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# Health-related Quality of Life and Female Urinary Incontinence

Evaluation of Measurement and Predictive Factors  
in Specialized Health Care



ACADEMIC DISSERTATION

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*To Jukka, Sonia and Joonas*

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# LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, referred to in the text by their Roman numerals. Some unpublished data is also presented.

- I Stach-Lempinen B, Kujansuu E, Laippala P and Metsänoja R (2001): Visual Analogue Scale, Urinary Incontinence Severity Score and 15D- psychometric testing of three different health-related quality-of-life instruments for urinary incontinent women. *Scand J Urol Nephrol* 35: 476-83.
- II Stach-Lempinen B, Sintonen H and Kujansuu E: The relationship between clinical parameters and health-related quality of life as measured by the 15D in incontinent women before and after treatment. (accepted in *Acta Obstet Gynecol Scand*).
- III Stach-Lempinen B, Kirkinen P, Laippala P, Metsänoja R and Kujansuu E (2004): Do objective urodynamic or clinical findings determine impact of urinary incontinence or its treatment on quality of life? *Urology* 63:67-72.
- IV Stach-Lempinen B, Hakala A-L, Laippala P, Lehtinen K, Metsänoja R, and Kujansuu E (2003): Severe depression determines quality of life in urinary incontinent women. *Neurourol Urodyn* 22:563-8.
- V Stach-Lempinen B, Nygård C-H, Laippala P, Metsänoja R and Kujansuu E (2004): Is physical activity influenced by urinary incontinence? *BJOG* 111:475-80.

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# ABBREVIATIONS

BMI	Body mass index
HRQoL	Health-related quality of life
ICS	Incontinence Continence Society
IIQ	Incontinence Impact Questionnaire
I-QOL	Incontinence Quality of Life Instrument
HAS	Hamilton Anxiety Scale
HDS	Hamilton Depression Scale
KHQ	King's Health Questionnaire
Max pDet	Maximal detrusor pressure
MET	Metabolic unit
MUCP	Maximal urethral closure pressure
NHP	Nottingham Health Profile
OAB	Overactive bladder
QALYs	Quality adjusted life years
SF-36	The Medical Outcomes Trust SF-36 (short form)
SUI	Stress urinary incontinence
TVT	Tension-free vaginal tape
UDI	Urogenital Distress Inventory
UI	Urinary incontinence
UISS	Urinary Incontinence Severity Score
US	Urgency Score
UUI	Urge urinary incontinence
UUI(±SUI)	Urge urinary incontinence with/without stress incontinence
VAS	Visual Analogue Scale

# ABSTRACT

The purpose of this study was to validate two disease-specific health-related quality of life (HRQoL) instruments: Urinary Incontinence Severity Score (UISS) and specific Visual Analogue Scale (VAS), to establish predictors of HRQoL impairment and to assess the effect of incontinence treatment on the HRQoL and its modifying factors in women referred to a specialized health care unit for symptomatic urinary incontinence.

According to the predefined inclusion criteria, 123 consecutive women were eligible for the study. Eighty-two incontinent patients (mean age 52, range 28-80) were recruited for the study that included baseline investigation and re-evaluation 13 months (range 6-21) after treatment. Twenty-nine control women, who had urinary incontinence, but were not bothered by it, completed the HRQoL measurements. Patients underwent clinical and urodynamic evaluation, frequency/volume chart, 48h pad-test, estimated the degree of bother from urinary incontinence (UI) using VAS and completed two HRQoL instruments: disease-specific UISS and generic 15D. The psychiatrists evaluated the women's depression and anxiety using a structured interview of the Hamilton Depression Scale and the Hamilton Anxiety Scale. Physical activity was measured by a self-report questionnaire and an electronic motion sensor (Caltrac accelerometer) worn by the women for one week. Patients were classified on the basis of history and urodynamic evaluation into two diagnostic groups: stress urinary incontinence (SUI) (n=57) and idiopathic urge incontinence with or without stress incontinence UUI( $\pm$ SUI) (n=25).

Validation of the HRQoL instruments was done by standard psychometric methods. Internal consistency (Cronbach's alpha 0.85) and content validity of UISS was good. Both measures UISS and VAS were reproducible; Spearman rank correlation between test-retest was 0.88 and 0.85, respectively. The control women's UISS and VAS scores were significantly lower than patient's scores ( $p < 0.001$ ), which proves good discriminant validity. UISS and VAS proved to be extremely responsive to treatment for UI women. The generic 15D performed well and appears to be sensitive in detecting change in HRQoL due to treatment of urinary incontinent women.

Compared to age-matched female general population, the HRQoL of urinary incontinent women was significantly poorer (mean 0.914 versus 0.836,  $p < 0.001$ ). Urge or mixed incontinence impairs HRQoL more than stress incontinence (mean 0.789 versus 0.857,  $p = 0.002$ ). The correlation between pad test and VAS, and UISS at baseline was:  $r = 0.47$  ( $p < 0.001$ ) and  $r = 0.25$  ( $p < 0.05$ ) respectively. The UISS and 15D scores correlated poorly with urodynamic and frequency/volume chart findings. Major depression occurred in 44.0 % of

women with UUI( $\pm$ SUI) incontinence and in 17.5 % women with SUI [(OR 3.69), 95 % CI 1.30 -10.49]. In addition co-morbid major depression correlated with reduced incontinence-specific HRQoL. Incontinent patients were as physically active as the normal population which suggests that exercise habits may influence treatment seeking behaviour. Even after successful treatment, exercise habits were not changed.

Significant improvement was found in women's HRQoL measured by all three HRQoL instruments after treatment. Among patients with SUI the total score of the 15D was about the same as in the age-matched general female population, but among those with UUI( $\pm$ SUI) although improved significantly, did not achieve the HRQoL level of women with SUI at baseline. Poor level of HRQoL at baseline, greater decrease in urine leakage, SUI diagnosis and lower depression scores after treatment predicted greater for the better change in HRQoL scores. Among women with SUI, the surgical treatment predicted better improvement in HRQoL than conservative treatment.

The UISS, VAS and 15D proved to be sound HRQoL instruments for the evaluation of the effectiveness of urinary incontinence interventions. Severity of urinary incontinence measured objectively correlate poorly with HRQoL. The treatment of women with SUI had a greater impact on HRQoL improvement than treatment of urge or mixed incontinence. In specialized health care, the effectiveness of surgical treatment on incontinence-specific HRQoL was greater than conservative treatment. Co-morbid depression not only predicted greater impairment of incontinence-specific HRQoL but the high rate of major depression among women with UUI suggests an association between these two conditions.

# INTRODUCTION

Health-related quality of life (HRQoL) is now recognized as an important patient outcome in response to a disease and treatment, especially in benign disorders, in which survival is not an issue. Information on the effect of different disorders on HRQoL and change in it due to treatment are important for clinicians to build a knowledge base in different diseases and make comparisons between therapeutic interventions. For policymakers it can be one of the bases on which to calculate the service provision and expenditure of health resources (Guyatt et al. 1993).

Urinary incontinence (UI) affects 20-50 % of women during their lifetimes and with increasing life expectancy it will be an increasingly important and widespread health problem (Thomas et al. 1980; Abrams 1997). Although not a life threatening condition, UI causes various physical, psychosocial and sexual problems for millions of women and their families and considerable economic problems for health service providers. Costs to health care of the diagnosis and therapy of this extremely embarrassing condition are in the range of those for diabetes mellitus in most Western countries (Hu et al. 2003).

Despite significant impairment of the HRQoL, at most half of the women with regular incontinence seek treatment (O'Brien et al. 1991; Hannestad et al. 2002; Kinchen et al. 2003). Those who want treatment seek medical care on the basis of their own subjective assessment of the severity of UI and perceived effect on HRQoL, which does not appear to depend on the duration or severity of incontinence (Norton 1982; Wyman et al. 1987; Burgio et al. 1994; Kinchen et al. 2003).

Identification factors influencing the women's self perception of their UI problem and predictors of HRQoL changing in response to treatment are needed for efficacy in individual, successful treatment planning. Knowledge of how UI affects women's health-related quality of life compared to other disorders is necessary to maximize the probability of appropriate allocation of health resources. To obtain information about HRQoL we need scientifically validated (accurate), reproducible (precise) and responsive HRQoL instruments.

The previous literature concerned merely general population surveys or women in specific age groups, usually without urodynamic or clinical evaluation of diagnosis or severity of UI (Hunnskaar and Vinsnes 1991; Grimby et al. 1993; Kutner et al. 1994; Schlenk et al. 1998). There are no studies, on women referred to specialist units whose clinical evaluation and treatment demand significant health service resources. There is no knowledge of how women's mental state or physical activity influence the subjective perception of their UI problems. The information about predictors of HRQoL impairment and treatment outcome

measured by HRQoL instrument is limited (Norton et al. 1988; Melville et al. 2002).

The aim of this thesis was psychometric testing of two different health-related quality of life instruments for urinary incontinent women and to assess the HRQoL impairment of incontinent women referred to a specialist gynecological unit. Factors determining UI impact on the quality of life and subjective severity of urinary incontinence were established. The changes of HRQoL of urinary incontinent women resulting from treatment and its modifying factors were described.

# REVIEW OF THE LITERATURE

## Urinary incontinence

### *Definitions and classification of urinary incontinence (UI)*

Urinary incontinence is defined by the Incontinence Continence Society (ICS) as the complaint of any involuntary leakage of urine (Abrams et al. 2002b). UI is not a disease, but rather a symptom which has many underlying causes and risk factors. The etiology of incontinence is multifactorial; incontinence is caused by pathophysiological impairments to the lower urinary tract and neurological system, as well as a range of external factors (Payne 1998; Donovan et al. 1999).

Incontinence is classified into three common types: stress incontinence (SUI, involuntary leakage on effort or exertion, or on sneezing or coughing), urge incontinence (UUI, involuntary leakage accompanied by or immediately preceded by urgency), and mixed incontinence (MI, involuntary leakage associated with urgency and with exertion, effort, sneezing or coughing (Abrams et al. 2002b). The commonest type of female UI is stress (50 %), then mixed (32 %) and urge (14 %) (Minassian et al. 2003).

SUI is thought to occur as results of weakened pelvic floor muscles or sphincter pathology, producing urine loss whenever there is increased intra-abdominal pressure. UUI may be due to extrinsic pathology such as bladder stones, acute urinary infection or carcinoma. Other recognised associations are with bladder outlet obstruction and neurological dysfunction. The commonest cause is “idiopathic”, i.e. occurring in the absence of detectable pathology. Some evidence suggests that this condition may result from subclinical neurologic disease or primary smooth muscle disease (Abrams 2002a).

### *Prevalence and risk factor of urinary incontinence*

The reported prevalence of UI has varied considerably depending on the study population and different definitions. Generally, there is an increase in duration, frequency of leakage, amount of leakage, severity and perceived impact

incontinence from the community, via general practice, to hospital (Cheater and Castleden 2000).

Women are more prone to UI than men. Studies from developed countries suggest that in adults younger than 30 years, UI affects about 5 % of women and <1 % of men (Hampel et al. 1997). However even 50 % of young healthy nulliparous women (<30 years) reported sporadic episodes of SUI (Cheater and Castleden 2000). Nygaard et al. (1990) reported that 28 % of nulliparous college athletes suffer from incontinence during competition. For community-based men 30-60 years of age, the prevalence remains unchanged, at about 1 %, but rates for female incontinence ranges from 14 to 41 % (Cheater and Castleden 2000). For the elderly (>60 years), prevalence rates of 17-55 % have been reported for women and 11-34 % for men. The prevalence of incontinence in institutional settings (hospital, nursing and residential homes) increases dramatically (>50 %), although similarly wide differences in 22-90 % prevalence rate have been reported (Cheater and Castleden 2000).

In the Finnish population the prevalence of incontinence varied from 3.1 % among 20 year old female students (Mäkinen et al. 1991) to 20.1 % among 25-55 years old (Mäkinen et al. 1992a) and about 60 % among elderly women aged 70 and over or institutional patients (Vehkalahti et al. 1986; Nuotio et al. 2003).

The risk factors of urinary incontinence can be classified into urogynecological, constitutional, neurological and behavioural risk factors (Cheater and Castleden 2000). The risk of UI is associated with aging (Herzog and Fultz 1990; Simeonova and Bengtsson 1990; Hannestad et al. 2000), obesity (Burgio et al. 1991; Mommsen and Foldspang 1994; Nygaard et al. 2003), chronic cough, poor health (Minassian et al. 2003), diabetes (Brown et al. 1999a), stroke (Wetle et al. 1995), dementia (Skelly and Flint 1995) and functional impairment (Nygaard and Lemke 1996). Parity is an important risk factor for female stress and mixed UI in fertile and peri- and early postmenopausal ages but all the effects of parity seem to disappear in older age (Rortveit et al. 2001; Nygaard et al. 2003). There is conflicting information about the potential roles of menopause (Jolleys 1988), hysterectomy (Brown et al. 2000), constipation (Spence-Jones et al. 1994; Møller et al. 2000a) and cigarette smoking (van Geelen et al. 2000; Hannestad et al. 2003) in the development of incontinence.

Strenuous exercise such as jumping, high-impact landings and running may induce incontinence (Nygaard et al. 1994; Eliasson et al. 2002). The prevalence of UI increases in people with cognitive and /or physical impairment, stroke and other neurological conditions such as Parkinson's disease (Cheater and Castleden 2000).

### *Treatment-seeking behaviours*

There are many factors such as age, education, income and availability of health services which influence the use of health services but the most important factor is the patients' own subjective perception of their health (Hannay 1979; Kinchen

et al. 2003). Although UI is common problem, only a small number of women at present actually seek medical attention (Couture and Valiquette 2000).

Although there is also wide variation in individuals' responses to similar symptoms (Pinnock and Marshall 1997; Samuelsson et al. 1997) most epidemiological studies have shown that frequency and severity of UI is a strong predictor of help-seeking behaviour (Samuelsson et al. 1997; Hannestad et al. 2002). However, women seem to be able to cope adequately with their incontinence. A community-based survey of Dutch women aged 50-65 years found 78 % of those with moderate to severe incontinence did not feel worried about it, and 75 % did not feel restricted in their activities (Lagro-Janssen et al. 1991).

Thirty three percent in Holst and Wilson's study (1988) and 50 % in O'Brien's et al. study (1991) of the women with incontinence twice per month or more wanted treatment. In Brocklehurst's study (1993) (2,124 women, aged 30 and over) 7.5 % of women had been incontinent of urine in the previous two months and 47 % of them had consulted their doctors. Patients were not embarrassed in seeing their doctor. Sixty percent of all those affected were concerned or worried about their incontinence, and in almost half of those incontinence limited their daily social activities.

The epidemiological study (n=2,911, aged >20) conducted in Göteborg showed that only 6 % of incontinent women who consider this a hygienic or social problem sought medical attention for UI (Simeonova et al. 1999). The recently reported Norwegian EPINCONT study showed that only a fourth of the women with any incontinence, and half of the women with significant incontinence had consulted a doctor (Hannestad et al. 2002). Increasing age, impact, duration and severity (Roberts et al. 1998; Hannestad et al. 2002) were significantly associated with consultation rate, as urge and mixed types compared with SUI (Hagglund et al. 2001; Hannestad et al. 2002; Coyne et al. 2003). In the study by Samuelsson et al. (1997) however, the desire for treatment did not correlate with the type of incontinence.

There is no knowledge about other possible predictors such as mental state or physical activity, which may also modify the help-seeking behaviour of incontinent women.

Most urinary incontinent women delay seeking medical treatment for many years (Norton et al. 1988). In this study the length of delay was not directly correlated with reported distress. The common reasons reported for delay or for not consulting the physicians were: that the symptoms were not considered serious or were not seen as abnormal (O'Brien et al. 1991; Lionis et al. 2000), lack of knowledge of the condition and of available treatment (Shaw et al. 2001) or a low expectation of benefit from treatment (O'Brien et al. 1991). Probably the most common reason especially among the elderly was embarrassment about discussing the problem with a doctor (Holst and Wilson 1988; Norton et al. 1988; Ushiroyama et al. 1999; Ueda et al. 2000). UI was considered as normal part of ageing or childbirth, or it was felt that such symptoms were inappropriate for medical intervention (Shaw et al. 2001).



Overall, community-based studies indicate that approximately 6 % of the total population, particularly women, will have UI of sufficient severity to interfere with their quality of life (Cheater and Castleden 2000). However, it has been estimated that over the next 30 years, growth in demand for services to care for female pelvic floor disorders, including UI will increase at twice the rate of growth of the same population. Also in a Scandinavian study (female population based study n=641, age=20-59), although only 9 % in the urinary incontinent group had ever consulted a doctor for incontinence, 60 % desired treatment (Samuelsson et al. 1997).

## Health-related quality of life (HRQoL)

### *General aspects of HRQoL*

The notion of quality of life is alluded to in the WHO description of health “as a state of complete physical, emotional and social well-being and not merely the absence of disease or infirmity” (WHO, 1947). Health-related quality of life is a multidimensional concept, and has come to mean a combination of patient-assessed measures of health, including physical function, role function, social function, emotional or mental state, burden of symptoms and sense of well-being (Coulter 1993).

### *Types of HRQoL measures and their applications*

Measures of HRQoL can be classified into three main categories: generic instruments that provide a summary of HRQoL, condition-specific instruments that focus on problems associated with single disease states and dimension-specific instruments aiming to measure single aspects of quality of life, such as pain or anxiety (Patrick and Deyo 1989).

**Table 1.** *Application of HRQoL instruments (Kelleher et al. 1995).*

- 
- Screening and monitoring of clinical conditions (including clinical audit)
  - Individual patients care in addition to a clinical interview
  - Population and observational studies
  - Outcome measures in:
    - health services
    - evaluation research
    - clinical trials
    - cost- utility analyses (economic evaluation)
-

The major advantages of generic measures are that they can be used in various populations regardless of the disease concerned. They are applicable to different patient groups and permit comparisons across patients with and without medical complaints. Economic evaluation allows comparison of different courses of action in terms of their costs and their consequences (Wennberg 1990).

Generic instruments include single health profiles and utility measures. Health profiles are instruments that attempt to measure all the important aspects of HRQoL (15D, SF-36). The utility measures of HRQoL are derived from economic and decision theory; they reflect the preferences of patients for treatment process and outcome. They can be used in cost-utility analyses that combine duration and quality of life. In utility measures, HRQoL is summarized as a single number along a continuum that usually extends from death (0.0) to full health (1.0). When a utility scale score is combined with patient survival in longitudinal studies, the outcome is called Quality-Adjusted Life Years (QALYs) (Guyatt et al. 1993).

The generic questionnaires include (necessitate) non-specific questioning, and scoring systems applicable to widely varying states of health, and therefore they may lack sensitivity when applied to women with non-life-threatening conditions such as UI. They may be unable to detect clinically important improvement in HRQoL when incorporated into clinical trials (unresponsive to change in specific conditions) (Guyatt et al. 1987; Guyatt et al. 1993).

Disease or condition specific measures are designed for a particular patient group and focus on aspects that are specific to the condition and are clinically relevant (important). Therefore, they should better reflect patient change in response to treatment.

Of the dimension-specific measures, Visual Analogue Scale (VAS) has been commonly used to assess pain along a 10 cm line ranging from “no pain” to “worst pain” and has also been used to assess urinary incontinence (Revill et al. 1976; Parkin and Davis 1986; Frazer et al. 1989; Vinsnes and Hunskaar 1991; Bo 1994; Seim et al. 1997; Dowell et al. 1999). Although the VAS approach has the merit of simplicity, there is some evidence that patients may not find it as simple and appealing as do researchers. Furthermore it has been suggested that the one-item VAS test demonstrates low reliability in comparison with longer scales (Steiner and Norman 1995). Dimension-specific measures can be used to supplement condition specific or generic questionnaires.

Disease-specific measures are of greatest interest to the patients themselves and to the clinicians who treat them, whereas generic measures, because they permit comparison across conditions and populations, are of greatest interest to the policy or decision maker. Thus, use of both categories of measures will be appropriate when the results could interest both audiences.

# Developing and psychometric assessment of HRQoL measure

## *Structure and modes of administration of HRQoL measures*

As HRQoL is a subjective measure, the instruments used to quantify it take the form of questionnaires and as such require validation to confirm their accuracy.

Some HRQoL measures consist of a single question that essentially asks “How is your quality of life?” (Guyatt et al. 1993). This question may be asked in a simple or a sophisticated fashion, but either way it yields limited information. More commonly, HRQoL instruments are self- or interviewer-administered questionnaires made up of a number of items or questions. These items are added up in a number of domains (sometimes also called dimensions). A domain or dimension refers to the area of behaviour or experience that we are trying to measure. Usually items are equally weighted, which assumes that their value is equal (Steiner and Norman 1995).

Self-administered questionnaires are the most practical, efficient and inexpensive method of obtaining patient-based information (Slevin et al. 1988; Aaronson 1989). Self-administration implies that patient capability (mental status, language, reading and writing ability, and so forth) has been considered when developing and using the questionnaires (Aaronson et al. 1988). With international studies becoming the norm in clinical trial it is imperative that questionnaires should be applicable in several languages and cultures. HRQoL scores are culture- and language-dependent tools, which should be carefully translated and validated in particular countries before taking them into use (Guyatt et al. 1993; Kujansuu 1997; Patrick et al. 1999).

Validation of a health-related quality of life instrument concerns reliability, validity and responsiveness, which are the three pillars of a good questionnaire.

## *Reliability*

The reliability of a questionnaire refers to its ability to be consistent and reproducible. Internal consistency is a measure of the homogeneity of items in a scale. When a number of items address the same issue, their scores should correlate and the calculation of Cronbach’s alpha provides a statistical assessment of this interrelationship between items (Cronbach 1951). Values greater than 0.7 are considered acceptable, greater than 0.8 are good and greater than 0.9 are excellent (Steiner and Norman 1995).

The reproducibility of the measures is concerned with the degree to which they can be repeated (Sintonen 1994a; Sintonen 1995). This is evaluated by correlation coefficients, such as Pearson’s  $r$ , Spearman’s  $\rho$  or intraclass correlation coefficients. A value of 0.8 or greater is indicative of high

reproducibility regardless of the correlation coefficients used (Steiner and Norman 1995).

## *Validity*

### *Content validity*

Validity examines whether the instrument measures what it is intended to measure. Content validity is most often addressed in the early phase of questionnaire development. It concerns how representative the contents are and it is often achieved through a literature review and consultations with experts and patients (Steiner and Norman 1995).

Another aspect of content validity is that the measure should be readily understood and unambiguous to the target population. Levels of missing data may be measures as this in an indicator of inappropriate questions.

### *Criterion validity*

The criterion validity of a measure is examined by correlating it with another measure, ideally a “gold standard”. If the measure correlates with the criterion measure when given at the same time, the measure shows concurrent validity (Guyatt et al. 1993; Steiner and Norman 1995). Criterion validity is applicable when a shorter version of an instrument (the test) is used to predict the results of the full-length index. Since there is no gold standard, the criterion validity of HRQoL measures cannot be proven.

### *Construct validity*

The most rigorous approach to establishing validity is called construct validity. HRQoL instruments should be able to reflect differing levels of symptoms in differing populations. Construct validity involves comparisons between measures and examines the logical relations that should exist between a measure and characteristics of patients and patient groups. Construct validation involves gathering external empirical evidence, convergent or discriminant, so that meaningful interferences can be made with the measure. To show convergent validity the measure should correlate highly with other variables and other measures of the same construct, to which it should correlate on theoretical grounds (Steiner and Norman 1995).

## *Responsiveness*

Responsiveness is studied to ascertain that a given questionnaire reflects a clinically important change in patient condition (Guyatt et al. 1993; Steiner and Norman 1995). Responsiveness will be deteriorated and the extents to which patients that have no change provide more or less the same scores. Most commonly the questionnaire studied is completed before and after a treatment of known efficacy and scores are compared to determine whether they reflect change due to treatment (Guyatt et al. 1987; Kazis et al. 1989). Patient perception of change is measured and the correlation of reported change in status with differences in quality of life scores is examined (Deyo and Inui 1984). Effect size calculations are also used. An effect size of 1.00 is a equivalent of a change in scores of one standard deviation in a original sample and it is considered a large effect size (Jenkinson et al. 1995).

HRQoL measures should also be interpretable that is, clinicians and policy makers must be able to identify differences in scores that correspond to trivial, small, moderate and large differences (that is the difference in the HRQoL). A number of strategies are available to make HRQoL scores interpretable (Deyo and Inui 1984; Guyatt et al. 1987; Steiner and Norman 1995) but interpretation of the results of HRQoL data has always been difficult. A statistically significant change of scores does not always mean it is clinically significant. Yalcin and Bump proposed global impression questionnaires Global Impression of Severity (PGI-S) and (Patient Global Impression of Improvement (PGI-I) scales to help in the translation of the scores of HRQoL measures into patient's perception of severity and treatment satisfaction (Yalcin and Bump 2003).

## Measurement of HRQoL in urinary incontinent women

### *Generic HRQoL instruments*

Although generic HRQoL questionnaires which measure function and well-being in general terms do not contain specific questions on UI, they have been widely used, either alone or in combination with a disease-specific measure, in studies concerning urinary symptoms, in comparative studies across the population of patients with other chronic disorders or the normal population, and in economic evaluation (Hunnskaar and Vinsnes 1991; Grimby et al. 1993; Dugan et al. 1998; Schlenk et al. 1998; Donovan et al. 1999; Burgio et al. 2002; Manca et al. 2003).

The Nottingham Health Profile (NHP) contains 38 dichotomous items grouped in six sections, including physical mobility, pain, sleep, social isolation, emotional reactions and energy level (Hunt et al. 1985). The NHP was administered to 433 elderly Swedish women and only two sections (emotional impairment and social isolation) showed a significant difference between

continent and incontinent women, but there were no differences between total score of the NHP in these two groups (Grimby et al. 1993). The NHP is short and easy to complete but tends to focus on the more severe end of the spectrum of ill health, therefore most respondents in normal population will tend to have scores near zero. Responsiveness was not reported.

The Sickness Impact Profile (SIP) (Bergner et al. 1981) contains 136 items divided into 12 categories, including sleep and rest, eating, work, home management, recreation and pastime, ambulation, mobility, body care and movement, social interaction, alertness behaviour, emotional behaviour and communication. Hunskaar and Vinsnes (1991) used the SIP to assess HRQoL impairment among 70 women attending a self-referral centre for incontinent patients (36 women aged between 40-60 years and 40 aged  $\geq 70$  years). They demonstrated that impact of urinary incontinence on HRQoL was both age- and symptom-dependent. Sleep, rest, emotional behaviour, mobility, social interaction and recreational activities were most commonly affected. The SIP is considerably longer than other generic instruments, making it somewhat unwieldy to use.

The Medical Outcomes Trust SF-36 is the most frequently used generic HRQoL instrument in studies among incontinent women (Ware 1989). It contains 36 items. They cover eight dimensions, including physical functioning, role limitations due to physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health (Hunt et al. 1985). Item scores for each domain are summed and transformed into a scale from 0 (worst) to 100 (best). The Short Form (SF-36) has undergone extensive validation and has greater sensitivity to change than the NHP (Hunt et al. 1985; Jenkinson et al. 1995).

The SF-36 showed good validity when used in men or women with urinary incontinence (Kutner et al. 1994). Test-retest reliability has been moderate to high ( $r=0.6$  to  $0.8$ ). Internal consistency of the scales was  $0.78$  to  $0.93$ . Therefore, McHorney et al. (McHorney et al. 1994) claimed that the SF-36 is appropriate for group comparison but not for individual comparison. The weakness of SF-36 is poor responsiveness reported in several intervention studies (Sand et al. 1995; Johannesson et al. 1997; O'Connor et al. 1998; Kobelt et al. 1999).

For economic evaluation, quality of life measures should have utility scaling. The utility measurement produces a single number (ranging from zero=death to 1=best possible health) for measured HRQoL. Examples of generic utility instruments are 15D (Sintonen 1994a) and EuroQoL-5D (EuroQoL 1990). The EuroQoL-5D is a simple five-dimension (three levels in each dimension) generic HRQoL questionnaire which produces a single index score from which quality adjusted life years (QALYs) may be calculated. It has been used in a cost-utility analysis of tension-free vaginal tape (Manca et al. 2003). The advantage of 15D is that it can be used as a profile and single index score measure. The 15D was found to be superior to the EuroQoL-5D in discriminatory power and responsiveness to change (Sintonen 2001).

### *Incontinence specific HRQoL instruments*

The 1990s saw the development of many disease specific quality of life measures. Many were constructed for a particular study with no report of their psychometric performance (Bø 1994; Seim et al. 1997).

Norton first (1982) developed a questionnaire to measure the effect of being incontinent. In the pilot study, 30 women who were attending a urodynamic clinic were asked to list all the ways in which urinary leakage had affected their lives. The final questionnaire consisted of 10 questions about the effects of incontinence upon physical health, mental well-being, domestic chores, social life, relationships with family, husband or boyfriend, work, dress and whether fear or odour or embarrassment restricted activities. The four possible responses – a great deal, quite a lot, slightly or not at all- had to be ticked as appropriate. This instrument was the base of the Incontinence Impact Questionnaire (IIQ), which was developed by the Continence Program for Women Research Group (Wyman et al. 1993). The IIQ was designed to assess the impact of all forms of incontinence on quality of life. Further work has been accomplished on the original IIQ, which has led to the development of two further questionnaires, the Urogenital Distress Inventory (UDI), which measures the prevalence of urinary incontinence and the bother it causes, and the Incontinence Impact Questionnaires, which assesses impact on quality of life (Shumaker et al. 1994). Short versions of these are now available (Uebersax et al. 1995). The validity of the IIQ questionnaire was recently questioned by FitzGerald et al. (2001) who assessed 55 patients with stress incontinence who underwent incontinence surgery. The patients completed UDI-6 and IIQ-7 before and three months after surgery. There was an assessment of the objective and subjective outcome of the treatment. Post-operative IIQ-7 scores were similar when those who were objectively cured of their SUI were compared with those whose procedures objectively failed. Hence the IIQ was not responsive to objective change in continence status. Later analysis of reliability showed a statistically significant decrease in total UDI and IIQ scores between test and retest assessment, although the authors suggest that the decrease was clinically trivial, possibly due to a research effect (Hagen et al. 2002). Van der Vaart et al. (2003) revisited the UDI and IIQ recently with the identification of a fifth subscale of the IIQ (in addition to the original four subscales: mobility, physical, social, and emotional functioning) about embarrassment and a recommendation to use this version in outcome analysis of treatments for urogenital symptoms in women.

The Incontinence Quality of Life Instrument (I-QOL) was designed to measure the impact of urinary incontinence primarily for use as an outcome measure in research (Wagner et al. 1996). The I-QOL has been adapted successfully into eleven languages and the cross-sectional psychometric properties of the US version were confirmed in four European countries (Patrick et al. 1999a). Although it is a reliable questionnaire, the responsiveness was poor with an effect size of 0.4 (Patrick et al. 1999b).

The Bristol Female Lower Urinary Tract Symptoms (BFLUTS) instrument focuses on the degree of bother caused to patients by a particular symptom, rather than whether the symptom is present, absent or of varying severity (Jackson et al. 1996).

The King's Health Questionnaire (KHQ) was designed to investigate the impact of incontinence on quality of life in women and also contains few questions about other urinary symptoms (Kelleher et al. 1997). The initial psychometric testing was based on the assessment of women referred to a tertiary urogynaecology unit without a control group. There were no results on the correlation between clinical measurement of incontinence severity (amount of urine leakage, incontinence episodes) and HRQoL impairment. The KHQ showed good validity and reliability among men and women with overactive bladder (OAB) symptoms (Reese et al. 2003). The KHQ has been validated and translated into seven languages. Responsiveness has not been reported, although it has been used to assess the results of surgery (Bidmead et al. 2001) and medical treatment (Kelleher et al. 2002; Reese et al. 2003).

Recently, Amarenco et al. (2003) presented the European psychometric validation of a new incontinence-specific HRQoL instrument CONTILIFE<sup>®</sup>. Internal consistency was good except for the effort activities dimension. Construct validity varied in different countries. Responsiveness to clinical improvement was good (effect size  $\geq 0.5$ ) except for the sexuality and well-being dimensions.

In addition to the HRQoL instruments described above, which can be used in varying types and severity of UI, there are also a few questionnaires available, designed for specific types of incontinence, such as urge or stress and OAB.

Brown et al. (1999b) developed the Urge-Incontinence Impact Questionnaire (U-IIQ) and the Urge-Urinary Distress Inventory (U-UDI) by adaptation IIQ and UDI. These instruments focus on the aspects of urge or mixed incontinence and showed good reliability, validity and responsiveness to change after treatment (ES -1.07- -1.71) (Lubeck et al. 1999).

After the ICS committee defined OAB diagnosis, this aroused the need for a questionnaire specific to patients with OAB.

OAB-q is a self-administered questionnaire which contains an OAB symptom and HRQoL scale (Coyne et al. 2002). The validation study has been performed in two large samples: a community sample who screened positive for OAB in a telephone survey (n=254) and patients seeking treatment for OAB symptoms (n=736). The OAB-q proved to be a reliable and valid instrument that discriminates between normal and clinically diagnosed continent and incontinent OAB participants. The responsiveness of this new instrument has not yet been tested in an intervention study.

The Symptom Impact Index (SII) is a short 3-item questionnaire that was developed for use with the 5-item Symptom Severity Index to estimate the impact of SUI rather than other urinary symptoms on quality of life (Black et al. 1996).



There are a number of reliable and valid disease-specific instruments for assessing the impact of incontinence on HRQoL (Table 2). Despite attempts to find a universally accepted questionnaire, some authors prefer one over the others. Choice of instrument depends on the study design and population. The KHQ, IIQ (long version) and I-QOL from general instruments and the U-IIQ and OAB-q for urge and OAB, are promising instruments for research but their responsiveness demands more evaluation. Although the sensitivity to change was studied, the clinical meaningfulness of changes in HRQoL scores after intervention needs more exploration. Moreover we need psychometrically robust useful instruments for busy clinicians to use in routine work with patients. These three general instruments are, however too lengthy for incorporation into everyday use.

### *The impact of urinary incontinence on HRQoL*

On the basis on epidemiological studies, regardless of type, incontinence has been shown to have a detrimental impact on patient HRQoL and the quality of life of incontinent persons has been significantly poorer than that of the general population (Wyman et al. 1987; Hunskaar and Vinsnes 1991; Grimby et al. 1993; O'Connor et al. 1998; Kobelt et al. 1999; Simeonova et al. 1999; Hagglund et al. 2001; Coyne et al. 2003). Patients with UI report feelings of embarrassment, shame and stigmatization, interference with daily activities and psychological distress (Lagro-Janssen et al. 1992; Grimby et al. 1993). Studies have documented that UI has negative effects on social activity by limiting places visited and by interfering with social relationships. Access to toilets is often reported as a factor that limits social activity, with incontinent women altering their lifestyles to avoid places without easy access to toilets. This can result in social isolation secondary to the avoidance of travelling and meeting places such as shops, church, theatres and dances (Norton 1982; Wyman 1994; Swithinbank and Abrams 1999). Fluid restriction to control incontinence (Brink et al. 1987) and the inability to exercise for fear of leakage (Norton 1982; Norton et al. 1988) have been reported. OAB with and without UUI has been associated with poorer quality of sleep (Stewart et al. 2003). Urinary incontinence adversely affected sexual function (Sutherst 1979; Diokno et al. 1990).

There is a little knowledge about HRQoL across chronic disorder populations and also of comparison of HRQoL of incontinent patients with others patients' groups. Schlenk et al. (1998) examined HRQoL using SF-36, across patients with UI, prostate cancer, COPD, AIDS, fibromyalgia and hyperlipidemia, and compared HRQoL in these patients with normative data. The results demonstrated that not only did the prostate cancer and hyperlipidemia patients have the highest HRQoL across the chronic disorders, but their HRQoL was comparable to normative data on healthy persons. A comparison of the scores of UI patients with those of other patient groups is useful only if the samples are at least approximately age-matched as above, since HRQoL is an age-dependent variable.

**Table 2.** Disease-specific quality of life questionnaires for women with urinary incontinence.

Questionnaire	Population sample	Number of items	Internal reliability Cronbach's alpha	Test-retest reliability	Validity	Responsiveness	References
IIQ	UI-women n=162	30	0.75	moderate	good	very good (12 weeks)	(Shumaker et al. 1994)
Incontinence Impact Questionnaires			acceptable				
IIQ-7	UI-women n=162	7	not reported	not reported	not reported	not reported	(Uebersax et al. 1995)
Short form							
I-QOL	UI-men and women n=62	22	0.95	very good	good	poor (2 weeks)	(Wagner et al. 1996; Patrick et al. 1999b)
Incontinence Quality of Life Instrument	UI-women n=288		very good				
BFLUTS	UI-women n=85	20	0.78	good	good	not reported	(Jackson et al. 1996)
Bristol Female Lower Urinary Tract Symptoms			acceptable				
KHQ	UI-women n=285	21	0.72-0.92	good	good	reported only for OAB-men and women (10 weeks)	(Kelleher et al. 1997)
The King's Health Questionnaire	OAB-men n=92		acceptable				(Reese et al. 2003)
CONTILIFE	SUI- women n=505	28	0.71-0.94	not reported	moderate	moderate (4weeks)	(Amarenco et al. 2003)
U- IIQ	UII-women n=83	32	0.82-0.96	ICC 0.68-0.83	good	good (12 weeks)	(Brown et al.1999)
	UII-men and women n=257		very good	good			(Lubeck et al. 1999)
OAB-q	OAB-women and men n=990	33	0.80-0.94	not reported	good	not reported	(Coyne et al. 2002)
SII	SI-women n=442	3	0.8	good	moderate	not reported	(Black et al. 1996)
Symptom Impact Index			good				

For example, the comparisons by Schlenk et al. (1998) do not meet this requirement. Johannesson et al. (1997) compared HRQoL among patients with detrusor instability and those with rheumatoid arthritis. Women with detrusor instability suffer greater impairment in vitality and social function, and greater emotional problems than do women with rheumatoid arthritis or neither condition.

## Predictors of HRQoL impairment for incontinent women

### *Demographic factors*

An individual's perception of UI as a significant health problem may be modified by a number of factors, including age, social class, support, and interpersonal relationships.

The effect of *age* on the subjective severity of UI has not been widely reported and studies yield conflicting results. In the Hunskaar and Vinsnes study (1991), although SUI was more severe in older women, younger women revealed more impairment in the domains of quality of life than older women, particularly in the realm of recreational activity. Older women may have accepted or coped with urine leakage more effectively because they accept it as a normal part of the ageing process. Sandvik et al. (1993) also found that younger women with stress incontinence appear to be more distressed than older women. In a study of women presenting at a urodynamic clinic, Norton (1982) found no relationship between age and HRQoL impairment. The symptoms of UI and OAB among young adult women (age 20-30) have the same detrimental effect on HRQoL as among older women (van der Vaart et al. 2003).

The different study populations (self-referral vs tertiary level) may explain the varied results. Probably age *per se* is not a major predictor of HRQoL impairment, rather other factors such as exercise and working habits, sexual activity, mental state and severity of leakage influence more the subjective perception of UI.

It is a well known fact (Norton et al. 1988) that urinary incontinent women have not sought treatment until many years after the symptoms have started. However, quality of life impairment does not appear to be related to symptom *duration* (Kelleher and Cardozo 1993; Sandvik et al. 1993). Only in one study (Lam et al. 1992) did the number of social problems increase with the duration of UI. This finding may result from the potential confounding of duration with increasing severity of UI over time. Recently Kinchen et al. (2003) found that symptom duration over three years was associated with treatment seeking.

The *type of UI* experienced appears to affect the degree of perceived impairment of quality of life. The majority of studies have documented that women with urgency-frequency problems or urge incontinence, or both report

the most impairment across several domains of quality of life (Wyman et al. 1990; Hunskaar and Vinsnes 1991; Grimby et al. 1993; Kelleher et al. 1997; Coyne et al. 2003). Women with UUI are less able to predict incontinence episodes and usually loss of urine is considerably greater (Wyman et al. 1993).

Not all authors have found this relationship, however. Samuelsson et al. (1997) found no difference between the impact of stress and urge incontinence on the aspects of well-being studied. In this study incontinence diagnosis based on the questionnaire and only 2 % of incontinent women had UUI, which can explain these findings. Likewise Burgio et al. (1991) in epidemiological study concerning only middle-aged women, found no relationship between the type of incontinence and any of the 12 psychological measures.

In the general population case-control study, by Coyne et al. (2003) there were no differences in HRQoL scores between different incontinence groups measured by generic SF-36, although measured by disease-specific OAB-q questionnaire urge and mixed incontinence had a greater impact on HRQoL than SUI. This emphasises the fact that not only the study population but the methods used to assess HRQoL must be taken into consideration in the comparison between studies.

### *Lower urinary tract symptoms and clinical parameters*

Population based studies have shown that the severity of incontinence assessed by patients self-reported incontinence episodes, amount of urine leakage or need to use protective pads correlated with quality of life impairment (Lam et al. 1992; Samuelsson et al. 1997; Dugan et al. 1998; O'Connor et al. 1998). In the study by Dugan et al. (1998) on community-dwelling elderly (aged 60 years and older) the impact of incontinence measured by IIQ-7 was greater for those who reported more days in bed due to health problems and having larger amounts of urine lost per accident and frequency of UI. Among patients with urge or mixed incontinence Johannesson et al. (Johannesson et al. 1997) found a statistically significant, linear correlation between SF-36 scores and number of micturitions and leakage (index) but correlation coefficients were weak varied -0.10- -0.23. In the study by O'Connor et al. (1998), HRQoL was significantly related to severity of symptoms in six of the eight domains of SF-36 among patients with urge.

In studies based on the women's population referred to the incontinence clinics there is no agreement regarding the effect of the reported severity of UI on HRQoL. However, in most of the studies, the correlation between the number of incontinence episodes or pad test and the psychosocial impact scores (Norton 1982; Wyman et al. 1997) or the scores of disease-specific HRQoL measures (Theofrastous et al. 1995; Nager et al. 2001) was rather modest. Two studies did, however, reveal that both IIQ long version scores (Shumaker et al. 1994) and I-QOL scores (Patrick et al. 1999) were significantly worse with increasing episodes and urine leakage. Correlation of severity measures with general health (measured by generic HRQoL instruments) was mostly negligible (Hunskaar and Vinsnes 1991; Shumaker et al. 1994).

To date, only two studies have been conducted in order to correlate urodynamic findings to the effect of urinary incontinence on HRQoL measured by standard instruments (Theofrastous et al. 1995; Nager et al. 2001).

Theofrastous et al. (1995) found no correlations between any urodynamic parameters and two standard instruments UDI and IIQ among patients with SUI. The power of this observation is limited by a relatively small sample size (only 33 subjects who completed HRQoL scales). Nager et al. (2001) likewise found no correlation between MUCP and leak point pressure with pad loss or quality of life measures and only modest correlation between the amount of fluid lost on pad testing and HRQoL score among 52 women with SUI.

There is no previous data comparing validated HRQoL instruments with cystometry. Urinary urgency seems to be the most significant symptom to affect HRQoL in continent and incontinent patients with OAB (Coyne et al. 2003). In particular, among those incontinent OAB patients the urinary urgency had the greatest impact of all urinary variables on HRQoL, whereas the number of incontinent episodes was not a significant contributing factor (Coyne et al. 2003). These findings suggest that the impact of UI on the HRQoL is not solely a function of its severity, but also depends on individual coping abilities.

### *Physical activity*

The general opinion is that incontinent women modify their behaviour by wearing pads during exercise, changing or ceasing the exercise for fear of leakage and odour (Norton 1982; Nygaard et al. 1990; Brown and Miller 2001).

In a general population study on Australia (Brown and Miller 2001) there was a cross-sectional association between incontinence and physical activity, such that women with more frequent urinary leakage were also more likely to report low levels of physical activity. Two previous studies did not find any association between UI and physical activity among middle-aged women (Burgio et al. 1991; Møller et al. 2000b).

Nygaard and colleagues (1990) studied 326 women (mean age 38.5) presenting at a private gynaecology office and found 20 % of “incontinent exercisers” had stopped their exercise because of leakage, whereas 18 % changed the way a specific exercise was done and 55 % wore a pad during exercise. Only 35 % had discussed their incontinence with a health care professional.

Except for two epidemiological studies (Nygaard et al. 1990; Brown and Miller 2001), there is a lack of data about physical activities among incontinent women seeking treatment, how women’s physical activity affects on their quality of life impairment and how exercise habits change after treatment.

## Depression and urinary incontinence

### *Prevalence of depression in urinary incontinent women*

Major depression is a prevalent disorder seen in approximately 5 % of community respondents (Kessler et al. 1994), in 5 % to 9 % of primary care patients (Kessler et al. 1994; Poutanen 1996), and in 15 % of speciality clinic patients (Katon and Schulberg 1992). The rate of major depression among general obstetric-gynecological outpatient populations varied from 6 % to 10 % (Spitzer et al. 2000). Panic disorders are also a common psychiatric co-morbidity that are reported in 1-3 % of community responders and in 4-8 % of patients in primary care (Katon et al. 1986) and which is strongly associated with depression (Kessler et al. 1994).

Since the 1970s the urogynecological literature has suggested that there is an association between various psychiatric disorders, especially depression and urinary incontinence, but the relationship between these disorders is not well understood (Frewen 1978; Frewen 1984; Freeman et al. 1985; Macaulay et al. 1987; Macaulay et al. 1991).

The prevalence of major depression among urinary incontinent women varied widely due to methodological variations and different study populations. Nygaard et al. (2003) using a short form of the Composite International Diagnostic Interview, found in a population-based cross-sectional study that middle-aged women with severe incontinence were 80 % (OR 1.82 , 95 %CI 1.26-2.63) more likely to have depression than continent women. However, the association did not hold for depressive symptoms measured by the revised Center for Epidemiologic Studies Depression Scale (CES-D). Recently Stewart et al. (2003) also using the CES-D scale found in a population based study that people (men and women) who suffer from overactive bladder had higher depression scores than matched controls in US.

Roughly a quarter of all UI patients in the Macaulay study (1991) were as depressed and anxious as psychiatric in-patients. Zorn et al. (1999) have noted major depression in 30 % of the incontinence group versus 17 % of controls. In a prospective randomized controlled study of 668 community-dwelling elderly (>age 69), Dugan and co-workers (2000) found that 43 % of those with incontinence were depressed, compared to only 30 % of continent subjects. There was a positive correlation with the degree of urine loss and depression. In a sample of 218 incontinent women at a special urogynecology clinic the prevalence rate of current psychiatric disorders was: 16 % major depression, 7 % panic disorders, 18 % either diagnosis (major depression and/or panic disorders) and 4 % both diagnoses (Melville et al. 2002).

### *Characterization of urinary incontinence in depression*

The majority of studies have found either a tendency of increased depression in urge or mixed incontinence, or a significantly higher prevalence of depression in urge or mixed rather than in stress incontinent patients (Frewen 1978; Frewen 1984; Freeman et al. 1985; Zorn et al. 1999; Melville et al. 2002) whereas some have no found differences in psychological characteristics between patients with urge and those with stress incontinence (Bodden-Heidrich et al. 1999). Most studies used instruments that measured depressive symptoms rather than instruments that provided major depression diagnoses. Also different study populations may also have led to inconsistent findings.

A study of 115 incontinent patients showed that 60 % of patients with UUI had significant depressive symptoms compared with 14 % of patients with SUI (Zorn et al. 1999). Melville et al. (2002) found that there was 9.2 OR (95 %CI, 1.8-48.09) for major depression that was associated with having urge UI and a 13.5 OR (95 %CL, 3.0-61.5 %) for major depression that was associated with having mixed UI.

In summary, an association between urinary incontinence especially urge or mixed, and depression exists, but the strength of this association depends on both the study population and the instrument used to assess and to classify depression.

### *Factors linking incontinence and depression*

There are different explanatory models of the association between incontinence and depression. UI as a chronic medical disorder may lead to significant anxiety and somatic concerns and depression (Macaulay et al. 1987; Norton et al. 1990; Walters et al. 1990; Lagro-Janssen et al. 1992). Feelings of anxiety and depression concern are normal reactions when individuals have uncomfortable and “bothersome” symptoms.

A psychosomatic background, especially of urge urinary incontinence (UUI) had also been presented once (Frewen 1978) but later research did not support this hypothesis (Norton et al. 1990; Lagro-Janssen et al. 1992). The aetiology of urge incontinence is multifactorial and with the exception of cases in which a neurologic lesion can be demonstrated, about 80 % of UUI causes remained unclear (Payne 1998; Abrams 2002a). Recently the researchers have postulated a new hypothesis that depression and UUI may share a common neurochemical pathogenesis. Experimental studies in animals have revealed that spinal reflex circuits involved in voiding function exhibit a dense serotonergic innervation, multiple 5-hydroxytryptamine (5-HT) receptors, and sensitivity to 5HT-receptor agonists and antagonists, and 5-HT reuptake inhibitors. Activity in the serotonergic pathway generally enhances urine storage by facilitating the vesical sympathetic reflex pathway and inhibiting the parasympathetic voiding pathway. Lowering monoamines such as serotonin and norepinephrine in the central nervous system led to depression and a hyperactive bladder in

experimental animals. Patients with altered central nervous system monoamines may manifest both depression and an overactive bladder (Steers and Lee 2001).

Ongoing animal studies and early human studies have also shown that alpha 1 adrenoreceptors and serotonin (5-HT) receptors in the Onuf nucleus of the sacral spinal cord, facilitate urethral sphincter contraction. Blocking the reuptake of endogenous norepinephrine and 5-HT increases activation of alpha-1 adrenergic and 5-HT2 receptors, enhancing pudendal nerve activity which strengthens the sphincter contraction and could help to prevent urine leakage during stress (Thor 2003).

### *The impact of co-morbid depression on symptom perception and HRQoL*

The effect of depression and panic disorders on incontinence specific HRQoL has been reported by only one study (Melville et al. 2002). Major depression had an independent effect on HRQoL measured by I-QOL, separate from the HRQoL effects that are associated with UI type and objective test of severity of UI. Compared with the group with no psychiatric diagnosis, the group of patients with coexistent major depression scored significantly poorer on I-QOL total score and the avoidance and limiting behaviour, psychosocial impact, and social embarrassment subscale scores. Co-morbid major depression significantly increased patient's reporting of UI severity, despite similar demographic, medical illness, and UI clinical parameters (Melville et al. 2002).

## HRQoL as an outcome measure in the assessment of incontinence treatment effectiveness

The measurement of the impact of different incontinence treatments on HRQoL is important not only from the patient's point of view but also in the assessment of effectiveness, cost-effectiveness and quality of public health. The International Continence Society's committee for the standardisation of outcome measures in clinical trials of continence care has strongly recommended the inclusion of quality of life data (Lose et al. 1998). However, data from validated and reliable generic or condition specific quality of life measures has been rarely reported.

The treatment of SUI include various physical therapy techniques and several surgical interventions. Pelvic floor muscle training, without known complications and inexpensive treatment, is the most commonly recommended as a effective first-line treatment but only few studies have evaluated the effect of the treatment on HRQoL (Bo et al. 2000; Goode et al. 2003). Adjuncts, such as biofeedback, electrical stimulation or vaginal cones are also commonly used with pelvic floor muscle training although the evidence regarding the effect of adding these treatments to pelvic floor muscle training is limited and HRQoL



was investigated in only two studies (Wyman et al. 1998; Elser et al. 1999; Hay-Smith et al. 2001). Recent trial with 200 women found that multicomponent behavioral training with or/without pelvic floor electrical stimulation and a self-help booklet reduced incontinence and improved HROoL measured by both disease-specific and generic instruments (Goode et al. 2003). Treatment effectiveness was measured immediately after an 8 weeks training program. Based on the short-term results the most common anti-incontinence operations: open colposuspension and tension-free vaginal tape significantly improved women's quality of life (Bidmead et al. 2001; Ward and Hilton 2004) with suggestions that tension-free vaginal tape is a cost effective alternative to colposuspension (Manca 2003). In general, the long-term effectiveness of both conservative and operative treatments on HRQoL is not clear. There is insufficient evidence to fully compare surgery with conservative interventions.

The pathophysiology of symptoms of urge incontinence and other overactive bladder symptoms is commonly multifactorial, and therapy that includes nonpharmacologic as well as pharmacologic interventions has been recommended (Hay-Smith et al. 2002; Ouslander 2004). Few studies have investigated the short-term effect of bladder training on HRQoL. Wyman et al (1997) found in a randomized controlled 6-week trial of bladder training in 123 older women with UI (both SUI and UUI) significant improvement in the HRQoL measured by IIQ and VAS on symptom burden. Burgio et al. (2002b) in a randomised controlled trial involving 222 older women (aged 55-92 years) with UUI treated for 8 weeks by behaviour training with or without biofeedback, reported significant improvements on three HRQoL instruments. There is lack of long-term follow up.

An new treatment option for UUI, posterior tibial nerve stimulation has shown good short-term efficacy in both objective parameters and I-QOL and SF-36 (Govier et al. 2001). Anticholinergic drugs are commonly used to treat UUI and OAB but they have met with severe criticism (Hay-Smith et al. 2002; Herbison et al. 2003). A Cochrane systematic review of anticholinergics for UUI concluded that the use of anticholinergic drugs by people with overactive bladder syndrome results in statistically significant improvement in symptoms but the clinical significance (as in terms of quality of life) of these differences is uncertain (Hay-Smith et al. 2002). Only two recent trials reported some HRQoL measure (Dorschner et al. 2000; Kelleher et al. 2002). For example Kelleher et al. (2002) found in open-label trial (n=838!) that sustained (12 months) treatment with tolterodine provides additional benefits in HRQoL as measured by the KHQ. No treatment differences were detected using the SF-36. It should be noted that in studies with such a large sample size, minor and even trivial differences are often statistically significant but not clinically. The long-term effectiveness of these interventions requires further study. Except evaluation of the effectiveness and cost-effectiveness of tension-free vaginal tape in comparison with the standard surgical interventions (open and laparoscopic colopsuspension, sling, or injectable agents) (Cody et al. 2003) no socioeconomic measures have been reported in other UI intervention trials.

# AIMS OF THE STUDY

The general aim of the study was to establish factors determining the health-related quality of life (HRQoL) impairment and the correlation of treatment-related factors to the change of HRQoL in women referred to a specialized health care unit for symptomatic urinary incontinence.

The specific aims of the present study were:

- psychometric testing of two incontinence-specific health-related quality of life instruments and assessment of functionality of generic HRQoL measure in urinary incontinence (I, II)
- to measure HRQoL impairment among the women studied and its correlation with clinical parameters (II, III)
- to assess the rate of depression and anxiety of the study population and to investigate whether mental state influenced the women's self-perception of urinary incontinence burden and their HRQoL (IV)
- to study the effectiveness of urinary incontinence treatment on HRQoL and its modifying factors (II, III, unpublished data)
- to measure women's physical activity, to assess the change of physical activity after treatment and describe the relationships between incontinence status, physical activity and HRQoL (V)

# STUDY POPULATION

## Patients

Written informed consent was obtained from the participants and the study protocol was accepted by the Ethics Committee of Tampere University Hospital. One hundred and twenty-three consecutive women, referred to the Department of Obstetrics and Gynecology at Tampere University Hospital for symptomatic UI between January 1996 and March 1997 were originally eligible for the study.

Exclusion criteria included: diabetic neuropathy, urogenital prolapse (gradus III), recently diagnosed cancer or other serious chronic conditions that may have caused neurogenic bladder dysfunction, and patients who had undergone incontinence surgery in the last five years. Sixteen women did not wish to participate in the study and 25 were excluded due to the reasons presented in Table 3. Finally 82 patients were left in the study.

**Table 3.** *Reasons for exclusion of patients.*

	N
Urogenital prolapse gr III	6
Previous UI surgery within 5 years	6
Diagnosis of mental disorder	5
Diabetic neuropathy	2
Bladder cancer	1
Physical immobility	2
Normal urodynamics, no clinical signs of urinary incontinence	3

## Control group

The control group consisted of healthy women who reported urinary leakage but did not want any medical intervention. Women were recruited from participants in a PAP smear and mammography-screening programme during 1998/1999 in the town of Lappeenranta and then screened by telephone for eligibility. They participated in our study by completing self-administered surveys, objective and subjective clinical measurements except urodynamic measurements.

# METHODS

## Clinical measurements

All patients were evaluated by history, bimanual gynecological examinations including assessment of prolapses, mucosa status and cough test, urine culture, residual urine measurement, urodynamic evaluation, standardised 48h pad-test and 48 h frequency/volume chart.

During bimanual gynecological examination the doctor assessed by palpation the patients' ability to detect and contract the pelvic muscles. We used three a point scale: 1 no voluntary contraction, 2 weak contraction and 3 good contraction. This was not validated, however, all women sent to physiotherapy underwent re-evaluation by palpation and assessment of pelvic muscle activity using a biofeedback probe.

Leakage of more than 8g/24 h was considered significant (Versi et al. 1996). Urodynamic testing (two-channel) contained filling cystometry with provocation (change of position, running water, walking and coughing), urethral pressure measurement and uroflowmetry in cases with urine residual above 100 ml or symptoms of voiding difficulty. Cystoscopy was performed for all patients with urge incontinence.

The patient's history was quantified using the Urgency Score (US) questionnaire (Kauppila et al. 1982). The US is designed to detect urge incontinence based on patient history. It consists of 10 items scored 0-2. The items include frequency, urgency, urge incontinence, nocturia and inability to stop voiding. The sum of scores  $>7$  indicates a high risk of urodynamically proven urge incontinence.

Patients were divided in two diagnostic groups: stress urinary incontinence (SUI) and idiopathic urge incontinence with or without stress incontinence (UUI( $\pm$ SUI)). SUI was diagnosed on the basis of urodynamics and if the patient had a positive stress test with a comfortably filled bladder in the supine or standing position, US was less than 8 and filling cystometry was normal. Urge incontinence was diagnosed when urine loss followed urgency and cystometrogram showed bladder contractions exceeding 15 cm of water or if we observed increased bladder sensation during filling cystometry, US exceeded 7, in the presence of urine leakage greater than  $> 8\text{g}/24\text{h}$  and absence of SUI.

## HRQoL and symptom severity measures

### *15D - generic HRQoL questionnaire*

The 15D is a generic, highly reliable, sensitive and responsive to change, standardised measure of HRQoL that can be used both as a profile and single index score measure. Its self-administered health state descriptive system is composed of 15 dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress vitality and sexual activity. Each dimension is divided into five ordinal levels (1= best level, 5 = worst level) (Appendix I). The woman chooses from each dimension the level that best describes her health status at the moment. The single index 15D score on a 0-1 scale, representing the overall HRQoL, is calculated from the health state descriptive system by using a set of population-based preference or utility weights (Sintonen 1994a; Sintonen 1995; Sintonen 2001). A change of about  $\pm 0.03$  in the score is clinically (relevant for people in the sense that they feel the difference) or practically important (Sintonen 1994b). The data on the HRQoL of the general population as measured by the 15D were obtained from the Finnish Health Care Survey in 1995/95 (Arinen et al. 1998). The age distribution of women in the survey sample was matched with that of the incontinent women with appropriate weighting.

### *Urinary Incontinence Severity Score (UISS) - disease-specific HRQoL questionnaire*

The Finnish Gynecological Society's urogynecologic working group designed the Urinary Incontinence Severity Score questionnaire (UISS), which has been widely used in clinical practice, to assess symptom severity and the impact of urinary incontinence on everyday life, but psychometric assessment of this instrument was lacking (Mäkinen et al. 1992b) (Appendix II).

The UISS consists of ten questions with a three-point scoring system (0=not at all, 1= sometimes, 2= often, Appendix 1). Items were devised from clinical experience and reviews of the literature. There are four items designed to quantify the amount of leakage and need to use pads and six items referring to the degree to which UI affects aspects of women's daily lives including social interaction, physical activities and sexual function. The questionnaire includes items not pertinent to all patients (work, sexual life). Thus, according to the original assumption, the UISS is expressed as the percentage of the patient's score of the possible maximum produced by the questions the patient answered. Here the sum of the scores is calculated.

### *Specific Visual Analogue Scale (VAS)*

The Visual Analogue Scale used was a 100 mm horizontal line marked from zero to ten on which the patients could mark their own point. The question above the Visual Analogue Scaleline was: “How bothered are you by incontinence at this moment?” The 0 point was explained as “not bothered” and the 10-point as “severely bothered”(Appendix II).

## Psychometric assessment of HRQoL instruments

Standard psychometric methods were used to evaluate reliability (calculation of Cronbach’s alpha) and reproducibility (Steiner and Norman 1995). For the UISS and VAS test-retest reproducibility 39 patients and 25 controls completed the questionnaires twice with a one-week interval.

To assess content validity we measured the levels of missing data, as an indicator of inappropriate questions. Furthermore, to see that all areas of life influenced by UI were recorded, the women completed a separate questionnaire in which they had the opportunity to submit supplementary information about personally important issues not included in the UI severity score questionnaire.

Assessment of criterion validity was problematic because at that time there was no valid urinary incontinence–specific questionnaire that had been accepted as a “gold standard”. Then, UISS was compared with the recordings on 15D and VAS. To evaluate construct validity we compared UISS and VAS between the controls and the patients. We also examined the correlations between UISS, VAS, 15D and clinical measure: the 48-h pad test both in the pre- and post-treatment evaluation.

Responsiveness is studied to ascertain that a given questionnaire reflects a clinically important change in patient condition (Guyatt et al. 1987). The change scores were calculated using the difference between pre-treatment and post-treatment visits. Furthermore, the responsiveness of UISS and VAS was measured by Guyatt’s statistic (effect size), which is the ratio of the mean change score (for each group) divided by the standard deviation for the stable group. The stable group consisted of patients who had no change in the pad weight. A statistic of 1.00 or greater (or –1.00 or less when improvement is denoted by a negative change score) is considered indicative of a measure highly responsive to change (Guyatt et al. 1987; Steiner and Norman 1995).

## Assessment of mental state

Two psychiatrists evaluated the patients’ depression and anxiety using a structured interview version of Hamilton Depression Scale (HDS) and Hamilton Anxiety Scale (HAS) in the version of Bech and co-workers (Hamilton 1959;

Bech 1993). This enlarged HDS consists of the 17 original Hamilton items (1-17) and 18-23 from the Melancholia Scale (Bech 1993). According to the HDS/MES criteria for depression, total scale scores are interpreted as follows: 0-7, no depression; 8-12, minor depression; 13-15, less than major depression; 16 or more, major depression.

Whereas the HAS scores are interpreted as follows: 0-5, no anxiety; 6-14 minor anxiety; 15 or more, major anxiety (Bech 1993). The patients with suspected mental disorder, major depression or anxiety were referred to psychiatric treatment.

## Assessment of physical activity

Data on physical activity, at baseline and one year after treatment, was collected using two different methods: a self-report questionnaire (Mälkiä et al. 1988; Mälkiä et al. 1994) and an electronic motion sensor: Caltrac accelerometer (Pambianco et al. 1990) worn by the women for one week.

### *Questionnaire*

The women were asked to assess physical activity at work and leisure during the preceding 12 months by completing the same questionnaire which was used in the Mini-Finland Study (Mälkiä et al. 1988; Mälkiä et al. 1994). Complete questionnaires are presented in Appendix III. Physical activity at work, leisure and in sport were expressed in METs (metabolic unit). One MET is defined as the energy expenditure for sitting quietly, which for the average adult is approximately 1 kcal x kg<sup>-1</sup> body weight x h<sup>-1</sup> (Ainsworth et al. 1993; Jacobs et al. 1993). Physical activity at work was assessed according to a 7-point scale range from 0= not at work (1.5 MET) to 6 =very heavy manual work (10 MET) accompanied by illustrations and descriptions of the various types of work corresponding to each scale point (Edholm 1967).

Exercise during leisure was first graded into 3 levels: 1 little physical exercise; 2 physical exercises in connection with other hobbies or irregular physical exercise and regular physical exercise. As regards regular physical exercise questions were asked about the type of activity or sport and about the frequency, duration and intensity, the latter being structured according to feelings of getting out of breath and of sweating. As regards exercise while going to work, questions were asked in three categories: travel by motor vehicle, bicycle, or on foot during summer and winter separately. Each activity level was changed into a corresponding MET (American College of Sports Medicine 1986; Mälkiä et al. 1988; Ainsworth et al. 1993).

From the different MET values we quantified: the energy intensity at work, the highest and mean intensity during leisure time, the mean of intensities while



going to work, the sum index of these three intensities and the highest MET value from all activities.

### *Caltrac*

The Personal Activity Computer (Caltrac; Point of View Oy) is a small, portable accelerometer which measures vertical acceleration and deceleration of the body and translates motion into activity scores when worn by human subjects (Pambianco et al. 1990; Miller et al. 1994). It has shown high test-retest reliability and has demonstrated a strong relationship with several measures of energy expenditure in laboratory tests (Miller et al. 1994). Patients wore the Caltrac attached to a belt for seven consecutive days except during sleeping time and registered the Caltrac scores in the diary. The physical activity was divided into three classes: 1) physical activity at work, 2) leisure-time activity (normal living: daily chores, social activity, hobbies) and 3) sport/exercise (Appendix IV).

The activity mode in Caltrac showed the energy expenditure during physical activity expressed in kilocalories. Each time a new class of activity started the women marked the scores in their diaries. Therefore from each individual woman, scores for total physical activity per week, specific scores for work, leisure and sport were obtained. We moreover estimated the highest intensity of physical activity.

## Treatment

After initial evaluation, all patients were given conservative (n=53) or operative treatment (n=27) according to severity and type of UI and based on the prevailing treatment rules. Two patients did not want treatment because they felt better after the first visit.

We referred to physiotherapy well motivated women with mild or moderate SUI (grade I or II) who had a weak pelvic floor muscle and had not been treated previously. The conservative treatment alternatives were pelvic floor exercises accompanied by electrostimulation in some cases. Physiotherapy was carried out and followed through in the physiotherapy department of Tampere University Hospital and usually consisted of 2-3 visits over six months and a follow-up visit six months later. Bladder training and anticholinergic drugs were used for the treatment of women with UUI. Vaginal oestradiol 25 micrograms twice weekly was prescribed for all patients who used neither local oestrogen nor hormone replacement therapy (HRT) before the study. Surgical intervention was undertaken in eight cases of low-pressure urethra (MUCP<20 cm H<sub>2</sub>O) a sling operation, colposuspension was done in 17 cases; one patient had a TVT and one bone anchoring sutures.

## Treatment efficacy assessment

The post treatment evaluation was completed in December 1999. Sixty-six (80 %) patients for study I were re-evaluated 6-21 months (mean 13, SD 3.0) after treatment. Sixty-nine (84 %) patients for studies II-V (52 with SUI and 17 with urge or mixed UI) were re-evaluated 6-21 (mean 13.0, SD 3.0) months after treatment. This included all surgical patients and 31 patients who underwent physiotherapy and 11 patients with pharmacological therapy. Treatment outcome was assessed according to objective parameters, patients' satisfaction and HRQoL measures. For the patients with SUI treatment efficacy was assessed by 48 h pad test, cough test with a comfortably filled bladder in the supine position. In addition patients with urge or mixed incontinence, underwent control cystometry and frequency/volume chart.

## Statistics

Means, range and/or standard deviation (SD) were used to describe continuous normally distributed data. Skew continuous data were described using median, range and/or quartiles ( $Q_1$ ,  $Q_3$ ). Differences in means between the independent groups were tested using Student's t-test and in medians using Mann-Whitney u-test or Kruskal-Wallis test. In the case of normally distributed data the correlation between variables was analysed using Pearson correlation coefficient and otherwise Spearman's rank correlation coefficient was used.

Cross-tabulated data was analysed with Pearson's chi-square test and odds ratio (OR) with 95 % confidence interval (95 % CI).

Internal consistency of UISS was measured using Cronbach's alpha. The test-retest-analysis is based on Spearman rank correlation coefficient. Responsiveness of UISS and VAS was measured by Guyatt's statistic, which is the ratio of the mean change score (for each group) divided by the standard deviation for the stable group. The stable group consist of patients who had no change in the pad weight. A statistic of 1.00 or greater (or -1.00 or less when improvement is denoted by a negative change score) is considered indicative of a measure highly responsive to change.

The differences in means between baseline and follow-up evaluation were tested by paired samples t-test and in medians by Wilcoxon signed rank test and respectively. The change of binary data was tested by McNemar's test.

Linear regression analyses were used to create separate models to explain 15D, UISS, VAS and changes of them between baseline and post-treatment control. Adjusted  $R^2$  ( $R^2$ ) and analysis of variance is used to reflect the overall goodness of fit in linear regression analysis. Stepwise linear regression analysis was used to explore, whether patient characteristics and UI-related clinical parameters explain the 15D score. Univariate regression analyses were used to test the relationship between each potential predictor for both UISS scores and

VAS at baseline. Significant variables of the univariate analyses were selected to the multivariable stepwise regression model.

Potential predictors selected for univariate analyses included: age, type of incontinence, parity, years of menopause, previous operations (hysterectomy, incontinence operation), using HRT, urge score >7, BMI, 48h pad test, frequency of day-time and night-times urination, pelvic muscle examination, atrophic mucosa, cystocele, urodynamics parameters (postvoid residual, MUCP < 25 cm H<sub>2</sub>O, stress incontinence threshold <50 cm H<sub>2</sub>O, first sensation to void, strong sensation, bladder capacity, bladder compliance and detrusor pressure), the HDS and HAS scores, physical activity [based on the questionnaire (MET values) and based on the Caltrac scores].

The above mentioned variables and the UISS and VAS scores in baseline, the change in pad test, HDS and HAS scores after treatment and methods of treatment (conservative versus operative) for women with SUI were selected for regression analysis to find the predictors of change of the UISS and VAS scores.

The limit for significance was set equal to 0.05. In the stepwise regression analysis the limit for significance was set at 0.05 to enter and 0.10 to remove. Data analysis was performed using the SPSS /Win (version 8.0 and Version 10.0) and Statistica/Win (version 6.0) statistical programs.

# RESULTS

## Study population

### *Patients*

Of the 85 women, 82 had objective evidence of UI, 57 patients had SUI and 25 had UUI either alone (n=14), or mixed with stress incontinence (n=11). Patients' characterisation at baseline is presented in Table 4.

**Table 4.** *Patient characteristics at baseline (n=82).*

	n	%
Age (years) mean 52.1; range 28-80		
28-39	10	12.2
40-54	41	51.2
55-69	27	31.7
70+	4	4.9
Duration of symptoms (years) median 7.5, range 1-40		
<1	3	3.7
1-5	32	39.0
6-15	33	40.2
≥16	14	17.1
Parity, median 2, range 0-6		
0	4	4.9
1-2	50	61.0
≥3	28	34.1
Type of UI		
SUI	57	70.0
UUI(±SUI)	25	30.0

Pad test results, age, duration of the incontinence and parity did not differ between incontinence types. Forty eight women [all with UUI( $\pm$ SUI)] completed and returned the 48h frequency/volume chart. Women with UUI( $\pm$ SUI) had higher frequency (mean 9.8, SD 3.0) than those with SUI (mean 7.3, SD 2.5,  $p=0.003$ ). UISS and VAS scores were similar for patients with different types of UI.

### *Control group*

During an initial telephone interview we selected 29 eligible women, (mean age 55, median 55, range 44-68) who had UI but were not bothered by it. Twenty four had stress UI (83 %), 3 urge UI (10 %) and 2 mixed UI (7 %). There was no statistical difference between age of patients and controls ( $p=0.081$ ), or distribution of diagnoses ( $p=0.38$ ).

### *Withdrawals*

Thirteen patients (16%) were lost from one-year follow-up. The patients lost to follow-up had higher urge score [median ( $Q_1$ - $Q_3$ ); 9.0 (6.5-11.0) vs. 5.0 (3.0-8.0)  $p=0.006$ ] and more urge and mixed incontinence than participating patients (62 % vs. 25 %;  $p=0.008$ ). There were no differences between them and other patients in pad test, duration of incontinence, parity, age, hysterectomy, use of HRT and VAS, UISS or 15D score.

## Psychometric assessment of the Urinary Incontinence Severity Score and specific Visual Analogue Scale (I)

### *Reliability*

Internal consistency of UISS measured by Cronbach's alpha for 77 patients and 26 control subjects answering all ten questions was 0.85 and deleting any item did decrease its value. Test-retest Spearman rank correlation coefficient for UISS ( $n=51$ ) was 0.88 ( $p<0.001$ ) and for VAS ( $n=60$ ) was 0.85 ( $p<0.001$ ).

## Validity

### Content validity

When the women were interviewed, they added only very special activities as influenced by urinary incontinence. The mean number of missing items was 2.19 % (range 0 -12). The question referring to work was unanswered by 12 % and that referring to sexual life, by 4 % of subjects.

### Criterion validity

One hundred and ten women completed the UISS, VAS and 15D questionnaires at the same time. At baseline there was a significant correlation between VAS and UISS (n=103; Spearman rank correlation coefficient  $r = 0.73$ ,  $p < 0.001$ ). The UISS and VAS correlation with the total score of 15D was  $r = -0.45$ ,  $p < 0.001$  and  $r = -0.23$ ,  $p < 0.001$  respectively. After treatment the correlation between the scores of UISS and VAS was also strong ( $r = 0.85$ ,  $p < 0.001$ ) and UISS and VAS correlation with the total score of 15D was moderate  $r = -0.50$  ( $p < 0.001$ ) and  $r = -0.40$  ( $p = 0.001$ ), respectively.

### Construct validity

The correlation between pad test and UISS, VAS and 15D at baseline (n=102) was  $r = 0.59$  (Spearman rank correlation coefficient  $p < 0.001$ ),  $r = 0.67$  ( $p < 0.001$ ) and  $r = 0.29$  ( $p = 0.004$ ), respectively. There was no correlation between HRQoL measures and any parameters from the frequency/volume chart (n=76). The mean, median and standard deviation of score on UISS and VAS among control women and patients is shown in Table 5.

**Table 5.** Construct validity.

	UISS patients n=77	UISS controls n=26	Mann- Whitney p-value	VAS patients n=86	VAS controls n=29	Mann- Whitney p-value
Mean	10.8	3.2		7.2	2.3	
(SD)	(3.9)	(1.5)		(2.0)	(1.9)	
Median	11.0	3.0	$p < 0.001$	8.0	2.0	$p < 0.001$
(Q <sub>1</sub> - Q <sub>3</sub> )	(8.0 – 14.0)	(2.0 – 3.0)		(6.0 – 9.0)	(1.0 – 3.0)	

## Responsiveness

Thirty nine patients had diminished pad weight in pad test after treatment (improved), 12 patients had no change (stable) and in five patients pad weight increased (deteriorated). The UISS and VAS in the improved group had responsiveness (Guyatt's) statistics: 1.48 and 1.74, respectively (Table 6).

**Table 6.** Responsiveness of the VAS and UISS by 48-hour pad test.

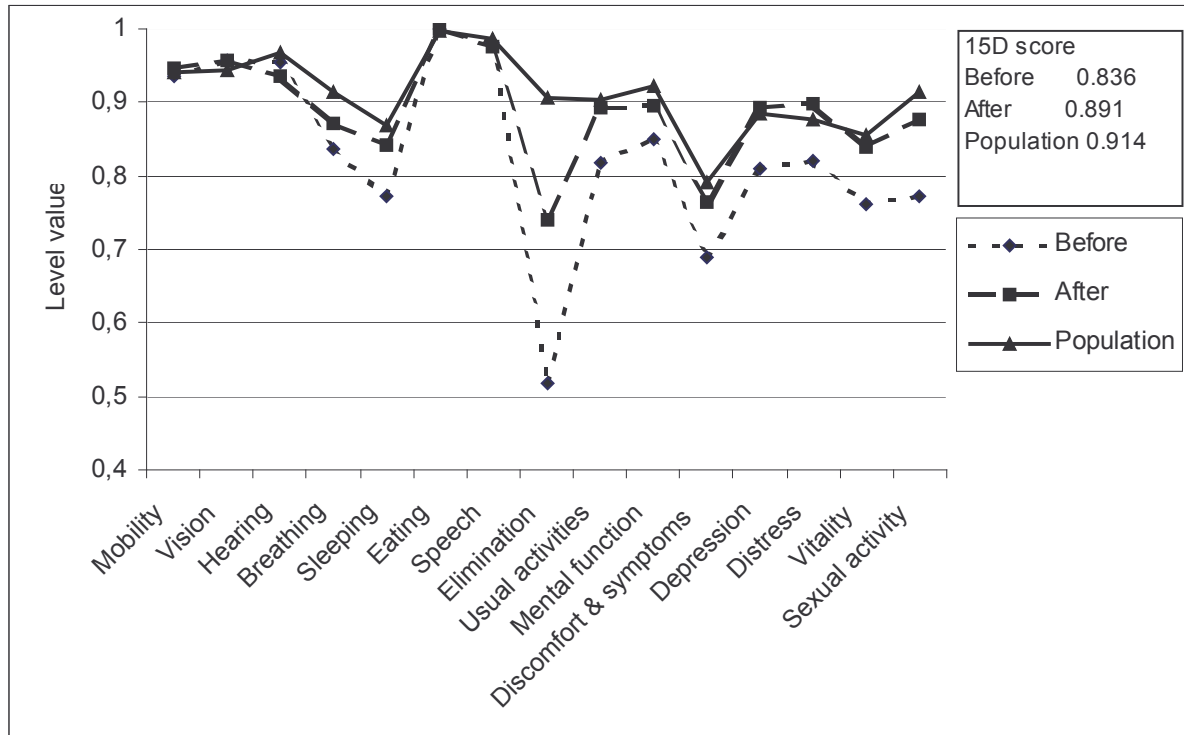
Scale	Stable (N=12)			Objectively improved (N=39)		
	Baseline	End point	Guyatt's <sup>a</sup> statistic	Baseline	End point	Guyatt's statistic
VAS	6.0 (2.1)	4.8 (3.1)	0.58	7.6 (1.9)	2.7 (2.5)	(1.74)
UISS	9.6 (3.2)	7.2 (4.6)	0.56	11.1 (3.4)	4.4 (4.5)	(1.48)

<sup>a</sup> Guyatt's statistic – the ratio of the mean change score (for each group) divided by the standard deviation for the stable group.

## Urinary incontinence impact on the general HRQoL measured by 15D (II)

At baseline the mean 15D score of UI women participating in the intervention study (n=82) was statistically and clinically significantly lower than that of age-matched women in general population (mean 0.836 vs. mean 0.914,  $p < 0.001$ ). The state of the UI patients was statistically significantly worse on the dimensions of elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity. Women with SUI had a statistically and clinically significantly higher HRQoL score than those with UUI ( $\pm$ SUI) mean 0.857 vs. mean 0.789,  $p = 0.002$ ). The state of the latter patients was statistically significantly worse on the dimensions of breathing, elimination, usual activities, distress and vitality (Figure 1 and 2).

**Figure 1.** Mean 15D scores and profiles (mean scores on the dimensions) of the UI patients at baseline and on average 13 months after treatment and of age-matched female general population.



### Correlation between clinical parameters and HRQoL measured by the 15D, Urinary Incontinence Severity Score and specific Visual Analogue Scale (II, III)

The correlations between pad test, frequency, main urodynamics parameters and HRQoL measurements are presented in Table 7. Forty eight women, all with UUI(±SUI) completed and returned the 48h frequency/volume chart. There were no correlations between any parameters of urodynamic findings or the frequency/ volume chart and UISS.



**Table 7.** Correlation of HRQoL scores with urodynamic parameters pad test and frequency expressed in Spearman or Pearson rank correlation coefficient among 82 urinary incontinent women in baseline.

	Urine leakage	Frequency <sup>1</sup>	MUCP	SUI threshold	FS	Bladder capacity	Max pDet	Compliance
VAS	0.46 <sup>***</sup>	0.45 <sup>*</sup>	-0.29 <sup>**</sup>	-0.27 <sup>*</sup>	0.26 <sup>**</sup>	-0.09	0.30 <sup>*</sup>	0.03
UISS	0.25 <sup>*</sup>	0.18	-0.20	-0.20	0.09	-0.11	0.20	0.16
15D <sup>2</sup>	-0.05	0.13	0.06	-0.02	0.14	0.27 <sup>*</sup>	-0.17	-0.25 <sup>*</sup>
ELIM <sup>2</sup>	-0.24 <sup>*</sup>	-0.25	0.19	0.05	0.05	0.17	-0.22	-0.15
							p=0.051	

MUCP = maximal urethral closure pressure; SUI threshold = stress urinary incontinence threshold; FS = first sensation to void; Max pDet = maximal detrusor pressure; ELIM = dimension of elimination of the 15D; <sup>1</sup> patients with Urge±SUI; <sup>2</sup> Pearson correlation coefficient; \* p<0.05; \*\* p<0.01; \*\*\* p<0.001

## Depression and anxiety in urinary incontinent women (IV)

Twenty six percent of the 82 incontinent women had major depression (HDS  $\geq 16$ ). Twenty nine percent had major anxiety (HAS  $\geq 15$ ). Major depression was significantly less common among patients with SUI than patients with UUI( $\pm$  SUI) (Table 8). There were no differences between evidence of major anxiety in these two diagnostic groups.

**Table 8.** *Rates of anxiety and depression among patients according to Hamilton Depression Scale and Hamilton Anxiety Scale interview in different diagnoses of urinary incontinence.*

	Stress incontinence n=57 (%)	Urge incontinence ( $\pm$ stress) n=25 (%)	P value*	Odds Ratio (95 % CI)
Major depression <sup>1</sup>	10 (17,5)	11 (44.0)	0.026	3.69 (1.30-10.49)
Major anxiety <sup>2</sup>	14 (24.6)	10 (40.0)	0.190	2.05 (0.75-5.57)

<sup>1</sup> = Hamilton Depression Scale  $\geq 16$ ; <sup>2</sup> = Hamilton Anxiety Scale  $\geq 15$ ; \* = Pearson chi-square test

Twelve percent women had major depression (HDS  $\geq 16$ ) in the follow-up in comparison with 26 % at baseline (p=0.021). Twenty four percent had major anxiety (HAS  $\geq 15$ ) in the follow-up (versus 29 % at baseline, p<0.065)

Twenty-two patients had severe incontinence defined as UISS  $\geq 14$  points (above Q<sub>3</sub>). These women had more major depression than women who had UISS scores under 14 points (45.5 % versus 18.3 %, p=0.013, OR 3.71, CI 1.28-10.77) . There were no differences between these two groups in amount of urinary leakage, frequency or the presence of anxiety.

According to VAS, 23 patients assessed UI as severe VAS  $\geq 9$  (above Q<sub>3</sub>). The only distinctive parameter in this group was the pad test. Patients in this group had greater urinary leakage (g/24h) than those who assessed under 9 [median (range Q<sub>1</sub>-Q<sub>3</sub>): 60 (34-66) vs 25 (9-45), p= 0.001].

## Predictors of HRQoL impairment measured by the 15D, Urinary Incontinence Severity Score and specific Visual Analogue Scale (II, III, IV, unpublished data)

### *15D*

In multivariate stepwise analysis higher age and urge or mixed incontinence diagnosis predicted poorer HRQoL at baseline measures by 15D ( $R^2 = 0.138$ ,  $F = 6.85$ ,  $p=0.002$ ) (tested were also parity, MUCP, bladder capacity, maximum detrusor pressure and pad test). The model suggests that with age controlled, the HRQoL of UUI( $\pm$ SUI) women is 0.0575 worse than that of SUI women.

### *Urinary Incontinence Severity Score (unpublished)*

In univariate linear regression analyses Hamilton Depression Scale scores ( $\beta=0.30$ ,  $p=0.006$ ), pad test ( $\beta=0.25$ ,  $p=0.033$ ), Urge Score  $> 7$  ( $\beta=0.24$ ,  $p=0.031$ ) were related to UISS at baseline.

In multivariate stepwise regression analysis higher depression score ( $\beta=0.35$ ), US  $> 7$  ( $\beta=0.26$ ) and greater leakage in pad test ( $\beta=0.23$ ) predicted poorer HRQoL at baseline measured by UISS ( $R^2 = 0.21$ ,  $F=7.57$ ,  $p<0.001$ ).

### *Specific Visual Analogue Scale (unpublished)*

In univariate analyses SUI threshold  $<50$  H<sub>2</sub>O cm ( $\beta=0.27$ ,  $p=0.015$ ), MUCP  $< 25$ H<sub>2</sub>O cm ( $\beta=-0.23$ ,  $p=0.040$ ), and marginally significant first desire ( $\beta=0.22$ ,  $p=0.050$ ), urine leakage measured by pad test ( $\beta=0.21$ ,  $p=0.079$ ), the sum of leisure activity measured by Caltrac ( $\beta=-0.22$ ,  $p= 0.073$ ) and detrusor pressure ( $\beta=0.21$ ,  $p= 0.060$ ) were related to VAS at baseline.

Because both stress incontinence threshold and MUCP  $< 25$ H<sub>2</sub>O cm reflect diminished urethral resistance, we chose more standard MUCP for the multivariate model (other tested parameters were first desire, urine leakage, sum of leisure activity measured by Caltrac and detrusor pressure during cystometry).

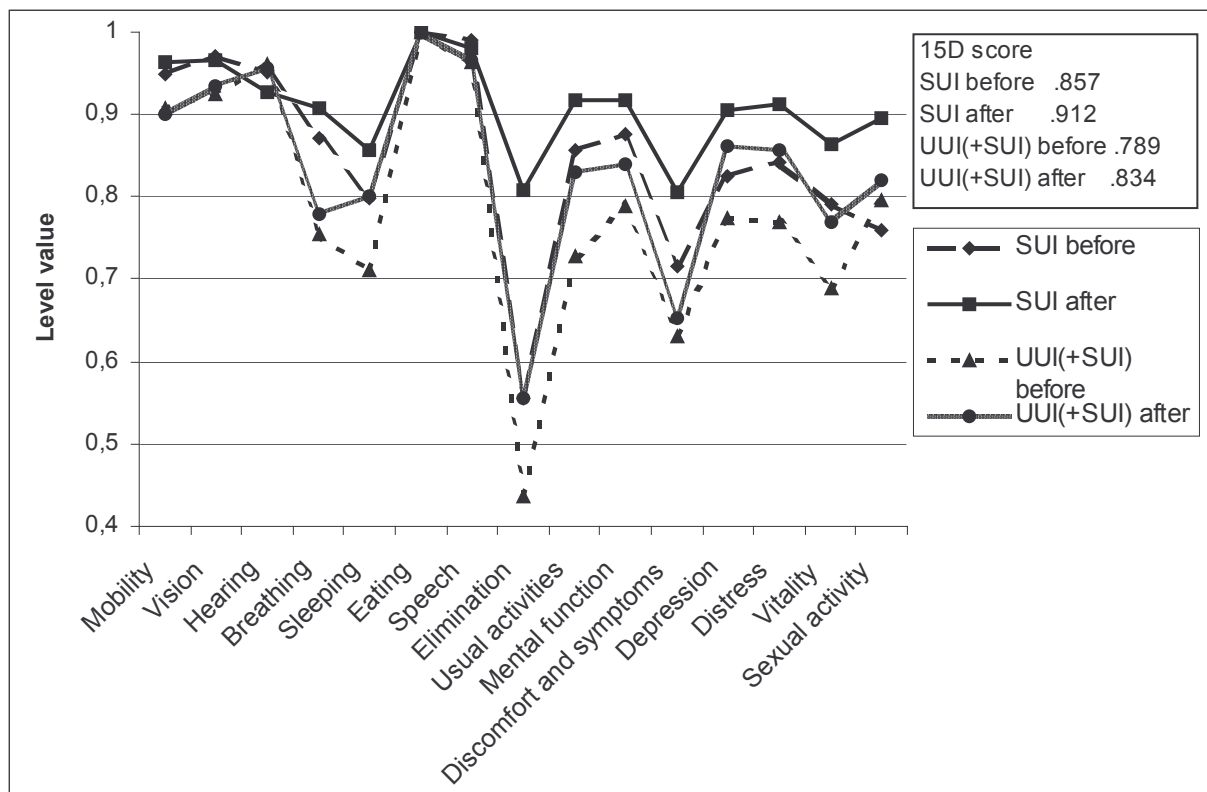
First desire (which reflects urgency) ( $\beta=0.36$ ) and greater urine leakage in pad test ( $\beta=0.28$ ) predicted a more severe degree of burden measured by VAS at baseline ( $R^2 =0.15$ ,  $F=6.19$ ,  $p=0.004$ ).

## Impact of the urinary incontinence treatment on women's HRQoL (II, III)

The 15D scores and 15D profiles (mean scores on the dimensions) in different types of UI before and after treatment are shown in Figure 2. Among SUI

patients there was a significant improvement from baseline on the dimensions of elimination, mental function, discomfort and symptoms, depression, distress, vitality and sexual function. The scores of sexual function improved equally among operated women and those who underwent conservative therapy. The change in the 15D score was both statistically and clinically significant. Among UUI( $\pm$ SUI) patients there was a significant improvement from baseline on the dimensions of distress and vitality only, but the change in the 15D score was both statistically and clinically significant.

**Figure 2.** 15D scores and 15D profiles (mean scores on the dimensions) in different diagnoses of UI before and after treatment.



The HRQoL and VAS scores and clinical parameters before and after treatment in different diagnoses of UI are presented in Table 9. Significant improvement was found in women’s HRQoL measured by UISS and VAS. Urine leakage, measured with pad test was significantly reduced in patients with SUI but not among patients with urge or mixed incontinence. Urinary frequency was reduced significantly in patients with UUI( $\pm$ SUI) incontinence.

In baseline evaluation operated women had more severe leakage than those who were referred to physiotherapy [pad test, median (Q<sub>1</sub>-Q<sub>3</sub>) 59.5 (20.0-83.0) vs. 29.0 (10.0-45.5), p=0.013]. They had higher UISS score [median (Q<sub>1</sub>-Q<sub>3</sub>) 12.0 (9.0-15.5) vs. 10.0 (7.0-12.0), p=0.039] but there were no differences

between VAS scores [median (Q<sub>1</sub>-Q<sub>3</sub>) 8.0 (7.5-9.0) vs. 7.0 (6.0-9.0)] and 15D scores [mean (SD) 0.859 (0.0836) vs. 15D 0.851 (0.0776) (p=0.70)]. There were no differences between other baseline parameters (age, duration, deliveries, years of menopause mental state and any parameters of physical activity).

Operated women had significantly greater change in pad test than those treated conservatively [mean (SD)-66.2 (75.0) vs. -17.4 (25.2) p=0.012]. Also the mean change in UISS [mean (SD) -10.0 (4.3) vs. -3.8 (4.4)] and VAS scores [mean (SD) -6.4 (2.3) vs. -2.5 (2.6)] were significantly bigger in operative group ( p<0.001 for both). However there was no difference between change in total 15D scores among this two treatment groups [mean (SD) 0.059(0.048) vs 0.039(0.01), p=0.24].

Among patients with UUI(±SUI) the mean change in pad test was significantly lower than among SUI patients [mean (SD)2.8(44.9) versus -38.7(57.3), p=0.009]. The mean change in UISS was -2.9(3.4) for UUI(±SUI) and -6.8(5.3) for SUI, p=0.006). The mean change in VAS was -2.6(3.0) and -4.4(3.1) (p=0.045) for UUI(±SUI) and SUI respectively. There was no differences between mean change in 15D scores among these two diagnostic groups (0.046 (0.068) for UUI(±SUI) and 0.049 (0.055) for SUI (p=0.86).

## Predictors of change in HRQoL (II, III, IV, unpublished data)

The changes in pad test correlated fairly well with those in the VAS (r=0.50 p<0.001 Spearman's rho, r=0.36; p=0.006 Pearson), those in UISS total scores (r= 0.42 p=0.001 Spearman's rho; r=0.30, p=0.023) and those in 15D (r=-0.13, p=0.35, Spearman's rho, r=-0.34; p=0.014 Pearson). There was a correlation between change in urinary frequency and change in UISS (Spearman r=0.46, p=0.042) but not between change in 15D or VAS.

### *15D*

In a stepwise regression analysis only the 15D score at baseline and change in urine leakage (pad test) had a statistically significant effect on the change in the 15D score from baseline to post-treatment measurement (other variables tested were age, UMCP<25 cm H<sub>2</sub>O, bladder capacity, duration of UI and type of UI). The lower was the 15D score at baseline (beta=-0.27) and the greater the decrease in urine leakage (beta=-0.36), the greater was the change in the 15D score for the better (R<sup>2</sup> =0.155, F=5.78, p=0.006) (Table 10).

### *Urinary Incontinence Severity Score (unpublished)*

In the univariate linear regression analyses the UISS at baseline (beta=-0.52, p<0.001), HDS measured post treatment (beta=0.35 p=0.004), diagnosis of UI (beta=0.33, p=0.006), change in pad test (beta=0.30, p=0.024) and UMCP<25 H<sub>2</sub>O cm (beta=0.24, p=0.048) were related to change in UISS score before and about 1 year after treatment.

**Table 9.** *Comparison of changes in the baseline and post-treatment UISS, VAS and 15D and clinical outcome according to diagnoses of urinary incontinence.*

	Baseline	Post-treatment	P
SUI			
Pad test g/24H median (Q <sub>1</sub> -Q <sub>3</sub> )	32 (16-60)	5 (2-17)	< 0.001 <sup>1</sup>
VAS median (Q <sub>1</sub> -Q <sub>3</sub> )	8 (7-9)	2 (0.25- 4)	< 0.001 <sup>1</sup>
UISS median (Q <sub>1</sub> -Q <sub>3</sub> )	11 (8-13)	3.5 (0.75-7)	< 0.001 <sup>1</sup>
15D mean(SD)	0.863 (0.0751)	0.912 (0.0843)	<0.001 <sup>2</sup>
Elim	0.578 (0.25)	0.808 (0.199)	<0.001 <sup>2</sup>
UUI(±SUI)			
Pad test g/24 h median (Q <sub>1</sub> -Q <sub>3</sub> )	26.5 (7.7-62.7)	6.25 (0-37)	0.591
Frequency median (Q <sub>1</sub> -Q <sub>3</sub> )	9 (7-12)	6 (5-9)	0.034 <sup>1</sup>
First sensation ml median (Q <sub>1</sub> -Q <sub>3</sub> )	130 (72-175)	200 (100-250)	0.017 <sup>1</sup>
Bladder capacity median (Q <sub>1</sub> -Q <sub>3</sub> )	400 (300-490)	450 (440-500)	0.013 <sup>1</sup>
VAS median (Q <sub>1</sub> -Q <sub>3</sub> )	7 (5.5-8.5)	5 (1.5-6.5)	0.004 <sup>1</sup>
UISS median (Q <sub>1</sub> -Q <sub>3</sub> )	12 (7-14)	8 (4-12)	0.002 <sup>1</sup>
15D mean (SD)	0.788 (0.0708)	0.834(0.0788)	0.013 <sup>2</sup>
ELIM mean SD	0.448(0.183)	0.556(0.230)	0.12 <sup>2</sup>

*1 Significance by Wilcoxon ranked paired test.; 2 Significance by Student's paired test*

In multivariate stepwise regression analysis the stress incontinence diagnosis the higher UISS at the baseline and lower depression score measured post treatment had a statistically significant effect on the change in the UISS from baseline to follow-up for the better (n=55, R<sup>2</sup>=0.34, F=10.16, p<0.001) (Table 10).

### *Specific Visual Analogue Scale (unpublished)*

In univariate linear regression analyses the VAS baseline (beta=-0.48, p<0.001, HDS total scores at baseline (beta=0.39, p=0.001) and in followed-up (beta=0.30, p=0.013), HAS total scores at baseline (beta=0.37, p=0.002) and in followed-up (beta=0.31, p=0.012), change in pad test (beta=0.35, p=0.007)

diagnosis of UI (beta=0.24, p=0.047) and MUCP<25H<sub>2</sub>O cm (beta=0.24, p=0.048) were related to the change in VAS.

The higher VAS scores at the baseline, lower depression score measured post treatment and the greater change in pad test had a statistically significant effect on the change in the VAS from baseline to follow-up for the better (n=55, R<sup>2</sup>=0.37, F=11.77, p<0.001) (Table 10).

**Table 10.** *Linear regression model explaining the variation in the change in 15D, UISS and VAS*

		beta	p
$\Delta 15D$	R <sup>2</sup> 0.16		
	- Change in pad test	-0.36	0.007
	- 15D score at baseline	-0.27	0.037
$\Delta UISS$	R <sup>2</sup> 0.34		
	- UISS at baseline	-0.48	p<0.001
	- HDS post treatment	0.37	p=0.002
	- SUI diagnosis	0.25	p=0.031
$\Delta VAS$	R <sup>2</sup> 0.37		
	- VAS at baseline	-0.43	p<0.001
	- HDS post treatment	0.33	p=0.003
	- Change in pad test	0.23	p=0.041

In stepwise linear regression analysis, the operative treatment of SUI predicted lower score in both VAS (R<sup>2</sup>=0.36, F=15.3, p<0.001) and UISS (R<sup>2</sup>=0.28, F=11.0, p<0.001) in follow-up, than conservative treatment. The model suggests that, when the baseline scores were standardised, the VAS among the operated group was 3.4 lower than in the group treated conservatively. The UISS score was 4.60 lower in the operated group. Operated women with SUI had 0.020 higher 15D scores in follow-up than those treated conservatively, but the difference was neither statistically, nor clinically significant.

## Physical activity of incontinent women (V)

All 82 women correctly completed the questionnaire about their physical activity. During the pre-treatment investigation three of the Caltracs mechanically failed and nine women did not complete the diary completely.

Finally, there was data on 72 women available at baseline. After treatment all Caltracs worked but only 50 (72 %) women completed the diary correctly.

Of all patients 26 (31.7 %) were not at work, 20 (24.4 %) were working in occupations assessed as light or other sedentary work, 30 (36.6 %) physically light standing or medium heavy work and 6 (7.3 %) heavy or very heavy manual work.

Eleven (13.4 %) reported little leisure time exercise, 34 (41.5 %) exercised irregularly or in connection with other hobbies and 37 (45.1 %) women exercised regularly. There were no differences between those groups in age, amount of urine leakage, parity and duration of symptoms, urodynamics parameters, frequency, and quality of life scores. Twenty-one (25,6 %) of all women reported exercise of more than three times per week.

Walking was the most popular kind of regular physical exercise among incontinent women, undertaken by 65 % of women (the next were: fitness gymnastics (46 %), bicycling (41 %), swimming (32 %) and cross-country skiing (27 %).

There was no linear correlation between physical activity and urine leakage (likewise among women with SUI) but incontinent women with leisure time activity above  $Q_3$  ( $\geq 6$  MET,  $n=23$ ) had more leakage in 48-hour pad test than others. They were younger [median ( $Q_1$ - $Q_3$ ) 48 (43-52) vs 52(45-62),  $p=0.039$ ] and they had smaller body mass index [median ( $Q_1$ - $Q_3$ ) 26(23-27) vs 27 (25-32),  $p= 0.023$ ] than others. They had a similar UISS and VAS scores. The contractility of pelvic floor muscles did not correlate with the intensity of the physical activity.

One year after treatment, there was no change in any parameters of physical activity parameters measured by Caltrac or assessed as METs on the basis of the questionnaires. The physical activity of those women who reported only little or irregular physical exercise before treatment, did not increase. The physical activity habits among women who were completely dry (pad test negative  $n=37$ ) likewise remained unchanged (Table 11). There were no more regular exercisers among those objectively cured women, than among those suffering from urine leakage (pad test greater than 8g/24h) (41 % vs. 36 %  $p= 0.69$ , OR 0.80, CI 0.28-2.33). We analysed all data separately for women with SUI and those with UUI( $\pm$ SUI) incontinence but the results remained the same.



**Table 11.** Comparison of changes at baseline and post-treatment in physical activity parameters among women completely continent after treatment (unpublished).

	At baseline median (Q <sub>1</sub> -Q <sub>3</sub> )	Post-treatment median (Q <sub>1</sub> -Q <sub>3</sub> )	p
Cure N=37			
MET sum <sup>3</sup>	9.3 (6.1-12.2) n=37	9.0 (5.9-12.2) n=34	0.31
MET sport <sup>4</sup>	4.0(3.0-5.4) n=37	3.8(3.0-4.8) n=35	0.21
Caltrac sum (kcal/week) <sup>5</sup>	3605(2682-4915) n=32	3181(2372-4246) n=26	0.089
Caltrac sport (kcal/week) <sup>6</sup>	540(15-1108) n=32	477(0-788) n=26	0.30

*P* - values based on Wilcoxon ranked paired test; <sup>1</sup> sum of METs at work, leisure and sport; <sup>2</sup> mean METs at sport; <sup>3</sup> sum of Caltrac scores at work, leisure and sport; <sup>4</sup> sum of Caltrac scores at sport

# DISCUSSION

## Evaluation of measurement of HRQoL

Health-related quality of life is a subjective measure; the instruments used to quantify it take the form of questionnaires and as such require validation to confirm their accuracy. For an assessment questionnaire to be accepted it must be simple, relevant and capable of rapid completion. Moreover, the language must be clear to the treatment population. If a questionnaire in a different language is used, back-translation, pre-testing and cultural adaptation is required (Guyatt et al. 1993).

### *Urinary Incontinence Severity Score*

At the time we were planning this study there were no, valid urinary incontinence specific, HRQoL instruments available. The UISS was developed by the Finnish Gynecological Society's urogynecological the working group in 1992 on the bases of clinical experiences (Mäkinen et al. 1992b). Although the UISS has not been validated it has been widely used in clinical practice to measure the impact of UI on women's daily lives and to guide the level of treatment rather than to assess treatment outcome from the patient's point of view.

There are three categories of incontinence specific HRQoL questionnaires: general, urge or OAB-specific and stress UI specific. The UISS worked well with various types of UI and this made it possible to use it amongst adult women independent of diagnosis of UI. Of general instruments KHQ is well-validated for use in incontinent women with stress, urge and OAB, and men with OAB (Kelleher et al. 1997; Reese et al. 2003). I-QOL and IIQ also appear to be reliable and valid for use in women with both diagnoses of UI (Wagner et al. 1996; Patrick et al. 1999a).

This is important that questionnaires must be tested in the population in which they are to be used. For example, the validity of the IIQ questionnaire (long and short forms) which was originally tested among patients referred to a speciality incontinence unit, was recently questioned in women without urodynamic diagnosis (Harvey et al. 2001). We had tested UISS among two

different female populations (control group and intervention group) but the functionality of UISS among women in primary health care needs further evaluation.

The UISS consists of only a few (central) simple questions. Brevity is a very important criterion for a measure before it is accepted widely among researchers and especially busy clinicians. The completion of the long version of the IIQ (30 items) (Shumaker et al. 1994), the I-QOL instrument (22 items) (Patrick et al. 1999) or the KHQ (21 items) (Kelleher et al. 1997) is time consuming and interpretation of the results is difficult for the clinician. The short version of IIQ is concise but does not include a domain about sexual life (Uebersax et al. 1995); a very important aspect of incontinent women's life. Furthermore, no validity and reliability analyses for IIQ-7 were given.

The UISS was used as a self-administered questionnaire which is the most practical, inexpensive method, and implies that patient capability (mental status, language, reading and writing ability and so forth) has been considered when using the questionnaire (Aaronson 1989).

The five items of UISS (items 4-8), which properly address the quality of life, assess: role limitations (items 4, 5), embarrassment (6); physical and social limitations (7), and sexual life (8). There is, however, a lack of domains about sleep disturbance, which is reported especially by women with urge symptoms. Instead, item number 9, referring to irritation of external genital organs, which is not a very specific problem for UI, rather for the use of pads, could be replaced by the more relevant above mentioned issue of UI.

Four other items (1, 2, 3 and 10) assess severity of symptoms and the use of protection. Questions 2 and 3 are applicable only to women with stress UI. There is no specific question for established severity of urge incontinence. Question 1 is unclear; it would be more precise (illustrated with examples) for urine leakage associated with a strong desire to pass urine or urgency. OLD: Do you experience urine leakage not related to effort or position (for example lying down) NEW (proposal): Do you experience urine leakage associated with a strong desire to pass urine, or not related to effort or position?

Responsiveness, which means sensitivity to detect clinical change, is the most important attribute of instruments used to assess the impact of treatments on the quality of patients' lives (Guyatt et al. 1987).

Of the general incontinence instruments, the IIQ has shown responsiveness in all domains over a 3-month treatment period (Shumaker et al. 1994). The IIQ-7, in a recently published study, was not responsive to objective change in continence status (FitzGerald et al. 2001). The I-QOL has shown poor/moderate (effect size 0.4) responsiveness in a short, two-week treatment period (Patrick et al. 1999). The responsiveness of the KHQ was strictly assessed only in patients with OAB (Reese et al. 2003) but it has also worked well in intervention study among women with SUI (Bidmead et al. 2001). In this study the UISS has been shown to be extremely sensitive to changes in our intervention study.

The validation of HRQoL questionnaires is a lengthy process and concepts of validity and responsiveness may change. Validation does not end when the first

study with data concerning validity is published but continues with repeated use of an instrument (Guyatt et al. 1993). The UISS proved to be a sound HRQoL instrument which we evaluated using standard techniques in health measurement. It is applicable for research and very useful in clinical routine. However, to improve content and construct validity the UISS needs some of previously suggested revisions and it should also be tested among incontinent women in primary health care.

### *Specific Visual Analogue Scale*

The Visual Analogue Scale is a generally accepted tool in research concerning measurement of the impact of disease and effects of medical interventions on HRQoL and has also been used in UI studies (Revill et al. 1976; Parkin and Davis 1986; Frazer et al. 1989; Vinsnes and Hunskaar 1991; Bo 1994; Seim et al. 1997; Dowell et al. 1999; Fultz et al. 2003; Melville et al. 2003). Studies on the reliability and responsiveness of the VAS designed to measure subjective evaluation of female UI, are so far lacking.

In this study we wanted to establish the bother caused by urine leakage and on this issue the VAS was capable of discriminating between different levels of perceived severity in the control and patient groups. The high correlation between UISS and VAS also proves its good construct validity. The VAS demonstrated responsiveness to change over time.

The weakness of HRQoL questionnaires is their dependence on the culture and language in which they were developed (Guyatt et al. 1993). Visual Analogue Scale could be an efficient language-independent instrument that provides simplicity of use, clarity and ease of interpretation for the clinician.

Although VAS does not replace a proper quality of life instrument it is useful for the rapid appraisal and follow-up of women with UI independent of the culture, language and intellectual level of patient and can be used complementary to generic or condition specific questionnaires.

### *15D*

The HRQoL is an important outcome in economic evaluation. This emphasises the necessity of using valid, reproducible, and above all, responsive generic HRQoL instruments.

In this study the 15D proved to be sensitive in detecting changes in HRQoL due to treatment of UI. The SF-36 has been the most frequently used generic HRQoL instrument in the intervention studies among women with UI. However, responsiveness to change has been reported to be poor in several studies (Sand et al. 1995; Johannesson et al. 1997; Kobelt et al. 1999; Burgio et al. 2002b; Kelleher et al. 2002; Goode et al. 2003). Sand et al. (1995) assessed the efficacy of transvaginal electrical stimulation in treating women with SUI. A significant

benefit was demonstrated by objective and subjective (severity of UI on a Visual Analogue Scale) measures, but no improvement was seen in the SF-36 scores. The SF-36 has also been integrated into two large willingness-to-pay surveys and a recently published intervention study of patients with overactive bladder (Kelleher et al. 2002). In these studies, despite the fact that treatment interventions led to an improvement in HRQoL measured by disease-specific instrument, there was no improvement in the SF-36. The responsiveness of NHP, another generic instrument that has been used among UI patients, has not been reported.

The 15D as a profile measure performs clearly better than the EuroQoL-5D. Moreover, the 15D is particularly valid for deriving quality-adjusted life years (QALYs) gained for resource allocation purposes (Sintonen 2001). The 15D combines the advantages of a profile and single index score measure and appears to be responsive to change in the treatment of UI.

## Urinary incontinence impact on general HRQoL

According to our results, and results from many previous studies, (Grimby et al. 1993; Dugan et al. 1998; Donovan et al. 1999; Coyne et al. 2003) UI impairs women's general HRQoL significantly. To put the average baseline 15D scores of UI patients into perspective, depression patients (average age 48 years) had a baseline score of 0.72 (Lönnqvist et al. 1994), gastrointestinal surgery patients (average age 53) a baseline score of 0.88 (Räsänen et al. 2001) and a representative sample of type 1 diabetes patients with long-term complication (aged 45-54 years) a score of 0.84-86 (Hahl et al. 2002). Thus the impairment due to UI is of the same magnitude as that caused by many other prevalent chronic disorders. With ageing of the population the prevalence of UI will increase. Significant resources are needed to serve women with UI. Luber et al. (2001) estimated that the demands for the care of UI and other pelvic floor disorders will increase at twice the rate of growth of the same population. Furthermore, UI is under-reported and under-treated (Cheater and Castleden 2000). Knowledge of UI and its treatment is increasing. The younger generation of women are not embarrassed to speak about incontinence. Urinary incontinence will no longer be tabu. New, more effective treatment options and mini-invasive operative procedures will be developed.

We need cost-effective programmes to care for patients with UI and especially for the appropriate positioning of care stratification: between speciality and primary units, between physicians and therapists (Luber et al. 2001).

# Predictors for HRQoL impairment of incontinent women

## *Diagnosis of urinary incontinence*

In this study we have shown that both urodynamically diagnosed urge incontinence and the amount of bladder symptoms measured by Urgency Score were independent predictors for poor quality of life measured by both instrument generic 15D and disease specific UISS. This is in accordance with most studies (Wyman et al. 1987; Hunnskaar and Vinsnes 1991; Grimby et al. 1993).

However, there are also reports finding no difference between incontinence types (Burgio et al. 1991; Samuelsson et al. 1997). Samuelsson et al. (1997) found no difference between the impact of stress and urge incontinence on the aspects of well-being studied. Both studies are population studies and their samples consisted of the primary health care patients and diagnosis of UI was established on the basis of anamnesis, which probably explained the differences of the findings.

The greater effect of UUI( $\pm$ SUI) on HRQoL may be associated with several factors: the urine loss may be less predictable, the volume may be greater, and it may affect sleep to a greater extent (Wyman et al. 1987).

## *Urine leakage*

The correlation between urine leakage and VAS, UISS and 15D depends on the study population. In the first study, which consisted of women referred to a specialist unit and controls who did not want any medical intervention, the correlation was good for VAS and UISS and moderate for total 15D scores. However, in the intervention study group, the correlation was moderate for VAS, weak for UISS and there was no correlation between total 15D scores and amount of leakage.

Our findings are in agreement with most of the previous results that in the population based study, UI severity correlates well with HRQoL impairment. However, in the populations referred to the incontinence clinics, correlation between the number of incontinence episodes or pad test and the scores of disease-specific HRQoL measures (Norton 1982; Wyman et al. 1987; Theofrastous et al. 1995; Nager et al. 2001) was weak or moderate and negligible for generic measures (Hunnskaar and Vinsnes 1991; Kelleher and Cardozo 1993; Shumaker et al. 1994). The tolerance of urine leakage has a wide spectrum. For example, the recently published Yalcin and Bump study (2003) revealed that amongst the women who responded to the Global Impression Severity scale, those who reported normal urinary tract condition had 12.9 (mean) incontinence episodes per week and median stress pad test 15g (range 2-399g), and those who

reported mild had 14.4 episodes per week and 9g (2-313) urine leakage in pad test.

In this study from the clinical measures the amount of urine leakage was the best although modest predictor of HRQoL impairment.

### *Bladder factors*

To the best of our knowledge, there is no previous data comparing validated HRQoL instruments with cystometry. In this study, from the cystometric parameters first desire and maximal detrusor pressure correlated with VAS, bladder capacity and compliance correlated, although weakly, with the 15D score. Also frequency correlated with VAS. Patients with detrusor overactivity incontinence often suffer from greater leakage and those with a small bladder capacity usually suffer from severe symptoms, which significantly disturb both daily activities and sleeping.

Contrary to what might be expected, the apparent severity of UII justified by cystometry does not correlate with impact on women's HRQoL measured by UISS.

### *Urethral factors*

From the urethral pressure parameters maximal urethral closure pressure and low stress incontinence threshold correlated with VAS registration of bother from incontinence, but there was no correlation with UISS and 15D.

There is limited data on comparison of urethral pressure measurement findings with validated HRQoL instruments. Theofrastous et al. (1995) found no correlations between any urodynamic parameters and pad test and two standard instruments, UDI and IIQ, among patients with SUI. Nager et al. (2001) likewise found no correlation between MUCP and leak point pressures with pad loss or HRQoL measures among 52 women with SUI.

Probably VAS and UISS, although both valid, reflect different aspects of UI and cannot be used alternatively but rather to complement each other. The correlation between urodynamics and HRQoL measures is weak and depends on the instruments used. Our results corroborate that physiological measures provide information for clinicians, but they take no account of patient's perceptions of their problems.

Filling cystometry with provocation is the crucial diagnostic test to examine bladder function and pathophysiology of UI. The benefits from urethral pressure measurement are small. Both urodynamics examinations provide only little information about the severity of symptoms and impact on HRQoL.

## *Depression*

In our study depression was a strong predictor of quality of life impairment. There is only one study examining the impact of co-morbid psychiatric disorders on the HRQoL of UI women (Melville et al. 2002). The authors found that in women with urge or mixed UI, co-morbid major depression is associated with symptom amplification, additional impact, and additive functional impairment. Women have made the decision to seek treatment on the basis of their own subjective experiences. Based on our findings, depression plays an independent role in the patient's subjective assessment of severity of UI and may determine seeking treatment.

The high rate of severe depression (26 %) and anxiety (29 %) in our highly selected study population is in accordance with some previous studies, which have indicated that patients with UI were more depressed and anxious than the normal population (Macaulay et al. 1987; Black et al. 1998; Zorn et al. 1999; Dugan et al. 2000; Melville et al. 2002; Nygaard et al. 2003) and more than the health centre patients (with prevalence of severe depression varied from 5.1 % to 9.2 %) (Dhadphale et al. 1989; Poutanen 1996). Our prevalence for psychiatric disorders among incontinent women is significantly higher (26 % vs 10 % for major depression and 29 % vs 12 % for anxiety) than among a general obstetric-gynaecology outpatient population (Sundström et al. 2001). The rate of major depression in our patients is comparable to that found in speciality clinics with other chronic diseases such as coronary disease, diabetes mellitus or gastrointestinal disorders (Hance et al. 1996; Walker et al. 1996; Anderson et al. 2001) which confirms the importance of considering psychiatric co-morbidity in patients seeking speciality care.

In this study women with urge and mixed incontinence were more likely to have major depression than those with SUI. Comparison between studies is very difficult because of methodological variations and studied populations. Some authors have found no increased rate of depression in urge incontinent patients in comparison with those with stress UI (Lagro-Janssen et al. 1992; Chiara et al. 1998; Bodden-Heidrich et al. 1999). Recent studies based on more precise diagnostic evaluation, however, have shown significantly higher prevalence of depression in UUI than in SUI patients (Zorn et al. 1999; Dugan et al. 2000; Melville et al. 2002). In our study, experienced psychiatrists using a precise methods- structural interview, carried out depression and anxiety assessment, which is a method considerably superior the self-report questionnaires usually used in previous studies (Maier 1990; Paykel 1990).

Despite the non-causal nature of this study, our results suggest a strong association between idiopathic urge incontinence and depression. On the basis of animal studies, it is possible that both depression and incontinence may share a common hormonal biochemical, or neurological pathway, given recent evidence that serotonergic pathways are linked to both clinical depression and the regulation of voiding function (Steers and Lee 2001). Among the drugs modulating the bladder function through 5-HT receptor, duloxetine, a potent and



selective inhibitor of 5-HT and norepinephrine is presently undergoing clinical trials for stress urinary incontinence (Viktrup and Bump 2003). Prolonging the effect of naturally released norepinephrine and serotonin with duloxetine could also augment the body's normal processes for controlling urine storage and micturition (Khaled and Elhilali 2003). 5-HT receptors antagonists and re-uptake inhibitors represent important targets for the development of new treatments of OAB and UI.

On the basis of actual knowledge, screening for depression, is recommended for patients with UI. There are many different screening methods for depression but a recently published study from New Zealand (Arroll et al. 2003) presented a questionnaire which consisted of only two questions. These would detect most cases of depression in general practice and also offer suitable methods for screening UI women.

Identification of depression is important not only because it causes significant symptomatic distress but also because co-morbid major depression may impair the prognosis of diseases and influence compliance with treatment (Gill and Hatcher 1998; DiMatteo et al. 2000). Patients with major depression may manifest symptom amplification and are more likely to report incontinence, and seek treatment, than non-depressed incontinent women. The presence of depression can predict those for whom treatment is less likely to succeed. Incontinent women with co-morbid depression and anxiety may be difficult to motivate to follow through especially with long conservative treatment options such as bladder drill and physiotherapy. When age, gender and severity of medical illness are controlled, the direct medical costs of patients with depression are approximately 50 % higher than for patients who do not have depression (Unutzer et al. 1997).

Although it is important not to overestimate the significance of depression in urge incontinence; new understanding of the relationship between the two conditions has important implications for treatment. Future investigation will hopefully show whether idiopathic urge incontinence and depression share a common pathogenesis.

## Impact of incontinence treatment on HRQoL and its modifying factors

In our longitudinal study re-evaluation took place approximately 13 months after treatment and especially the follow-up of the women with urge and mixed incontinence was considerably longer than in the previous studies. A significant improvement was found in women's HRQoL measured by 15D, UISS and VAS.

Among patients with SUI the HRQoL after treatment the total score of the 15D was about the same as in the age-matched general female population. The sexual activity of women with SUI improved dramatically. Interestingly, both operative treatment and pelvic floor rehabilitation led to significant improvement

in sexual activity. Few earlier studies have shown that UI adversely affects sexual function (Sutherst 1979; Hilton 1988; Norton et al. 1988). On the basis of our findings, SUI appears to have a significant, if not widely appreciated effect on woman's sexuality.

The general HRQoL (measured by 15D) of women with UUI( $\pm$ SUI) improved significantly after treatment, but in spite of this they did not achieve the HRQoL level of women with SUI at baseline.

The role of patient's personal experience (and perhaps also placebo effect) of the impact of UUI on HRQoL emphasised the fact that, although there was no significant decrease in the urine leakage after treatment, the patients experienced a subjective improvement of their symptoms measured by all three instruments. Similarly Wyman J et al. (1997) found only a modest correlation between changes in HRQoL variables and changes observed in incontinence frequency and pad test weights in a short-term randomised controlled 6-week trial of bladder training in 123 older women with UI.

Treatment of patients with UUI( $\pm$ SUI) is more complicated than treatment of patients with SUI. Few published studies suggest that OAB is a chronic condition that persists urodynamically and symptomatically (Garnett and Abrams 2003). At present treatments do not provide a cure, only alleviation of symptoms. In a recent systematic review of 32 trials involving 6800 participants, Herbison et al (2003) found significant but relatively small differences between widely used anticholinergic medication and placebo in objective severity of urge UI. In an other review there was no long-term improvement in urge patients' HRQoL (Hay-Smith et al. 2002). Our treatment protocol for urge or urge-predominantly mixed cases was also deficient but based on the prevailing treatment rules. To attain better outcomes, it will probably be necessary to combine different treatments, which demands co-operation between patients, physicians and physiotherapists (Burgio 2002a) but the effectiveness and cost-effectiveness of those interventions needs further evaluation.

The main goal of UI treatment is improvement of quality of life. The knowledge of predictors of HRQoL change and of impact of different treatment on HRQoL is essential for selecting an appropriate intervention to achieve the best possible health effects for patients.

To put together all predictors revealed, this study has shown that the UI diagnosis, actual amount of urine leaking, and women's depressiveness have an important independent aspect in determining treatment success although predictors varied depending on the HRQoL instruments used. This should be considered, especially in economic analyses of incontinence treatment so that the result may depend on the HRQoL instrument used. Urinary incontinent women may have several concomitant disease-connected factors impairing their quality of life. These may have profound undiscovered influences on the perceived result of treatment. The presence of co-morbid depression must be considered when there is a discrepancy between the patient's dissatisfaction and objective findings of UI.

There are few studies about the influence of depression and anxiety on the outcome of UI treatment (Rosenzweig et al. 1991; Berglund and Fugl-Meyer 1996; Berglund and Lalos 1996). Berglund and Lalos found (1996) that depression measured BDI (Beck Depression Inventory) scores or symptoms of depression in women after surgery for SUI rose postoperatively even when incontinence was corrected (Berglund and Lalos 1996). Rosenzweig et al. (1991) reported that depression became worse after unsuccessful surgery but was not statistically improved with a successful procedure. It is not possible to conclude from the prevalence data whether depression is a result of previous failed incontinence treatment or the reason for the failure thereof.

The study population in our data represents a fraction of incontinent patients seeking ultimate relief from their symptoms through specialized health care. In this population with relatively severe UI, the surgical treatment predicted greater improvement in HRQoL than conservative treatment for women with SUI. However, this conclusion should be interpreted with caution, since in spite of controlling for the baseline differences in the outcome variable, the treatment groups may differ in some important variables, which were not controlled. It has been speculated that even with a 30 % cure rate it is less expensive to first try conservative treatment, and then if it fails, to perform an incontinence operation. Future recommendation as a first line treatment would require evidence of patient benefit and cost-effectiveness trials with long-term outcome and comparison with operative treatment.

## Urinary incontinence and physical activity

This is the first study measuring by objective means, the physical activity of incontinent women seeking treatment and the effect of treatment on exercise habits. We found that incontinent women who are referred to a specialized incontinence unit for treatment were physically very active and that even after successful treatment, exercise habits were unchanged.

There were no differences in distribution of physical activity in women of working age (< 65 years), by comparison with the normal Finnish population (Mälkiä et al. 1994). The prevalence of regularly exercising women in our study did not differ from that reported in the general population, which suggests that physically very active women who seek treatment want to continue exercises and to be dry (<http://www.ktl.fi/publications/2001/b2.pdf>).

Recently, Brown and Miller (2001) in a general population study from Australia found that physical activity was impaired with increased urine leakage. Nygaard et al. (1990) found that 20 % of “incontinent exercisers” stopped exercising because of leakage, whereas 18 % changed the way a specific exercise was done and 55 % wore a pad during exercise. Thirty five percent had discussed their incontinence with a health care professional. On the basis of epidemiological studies women appeared to be very adaptive to their

incontinence problem. It seems that there are different behaviours among “incontinent exercisers”. In those who “cope” women stop or change their exercise habits and/or wear pads and manage with leakage. It is possible that intensity of sport or fitness habits has an effect on treatment-seeking behaviour. For example, physically active women do not want to change their exercise habits and are unwilling to wear pads, and actively seek relief for their problem.

Two other previous studies found no any association between UI and physical activity among middle-age women (Burgio et al. 1991; Møller et al. 2000).

Although we found no linear correlation between the amount of leakage and physical activity, physically very active women had greater leakage than more “passive” women. It is interesting that among the latter the level of quality of life impairment was the same as among very active women, although inactive women had significantly less urine leakage. It is possible that for women who exercise very intensively, the amount of leakage is the most important factor impairing incontinence-specific quality of life. On the other hand, other factors could play an important role in the modification of quality of life of physically passive women.

The contractility of the pelvic muscle did not correlate with the level of physical activity. Women need special instruction and supervision for exercise of the pelvic floor muscles. Recent studies have shown that pelvic floor exercise is very effective treatment for both SUI and UUI (Bø et al. 1999; Burgio et al. 2002a) and the guidance, how to identify, exercise and use those muscles should be routine during fitness and aerobic training for women of all ages to prevent UI and improve bladder control.

There are many factors, which modify the habits of exercise. Urine leakage has been considered as one of the evident restrictive factors. However, our results do not confirm that becoming dry results in increase in physical activity. Our study sample is small, which might cause inability to detect differences in physical activity. The results must therefore be interpreted cautiously. Regardless of treatment outcome, physical activity did not change. One year after treatment, exercisers continued their sports and others were as passive as before, even though they had become dry. Possible one-year follow-up is too short a time to detect a change in physical activity among continent women.

# SUMMARY AND CONCLUSIONS

- The Urinary Incontinence Severity Score and specific Visual Analogue Scale measuring degree of incontinence bother, proved to be valid, reproducible and responsive to treatment disease-specific HRQoL instruments. VAS could be an efficient language and culture-independent instrument that can be used in conjunction with generic or condition specific questionnaires for rapid appraisal and follow-up of urinary incontinent women. The generic 15D, which in contrast to other generic measures, appears to be responsive to change in the treatment of UI. All three measurements are robust HRQoL instruments for the evaluation of effectiveness and quality of incontinence treatment in research and clinical practice.
- Urinary incontinence significantly impairs women's HRQoL. The HRQoL of women with urge or mixed incontinence is poorer than that of women with stress incontinence. From the clinical parameters the amount of urine leakage best, although modestly, correlated with HRQoL. The correlation of HRQoL impairment with urodynamic and frequency/volume chart findings was generally poor, and varied depending on the instruments used. HRQoL measures are important tools in the assessment of treatment outcome, but treatment decisions cannot be based solely on subjective perception of the severity of urinary incontinence because the severity of UI does not appear to correlate well with HRQoL.
- Major depression was highly prevalent in women with UI. Co-morbid major depression significantly impacts on women's incontinence-specific HRQoL. The significantly higher rate of major depression among women with urge than those with stress UI also suggests pathophysiological association between these two conditions. Screening for depression, especially for patients with urge or mixed incontinence and for those with great impact on HRQoL is recommended.
- One year after treatment women's HRQoL measured by both generic and incontinence-specific instruments improved significantly. The effectiveness of treatment on HRQoL was greater for women with stress incontinence than for those with urge or mixed. The challenge for the future will be to improve the success of treatment for women with urge incontinence. In addition to a diagnosis of stress incontinence, greater impairment of HRQoL at baseline, greater decrease in urine leakage and lower depression scores after treatment also predicted greater change for the better in HRQoL scores.

In specialized health care surgical treatment of women with stress incontinence seems to have a greater effect on incontinence-specific HRQoL than conservative treatment.

- The prevalence of regularly exercising women in our study did not differ from those reported in the general population, which suggests that exercise habits may influence treatment seeking behaviour. Regardless of treatment outcome, exercise habits did not change. One year after treatment, exercisers continued their sports and others were as passive as before even though they had become dry.

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# ORIGINAL PUBLICATIONS