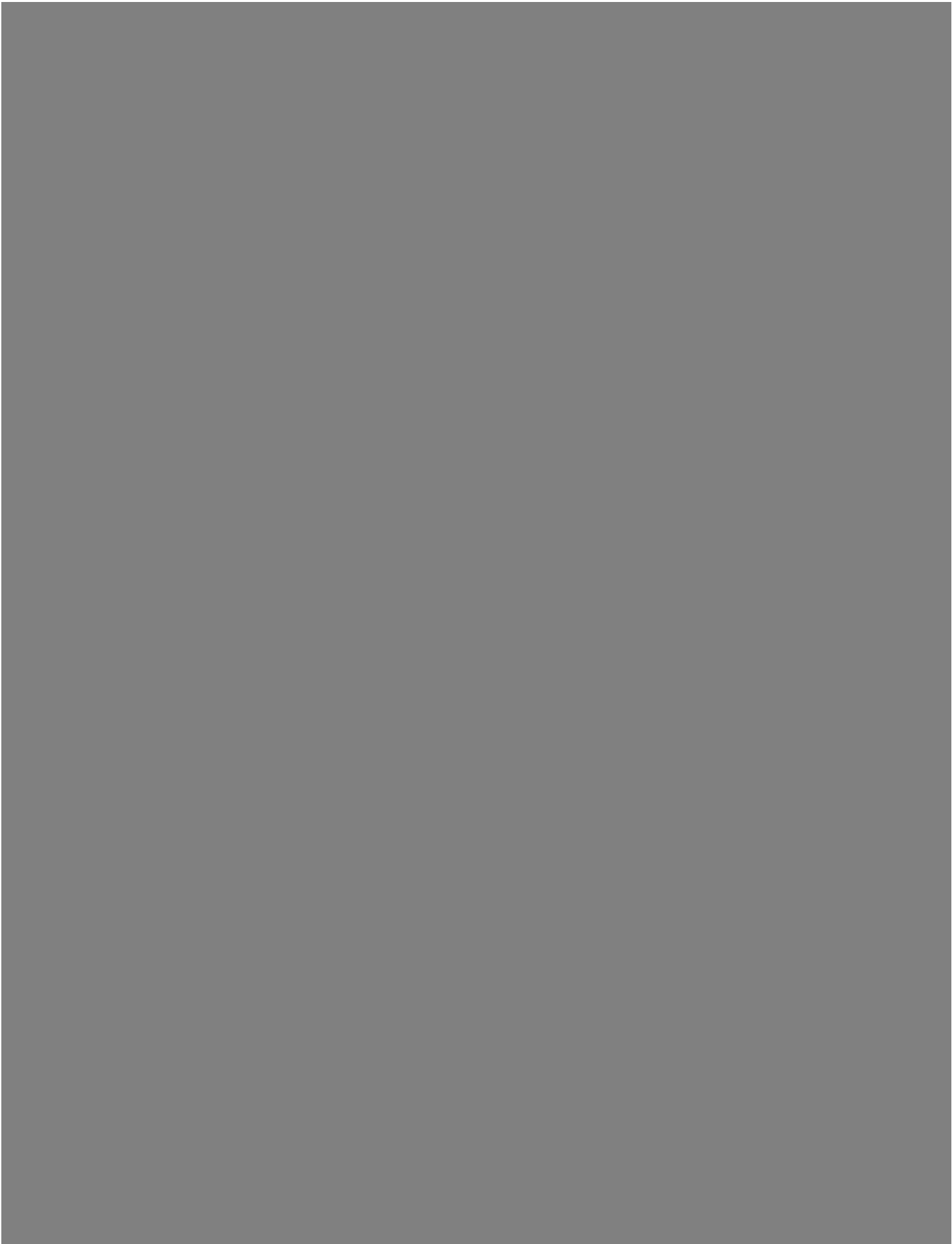
As clinicians it is our duty to provide evidence-based health care for our patients. We need to find ways of improving the management and treatment of women with LUTS and or other bladder conditions such as detrusor overactivity.

The discovery and evaluation of factors that might be useful as modifiable targets for interventions to improve outcomes is known as prognostic factor research (Riley et al, 2013)⁸⁴. A prognostic factor has been identified as any measure that, among people with a given health condition (start point), is associated with a subsequent

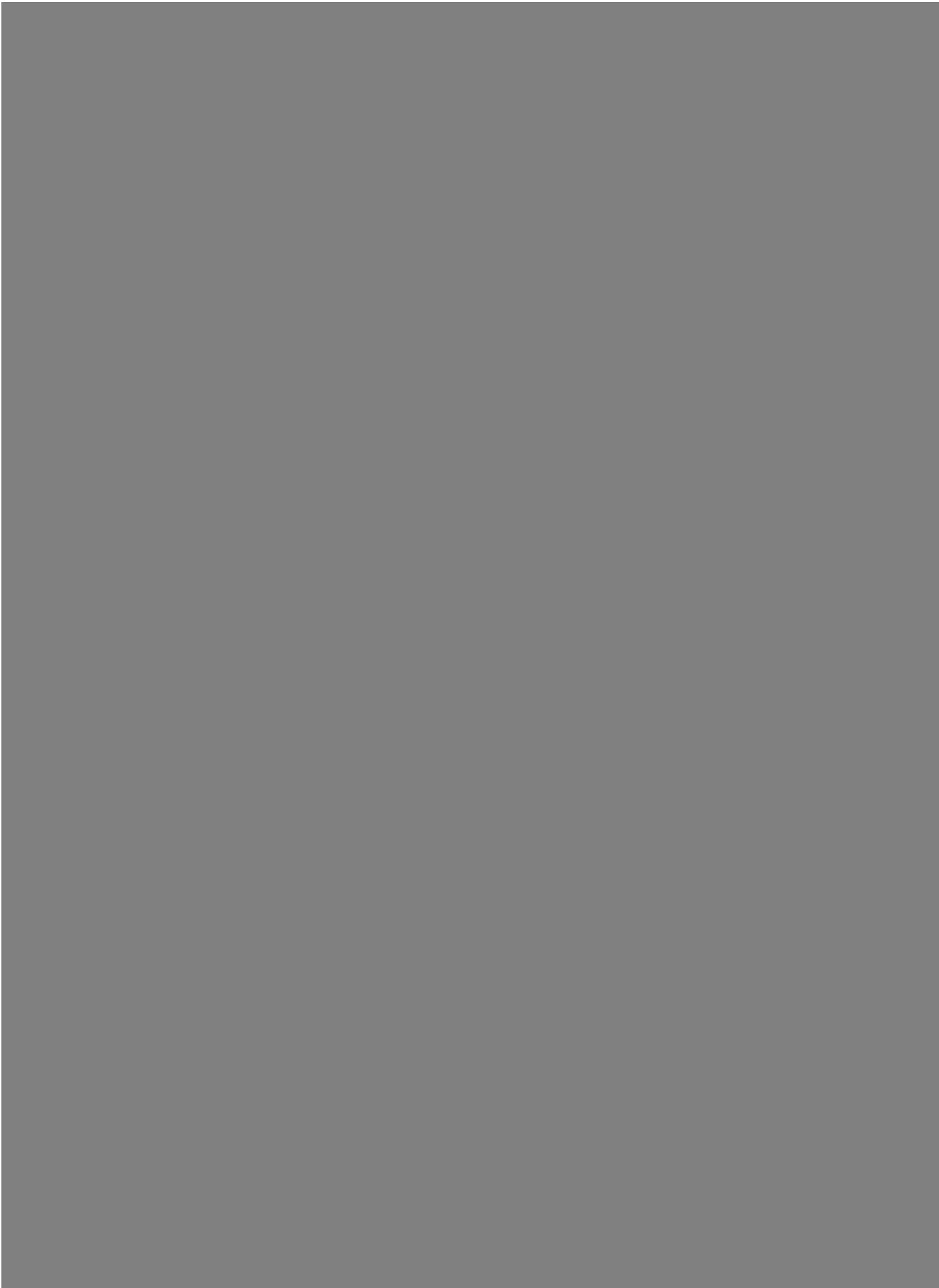
clinical outcome (endpoint). This particular type of research could be useful within the urogynaecology remit as many women are living with their bladder conditions for a longer period. In considering prognostic research we need to evaluate the broader healthcare impacts ⁹⁵ (age, health conditions, treatment response) and build a prediction model. The first step in building any prediction model is to assess the factors that may have predictive ability- for example (BMI, parity, surgical history, age of patient, ethnicity etc.). These factors individually may not have the ability to be used as a stand-alone test; however they could be incorporated as factors within the model.

In future, we need to assess the value added by OAB and SUI scores on ePAQ to the information already obtained from routinely used initial non-invasive tests (history, bladder diary).



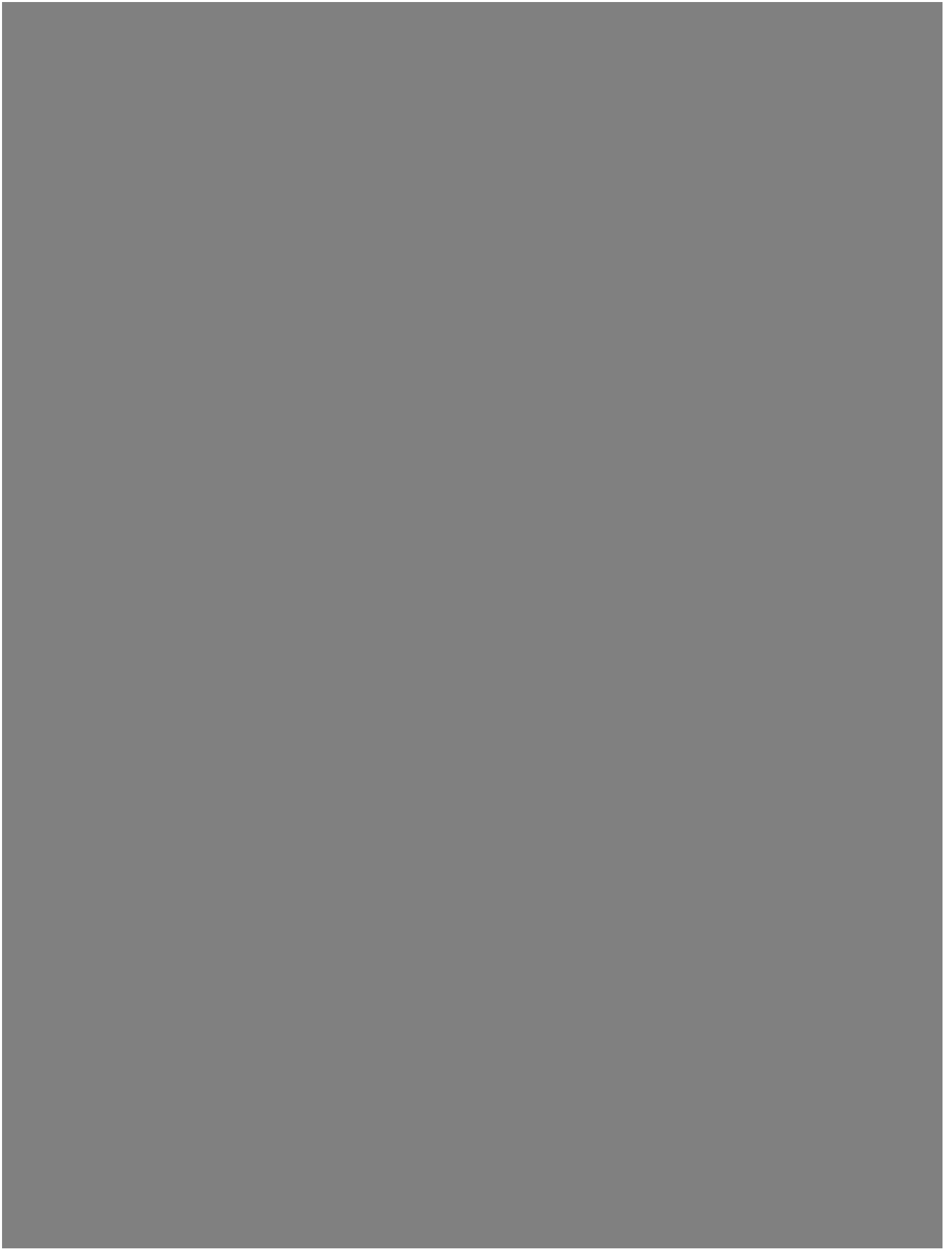


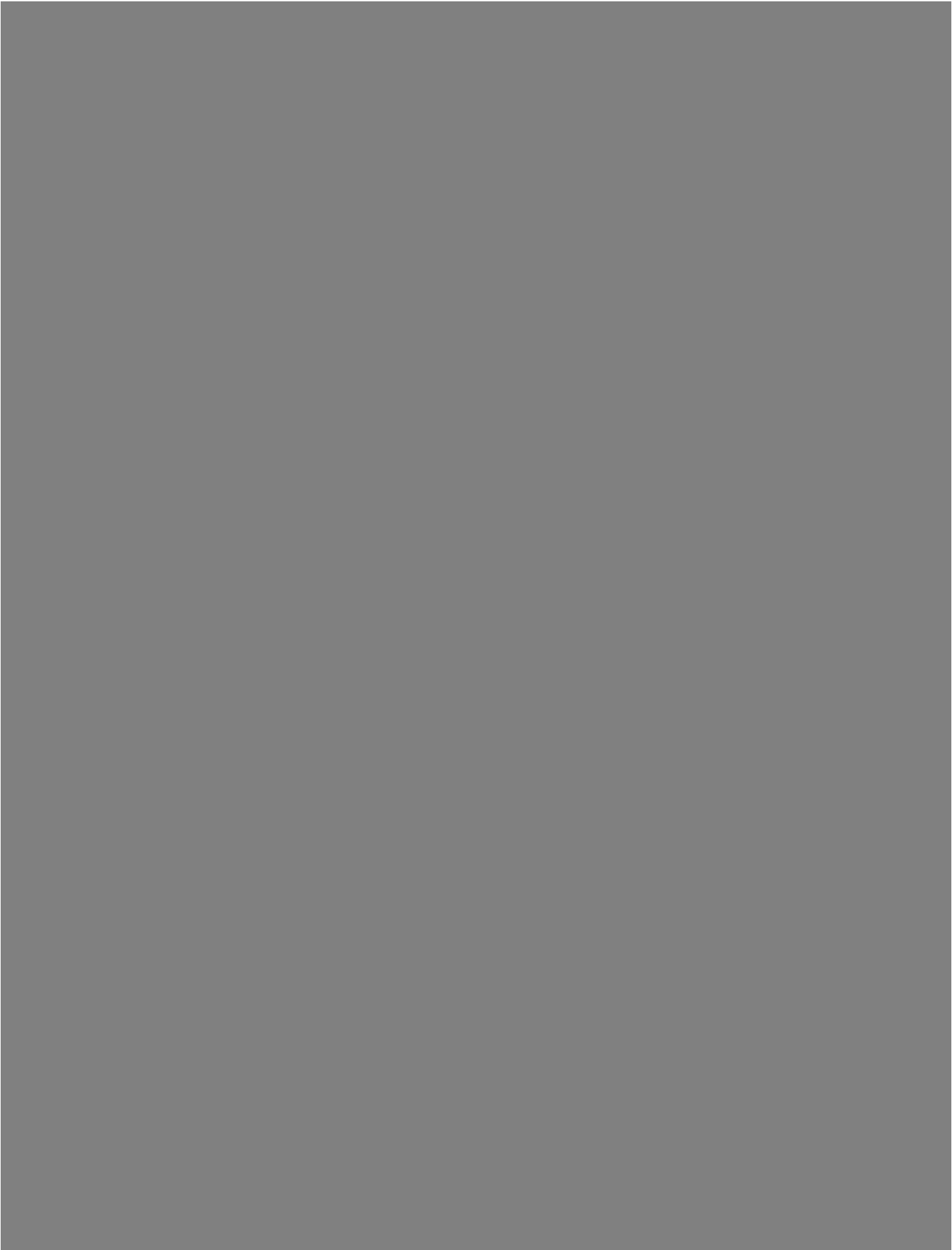


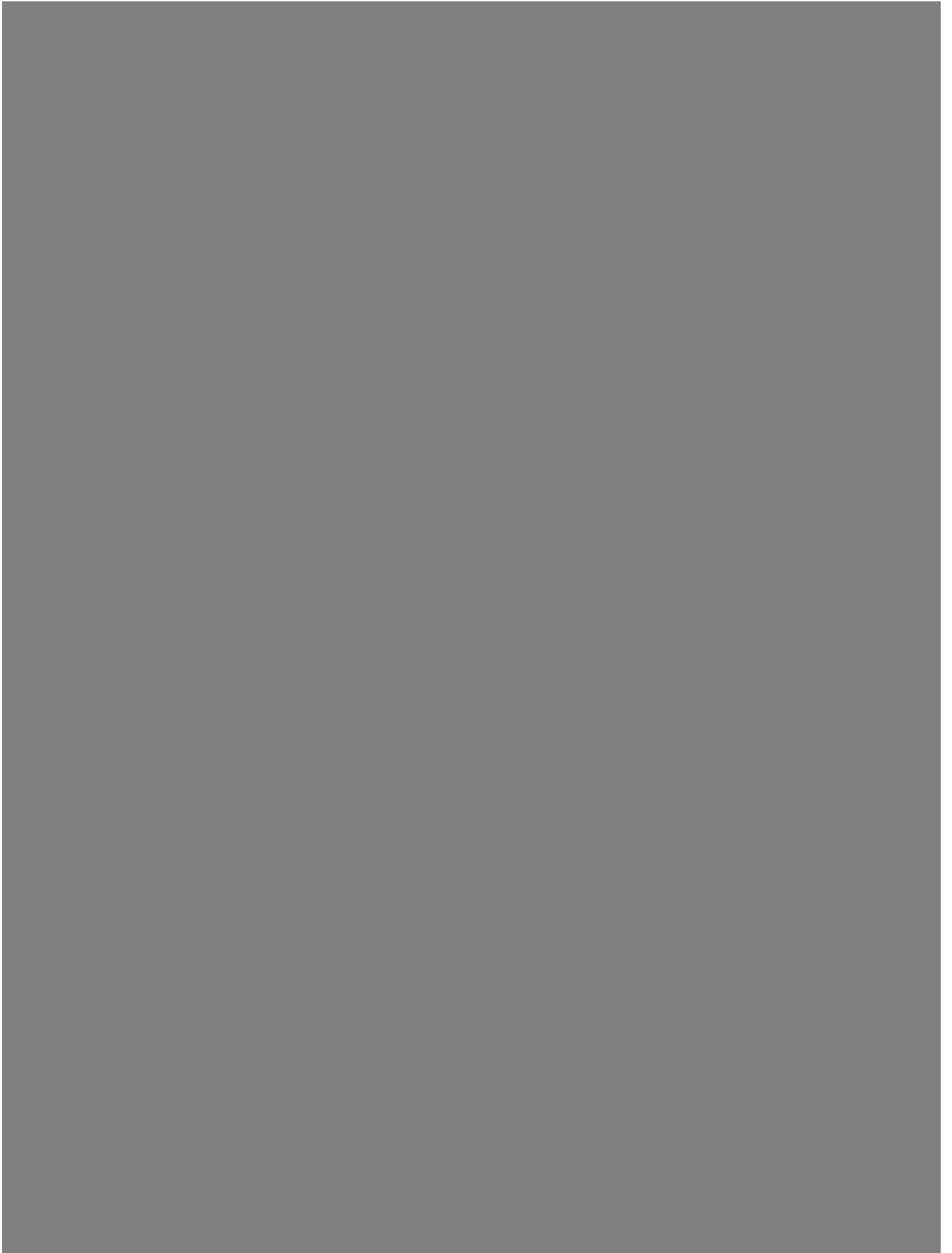








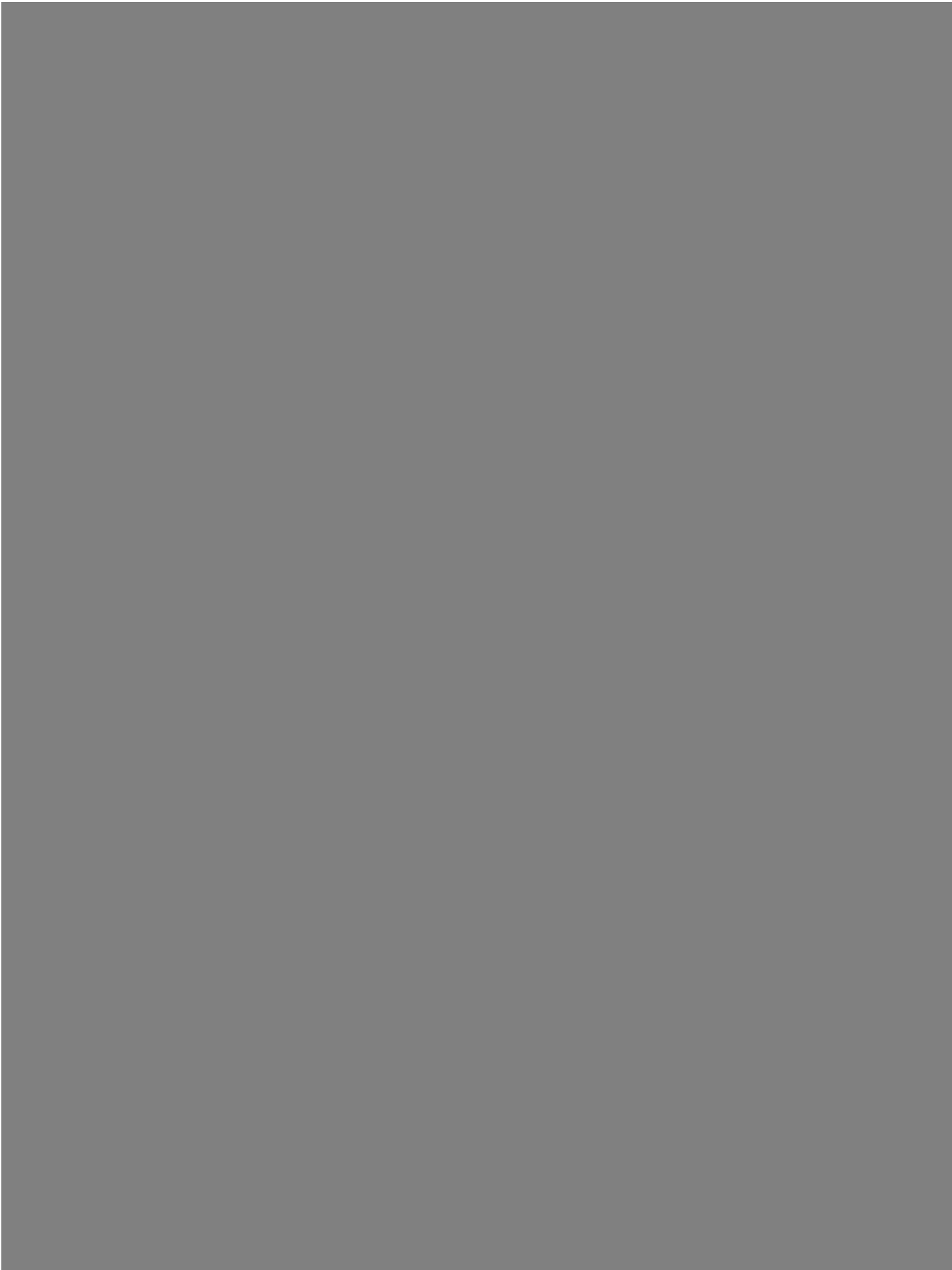














PUBLICATIONS AND PRESENTATIONS FROM THIS THESIS

Published manuscripts

1. **McCooty, S. Latthe, P. (2012) Quality control in urodynamics. Nursing standard. 27, 43; 35-38.**

S. McCooty conducted the UDS audit, and wrote the manuscript.

P. Latthe conceived the idea of the manuscript and contributed to the critical revision of the manuscript.

2. **McCooty, S. Latthe, P. (2014) Electronic pelvic floor assessment questionnaire: a systematic review. British Journal of Nursing, (urology supplement), 23 (18): S32-S37.**

S. McCooty was the first reviewer and wrote the manuscript. P. Latthe conceived the idea, acted as the second reviewer and contributed to the critical revision of the manuscript.

3. **McCooty, S. Nightingale, P. Latthe, P. (2016) The predictive value of ePAQ in the urodynamic diagnoses. BJOG- An International Journal of Obstetrics and Gynaecology- Online supplement from RCOG World.**

Congress Birmingham UK 2016- Stream 10- Urogynaecology (FC10.006).

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S.McCooty conducted the research study and wrote the abstract,

P Nightingale generated the statistical analysis and P Latthe conceived the idea and contributed to the critical revision of the abstract.

4. **McCooty, S. Nightingale, P. Latthe, P. (2017) The predictive value of ePAQ in the urodynamic diagnoses- A prospective cohort study. Neurourology and Urodynamics. 2017; 9999: 1-8.**

S.McCooty conducted the research study and wrote the manuscript.

P Nightingale generated the statistical analysis and P Latthe conceived the idea and contributed to the critical revision of the manuscript.

Presentations from this thesis

1. McCooty, S. Perkins, K. Tooze-Hobson, P. Latthe, P. Predictive value of ePAQ in the urodynamic diagnoses in women- Discussed poster presentation at the United Kingdom Continence Society (UKCS) held in Liverpool, UK, from 18/04/2012-20/04/2012.
2. McCooty, S. Predictive value of ePAQ- Urogynaecology across Mid-Counties Study Day held in at The Lygon Arms, Worcestershire, UK, on 11/03/2013

3. McCooty, S. Predictive value of ePAQ- Non discussed poster presented at the United Kingdom Continence Society (UKCS) meeting held in Bradford, UK, from 17/04/2013-19/04/2013.
4. McCooty, S. Predictive value of ePAQ- Non discussed poster at International Continence Society (ICS) conference held in Barcelona from 26/08/2013 to 30/08/2013.
5. McCooty, S. The predictive value of ePAQ in the urodynamic diagnoses in women with lower urinary tract symptoms- presentation at the Research and Development Showcase event, Birmingham Women's NHS Foundation Trust, UK on 17/11/2015.
6. McCooty, S. Nightingale, P. Latthe, P. The predictive value of ePAQ in the urodynamic diagnoses- Oral presentation at the Royal College of Obstetricians and Gynaecologists (RCOG) World Congress, Birmingham, UK on 21/06/2016.

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