Lower Urinary Tract Symptoms, Quality of life and Coping styles

The longitudinal Krimpen study in community-dwelling older men

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Lower Urinary Tract Symptoms, Quality of life and Coping styles
The longitudinal Krimpen Study in community-dwelling older men

Klachten van de lage urinewegen, kwaliteit van leven en copingstijlen
De Krimpen Studie, een longitudinaal onderzoek onder oudere mannen
in de open populatie

Proefschrift

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de Erasmus Universiteit Rotterdam
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Chapter 4

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Chapter 5

Kok ET, Groeneveld FPMJ, Busschbach JJV, Hop WCJ, Bosch JLHR, Thomas S, Bohnen AM. Influence of coping styles on quality of life in men with new and increasing lower urinary tract symptoms: The Krimpen Study in community-dwelling men. ***Submitted***

Chapter 6

Kok ET, Groeneveld FPMJ, Gouweloos J, Jonkheijm R, Bosch JLHR, Thomas S, Bohnen AM. Determinants of seeking of primary care for lower urinary tract symptoms: The Krimpen Study in community-dwelling men. ***European Urology; in press***

Chapter 7

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Chapter 8

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Chapter 9

Kok ET, McDonnel J, Stolk EA, Stoevelaar HJ, Busschbach JJV. The valuation of the International prostate Symptom Score (IPSS) for use in economic evaluations. ***Eur Urol. 42:491-7, 2002***

LIST OF ABBREVIATIONS

LUTS	Lower urinary tract symptoms
BPH	Benign Prostatic Hyperplasia
QOL	Quality of life
IPSS	International Prostate Symptom Score
GP	General practitioner
SIP	Sickness Impact Profile
ISH	Inventory of Subjective Health
BII	BPH Impact Index
UCL	Utrecht Coping List
Qmax	Maximum urinary flow rate
TURP	Transurethral Electro-Resection of the prostate
DRE	Digital rectal examination
TRUS	Transrectal ultrasound
PSA	Prostate specific antigen

1

General introduction; research questions

INTRODUCTION

During the past decades, much knowledge on the epidemiology and natural history of lower urinary tract symptoms (LUTS) and the efficacy and safety of treatment approaches has been gained from research published in the international literature. Worldwide the prevalence of men with LUTS is documented[1-7], and interest on the impact of LUTS on the quality of life (QOL) continues to grow[8-14]. Remarkably, most studies on which this knowledge is based have a cross sectional study design. The Krimpen Study, a community-based study in the Netherlands, offers the opportunity to study factors associated with LUTS in a longitudinal study design. In that study data on LUTS, QOL and coping styles were collected at regular intervals. Based on this large database the normal values and determinants of urogenital tract (dys)function in older men have already been determined [15]. However, a cluster of questions with regard to the impact of changes in LUTS on changes in QOL remains unanswered. This thesis, based on the longitudinal data of the Krimpen Study, focuses on the relationship between changes in LUTS and changes in QOL, taking into account the impact of coping behaviour in men with new and increasing LUTS. To study the clinical relevance of QOL and coping behaviour in these men the relationship with the general practitioner (GP) consultation and the GP policy was determined. Therefore, the following seven research areas were formulated.

1.1. CASE DEFINITION OF BENIGN PROSTATIC HYPERPLASIA

Benign prostatic hyperplasia (BPH) is a highly prevalent and important underlying cause in the age group of men with LUTS[16]. The three characteristics upon which the condition clinical BPH is based are LUTS, bladder outflow obstruction, and prostate enlargement[16]. These characteristics can be expressed as quantitative parameters. There is no consensus concerning the choice of the three possible parameters or the cut-off point between normal and abnormal for the numerical values of these parameters. For example bladder outflow obstruction can be expressed by the parameter “urethral resistance during voiding” for which several different versions can be used such as the Schäfer grade, URA, and the AG-number. A proxy for these options is often chosen in the form of maximum urinary flow rate (Qmax). Cut-off points between normal and abnormal Qmax are often set at 10 or 15 ml/sec. Inasmuch as it is accepted that the prevalence of BPH increases with age, we have previously tested several possible case definitions for BPH based on various combinations of parameters and various numerical cut-off values for these parameters, and determined whether these case definitions resulted in an increasing prevalence with advancing age[2]. We further postulated that the case definition that gave the best prediction of a GP consultation for LUTS/BPH should be considered to be the most appropriate one. It should be emphasized that measurement and characterization of the men included in this study were not communicated to their GP (an exception to this rule was the serum prostate specific antigen (PSA) value in case a biopsy was warranted). In this way, a prospective study of the predictive value for GP consultation of the different case definitions could be performed. Therefore, the first research objective of this thesis addressed this topic:

To explore which case definition of clinical BPH is most predictive for GP consultation for lower urinary tract symptoms suggestive of BPH

1.2. CHANGES IN LUTS AND QUALITY OF LIFE

LUTS can be very bothersome for patients, and especially symptoms such as frequency, nocturia, urgency, urge incontinence and dribbling can seriously affect the patient's QOL by interfering with their daily activities. However, since the mere presence of symptoms does not necessarily reflect the magnitude of the experience of them, it is still unknown in which way LUTS changes the QOL and how this change can be compared to the impact of other diseases on QOL.

Quality of life instruments used in economic evaluation are suitable to estimate the impact of a condition on QOL and to make comparisons and relative statements across different conditions, interventions and diseases. If the International Prostate Symptom Score (IPSS) could be validated in this way, GPs, urologists and policymakers would have a sensitive tool to describe the impact of LUTS on QOL and to facilitate economic evaluation of various treatment options. The second and third research objectives of this thesis addressed these topics:

To determine if, and to what extent, changes in lower urinary tract symptoms are related to changes in quality of life.

To describe how the IPSS, in a context of lower urinary tract symptoms, was valued, and how these values should be interpreted.

1.3. LUTS, QOL AND COPING STYLE

It is not known whether a change in QOL is directly influenced by a change in LUTS or whether such change in QOL is mainly related to other factors, such as characteristics of men's personality, e.g. coping style. In daily life people get involved with (problematic) circumstances that require adaptation. However, the way one deals with this situation differs per individual. Various factors have been postulated that explain how individuals perceive, interpret and react in a certain situation. One of these factors is "coping". Coping is largely determined by situational characteristics[17-20] as well as a relatively stable personality style[21, 22]. In Lazarus' paradigm coping is the way an individual behaviourally, cognitively and emotionally reacts in adaptation to problematic situations. This coping process changes constantly, depending on new information or results of earlier behaviour. Lazarus differentiated coping into two strategies, first as a response to stressors in terms of problem solving and secondly as emotion-regulating behaviour[23].

In practice, however, it is difficult to differentiate between the various coping strategies and to classify them such that they can be used in studies exploring the relationships between determinants and consequences of behaviour and illness. One of the approaches to measure coping is to define coping as a personality trait[24]. The Utrecht Coping List (UCL)[22], that measures the coping of the men in the Krimpen Study, belongs best to the approach that interprets coping as a certain personality style. This approach is based on the assumption that people are behaviourally and cognitively consistent in different problematic situations, based on former experiences and education.

It is established that coping affects psychological, physical and social well-being[25-30]. Nevertheless, the influence of coping is often expressed in a qualitative rather than in a quantitative way, which makes comparison between the impact of coping styles and other influencing factors difficult. The question as to which coping style is more effective in specific situations has not been studied previously in a prospective study design. For this study question, the UCL is a suitable instrument[31].

If different coping styles are related to QOL in men with new and increasing LUTS, this will be relevant information for the GP when considering his policy for LUTS. Discussing the coping style with the patient may be an effective way to influence QOL in chronic diseases like LUTS, which have relatively limited treatment options. Therefore, the fourth research objective of this thesis addressed this topic:

To determine the influence of coping on quality of life in men with new and increasing lower urinary tract symptoms.

1.4. GP CONSULTATION AND GP'S INITIAL TREATMENT DECISION IN MEN WITH NEW AND INCREASING LUTS

Due to the ageing of the population, LUTS will become even more prevalent in the future and the number of men consulting their physician will increase. A consultation with a GP depends not only on the severity of the symptoms, but also on (a change in) QOL and the characteristics of the men's personality (such as coping style). Improved knowledge of the determinants for GP consultation in men with LUTS will contribute to an appropriate use of health care focused on the needs of elderly men.

Treatment for LUTS includes watchful waiting, pharmacological treatment and referral for possible surgical interventions. Characteristics of both the patient and the GP may influence decisions related to treatment alternatives. Previous studies mainly focused on referral rates and characteristics of the GP rather than on the management of newly developed LUTS[32-39] . The impact of the patient's QOL and the influence of the coping styles of the patient and the GP on the GP's initial treatment choice have not yet been established in men with LUTS. The fifth, sixth and seventh research objectives of this thesis addressed these topics:

To determine which determinants predict future primary care seeking in men with lower urinary tract symptoms.

To determine patient characteristics associated with the GP's initial treatment decision (watchful waiting versus pharmacological treatment/referral) in men with lower urinary tract symptoms.

To determine whether the coping style of the GP influence his treatment decision (watchful waiting versus pharmacological treatment/referral) in men with lower urinary tract symptoms.

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2

Study design of the Krimpen Study

The Krimpen Study is a longitudinal study on the natural history of LUTS and general well-being among men aged 50 to 78 years, living in Krimpen aan den IJssel[1] .

2.1. STUDY POPULATION

Names and addresses of all the 3,924 registered men aged 50 – 78 years were obtained (reference date June 1995) from all general practices of Krimpen aan den IJssel, a commuter town near Rotterdam (The Netherlands) with approximately 28,000 inhabitants. All men without radical prostatectomy, prostate or bladder cancer, neurogenic bladder disease or negative advice from their GP (in case of a serious disease with a short life-expectancy) and who were able to complete questionnaires and to attend the health centre were found eligible and were invited for the study. In all cases, the GP decided whether the patient could enter the study before invitation. The GP's reasons for excluding any patient were checked by the researchers in the electronic medical GP records. Recruitment took place from August 1995 to January 1998.

2.2. THE STUDY

All men entering the study provided written informed consent and the Medical Ethics Committee of the Erasmus Medical Centre Rotterdam approved the study. The baseline study consisted of two phases. In the first phase the participants were asked to fill out a 133-item self-administrated questionnaire and to visit the health centre in Krimpen aan den IJssel (consisting of 16 practising GPs) for a medical examination. In the second phase of the baseline study, urological measurements were performed in cooperation with the Urology outpatient department of the Erasmus MC and the participants filled out a three-day frequency-volume chart. After the baseline study three consecutive rounds of follow-up were performed with an average follow-up period of 2.1 years, 4.2 years and 6.5 years, respectively. In each of these rounds all the above-mentioned measurements were repeated. The visit to the health centre in Krimpen aan den IJssel was only at baseline. Men who did not respond to the first or the second-follow up and did not meet the exclusion criteria were nevertheless also re-invited for participation in the third follow-up round. A flow chart of the study design is presented in Figure 1.

2.2.1. Questionnaire

Lower urinary tract symptoms (LUTS)

To study the presence of LUTS and related bother, the questionnaire included the International Prostate Symptom Score (IPSS)[2] and the BPH Impact score (BII)[3]. The seven-item IPSS was used to assess the occurrence and frequency of LUTS. The score range is 0 (no symptoms) to 35 (maximal symptoms). According to the classification of the American Urological Association (AUA), scores can be classified into three categories: mild (0 - 7), moderate (8 -19)

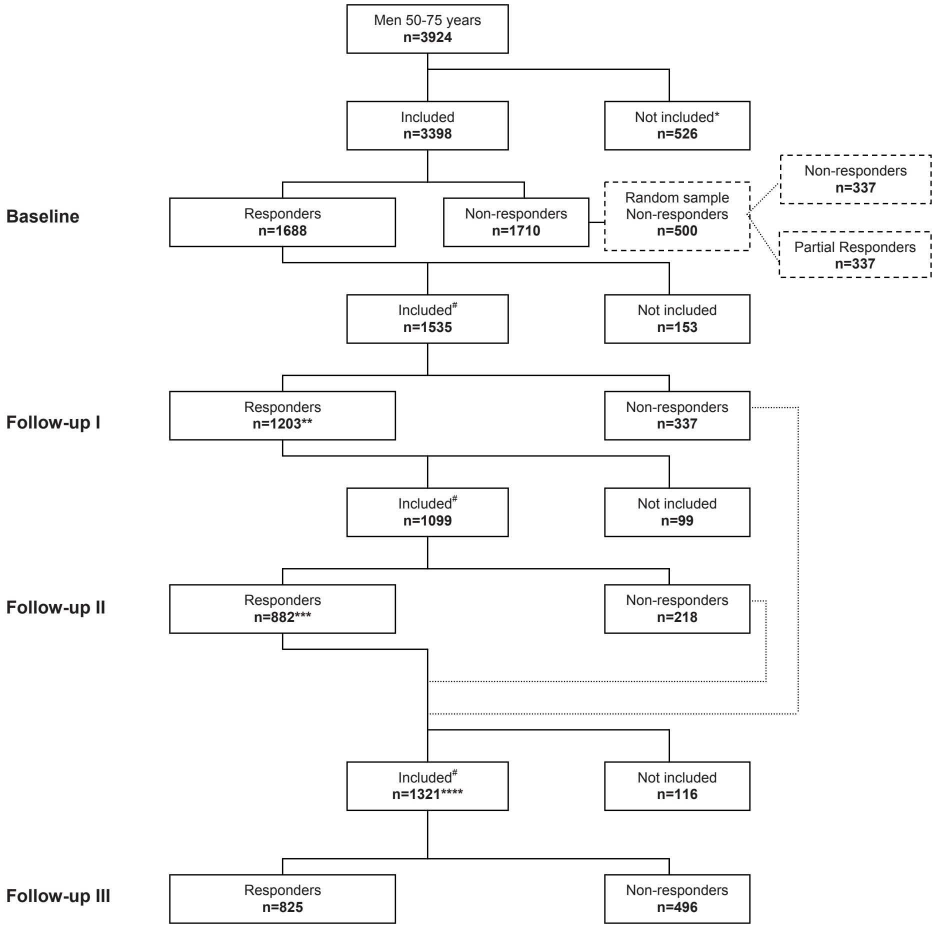

Figure 1. *Flowchart of the Krimpen Study*
** Men without radical prostatectomy, prostate or bladder cancer, neurogenic bladder disease or a negative advice from their GP (in case of a serious disease with a short life-expectancy), who were able to complete questionnaires and attend the research centre, were invited for the study; # If no prostate cancer was detected, participants had not moved outside the municipality and were alive a re-invitation letter was sent to all responders for follow-up; ** five men did not participate in the baseline study, but entered the study in folluw-up I; *** one man did not respond in follow-up I, but re-entered the study in follow-up II; **** Men, who did not respond after baseline, first follow-up or second-follow up and did not meet the exclusion criteria were also re-invited for participation in the third follow-up round (882 + 337 + 218 – 116)*

or severe (20 -35)[2]. The BPH Impact Index includes questions on the bothersomeness of LUTS and the impact of LUTS on physical distress, health concerns and interferences with daily life activities[3]. Sexuality related questions of the International Continence Society (ICSsex questionnaire)[4] were also included in the questionnaire. The ICSsex questionnaire covers four items, each with a bother score ranging from no problem to a serious problem on a four-point scale. In addition the men were asked whether they were sexually active and, if not, how long ago their sexual activities ceased.

Quality of life (QOL)

To assess the generic QOL of the men the questionnaire included the mini-Inventory of subjective Health (ISH)[5] and the Sickness Impact Profile (SIP)[6]. The mini-ISH is a 13-item questionnaire on subjective health with a score range from 0 to 13.[5] The three domains of the SIP used in this study are 'Emotions' ('Emotions, feelings and sensations', 9 items), 'Recreation' ('leisure pastimes and recreation', 8 items) and 'Social' ('social interaction', 20 items). For each category, a score was computed based on weighting factors for each item, providing scores ranging from 0 to 100[6].

At the third follow-up the generic QOL questionnaire 'EQ-5D'[7] was added to the questionnaire. The EQ-5D has five questions and a visual analogue scale to measure overall QOL[7].

In contrast to the generic QOL questionnaires, disease-specific questionnaires measure QOL based on items closely related to the specific disease and are expected to be more sensitive for the effects of a specific disease on QOL. Therefore, to measure the effect of LUTS on QOL we used the QOL question of the IPSS[2] (IPSS-QOL) and the BPH Impact Index (BII) [8]. The latter question of the IPSS results in a separate QOL score (IPSS-QOL) and can be rated on a scale from 0 to 6[2]. The BII is a four-question index with a score of 0 – 13 designed to assess the impact of the symptoms of LUTS on health status [3].

For all QOL scales used (disease-specific and generic) a higher score indicates a worse QOL.

Coping styles

For the third follow-up round the questionnaire also included questions on coping styles. To assess coping behaviour the Utrecht Coping List (UCL) was used[9]. In the UCL, coping behaviour is regarded as a personal disposition, e.g. a trait. The respondent is asked to imagine his reaction to 'problems in general'. The UCL consists of 47 items describing a specific coping behaviour. Answers are on a 4-point scale ranging from 'seldom or never' to 'very frequently'. The instrument has been validated for use in a Dutch population[9]. The UCL consists of seven coping scales representing different coping styles. The names of the styles and examples of items (between brackets) are: **A**: active problem solving ('putting things in a row', 'seeking a way to solve a problem'), **P**: palliative reaction ('looking for distraction', and 'looking for good company'), **AV**: avoidance ('avoiding difficult situations' and ' letting things go'), **S**: seeking social support ('discussing the problem with friends or family' and 'asking somebody for help'), **PR**: passive reaction ('being overwhelmed by problems'), **E**: expression of emotions ('showing anger to the person who is responsible for the problem'), and **R**: Reassuring thoughts ('imagining that things could be worse'). A higher score on a coping style represents a higher level of use of the style. Note that there are neither abnormal styles nor normal values for the frequency that a specific style is used.

Ageing, erectile dysfunction and incontinence

In the third follow-up round the St. Louis University ADAM (androgen deficiency in aging male) questionnaire [10], the International Index of Erectile Function (IIEF)[11], the short form ICS male questions on incontinence (6 items) and a single question on impotence of the Massachusetts Male Aging Study (MMAS)[4] questionnaire were also added to the questionnaire.
The ADAM questionnaire of St Louis University[10] is used as a non-invasive screening tool to detect possible androgen deficiency in aging males and consists of 10 items. The IIEF is a validated self-administered measure that assesses erectile (dys)function [11].

Medical conditions and socio-demographic factors

The questionnaire included questions on treatment for chronic diseases (e.g. cardiovascular problems, hypertension, diabetes mellitus, Parkinson's disease, chronic obstructive pulmonary disease (COPD), chronic urinary tract infections and liver diseases), history of transurethral resection of the prostate, family history of prostate cancer, smoking habits and alcohol consumption, marital status and educational level.

Frequency-volume charts

The participants were asked to complete a 3-day frequency-volume chart on which each micturition was recorded in one-hour time units. On the third day, the volume of each voiding was recorded. Bedtime and time of rising were also recorded on the charts. The number of voids during patient-reported waking/sleeping hours was determined.
Recordings on the frequency volume charts are used to determine: nocturnal and diurnal voiding frequency, 24-hours voided volume, average volume per void (24-hour volume/frequency), functional bladder capacity (defined as the largest voided volume) and hourly urine production.

2.2.2. Measurements

Health centre

At the health centre, two study physicians checked the questionnaires and completed these with data on current medication (using the Anatomical Therapeutical Chemical classification). Urinalysis was performed using a dipstick (including levels of leukocytes, nitrate and glucose), mainly to exclude lower urinary tract infection. Erythrocyte levels were not assessed to avoid unnecessary investigations in men with microscopic haematuria. Finally, systolic and diastolic blood pressure, height and bodyweight were measured.

Urology outpatient department of the Erasmus MC

The men were subsequently invited to visit the urology outpatient department of the Erasmus MC for the following measurements: digital rectal examination (DRE), transrectal ultrasound (TRUS), uroflowmetry, post-void residual urine volume, and serum prostate specific antigen (PSA). Almost all men that have visited the heath centre also completed this second phase of the study.

On DRE, the volume of the prostate was estimated and the location of possible nodules was noted. The total volume of the prostate and the volume of the transition zone were measured by TRUS. We used the planimetric procedure to determine the prostate volume most accurately[12]. The measurements were performed using the Bruel and Kjaer Medical Falcon Ultrasone Scanner type 2101 equipped with a 7 MHz biplanar endorectal transducer type 8808. Also recorded were the width, height, length, perimeter and area of the prostate and the transitional zone of the prostate.

Uroflowmetry was done using a flow meter (Dantec Urodyn 1000, Copenhagen, Denmark). The following parameters were recorded: peak flow rate (Qmax), average flow rate, delay time, total voiding time, total flow time and the voided volume. The men were asked to visit the clinic with a full bladder and were instructed not to void in a toilet before that time.

The post-void residual urine volume was measured with a transabdominal ultrasound device (Aloka Model SSD-1700 Dyna View) with a 3.5 MHz electronic convex probe, using the formula $\pi/6$ * width* height* depth. The postvoid residual was not computed if a man was unable to void in the flowmeter. The initial pre-micturition bladder volume was calculated by summing the voided volume and the residual volume.

A blood sample (serum and plasma) was obtained by venapuncture. From this sample, the serum PSA level was determined using the Tandem-R method (Hybritech, Dan Diego, USA). Three portions of 3 ml each from the blood sample were stored in a freezer.

Prostate biopsies

The following protocol was used to detect prostatic carcinoma: prostate biopsies were performed (i) always at PSA values above 10 ng/ml at baseline and above 4 ng/ml during follow-up, (ii) at PSA levels between 2 and 10 ng/ml at baseline or between 1 and 4 mg/ml at follow-up in case of abnormal findings on DRE or TRUS (i.e. suspect for carcinoma), and (iii) at PSA values of 1 to 2 ng/ml if DRE was abnormal. No biopsies were taken to confirm the histopathologic diagnosis BPH.

2.2.3. Data assembly of GP data

In the Netherlands, all inhabitants are registered with a GP. When the patient visits an emergency room, a specialist, or a (substitute) physician in the weekend or at night, their own GP is always informed. Data about these visits, contacts and prescription of medication are stored in the computerized medical records. In the present study all practising GPs (n =16) in Krimpen aan den IJssel allowed access to their computerized medical records. The GP medical records of all the participants of the Krimpen study (n = 1688) were checked with the “N6” computer program (QSR International Pty. Ltd. Melbourne, Australia). This program

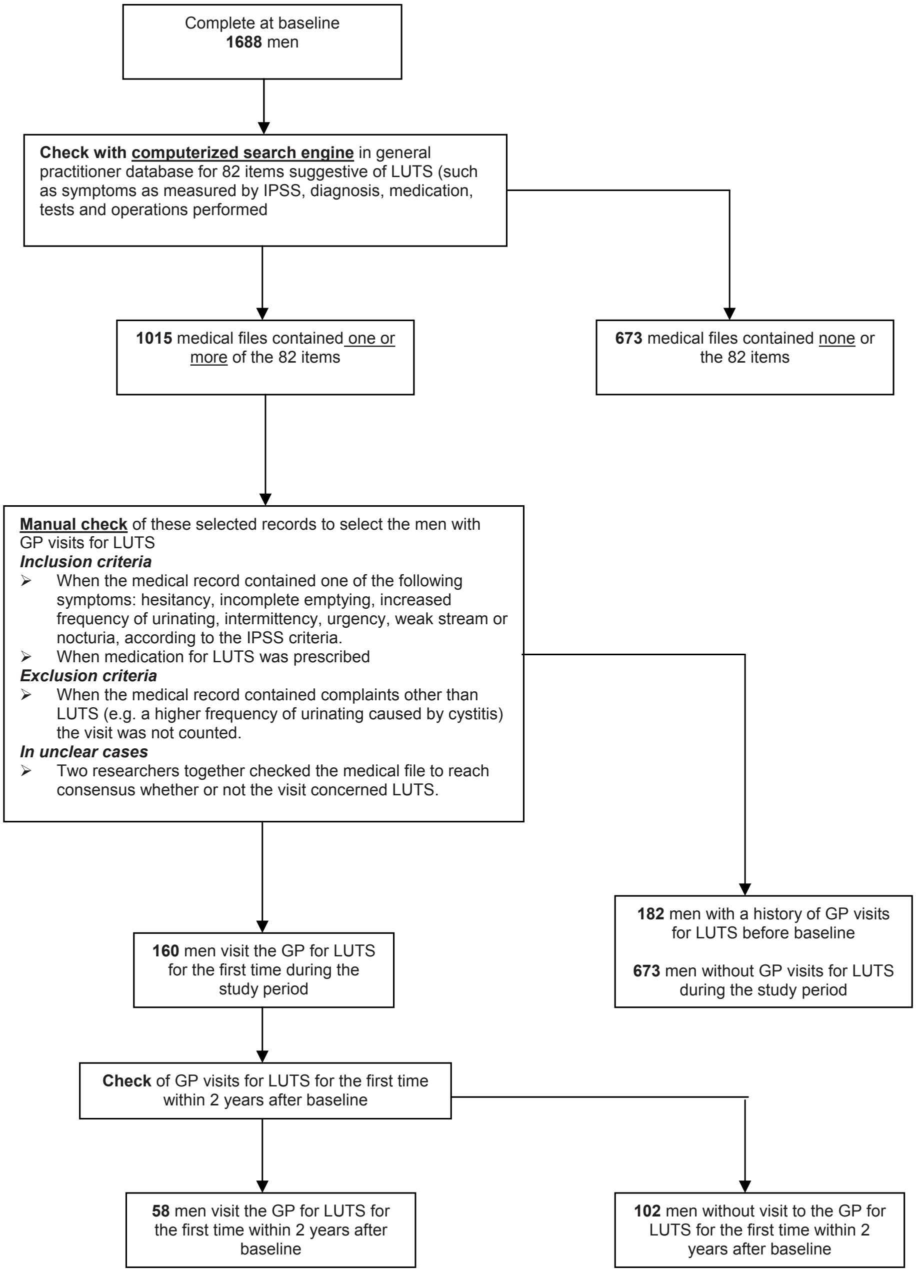

Figure 2. *Data assembly in general practitioner database*

can search text files on keywords and select files based on keywords. Two researchers independently analysed the files selected by the N6 program and filled in a score form separately. They both scored whether or not there was a history of LUTS (i.e. before the start of the study) and noted whether the participant had visited his GP for LUTS and the first date this took place. When a record showed another reason for LUTS-like symptoms clearly due a disease other than BPH (e.g. high frequency of urinating due to uncontrolled diabetes mellitus), the visit was not counted. Also the treatment choice was noted. When the medical file showed that a person had moved from the GP's practice (lost to follow-up) or was deceased, the date of this event was noted. To validate the use of the N6 program the medical files that showed no hits by the N6 (using 82 keywords) were checked manually. The check gave a 100% negative predictive value for the search by the N6 program (none of the files reported visits for LUTS). No loss of follow-up (missing files) occurred in the GP data. A flow chart of the GP data assembly is presented in Figure 2.

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3

A simple case definition of clinical Benign Prostatic Hyperplasia, based on the International Prostate Symptom Score, predicts general practitioner consultation rates

Urology; in press

ABSTRACT

Objective

To determine which case definition of clinical benign prostatic hyperplasia (BPH) has the best predictive value for GP visit for lower urinary tract symptoms (LUTS) suggestive of BPH. In relation, the incidence and prevalence rates of GP visit for LUTS are determined.

Materials and Methods

A longitudinal, population-based study from 1995 to 2003 was conducted among 1688 men aged 50 to 78 years old. Data were collected on physical urological parameters, quality of life and symptom severity based on the International Prostate Symptoms Score (IPSS). Information on health-care-seeking behaviour of all participants was collected from the general practitioners (GP) record using a computerised search engine, and an additional manual check of the electronically selected files.

Results

The incidence and prevalence rates of the men at risk were 19.6% and 14.0%, respectively; these rates increase with age. For sensitivity and the positive predictive value, the case definition of clinical BPH "IPSS >7" has the best predictive value for GP visit for LUTS within two years after baseline.

Conclusion

Because only marginal improvement (a higher specificity but a lower sensitivity) in the prediction of GP visit for LUTS is possible by adding the information on prostate volume and flow, for prediction of future GP visit for LUTS suggestive of BPH we suggest that the IPSS can be used and that estimation of the prostate volume and flow is not required.

INTRODUCTION

In 1991, Garraway[1] predicted that the operational definition of Benign Prostatic Hyperplasia (BPH) probably would change over time as knowledge of the natural history of BPH increases. Consensus seemed to be reached about the three characteristics upon which the condition clinical BPH is based: bladder outflow obstruction, LUTS and prostate enlargement.[2] However, research to determine cut-off points for these three elements of the case definition, ideal for enabling early cases of BPH to be picked up through screening, is still ongoing. An issue that can only be determined in a study which assess these cut-off points in a representative sample of men in the community. The Krimpen study is such a study providing knowledge about the natural history of Benign prostatic hyperplasia (BPH) in a representative sample of men.

Differences in predictive values of the case definition of clinical BPH based on various cut-off values might help to select the most useful case definition of clinical BPH. Therefore the aim of the present study was to explore which case definition of clinical BPH is most predictive for GP consultation for lower urinary tract symptoms (LUTS) suggestive of BPH. In accordance, the incidence and prevalence of GP visit for LUTS was established.

MATERIALS AND METHODS

Study design

The design of the Krimpen study on male urogenital tract problems and general health status has been described in detail [3]. Briefly, the Krimpen study was performed among all men aged 50 – 78 years living in a Dutch municipality near Rotterdam. Men without radical prostatectomy, prostate or bladder cancer, neurogenic bladder disease or a negative advice from their GP (in case of a serious disease with a short life-expectancy), who were able to complete questionnaires and attend the research centre, were invited for the study. The Medical Ethical Committee of the Erasmus Medical Centre Rotterdam approved the study.

First, data of 1688 responders (50%) were collected via a self-administered 113-item questionnaire, which included different questionnaires about symptom frequency, quality of life and also addressed the topics marital status, number of children, education level, smoking behaviour and drinking habits. Secondly, additional measurements: height, body weight, blood pressure measurement and urinalysis were performed at the research centre. Finally, in cooperation with the urology department of the Erasmus MC the following tests were performed: serum prostate-specific antigen (PSA), digital rectal examination (DRE), transrectal ultrasound of the prostate (TRUS), uroflowmetry and poist void residual urine volume. Prostate biopsies were taken in men suspected of prostate cancer. Measurements were repeated in three consecutive rounds of follow-up with an average follow-up time of 2.1 years, 4.2 years and 6.5 years, respectively.

In order not to disturb the natural course of BPH, no information on test results, except for the value of the prostate specific antigen (PSA), was given to the participant and his GP.

Data assembly of GP data

A flow chart of the GP data assembly is presented in figure 1.

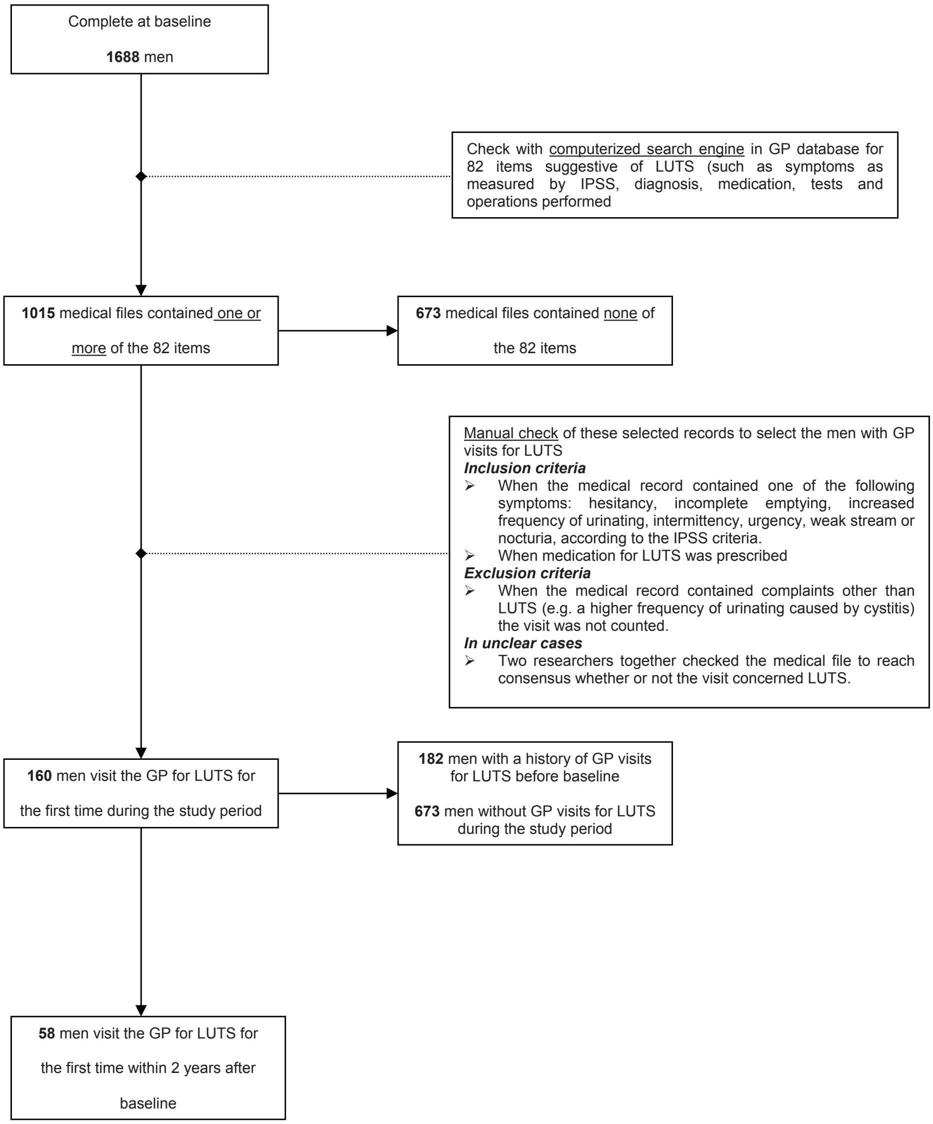

Figure 1. *Data assembly in general practitioner database*

In the Netherlands, all inhabitants are registered with a GP. When the patient visits any physician in the weekend or at night, his own GP is always informed. Data about all visits, contacts and prescription of medication are stored in the computerized medical records.
All practicing GP's (N=16) in Krimpen aan den IJssel gave access the GP medical records of all the participants of the study (N = 1688). These records were checked with the "N6" computer program (QSR International Pty. Ltd. Melbourne, Australia) that can search and select text files on keywords. Two researchers independently scored whether or not there was a history of LUTS (i.e. before the start of the study), whether the participant had visited his GP for LUTS and the first date this took place. When a patient had complaints other than for LUTS (e.g. a higher frequency of urinating caused by cystitis), the visit was not counted. When the medical file showed that a person had moved from the GP's practice (lost to follow-up) or was deceased, the date of this event was noted. To validate the use of the N6 program the medical files that showed no hits by N6 were checked manually; none of the files reported visits for LUTS.

Symptoms and Measurements

LUTS was assessed by the seven-item International Prostate Symptom Score (IPSS).[4] The total volume of the prostate and the volume of the transition zone were measured by transrectal ultrasound (TRUS). We used the planimetric procedure to determine the prostate volume most accurate.[5] The measurements were performed with a 7 MHz Bruel and Kjaer multiplane scanning probe. Post-void residual urine volume was measured using a transabdominal ultrasound device (Aloka, 3.5 MHz) and uroflowmetry (Q_max) was done using a flow meter (Dantec Urodyn 1000, Copenhagen, Denmark).

Definitions of clinical BPH

The case definitions of clinical BPH used in this study were based on the definitions used by Garraway et al. and on three definitions reported to be the most valid by Bosch et al.[1, 6] The variables used in these definitions were the IPSS, prostate volume (PV) and Q_ max: prostate volume is expressed in cc and Q_max in ml per second. The 7 case definitions are as follows **1)** IPSS > 7; **2)** IPSS > 7 + PV > 30; **3)** IPSS > 7+ PV > 30 + Q_max < 15; **4)** IPSS > 7 + PV > 30 + Q_max < 10; **5)** IPSS > 7 + PV > 20 + Q_max < 15. We added two other case definitions: **6)** prostate volume > 30 and **7)** PSA ≥ 2 ng/ml (as proxy for prostate volume) based on the median of the value of PSA in our population.

Statistical Analysis

First, characteristics of the men at risk to visit a GP for LUTS were determined. After this, age-specific prevalence and incidence of GP visit for LUTS and the percentages of men visiting their GP for LUTS within two years after baseline according to the various case definitions of clinical BPH was determined. Finally, logistic regression analyses were used to determine which case definition of clinical BPH best predicted a GP visit for LUTS within 2 years after baseline. Moreover, to analyse whether disease-specific quality of life (IPSS_QOL) predicts stronger GP visits for LUTS than symptom severity alone, also the predictive value of the IPSS_QOL was determined. All data were analysed in SPSS 11.

RESULTS

The total study cohort consisted of 1688 men. The search program N6 selected 1015 of the files. In these files we found 182 men with a history of GP visit for LUTS (GP or urologist) before the start of the study, leaving 1506 men (89%) at risk to attend their GP with LUTS on a later date. Of these 1506 men complete baseline data and GP data were available. Table 1 shows the characteristics of the study population.

Table 1. *Characteristics of the study population at baseline*

	Persons at risk (N= 1506)
Age (years)	**Percentages**
50-54	21.4
55-59	25.7
60-64	23.5
65-69	19.0
70-74	7.4
75+	2.9
IPSS	
Mild (0 – 7)	68.2
Moderate (8 – 19)	18.9
Severe (20 – 35)	2.0
Quality of life	**Percentages**
IPSS_QOL: delighted to mixed	96.6
IPSS_QOL: mostly dissatisfied to terrible	3.4
Measurements	**Mean (SD)**
Prostate volume	33.6 (14.2)
Transition zone volume	16.0 (11.9)
Maximum urinary flow rate	11.6 (6.9)
Post-void residual urine volume	21.7 (51.5)

Table 2. *Case definitions of clinical BPH as determinant for GP visits for LUTS suggestive of BPH within two years after baseline (N = 1481)*

Case definitions of clinical BPH at baseline	**N[+] to def.**	**% men visit GP**	**OR**	**CI95%**	**R2**	**p-value**	**Sens. %**	**Spec. %**	**PV+ %**	**PV- %**	**Accurate %**
Definition 1: IPSS>7*	309	10.1	5.35	3.09-9.27	0.09	<0.001	56	80	18	98	80
Definition 2: IPSS>7 + PV >30*	163	14.1	6.78	3.83-12.0	0.09	<0.001	43	96	14	98	88
Definition 3: IPSS>7 + PV >30 + Q_max<15*	130	16.2	7.71	4.24-14.0	0.10	<0.001	43	91	16	98	88
Definition 4: IPSS>7 + PV >30 + Q_max<10*	95	19.0	8.69	4.65-16.2	0.10	<0.001	37	94	19	97	90
Definition 5: IPSS>7 + PV >20 + Q_max<15*	211	12.8	6.98	3.89-12.5	0.11	<0.001	55	85	13	98	83
Prostate Volume > 30	433	5.5	2.72	1.49-4.96	0.03	0.001	48	72	6	97	51
PSA ≥ 2	743	6.5	2.35	1.38-9.67	0.02	0.002	73	49	6	98	71
IPSS_QOL mostly dissatisfied to terrible	49	18.4	6.65	3.05-14.5	0.04	<0.001	16	97	18	96	94

** IPSS, International Prostate Symptom Score; PV, prostate volume on Transrectal Ultrasound (cc); Q_max, maximum urinary flow rate (ml/sec): Prostate specific antigen (ng/ml); Sens., sensitivity; Spec., specificity; PV+/–, predictive value of being positive or negative according to the definition; Accurate, percentage of true positives and true negatives.*

[+] Number of men complied to definition

The total prevalence rate of first GP visit for LUTS during the study period was equal to 14.0%. The (period) prevalence increased linearly with age from 9% in men aged between 50-54 years to 20% in men aged between 70-74 years. The mean follow-up time of the participants was 5.75 years. Of the men at risk (N = 1506, total 8181 person years at risk), a total of 160 new first GP visits for LUTS were found which led to an incidence rate of 19.6 per 1000 person years. The incidence of the first visit for LUTS increased also linearly with age from 13% in men aged between 50-54 years to 32% in men aged between 70-74 years. Of the men at risk 58 men (3.9%) have visited their GP for LUTS for the first time within two years after baseline.

Table 2 showed that case definition 4 (IPSS>7 + prostate volume >30 cc + Q_max <10 ml/sec) gave the highest odds ratio (8.69), but the least number of men complied with this definition (n=95). Case definition 1 (IPSS>7) complied with the highest number of men (n=309), but showed the lowest odds ratio (5.35) and explained variance in GP visit for LUTS (R^2=0.09). The value of PSA has a high sensitivity, but a low positive predictive value. The IPSS_QOL has a higher OR than symptom severity alone, but a very low sensitivity. Regarding the sensitivity and the positive predictive value (PPV), definition 1 (IPSS>7) is the best. Thus, this definition is the best predictor for GP visit for LUTS suggestive of BPH within two years after baseline.

DISCUSSION

The present longitudinal study demonstrated that both the incidence rate and prevalence rate of men visiting their GP for LUTS increase with age. The total incidence and prevalence rates of the men at risk in this study population are 19.6% and 14.0%, respectively. Regarding the various case definitions of clinical BPH, the number of men visiting their GP for LUTS differs. The case definition *IPSS>7 + prostate volume >30 cc + Q_max <10 ml/sec* has the best predictive value for GP visit for LUTS: however, the smallest number of men complied with this case definition and only 37% of the men that visited the GP for LUTS belonged to this group. The case definition *IPSS>7* complied with the highest number of men. With regard to the sensitivity and the positive predictive value this case definition has the best predictive value for GP visit for LUTS suggestive of BPH.

In the Krimpen study 50% of the invited men responded. A questionnaire was sent to those that did not participate at baseline to investigate the characteristics of this group. As the prevalence of men with IPSS > 7 was lower in the non-participants [3], we have to conclude that the prevalence and incidence of first GP visit for LUTS in fact must be slightly lower than measured in the present study. However, because this study reports about the relationship between various case definitions of BPH and GP consultation this bias has not influenced our results of the predictive characteristics of the case definitions. Our results are also not biased by the knowledge of the study test prior to the GP visit. The participants themselves and their GPs enrolled in our study were not exposed to this information. Only the value of the PSA was given to the GP, in relation to the need to detect prostate cancer. In the present study, most probably, the possible fear of prostate cancer does not play an important role in GP consultation for LUTS, because men with prostate cancers have already been filtered out of the study population.

The finding that incident GP visit for LUTS increases with age corresponds with other studies.[7, 8] Verhamme et al. reported an incidence rate of 15 per 1000 man-years [8], which is somewhat lower than ours. However, their selection criteria for GP visit for LUTS included the criteria that men for whom no medication for BPH was prescribed or for whom the diagnosis of BPH was given, must have attended their GP at least two times with LUTS to count as such. In general it is known that the majority of men with LUTS (70-90%) do not present their LUTS to a GP. [1, 9] This is in accordance with our results showing that only 5.5–19% of the men with clinical BPH presented their symptoms to a GP within two years after baseline. These percentages could indicate underestimation of GP visit for LUTS due to the short follow-up time of two years, but a more reasonable explanation for the low incidence rate may be that the symptoms were not considered serious enough to visit a GP or that the men did not expect that their GP could relieve their symptoms.

From the perspective of clinical decision-making, it was concluded that post void residual, symptom severity and maximum flow rate are the most relevant determinants of the risk of BPH progression.[10] We conclude that to enable early cases of BPH to be picked up through screening only the symptom severity is needed to predict which man will seek care for LUTS suggestive of BPH.

The low explained variance of the models of the various case definitions in predicting GP visit for LUTS is not remarkable. Previous studies (including the Krimpen study) already showed that besides symptoms and urological parameters, also quality of life, worry and embarrassment and fear of cancer are important determinants for GP consultation in men with LUTS.[11-13] The present study shows that the predictive value of GP visit for LUTS of the disease-specific QOL was higher than the predictive value of symptom severity alone. Also in a multivariate model adjusted for symptom severity the OR of the IPSS_QOL was still significant, but decreased. (OR adjusted: 2.7). However, regarding the low sensitivity (16%) it is preferred to use symptom severity (IPSS) instead of the disease-specific QOL (IPSS_QOL) to predict future GP visit for LUTS.

As elevated PSA and elevated prostate volume both have a very low predictive value we suggest not using these separate parameters to predict future GP visit for LUTS. By adding information on prostate volume and flow to the IPSS only a marginal improvement (a higher specificity but a lower sensitivity) in the prediction of GP visit for LUTS is possible. Therefore we suggest that for prediction of future GP visit for LUTS suggestive of BPH the IPSS with a cut-off value of 7 points can be used, and estimation of the prostate volume and flow is not required. In this way in in epidemiological studies, the IPSS can be used to select the men at risk developing clinical BPH.

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Changes in disease-specific and generic quality of life related to changes in lower urinary tract symptoms

J Urol. 174:1055-8, 2005

ABSTRACT

Objective

We determined if and to what extent longitudinal changes in lower urinary tract symptoms (LUTS) are related to disease-specific and generic quality of life in men.

Material and methods

A longitudinal population-based study with a follow-up of 4.2 years on 1,688 was done in 1688 men who were 50 to 79 years old. Data were collected through self-administered questionnaires, including the Sickness Impact Profile (SIP, three domains), Inventory of Subjective Health (ISH), International Prostate Symptom Score (IPSS) and BPH Impact Index (BII). Moreover, they completed various physical and urological measurements. Mean IPSS and quality of life scores at baseline and follow-up were analysed for certain subgroups. Multiple linear regression were used to determine the change in quality of life in relation to baseline IPSS score, changes in IPSS between baseline and follow-up, and age.

Results

Although mean IPSS increased with time, the average generic quality of life improved and almost one third of the men reported a better disease-specific quality of life. Multiple linear regressions revealed that disease-specific quality of life was associated with IPSS at baseline, IPSS-changes between baseline and follow up, and age; however, generic quality of life scores were not associated with these parameters.

Conclusions

Changes in LUTS had on average little impact on disease-specific quality of life of 50 to 78-year-old men or on generic quality of life during the 4.2-year follow-up.

INTRODUCTION

Due to the population aging and the availability of new, minimally invasive treatments, increasing attention is being given to the impact of lower urinary tract symptoms (LUTS) on quality of life (QOL). In LUTS symptom severity has been reported to have a significant impact on physical and social functioning, mental health, and on the perception of health and general well-being.[1-7] The severity of LUTS, measured as the frequency of symptoms rated by the patient, and bother, as experienced by the patient, are important determinants for intervention. Since the presence of symptoms does not necessarily reflect the experience of them, the concept of QOL as a consequence of LUTS is of interest.

Data on the relation between LUTS severity and QOL is largely based on cross-sectional studies.[2-6] Because LUTS likely is to be associated with other morbidity, it follows that the relationship between LUTS and QOL may be confounded by such co-morbidity. This methodological problem can in part be overcome by measuring the relation between change with time in LUTS and in QOL. However, few studies have examined the relationship between long-term changes in LUTS severity and changes in QOL-scores with time.[1, 8, 9] Therefore, in this longitudinal study we determined if and to what extent changes in LUTS are related to changes in QOL.

MATERIALS AND METHODS

The Krimpen Study is an ongoing, longitudinal, community based population study of 50 to 78-year-old men, in which the natural history of LUTS and its relationship to general wellbeing was surveyed. After the baseline evaluation two follow-up rounds were completed. The design of the Krimpen Study has been extensively described previously.[10] Briefly, all 3,924 eligible men aged 50 to 78 years old in Krimpen aan den IJssel were invited to participate, of whom 50% responded. All men provided written informed consent. The Medical Ethics Committee of the Erasmus Medical Centre Rotterdam approved the study.

Participants completed a questionnaire, including the short version of the Inventory of Subjective Health (mini-ISH), three domains of the Sickness Impact Profile (SIP), the International Prostate Symptom Score (IPSS) and the benign prostatic hyperplasia (BPH) Impact Index (BII). Moreover, they underwent various physical and urological measurements. Based on the results of digital rectal examination (DRE) and prostate specific antigen (PSA) prostate biopsies were done to exclude prostate cancer.

If no prostate cancer was detected, participants had not moved outside of the municipality, they were alive, and no exclusion criteria were met, a re-invitation letter was mailed to all participants for follow-up. Two consecutive rounds of follow-up were performed with an average follow-up 2.1 and 4.2 years, respectively. In these rounds all measurements were repeated.

Quality of life questionnaires

Generic measurements are commonly used to measure changes in QOL due to a disease or treatment in terms that are applicable to every individual, irrespective of a specific diagnosis. These questionnaires enable the comparison of QOL data on different groups of patients.

In this study we used mini-ISH and SIP as the generic QOL questionnaires. Mini-ISH is a 13-item questionnaire on subjective health with a score range from 0 to 13.[11] The three domains of the SIP used in this study were 'emotions, feelings and sensations' ('Emotions', including 9 items), 'leisure pastimes and recreation' ('Recreation', 8 items) and ' social interaction' ('Social', 20 items). For each category, a score was calculated based on weighing factors for each item, providing scores from 0 to 100.[12]

In contrast to generic QOL questionnaires disease-specific questionnaires measure QOL based on items closely related to the specific disease and, therefore, they are expected to be more sensitive. To measure the effect of LUTS on QOL we used the QOL question of the IPSS (IPSS-QOL) and BII. The IPSS-QOL can be rated on a 0 to 6 scale.[13] The BII is a four-question index with a score of 0 to 13 designed to assess the impact of the symptoms of BPH on health status.[5]

For all scales used (disease-specific and generic) a higher score indicates worse QOL.

LUTS

LUTS were categorized according to IPSS as mild (0-7), moderate (8-19) or severe (20-35).[13] We defined clinical LUTS as moderate to severe symptoms (IPSS greater than 7).

A few groups have investigated which change in IPSS leads to an observable change in QOL.[14, 15] For example, in patients with clinically progressive LUTS Barry et al. reported that a worsening in IPSS of at least 3.1 points was needed for the patient to perceive the change.[15] On the other hand, in the Medical Therapy of Prostatic Symptoms (MTOPS) a worsening of total IPSS of at least 4 points according to an arbitrary demarcation (based on a 3 point improvement in symptom scores when recieving alpha blockers) was used to determine the number of patients with clinical progression of LUTS. [14] In the current study based on the distribution over the participants subgroups we defined changes in IPSS as follows: 1) clear worsening (4 points or greater); 2) slight worsening (less than a 4 points increase); 3) no change; 4) slight improvement (less than a 4 points decrease); and 5) clear improvement (4 point decrease or greater decrease).

Analysis

Analysis focussed on mean IPSS and QOL scores at baseline and tat second follow-up (mean follow-up time of 4.2 years). To determine if baseline LUTS-severity was a determinant of non-response at second follow-up we compared mean IPSS at baseline for those with and without data at second follow-up. Statistical comparisons between the groups were performed using the paired t-tests. Statistical significance was considered at the 0.05 level.

Pearson's correlations between all QOL measurements at baseline, and between all QOL measurements at baseline and IPSS at baseline were used to determine sensitivity of the QOL measures used. QOL changes with time in relation to LUTS were analysed in different subgroups depending on baseline IPSS and change in IPSS in time. Multiple linear regressions analysis was used to test the relationships between changes in QOL, changes in IPSS, different baseline-IPSS levels and age.

RESULTS

Table 1 lists characteristics of the study population according to age and IPSS. At the second follow-up 882 men (80.3%) participated of whom 19 had no IPSS data available during baseline measurement. In men without data at the second follow-up mean baseline IPSS was 6.2 compared with 5.2 in men with available data.

Of the men with complete data during the follow-up period of 4.2 years 178 showed clear worsening of LUTS, 88 showed clear improvement, and 597 showed slight or no changes in LUTS.

Table 1 also shows QOL-scores at baseline and at 4.2 years of follow-up. The mean generic QOL-scores improved significantly with time in all men as well as in men with significant LUTS. There was no significant change in disease-specific values (IPSS-QOL & BII) in all men However, in men with significant LUTS these two scores decreased significantly. An increase in IPSS-QOL with age was observed at baseline and at follow-up.

Table 2 shows the annual change in IPSS and IPSS-QOL in European men (Krimpen Study) compared with these changes in men in North America (Olmsted County) and Asia (Japan).[8, 9] In all studies the average annual IPSS-change generally increased with age. However, in the Krimpen Study and the Olmsted County study there was little or no average change in IPSS-QOL with time, which was fairly consistent across age groups. Japanese results showed a diffuse pattern over the age groups.

QOL-instruments were tested for mutual correlation (Table 3). Generic QOL-measures and the two disease-specific QOL-measures showed significant correlation, providing evidence for the sensitivity of the generic instruments. The correlation between the generic QOL instruments and IPSS baseline was low but statistically significant.

Overall, 28.6 % of the men reported a clear or slight improvement in LUTS after 4.2 years. The mean change in IPSS in the clear worsening subgroup was 6.6 in men with mild symptoms at baseline, 6.3 in those with moderate to severe symptoms at baseline. In men in the clear improvement subgroup the mean change in IPSS was – 4.6 in those with mild symptoms at baseline and – 7.5 in those with moderate to severe symptoms at baseline.

Table 4 shows changes in QOL related to changes in LUTS. With time generic QOL-scores decreased (indicating a better QOL), independent from baseline-IPSS and IPSS-change between

Table 1. *Study population characteristics, IPSS and quality of life scores at baseline and after 4.2 years of follow-up*

	Baseline		**Follow up**	
Age (years)	***% of men (N=882)***			
< 55	21.4		1.6	
55 – 59	27.6		23.9	
60 – 64	25.5		28.3	
65 – 69	17.7		23.0	
70 – 78	7.7		23.2	
IPSS	***% of men***			
Mild (0 – 7)	76.5		69.8	
Moderate (8 – 19)	21.4		26.9	
Severe (20 – 35)	2.1		3.3	
IPSS by age (years)	***Mean (Median) IPSS***			
50 - 59	4.9 (3)		5.1* (3)	
60 - 69	5.5 (4)		6.8 *(5)	
70 - 78	6.4 (6)		8.1 *(8)	
IPSS (all men)	***Mean IPSS***			
IPSS	5.2		6.1*	
Quality of Life	***Mean quality of life scores***			
	All men	*IPSS > 7*	*All men*	*IPSS > 7*
Mini-ISH	2.0	3.0	1.5*	2.1*
SIP Social (6; 11) †	5.3	7.7	4.3*	6.3*
SIP Emotional (3.5; 17.9) †	3.6	6.0	2.8*	4.0*
SIP Recreation (3; 11.9) †	9.8	13.8	7.7*	11.1*
IPSS-QOL	1.3	2.5	1.4	2.2*
BII	0.7	2.0	0.6	1.6*
Quality of Life by age (years)	***Mean (median) IPSS-QOL***			
50 - 59	1.2 (1)		1.2 (1)	
60 - 69	1.4 (2)		1.5 (2)*	
70 - 78	1.7 (2)		1.8 (2)*	

** Significant at p = 0.05*
†Mean reference values Jacobs (open population versus persons with non-specific abdominal complaints)

Table 2. *Annual IPSS and IPSS-QOL changes in 3 comparable studies*

	IPSS			IPSS-QOL		
Baseline age (years)	***Krimpen***	***OCS****[8]	***Japan***[9]	***Krimpen***	***OCS***	***Japan***
50 - 59	0.05	0.30	- 0.10	0.00	- 0.00	- 0.01
60 - 69	0.31	0.60	- 0.20	0.01	0.05	- 0.27
70 - 78	0.41	0.38	- 0.20	0.01	- 0.03	0.20

**OCS = Olmsted County (USA)*

Table 3. *IPSS and various quality of life measures (all correlations are significant at 0.05 level)*

At Baseline	Mini-ISH	SIP Social	SIP Emotional	SIP Recreation	IPSS-QOL	BII
IPSS	0.27	0.16	0.16	0.14	0.67	0.67
Mini-ISH		0.40	0.35	0.38	0.27	0.25
SIP Social			0.57	0.50	0.13	0.15
SIP Emotional				0.35	0.13	0.16
SIP Recreation					0.13	0.10
IPSS-QOL						0.62

For abbreviations: see Materials and Methods

Table 4. *QOL changes on various measures according to baseline IPSS and LUTS changes*

	Mini-ISH	SIP Social	SIP Emotional	SIP Recreation	IPSS-QOL	BII
All men	- 0.40*	- 0.95*	- 0.85*	- 2.09*	0.06	0.02
IPSS mild at baseline						
Clear worsening (n=144)	- 0.21	- 0.15	0.01	- 1.29	0.57*	0.55*
Slight worsening (n=384)	- 0.38*	- 0.60	- 0.80*	- 2.01*	0.20*	0.04
Slight improvement (n=114)	- 0.56*	- 3.20*	- 1.54*	- 4.87*	- 0.35*	- 0.25*
Clear improvement (n=18)	- 0.50	- 1.9	- 0.32	0.78	- 0.11	- 0.22
IPSS moderate to severe at baseline						
Clear worsening (n=34)	- 0.50	- 0.68	1.29	- 1.23	0.29	0.91*
Slight worsening (n=49)	- 0.76*	- 0.77	- 2.18	- 1.14	- 0.16	0.29
Slight improvement (n=50)	- 0.46	0.48	- 1.05	- 0.09	- 0.32*	- 0.6*
Clear improvement (n=70)	- 0.32	- 1.98*	- 1.96	- 2.88	- 0.77*	- 1.36*

Mean change computed by subtracting baseline from follow-up data with negative mean change indicating improved quality of life and statistical analysis between baseline and follow-up data performed using a paired t-test (IPSS groups were based on baseline IPSS (mild versus moderate to severe) and change in IPSS over time of < 4 points or ≥ 4 points.)
** Significant at p = 0.05 level*

Table 5. *QOL changes on various measures according to 4-points LUTS increase*

	Change in quality of life according to an increase of 4 points in IPSS (11.43%)
Mini-ISH (0-13)	0.07 (0.54%)
SIP Social (0-100)	0.41 (0.41%)
SIP Emotional (0-100)	0.32 (0.32%)
SIP Recreation (0-100)	1.05 (1.05%)
IPSS-QOL (0-6)	0.32 (5.33%)
BII (0-13)	0.49 (3.77%)

baseline and second follow-up. Table 4 also shows that in the QOL disease-specific measures there was significant improvement and significant worsening depending on the subgroups. It should be noted that, although in some subgroups IPSS-QOL worsened, the average score of this measurement nevertheless indicates general satisfaction with the condition.[13]

Men in the clear worsening, slight worsening, slight improvement and improvement subgroups showed no inter-group differences regarding age, smoking/drinking behaviour, marital status, number of children and level of education.

Changes in QOL with time were analysed for each QOL score separately. Table 5 shows changes in the generic and disease-specific QOL measures according to an increase of 4 points on the IPSS. Linear regression models, which included IPSS at baseline, change in IPSS between baseline and follow-up and age, showed that 0.8% of the change in Mini-ISH could be predicted by the model (explained variance = 0.8%, $p = 0.069$). For SIP Social, SIP emotional and SIP recreation the explained variance was 1.4% ($p = 0.006$), 0.7% ($p = 0.112$) and 1.1% ($p = 0.023$), respectively. This low explained variance indicates that better reported QOL measured by the generic instruments cannot be attributable to changes in LUTS (Table 3) .

Using the same explanatory variables for the disease-specific QOL changes 14.7% of the IPSS-QOL change could be predicted by this model (r^2 $p < 0.0001$), as 16.5% of the variance in BII (r^2 $P < 0.0001$).

DISCUSSION

The results of our longitudinal study show that changes in the severity of LUTS, defined as changes in symptom frequencies as measured by IPSS, have little impact on disease-specific QOL and hardly any impact on generic QOL in men aged 50 to 78 years old. Considering the suggested progressiveness of LUTS with time the only slight increase in mean IPSS in our study population during 4.2 years is remarkable. Selective loss of respondents is not an adequate explanation for this small increase. Men who quit the study after baseline measurement or at 2.1 years of follow-up also showed only a modest increase in IPSS with time.

The longitudinal annual change in the Olmsted County study also increased with age, although this annual change was higher than in our participants.[8] In contrast to these and our results, mean scores in men in the Japanese study decreased.[9] Differences in follow-up period (Japan shorter) and the number of data points in the Japanese study (Japan less) could be an explanation for these differences.

The overall health-status of our participants as measured by the generic QOL questionnaires improved during follow-up. Participants in our study had SIP-scores comparable to those in an unselected Dutch population but better QOL as measured by SIP than in patients with non-specific abdominal symptoms.[16] Only the mean score on the recreation domain of the SIP of our participants was higher than the score of the two reference-groups, which could be explained by the higher age of our participants.

In the current study disease-specific QOL of men deteriorates with increasing IPSS. However, most men seem to have had few problems with LUTS because the average score on PSS-QOL in the different subgroups indicates "in general satisfied". Thus, despite the significant changes measured in IPSS-QOL, we emphasize that this does not necessarily imply clinically relevant changes.

The positive change in generic QOL in this study could not be attributed to baseline LUTS severity or change in LUTS with time. Although the QOL-instruments were found to be sensitive and in a large part of the population we saw IPSS-changes of 4 or more points, we must to realize that the change in IPSS causes only a small change in disease-specific QOL. This change may be too small to cause a measurable effect on generic questionnaires.

Normally, one would expect the reported QOL to decrease with ageing. However, in the current study we found the opposite. Better generic QOL might be explained by participants reaching retirement age during the study period, more spare time, less work-related stress and other kinds of daily activities. This discrepancy between the increase in LUTS and worse disease-specific QOL on the one hand and the better generic QOL on the other might also be explained by coping strategies. Studies have shown that coping behaviour, that is the way one manages stressful situations and circumstances affects psychological, physical and social wellbeing.[17, 18] Because LUTS was not the topic of investigation in those latter studies, to our knowledge the relationship between coping behaviour and changes in perceived QOL in men with a change in LUTS-severity remains to be explored.

The results of our longitudinal study in the community show that there is an interaction between LUTS and QOL but it is not as large as expected. Obviously there are other populations or subgroups with more extreme changes in severity of LUTS that may show larger effects on QOL.

From our cross-sectional analyses we earlier concluded that LUTS was strongly related to suboptimal wellbeing.[6] Also based on cross-sectional data, others, concluded that men with moderate and severe LUTS identified in a large U.S. cohort have a poor health status in several important QOL dimensions.[3, 6] Bertaccinni et al. also suggested that LUTS largely influenced the perceived QOL of men.[19] Thus earlier conclusions about the relation between LUTS and QOL in cross-sectional data, including the Krimpen Study, seemed justified. However, after analysing the longitudinal data of the Krimpen Study the relationship between LUTS and QOL has to be reconsidered. The differences between the results based on cross-sectional and on longitudinal data are mainly attributable to study-design-differences, but may also be due to co-morbidity that occurs more frequently in patients with LUTS and is known to have a negative effect on QOL. Because, we have previously observed an association between LUTS, erectile-dysfunction and QOL, we suggest that in men with LUTS and a poor QOL the general practitioner or urologist should also assess for curable co-morbidity that could have adversely affect QOL. [6]

Longitudinally our data showed that there is a slight increase in disease-specific QOL with time. This is in line with data from North America and Asia.[8, 9]

No attention was paid to the impact of potential treatments in this population because our analyses are specifically targeted on changes. LUTS and QOL separately can be affected by treatment but it is not probable that treatment has impact on the relationship between LUTS and QOL. The influence of treatment for LUTS in relation to changes in QOL is a topic of future research in the Krimpen Study.

CONCLUSION

From our population-based study we conclude that a change in LUTS during a follow-up of 4.2 years had only a small impact on the disease-specific QOL and hardly any impact on the generic QOL of men 50 to 78 years old. These results imply that men with LUTS do not perceive a considerable influence of these symptoms on general wellbeing. This in turn could suggest the need for more restraint in the intervention policy for men with LUTS.

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5

Influence of coping styles on quality of life in men with new and increasing lower urinary tract symptoms

Submitted

ABSTRACT

Objective

It is not known whether a change in lower urinary tract symptoms (LUTS) has a direct influence on quality of life (QOL) or whether such change in QOL is also influenced by other factors, such as personal characteristics e.g. age, co-morbidity and coping style. The present study aims to determine the influence of coping on QOL in elderly men developing LUTS.

Materials and Methods

Longitudinal population-based study with a follow-up period of 6.5 years on 1,688 men aged 50 to 78 years. Data were collected through self-administered questionnaires, including the Sickness Impact Profile (SIP, three domains), Inventory of Subjective Health (ISH), International Prostate Symptom Score (IPSS), BPH Impact Index (BII) and the Utrecht Coping List (UCL). Various physical and urological measurements were completed. Multiple linear regressions were used to determine the change in QOL in men with incident LUTS in relation to coping behaviour.

Results

Overall no significant association is found between changes in LUTS with a change in QOL. However, a positive change in QOL is significantly associated with a change in LUTS when men use the coping style active problem solving and a negative relation exists with coping style reassuring thoughts.

Conclusion

Different coping styles have a different impact on the relation between a change in LUTS and a change in generic QOL in community-dwelling elderly men. The change in generic QOL determined by a change in LUTS in combination with the use of these coping styles is large compared to the influence of, for example, getting a new chronic disease. This makes a future exploration of the clinical treatment possibilities warranted.

INTRODUCTION

It is not known whether a change in quality of life (QOL) is directly influenced by a change in Lower urinary tract symptoms (LUTS) or whether such change in QOL is mainly caused by other related factors, such as personal characteristics e.g. age, co-morbidity and coping style. Coping style represents the way one manages stressful situations, and is known to affect psychological, physical and social well-being [1-6]. Coping can be conceptualised as a personality trait [7]. Discussing the coping style with the patient may be an effective way to influence QOL in chronic diseases like LUTS with relative limited treatment options. However, the association between coping, LUTS and QOL has not yet been studied. The Krimpen Study offers the opportunity to study these three factors in a longitudinal study design in which a change in QOL can be linked to a change in LUTS. The present study aims to determine the influence of coping on QOL in elderly men developing LUTS.

MATERIALS AND METHODS

The design of the Krimpen study on male urogenital tract problems and general health status has been described in detail [8]. Briefly, the Krimpen study was performed among all men aged 50 – 78 years living in a Dutch municipality near Rotterdam. Men without radical prostatectomy, prostate or bladder cancer, neurogenic bladder disease or a negative advice from their GP (in case of a serious disease with a short life-expectancy), who were able to complete questionnaires and attend the research centre, were invited for the study. The Medical Ethical Committee of the Erasmus Medical Centre Rotterdam approved the study.

First, all 1688 participants filled out a questionnaire, including the short version of the Inventory of Subjective Health (mini-ISH) [9], three domains of the Sickness Impact Profile (SIP) [10], the International Prostate Symptom Score (IPSS) [11], the BPH Impact Index (BII) [12] and the Utrecht Coping List (UCL) [7]. Secondly, additional measurements: height, body weight, blood pressure measurement and urinalysis were performed at the research centre. Finally, in cooperation with the urology department of the Erasmus MC the following tests were performed: serum prostate-specific antigen (PSA), digital rectal examination (DRE), transrectal ultrasound of the prostate (TRUS), uroflowmetry and poist void residual urine volume. Prostate biopsies were taken in men suspected of prostate cancer. Measurements were repeated in three consecutive rounds of follow-up with an average follow-up time of 2.1 years, 4.2 years and 6.5 years, respectively. Men, who did not respond after baseline, first follow-up or second-follow up and did not meet the exclusion criteria were also re-invited for participation in the third follow-up round. In the baseline study, the first, second and third follow-up respectively 1688, 1204, 882 and 825 men participated.

Quality of life questionnaires

We used the SIP as the generic QOL questionnaire [10]. The three domains of the SIP used in this study are 'Emotions' (9 items), 'Recreation' (8 items) and 'Social' (20 items). For each category, a score was computed based on weighing factors for each item, providing scores ranging from 0 to 100 [10]. In the present study the scores on the three domains were summed up. (significant correlation between the three SIP domains ranged from 0.4 – 0.6) A higher score on the SIP total indicates a worse QOL. A change in QOL was defined as the difference between the sum of the SIP domains at baseline and the sum of the SIP domains at the various follow-up rounds.

Coping Style

Coping styles are assessed using the Utrecht Coping List [7]. In the UCL, coping is regarded as a personal disposition, e.g. a trait. The respondent is asked to imagine 'problems in general'. The UCL consists of 47 items describing a specific coping behaviour. Answers are on a 4-point scale ranging from 'seldom or never' to 'very frequently'. The instrument was validated for use in a Dutch population [7]. The UCL consists of seven coping scales considered as coping styles. The names of the styles and examples of items (between brackets) are: **A**: active problem solving ('putting things in a row', 'seeking a way to solve a problem'), **P**: palliative reaction ('looking for distraction', and looking for good company'), **AV**: avoidance ('avoiding difficult situations' and ' letting things go'), **S**: seeking social support ('discussing the problem with friends or family' and 'asking somebody for help'), **PR**: passive reaction ('('being overwhelmed by problems'), **E**: expression of emotions ('showing anger to the person who is responsible for the problem'), and **R**: Reassuring thoughts ('imagining that things could be worse'). Data on coping was only collected at the third follow-up round.

LUTS

To assess the occurrence and frequency of LUTS we used the International Prostate Symptom Score (IPSS) [11]. The IPSS is a seven-item questionnaire that elicits the symptoms of nocturia, frequency, weak urinary stream, hesitancy, intermittency, incomplete emptying and urgency. The scoring range is 0 (no symptoms) to 35 (maximal symptoms). Change in LUTS was defined as the difference between the IPSS at baseline and the IPSS at the various follow-up rounds.

Co-morbidity

To adjust for the influence of other symptoms than LUTS on QOL we used the mini-ISH [9], a 13-item questionnaire. On every item the respondent is asked whether he has experienced it during the past two weeks. All items must be answered with 'yes' or 'no'. A higher score indicates more symptoms. We also registered if a new chronic disease (diabetes, hypertension, COPD or heart problems) occurred by asking whether the participant had seen his general practitioner or a medical specialist for this disease for the first time during the last three months before baseline of follow-up.

Statistical analyses

Only 7.7% (1.5% missing more than 1 question) of the respondents who returned the UCL did not complete this questionnaire. We imputed these missing values on the UCL with the mean value of the respondents who completed the questionnaire. Mean coping scores and 95% confidence intervals (CI) of the study population were determined and compared with reference scores of the Dutch population. Also mean changes in SIP total and IPSS were determined between baseline and follow-up. Pearson's correlation was used to determine the correlation between these changes.

To explore whether coping influence the impact of LUTS on generic QOL we performed multivariate linear regression analyses using the PROC MIXED procedure from SAS. This method allows for the repeated measurements within individuals and handles continues and categorical explanatory variables, missing data, and time-dependent covariates.

The following independent variables were entered in the model: total SIP score at baseline, baseline IPSS, age, change in IPSS, change in mini-ISH, change in number of chronic disease(s), age, the seven coping styles of the UCL separately and in interaction with a change in IPSS. After backward stepwise elimination of the non-significant variables, only the significant variables remained in the model ($P < 0.05$). Final analysis was performed using statistically significant variables only. The SAS (version 8.2) program was used for all analyses.

RESULTS

For 742 men (92% of the respondents at follow-up 3) data on coping behaviour were available. Table 1 presents the baseline characteristics of these men. Mean IPSS and QOL scores indicate a mild severity of LUTS and a reasonably good generic QOL. The scores on the seven separate coping styles of our respondents correspond with the mean scores of a Dutch reference group of men in the same age category.[7]

Table 2 shows that the mean changes in quality of life between baseline and follow-up are nihil. However, the high standard deviations indicate higher individual changes. No correlation was found between changes in QOL and changes in IPSS between baseline and follow-up.

Table 3 shows the final multivariate model of the linear regression analysis of the determinants influencing the changes in generic quality of life. Symptom severity at baseline, age, getting a new chronic disease and the coping styles passive reaction pattern and expression of emotions have a significant association with a worsening of generic QOL. Contrary, generic QOL at baseline and the coping style active problem solving are significant associated with an improvement of generic QOL. Overall we found no significant association between a change in LUTS and a change in QOL. However, the level of coping style active problem solving and reassuring thoughts determine the effect of a change in LUTS on a change in

Table 1. *Characteristics of the study population at baseline*

	Study population (N=742)		
Age (years)	**Percentages**		
50-54	23.5		
55-59	30.3		
60-64	23.8		
65-69	15.7		
70-78	6.6		
Symptoms and chronic diseases	**Mean (SD)**		
IPSS [0-35]	5.3 (5.5)		
Number of chronic diseases† [0-4]	0.2 (0.5)		
Quality of life	**Mean (SD)**		
SIP Total+ [0-300]	19.5 (28.9)		
Mini-ISH [0-13]	2.0 (2.4)		
	Krimpen Study		**Reference Population***
Coping styles	**Mean**	**95% C.I**	**20th-80th percentile**
Active problem solving (A) [7-28]	17.7	17.5-18.0	15-20
Palliative response (P) [8-32]	14.7	14.5-15.0	12-18
Avoidance and passive expectancy (AV) [8-32]	15.2	15.0-15.5	12-17
Seeking social support (S) [8-32]	11.2	11.0-11.4	9-13
Passive reaction (PR) [7-28]	10.3	10.1-10.5	9-12
Expression of emotion and anger (E) [3-12]	5.8	5.7-5.9	5-6
Reassuring Thoughts (R) [5-20]	11.3	11.1-11.4	10-13

**Values for the age category 55 to 65 years based on data from a study on employees of the Dutch Railway, and a random sample of the Dutch population (7).*

[+] Sip Total = Sip emotion + Sip social + sip recreation

[†] Number of chronic diseases (including: diabetes, hypertension, COPD and heart problems)

[Numbers between brackets represents scale]

QOL as evidenced by significant interaction terms. For example, a worsening of 8 points at the IPSS (for example; from no LUTS to mild LUTS) in combination with the minimal level of coping style reassuring thoughts (R) (min = 5 points) will worsen the score at the SIP total with 7 points ((8*0.08) + (8* 5 * 0.15) = 6.6). A change of 8 points at the IPSS in combination with the maximal level of this coping style (max = 20 points) will worsen the score at the SIP total with 25 points ((8*0.08) + (8* 20 * 0.15) = 24.6). In both cases the level of coping style A is minimal (value extrapolated to zero). Conversely, getting a new chronic disease results in a worsening of the total SIP score with 5 points. The model presented in table 3 explained a substantial proportion of the change in generic QOL ($R^{2} =$ 39%).

Table 2. *Mean changes in quality of life and IPSS between baseline and follow-up*

	Mean Change in SIP[+] (SD[*]) [0-300]	**Mean change in IPSS (SD[*]) [0-35]**	**Pearson's correlation between change in SIP and change in IPSS**
Between baseline and 2 years	0.58 (28.4)	1.78 (4.84)	0.05 (NS)
Between baseline and 4 years	-4.85 (27.03)	0.69 (3.86)	0.03 (NS)
Between baseline and 6 years	-4.25 (22.40)	0.20 (3.88)	0.06 (NS)

+ Sip Total = Sip emotion + Sip social + sip recreation
** Standard deviation*
NS: not significant

Table 3. *Final model of determinants influencing the change from baseline of the generic quality of life in men aged 50-78 years. (Multivariate model of determinants with p < 0.05; regression coefficient (B) and P-value is given)*

Variables	**B[†]**	**Se[†]**	**P-value**
Follow-up moment 0* (2 years from baseline)	0	0	0
Follow-up moment 1 (4 years from baseline)	-0.88	0.89	.32
Follow-up moment 2 (6 years from baseline)	3.74	1.00	< .001
Age (yrs)	0.22	0.10	.03
SIP Total Baseline	- 0.57	0.02	< .001
IPSS Baseline	0.51	0.12	< .001
Change in IPSS	0.08	0.67	.91
Getting a chronic disease (yes versus no)	4.97	0.95	< .001
Passive reaction pattern (PR)	1.44	0.26	< .001
Expression of emotions (E)	1.44	0.45	< .01
Active Problem Solving (A)	- 0.42	0.18	.02
Reassuring thoughts (R)	- 0.07	0.29	.81
Change in IPSS * coping style A[#]	- 0.08	0.03	.02
Change in IPSS * coping style R[#]	0.15	0.05	< .01

* Reference category
[†] Se, standard error
[#] Interaction terms

DISCUSSION

The present longitudinal study provides evidence that different coping styles have a different impact on the relation between a change in LUTS and a change in generic QOL in community-dwelling elderly men. A change in QOL is significantly positively associated with a change in LUTS when men use the coping style active problem solving and negatively with reassuring thoughts. The change in generic QOL determined by a change in LUTS in combination with the use of these coping styles is large compared to, for example, getting a new chronic disease (not considering coping styles).

Given the similarity of the scores at the 7 coping styles of our respondents and the Dutch reference groups, our study population can be considered as representative. Coping style is considered a personality trait. Therefore, we checked if there was in our data a relationship between coping style and LUTS (data not presented). Men with specific coping scores are equally prone to get LUTS. If there is no relation between incident LUTS and coping style, and we assume a causal relation between QOL and incident LUTS (which is reasonable), then the interaction of coping, LUTS and QOL is the result of a causal relation between coping and QOL.

In line with our previous study[13] the multivariate linear regression analysis showed that a change in LUTS separately was not significantly associated with a change in generic QOL. However, changes in LUTS in combination with the use of specific coping styles seem to affect generic QOL. For example, a man who always wanted to solve a problem efficiently (coping style active problem solving) getting LUTS will probably seek care for it probably resulting in a better QOL. But denying LUTS, which is treatable, by thinking that it is not really a serious problem and that it probably will disappear in time (coping style reassuring thoughts) can negatively affect generic QOL.

To our knowledge this study is the first that demonstrates that coping styles influence the impact of LUTS on QOL, and also quantified this influence compared to the influence of other important factors. The associations found between a change in LUTS and different coping styles as active problem solving and reassuring thoughts in relation to generic QOL are interesting for physicians. For example, it may be advisable to stimulate effective coping styles in patients and not to stimulate non-effective styles. This may implicate that physicians must pay attention to the coping style of the patient. However, proof of this needs further study in which an intervention is introduced to change the coping style of the patient, with the aim to influence the outcome QOL. Until this has been proven physicians should, because of the prognostic value of the coping style in relation to the change in generic QOL, take into account the influence of coping styles on generic QOL in their treatment.

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Determinants of seeking of primary care for lower urinary tract symptoms in community-dwelling men

European Urology; in press

ABSTRACT

Objective

To determine which factors predict primary care seeking in men with lower urinary tract symptoms (LUTS).

Materials and Methods

A longitudinal, population-based study with a follow-up period of 6.5 years was conducted among 1688 men aged 50 to 78 years old. Data were collected on transrectal ultrasonometry of prostate volume, urinary flow rate, ultrasound estimated postvoid residual urine volume, generic and disease-specific quality of life and symptom severity based on the International Prostate Symptoms Score (IPSS). Information on primary care seeking during 2 years of follow-up of all participants was collected from the general practitioners (GP) record using a computerised search engine, and an additional manual check of the electronically selected files.

Results

Prostate volume, post-void residual volume, IPSS and social generic QOL are important determinants of first GP consultation in men with LUTS. Measurements (physical urological parameters) and self-reported items (symptom-severity and quality of life) contribute almost equally to GP consultation in these men.

Conclusion

Both measurements of prostate volume and post-void residual urine volume as self-reported information about symptoms or QOL can help to select those who will benefit from medical care and help to reassure those men that are not likely to need near future help.

INTRODUCTION

As the past decades can be characterised by an increasing growth of diagnostic and therapeutic opportunities in health care, and resources as workforce and time become scarce, the efficiency of health care is followed critically.[1] Likewise, consultation of the general practitioner (GP) and GP policy are subject of discussion. In the Netherlands men who develop LUTS first consult their general practitioner (GP) for medical care. Improved knowledge of the determinants for GP consultation in men with lower urinary tract symptoms (LUTS) will contribute to an appropriate use of health care focused on the needs of elderly men. Previous studied factors that differed between men who sought medical care for LUTS and those who did not are retirement [2], scores on urinary symptom questionnaires [3, 4], being worried and embarrassed about urinary (dys)function [4], social influences[5], fear of cancer or surgery [6], and the patient's perception of the ability of the care provider.[7] These studies mostly investigated a specific factor of interest and were not prospective in study design; this limits their prognostic value. To understand which determinants predict GP visit for LUTS a longitudinal population based study including symptom severity, age and other important factors such as quality of life, urological parameters (prostate volume, post-void residual volume and maximum urinary flow rate), lifestyle (smoking behaviour and drinking habits) and education. The present study aimed to determine which of these determinants predict future primary care seeking in men with LUTS.

MATERIALS AND METHODS

Study design

The design of the Krimpen study on male urogenital tract problems and general health status has been described in detail [8]. Briefly, the Krimpen study was performed among all men aged 50 – 78 years living in a Dutch municipality near Rotterdam. Men without radical prostatectomy, prostate or bladder cancer, neurogenic bladder disease or a negative advice from their GP (in case of a serious disease with a short life-expectancy), who were able to complete questionnaires and attend the research centre, were invited for the study. The Medical Ethical Committee of the Erasmus Medical Centre Rotterdam approved the study.

First, data of 1688 responders (50%) were collected via a self-administered 113-item questionnaire, which included different questionnaires about symptom frequency, quality of life and also addressed the topics marital status, number of children, education level, smoking behaviour and drinking habits. Secondly, additional measurements: height, body weight, blood pressure measurement and urinalysis were performed at the research centre. Finally, in cooperation with the urology department of the Erasmus MC the following tests were performed: serum prostate-specific antigen (PSA), digital rectal examination (DRE), transrectal ultrasound of the prostate (TRUS), uroflowmetry and poist void residual urine volume. Prostate biopsies were taken in men suspected of prostate cancer. Measurements were repeated in three consecutive rounds of follow-up with an average follow-up time of 2.1 years, 4.2 years and 6.5 years, respectively.

In order not to disturb the natural course of BPH, no information on test results, except for the value of the prostate specific antigen (PSA), was given to the participant and his GP.

Data assembly of GP data

A flow chart of the GP data assembly is presented in figure 1.

In the Netherlands, all inhabitants are registered with a GP. When the patient visits any physician in the weekend or at night, his own GP is always informed. Data about all visits, contacts and prescription of medication are stored in the computerized medical records.

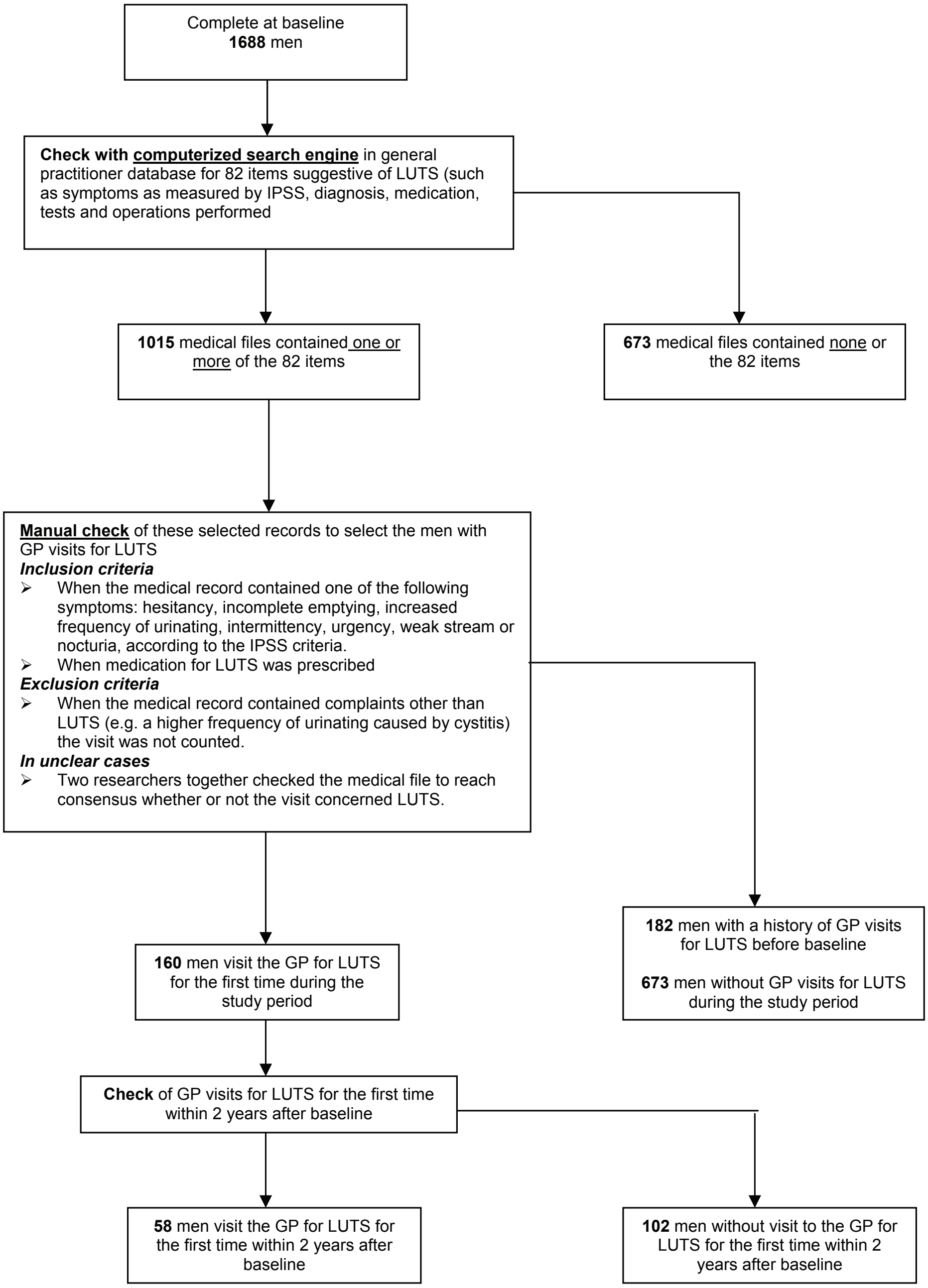
All practising GP's (N=16) in Krimpen aan den IJssel gave access the GP medical records of all the participants of the study (N = 1688). These records were checked with the "N6" computer program (QSR International Pty. Ltd. Melbourne, Australia) that can search and select text files on keywords. Two researchers independently scored whether or not there was a history of LUTS (i.e. before the start of the study), whether the participant had visited his GP for LUTS and the first date this took place. When the medical file showed that a person had moved from the GP's practice (lost to follow-up) or was deceased, the date of this event was noted. To validate the use of the N6 program the medical files that showed no hits by N6 were checked manually; none of the files reported visits for LUTS.

Symptoms and Measurements

LUTS was assessed by the seven-item International Prostate Symptom Score (IPSS).[9] The total volume of the prostate and the volume of the transition zone were measured by transrectal ultrasound (TRUS). We used the planimetric procedure to determine the prostate volume most accurate.[10] The measurements were performed using the Bruel and Kjaer® Medical Falcon Ultrasone Scanner type 2101 equipped with a 7 MHz biplanar endorectal transducer type 8808. Post-void residual urine volume was measured using a transabdominal ultrasound device (Aloka® Model SSD-1700 Dyna View, with a 3.5 MHz electronic convex probe) and uroflowmetry (Q_max) was done using a flow meter (Dantec Urodyn 1000, Copenhagen, Denmark).

Quality of life

To assess the generic QOL of the men we used the mini-Inventory of subjective Health (ISH) and the Sickness Impact Profile (SIP). The mini-ISH is a 13-item questionnaire on subjective health with a score range from 0 to 13.[11] The three domains of the SIP used in this study are 'Emotions' (9 items), 'Recreation' (8 items) and 'Social' (20 items). For each category, a score was computed based on weighing factors for each item, providing scores ranging from 0 to 100 [12].



Complete at baseline
1688 men

Check with <u>computerized search engine</u> in general practitioner database for 82 items suggestive of LUTS (such as symptoms as measured by IPSS, diagnosis, medication, tests and operations performed

1015 medical files contained one or more of the 82 items

673 medical files contained none or the 82 items

Manual check of these selected records to select the men with GP visits for LUTS

Inclusion criteria

- When the medical record contained one of the following symptoms: hesitancy, incomplete emptying, increased frequency of urinating, intermittency, urgency, weak stream or nocturia, according to the IPSS criteria.
- When medication for LUTS was prescribed

Exclusion criteria

- When the medical record contained complaints other than LUTS (e.g. a higher frequency of urinating caused by cystitis) the visit was not counted.

In unclear cases

- Two researchers together checked the medical file to reach consensus whether or not the visit concerned LUTS.

160 men visit the GP for LUTS for the first time during the study period

182 men with a history of GP visits for LUTS before baseline

673 men without GP visits for LUTS during the study period

Check of GP visits for LUTS for the first time within 2 years after baseline

58 men visit the GP for LUTS for the first time within 2 years after baseline

102 men without visit to the GP for LUTS for the first time within 2 years after baseline

Figure 1. *Data assembly in General Practitioner database*

In contrast to the generic QOL questionnaires, disease-specific questionnaires measure QOL on the basis of items closely related to the specific disease and are therefore expected to be more sensitive. To measure the effect of LUTS on QOL we used the QOL question of the IPSS (IPSS-QOL) and the BII. The IPSS-QOL can be rated on a 0 to 6 scale.[9] The BII is a four-question index with a score of 0 – 13 designed to assess the impact of the symptoms of BPH on health status.[13]

For all used QOL scales (disease-specific and generic) a higher score indicates a worse QOL.

Statistical analyses

To explore the possible effect of different variables on first GP visit for LUTS within two years after baseline we performed univariate and multivariate logistic regression analysis. First GP visit for LUTS means the first visit with complaints of LUTS *without a history of LUTS*.

Baseline variables were analysed as continuous variables but for post-residual volume greater than 50 ml, the different SIP domains, having children, living together, current smoker, using more than 2 drinks of alcohol a day, and educational level a dichotomous variable was constructed, because no normal distribution was present in this study population. The total domain score was 0 if the SIP domain score was equal to 0, and was 1 if the SIP domain score was above 0.

Variables with a p-value ≤ 0.25 in the univariate analysis were entered in the multivariate logistic regression analysis.[14] Variables with a p-value more than 0.05 to the effect in the multivariate models were excluded. The data were analysed in SPSS 11.

RESULTS

The study cohort consisted of 1688 men. The search program N6 selected 1015 of the files. In these files we found 182 men with a history of GP visit for LUTS (GP or urologist) before the start of the study, leaving 1506 men (89%) at risk to attend their GP with LUTS on a later date. Complete baseline data and GP data were available of these 1506 men. Table 1 shows that men at risk have slightly less LUTS and higher QOL than men of the total study population. Of the men at risk 58 men (3.9%)have visited their GP for LUTS for the first time within two years after baseline.

Table 2 shows the results of logistic regression analysis of determinants predicting GP visit for LUTS. Determinants univariate significantly associated with first GP visit for LUTS are: post-void residual volume, Q_max, prostate volume, age, symptom severity, disease-specific QOL (IPSS_QOL and BII) and social and emotional generic QOL ($p \leq 0.05$). Both irritative IPSS and obstructive IPSS were related to first GP visit for LUTS. The multivariate model with only urological determinants (prostate volume, post-void residual volume and maximum flow rate) gave a proportion of explained variance (R^2) of 10%. When symptom-severity (IPSS) and

Table 1. *Characteristics of the study population at baseline*

	Total study population* (N=1688)	**People at risk** (N=1506)**
Symptoms	**Mean (SD)**	**Mean (SD)**
IPSS	5.3 (5.4)	4.8 (4.9)
IPSS-irritative	2.9 (2.7)	2.7 (2.5)
IPSS-obstructive	2.4 (3.5)	2.1 (3.1)
Quality of Life (QOL)	**Mean (SD)**	**Mean (SD)**
Generic QOL		
SIP Social	5.9 (9.6)	5.6 (9.2)
SIP Emotional	4.0 (9.9)	3.9 (9.4)
SIP Recreation	10.8 (17.3)	10.6 (17.4)
Mini-ISH	2.0 (2.3)	2.0 (2.3)
Disease-specific QOL		
IPSS-QOL	1.4 (1.2)	1.2 (1.1)
BPH-II	0.7 (1.4)	0.6 (1.2)
Urological parameters	**Mean (SD)**	**Mean (SD)**
Prostate volume	33.7 (14.5)	33.6 (14.2)
Transition zone volume	16.2 (12.3)	16.0 (11.9)
Maximum urinary flow rate	11.5 (6.9)	11.6 (6.9)
Residual volume	21.8 (50.5)	21.7 (51.5)
Age	**Percentages**	**Percentages**
50-54	20.3	21.4
55-59	25.4	25.7
60-64	24.0	23.5
65-69	19.3	19.0
70-74	7.9	7.4
75+	3.1	2.9
Under treatment for:	**Percentages**	**Percentages**
Diabetes Mellitus	3.4	3.5
Hypertension	15.9	15.8
COPD	4.5	4.4
Parkinson’s disease	0.1	0.1
Cardiac disease	6.2	6.1
Chronic urinary tract infection	0.8	0.5
Liver disease	0.4	0.4
One or more of the above	24.8	24.5

** Total study population: 1688 baseline responders*

*** People at risk: men, without a history of LUTS, at risk to attend their GP for LUTS after start of the study.*

Table 2. *Univariate and multivariate logistic regression analyses of (possible) determinants at baseline for GP visit for LUTS within two year (N at risk = 1506; N of men with event = 58)*

Determinants	OR	95% CI	P-value
Univariate analysis			
IPSS*	1.13	1.09-1.18	<0.001
IPSS-irritative*	1.29	1.19-1.39	<0.001
IPSS-obstructive*	1.17	1.10-1.23	<0.001
Age*	1.09	1.05-1.13	<0.001
Post-void residual urine volume more than 50 ml $^+$	3.22	1.73-5.99	<0.001
Prostate volume*	1.04	1.03-1.05	<0.001
Transition zone volume*	1.04	1.03-1.06	<0.001
Transition zone Index*	1.06	1.04-1.08	<0.001
Maximum urinary flow rate*	0.93	0.88-0.98	0.006
Mini-ISH*	1.07	0.96-1.19	0.225
IPSS-QOL*	1.88	1.49-2.36	<0.001
BPH-II*	1.48	1.30-1.69	<0.001
Socially impaired$^+$	4.48	2.18-9.22	<0.001
Emotionally impaired$^+$	1.97	1.12-3.46	0.019
Recreationally impaired$^+$	1.89	1.10-3.26	0.021
Living together$^+$	0.58	0.14-2.42	0.456
Children$^+$	1.11	0.43-2.82	0.832
Smoking$^+$	1.23	0.68-2.22	0.499
More than two units of alcohol a day$^+$	0.62	0.28-1.38	0.237
Education level$^+$	1.37	0.66-2.85	0.398
Final multivariate model with determinants with p≤ 0.05; R^2 = 0.22			
Determinant†	**OR**	**95% CI**	**P-value**
IPSS*	1.14	1.08-1.19	<0.001
Prostate volume*	1.03	1.02-1.05	<0.001
Post-void residual urine volume more than 50 ml $^+$	2.57	1.24-5.32	0.011
SIP-social score $^+$	3.91	1.76-8.66	<0.001

** Continuous variable;*

$^+$ *Dichotomous variable;*

† *Only variables with significance of p <0.25 in univariate analysis were used for the multivariate model.*

quality of life (disease-specific and generic) were added to the model with only urological variables, the IPSS, prostate volume, post-void residual volume and the SIP social remained significant determinants of first GP visit for LUTS ($R^2 = 22\%$).

Using the variable transition zone index instead of prostate volume in the model, the transition zone index was significant (p = 0.05) but less significant than the prostate volume (p = 0.02) and did not result in a higher explained variance in GP visit for LUTS.

DISCUSSION

Our study demonstrates that prostate volume, post-void residual volume, IPSS and social generic QOL are important determinants of first GP consultation in men with LUTS. Urologic measurements and self-reported items contribute almost equally to first GP consultation for LUTS.

In the Krimpen study 50% of the invited men responded. The mean symptom and QOL scores of the responders indicate a mild severity of LUTS and a reasonably good QOL. A questionnaire was sent to those that did not participate at baseline to investigate the characteristics of this group. As the prevalence of men with IPSS > 7 was lower in the non-participants [8], we have to conclude that the prevalence and incidence of first GP visit for LUTS in fact must be slightly lower than measured in the present study. However, because this study reports about the relationship between determinants and GP consultation this bias has not influenced our results. Our results are also not biased by the knowledge of the study test results prior to the GP visit. The participants themselves and their GPs enrolled in our study were not exposed to this information. Only the value of the PSA was given to the GP, in relation to the need to detect prostate cancer. In the present study, most probably, possible fear of prostate cancer does not play a role in GP consultation for LUTS, because men with prostate cancers have already been filtered out of the study population. In this type of epidemiological research the reliability of the electronic medical record is a problem because the information entered by the physician is often variable. However, because of the large number of keywords (N=82) used in the search our concerns about missing hits are minimal.

Although the OR's of the IPSS and prostate volume are just above 1 they are not only statistically significant but also clinically significant. These variables are continuous variables which means that for example by an increase of 4 points at the IPSS the change on a first GP visit for LUTS will increase with 4.56 (4*1.14).

Like others[15,16] we found that maximum flow rate and age were univariately significantly associated with first GP visit for LUTS. We could not confirm the finding of Wolfs et al.[15] that being a current smoker was a determinant of GP visit for LUTS. Previous studies [17, 18] concluded that increased symptom severity, a poor maximum urinary flow rate (Q-max) and a high post-void residual urine volume are major risk factors for overall clinical progression of LUTS/BPH. These determinants, except the Q_max, are the same factors predicting GP visit for LUTS in our study. The univariate significant relation between the Q_max and first GP visit for LUTS disappeared after we adjust for other determinants in the multivariate analyses. In addition, we conclude that social generic QOL is an important factor to present LUTS to the GP.

An important underlying cause of LUTS, Benign Prostatic Hyperplasia seems to be explained mainly by the growth of the transition zone of the prostate. [19] In our study a greater transition zone volume gave an almost equal odds ratio (OR 1.036; 95% C.I. 1.03-1.06) than total prostate volume (OR 1.035; 95% C.I. 1.03-1.05), but did not increase the variance of the model

(-0.3 %). But, because our outcome measure is 'primary care-seeking' instead of, for example, acute urinary retention or need for surgery, this finding is not remarkable.

The explained variance (22%) of this model predicting GP visit for LUTS is somewhat low. Besides that the variance could have been limited due to variation over time in health status or symptoms of the participants, we conclude that there might be other determinants of GP visit for LUTS. This is consistent with the finding of Norby that other factors than symptom severity must influence the health care-seeking behaviour, since in their study less than 50% of men and women with severe LUTS had seen a physician within two years time.[20] As previous results of the Krimpen Study [21] demonstrate the impact of various coping styles on QOL in men with LUTS personal traits, like coping behaviour, may play a role; further research is needed to explore this assumption.

We conclude that the number of men in the community first visiting the GP for LUTS in 2 years time is still limited to a few percent. Almost a quarter of the first GP visit for LUTS in men can be predict by prostate volume, post-void residual urine volume, IPSS and social generic QOL. Both urologic measurements and self-reported information about symptoms and QOL can help to select those who will benefit most from medical care and help to reassure those men that are not likely to need near future help.

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7

Patient's quality of life and coping style influence general practitioner's management in men with lower urinary tract symptoms

Quality of Life Research; in press

ABSTRACT

Objective

To identify patient characteristics associated with general practitioner's (GP) initial treatment decision in men with LUTS and to test the hypothesis that a different coping style of patients results in different GP behaviour regarding treatment.

Materials and Methods

A longitudinal, population-based study with a follow-up period of 6.5 years was conducted among 1688 men aged 50 to 78 years old. Data were collected on quality of life, symptom severity based on the International Prostate Symptom Score (IPSS) and coping. Information on primary care seeking and GP's initial management during 2 years of follow-up of all participants was collected from the general practitioners record.

Results

Data were obtained of 68 men, without a history of LUTS, who had a first GP visit for LUTS during the study period. In 54.4% of the cases the GP prescribed medication, independent of symptom severity. In the group of men with a bad disease-specific QOL those with a high passive reaction pattern were treated less frequently than those with a low passive reaction pattern.

Conclusion

This quantitative study confirms the hypothesis that different coping styles of patients may result in different GP behaviour regarding treatment. The use of the coping style passive reaction pattern has a large influence on GP's initial management in men with LUTS.

INTRODUCTION

Treatments of lower urinary tract symptoms (LUTS) include watchful waiting, pharmacological treatment and referral for surgical interventions, and characteristics of both the patient and the general practitioner (GP) may influence decisions related to treatment alternatives. Characteristics such as the duration of the GP's training [1], sex [2] and psychosocial orientation [3] are known to influence the GP's decision to refer a patient to a specialist. Research on the influence of patient characteristics on referral has resulted in many unresolved controversies. Some studies suggest that referral rates rise, for example, with patient's age[4] or low socio-economic status[5, 6], whereas others suggest no effect of these factors[3, 7, 8]. However, these studies mainly focus on referral rates rather than on the management of newly developed LUTS.

Because the aim of treatment in men with LUTS is to improve their quality of life (QOL) patient characteristics may play an important role in treatment decisions [9]. Although coping behaviour of patients may well influence the policy of the GP [10], the impact of coping behaviour has not yet been established in LUTS.

This study aimed to identify patient characteristics associated with the GP's initial treatment decision (watchful waiting versus pharmacological treatment/referral) in men with LUTS and to test the hypothesis that a different coping style of patients results in different GP behaviour regarding treatment.

MATERIALS AND METHODS

Study design

The data presented here were obtained as part of the Krimpen study on male urogenital tract problems and general health status. The design of this large community-based cohort study has been described in detail [11]. Briefly, the Krimpen study was performed to gain information on male urogenital tract dysfunction and general well-being among all men aged 50 – 78 years living in a Dutch municipality near Rotterdam. Men without radical prostatectomy, prostate or bladder cancer, neurogenic bladder disease or a negative advice from their GP (in case of a serious disease with a short life expectancy), who were able to complete questionnaires and attend the research centre, were invited for the study. All men entering the study provided written informed consent. The Medical Ethical Committee of the Erasmus Medical Centre Rotterdam approved the study.

Data of 1688 responders (50%) were collected via a self-administered 113-item questionnaire, which included questions about symptom frequency, quality of life and also addressed the topics marital status, number of children, education level, smoking behaviour and drinking habits. Data on coping were also collected. Additional measurements such as height, body weight, blood pressure measurement and urinalysis were performed at the research centre.

In cooperation with the urology department of the Erasmus MC the following tests were performed: serum prostate-specific antigen, digital rectal examination, transrectal ultrasound of the prostate, uroflowmetry and post-void residual urine volume. Prostate biopsies were taken to detect prostate cancer.

Three consecutive rounds of follow-up were performed with an average follow-up period of 2.1 years, 4.2 years and 6.5 years, respectively. In each of these rounds all measurements were repeated. Men who did not respond after baseline, first follow-up or second-follow up and did not meet the exclusion criteria were nevertheless also re-invited for participation in the third follow-up round.

No information on test results, except for the value of the prosate specific antigen (PSA), was given to the participant or his GP.

Assembly of GP data

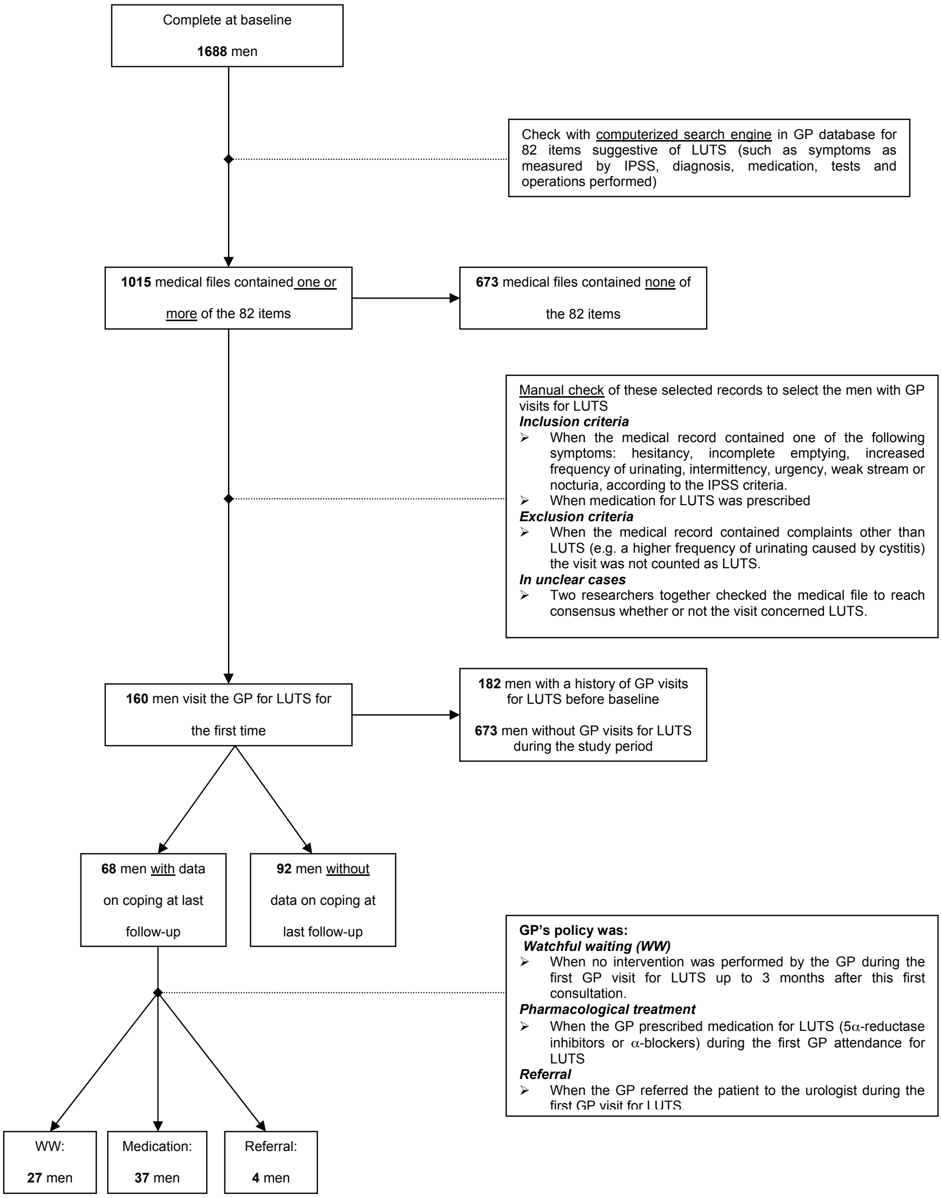
A flow chart of the GP data assembly is presented in Figure 1.

In the Netherlands, all inhabitants are registered with a GP. When the patient visits an emergency room, a specialist, or a (substitute) physician in the weekend or at night, their own GP is always informed. Data about these visits, contacts and prescription of medication are stored in the computerized medical records. All practising GPs (N=16) in Krimpen aan den IJssel gave access to their computerized medical records. The GP medical records of all the participants of the Krimpen study (N = 1688) were checked with the "N6" computer program (QSR International Pty. Ltd. Melbourne, Australia). This program can search text files on keywords and select files based on keywords. Two researchers independently analysed the files selected by the N6 program and filled in a score form separately. They both scored whether or not there was a history of LUTS (i.e. before the start of the study) and noted whether the participant had visited his GP for LUTS and the first date this took place. Also the treatment choice was noted. When the medical file showed that a person had moved from the GP's practice (lost to follow-up) or was deceased, the date of this event was noted. To validate the use of the N6 program the medical files that showed no hits by the N6 (using 82 keywords) were checked manually. The check gave a 100% negative predictive value for the search by the N6 program (none of the files reported visits for LUTS). No loss of follow-up (missing files) occurred in the GP data.

Questionnaires

LUTS

To assess the occurrence and frequency of LUTS we used the seven-item International Prostate Symptom Score (IPSS).[12]The scoring range is 0 (no symptoms) to 35 (maximal symptoms). Scores can be classified, according to the classification of the American Urological Relationshipship (AUA), into three categories: mild (0 - 7), moderate (8 -19) or severe (20 -35).[12]



Complete at baseline

1688 men

Check with computerized search engine in GP database for 82 items suggestive of LUTS (such as symptoms as measured by IPSS, diagnosis, medication, tests and operations performed)

1015 medical files contained one or more of the 82 items

673 medical files contained none of the 82 items

Manual check of these selected records to select the men with GP visits for LUTS

Inclusion criteria

- When the medical record contained one of the following symptoms: hesitancy, incomplete emptying, increased frequency of urinating, intermittency, urgency, weak stream or nocturia, according to the IPSS criteria.
- When medication for LUTS was prescribed

Exclusion criteria

- When the medical record contained complaints other than LUTS (e.g. a higher frequency of urinating caused by cystitis) the visit was not counted as LUTS.

In unclear cases

- Two researchers together checked the medical file to reach consensus whether or not the visit concerned LUTS.

160 men visit the GP for LUTS for the first time

182 men with a history of GP visits for LUTS before baseline

673 men without GP visits for LUTS during the study period

68 men with data on coping at last follow-up

92 men without data on coping at last follow-up

GP's policy was:

Watchful waiting (WW)

- When no intervention was performed by the GP during the first GP visit for LUTS up to 3 months after this first consultation.

Pharmacological treatment

- When the GP prescribed medication for LUTS (5α-reductase inhibitors or α-blockers) during the first GP attendance for LUTS

Referral

- When the GP referred the patient to the urologist during the first GP visit for LUTS.

WW: **27** men

Medication: **37** men

Referral: **4** men

Figure 1. *Data assembly in General Practitioner database*

Quality of life

To assess the generic QOL of the men we used the mini-Inventory of subjective Health (ISH)[13] and the Sickness Impact Profile (SIP)[14]. The mini-ISH is a 13-item questionnaire on subjective health with a score range from 0 to 13.[13] The three domains of the SIP used in this study are

'Emotions' ('Emotions, feelings and sensations', 9 items), 'Recreation' ('leisure pastimes and recreation', 8 items) and 'Social' ('social interaction', 20 items). For each category, a score was computed based on weighting factors for each item, providing scores ranging from 0 to 100 [14]. In contrast to the generic QOL questionnaires, disease-specific questionnaires measure QOL based on items closely related to the specific disease and are therefore expected to be more sensitive. To measure the effect of LUTS on QOL we used the QOL question of the IPSS[12] (IPSS-QOL) and the BPH Impact Index (BII) [15]. The IPSS-QOL can be rated on a scale from 0 to 6.[12] The BII is a four-question index with a score of 0 – 13 designed to assess the impact of the symptoms of LUTS on health status.[15]

For all QOL scales used (disease-specific and generic) a higher score indicates a worse QOL.

Coping Style

To assess coping behaviour we used the Utrecht Coping List (UCL)[16]. In the UCL, coping behaviour is regarded as a personal disposition, e.g. a trait. The respondent is asked to imagine 'problems in general'. The UCL consists of 47 items describing a specific coping behaviour. Answers are on a 4-point scale ranging from 'seldom or never' to 'very frequently'. The instrument was validated for use in a Dutch population [16]. The UCL consists of seven coping scales representing coping styles. The names of the styles and examples of items (between brackets) are: **A**: active problem solving ('putting things in a row', 'seeking a way to solve a problem'), **P**: palliative reaction ('looking for distraction', and looking for good company'), **AV**: avoidance ('avoiding difficult situations' and ' letting things go'), **S**: seeking social support ('discussing the problem with friends or family' and 'asking somebody for help'), **PR**: passive reaction ('being overwhelmed by problems'), **E**: expression of emotions ('showing anger to the person who is responsible for the problem'), and **R**: Reassuring thoughts ('imagining that things could be worse'). The scores representing the minimal and maximal level (scale) of the coping styles are given in table 1.

Co-morbidity

The GP's initial policy can be influenced by a contra-indication due to co-morbidity and corresponding pharmacological treatment. In the present study a person was assumed to have co-morbidity e.g. diabetes mellitus, Parkinson's disease, chronic inflammation of urinary tract or heart problems, if he indicated on the questionnaire that he consulted his GP or a medical specialist for at least one of these diseases during the last three months. We have validated the answer on the questionnaire with the GP record. The check gave a 100% positive predictive value for the answer on the questionnaire (all co-morbidities mentioned on the questionnaire were also reported in the GP record).

Statistical Analysis

Because the data on patient characteristics were assembled at various points in time (baseline, FU1, FU2 and FU3), data collected closest to and before the date of the first GP visit for

LUTS were used in the current analyses. In this way possible temporal variation in health status is also taken into account.

The relationship between patient characteristics (age; SIP social, emotion and recreation; mini-ISH; IPSS; IPSS_QO; BII; the seven coping styles separately; co-morbidity; educational level and marital status) and the GP's initial management (watchful waiting versus pharmacological treatment/referral) was evaluated by means of logistic regression (SAS PROC GENMOD). To correct for the influence of the GP on the treatment policy we used this technique to take correlation between men in the same GP practice into account. Analyses were performed both in univariate and multivariate models. Variables with a p-value ≤ 0.15 in the univariate analyses were entered into the multivariate model.

For the multivariate model a two-sided p-value of 0.05 was considered significant. For these variables odds ratios are presented with 95% confidence intervals ($CI_{95\%}$).

The SAS (version 8.2) program was used for all analyses.

RESULTS

Data were obtained of 160 men, without a history of LUTS, who had a first GP visit for LUTS during the study period (Figure 1). For 68 of these men data on coping behaviour were also available.

Table 1 presents the characteristics of these 68 men collected closest to and before their first GP visit for LUTS. The average age was 64.3 years (sd 6.8 years). Mean symptom scores and QOL scores indicate a moderate severity of LUTS and a reasonably good generic and disease-specific QOL. The coping styles of our respondents correspond with the mean scores of a Dutch reference group. [16]

Table 2 shows the GP's initial management in the men's first GP visit for LUTS. In approximately 55% of the cases the GP prescribed medication, independent of symptom severity.

Table 3 gives the results of the univariate logistic regression analyses of patient characteristics in the GP's initial management. Men using the coping style Palliative reaction and Passive reaction pattern received treatment less frequently. The odds ratios of these continuous variables were 0.93 ($C.I^{95\%}$: 0.89-0.97) and 0.85 ($C.I^{95\%}$: 0.79- 0.91), respectively. Of the other patient characteristics, men with co-morbidity, and a worse social or emotional generic QOL received treatment less frequently ($p<0.15$), while men having a worse disease-specific QOL more often received treatment ($p < 0.15$).

Table 4 gives the adjusted odds ratios and 95% confidence intervals as result of the multivariate logistic regression analyses of patient characteristics in the GP's initial management. Men with a worse disease-specific QOL received treatment more often. However, men with a worse disease-specific QOL using the coping style passive reaction pattern (PR) received treatment less frequently.

Table 1. *Characteristics of the study population before their first visit to the GP for LUTS*

	Men (N=68)	
	Percentage	
Co-morbidity		
Non	85.3	
Yes	14.7	
Marital status		
Alone	5.9	
Living together	94.1	
Educational level		
No education/ Primary school	14.7	
Higher education	85.3	
	Mean (sd)	
Age (years)	64.3 (6.8)	
IPSS (0-35)	9.0 (6.2)	
Quality of life		
Mini-ISH (0-13)	4.5 (8.6)	
SIP Social (0-100)	5.2 (9.1)	
SIP Emotion (0-100)	2.3 (6.5)	
SIP Recreation (0-100)	10.2 (17.5)	
IPSS_QOL (0-6)	1.9 (1.2)	
BII (0-13)	1.2 (2.0)	
Coping styles	***Mean (sd)***	***20th- 80th percentile Reference****
Active problem solving (A) [7-28]	17.0 (3.9)	15-20
Palliative reaction (P) [8-32]	15.5 (3.8)	12-18
Avoidance and passive expectancy (AV) [8-32]	15.0 (3.2)	12-17
Seeking social support (S) [8-24]	10.7 (2.8)	9-13
Passive reaction (PR) [7-28]	10.7 (2.8)	9-12
Expression of emotions and anger (E) [3-12]	6.0 (1.7)	5-6
Reassuring thoughts (R) [5-20]	11.2 (2.3)	10-13

** Values for the age category 55 to 65 years based on data from a study on employees of the Dutch Railway, and a random sample of the Dutch population (8).*

[Numbers between brackets represents minimal and maximal level (scale)]

Table 2. *General practitioner's management in men's first GP attendance for LUTS*

	Total (N=68)		Mild LUTS* (N= 37)		Moderate to severe LUTS* (N= 31)	
	N	**%**	**N**	**%**	**N**	**%**
Watchful waiting	27	39.7	16	43.2	11	35.5
Pharmacological treatment	37	54.4	20	54.1	17	54.8
Referral to urologist	4	5.9	1	2.7	3	9.7

**Mild (IPSS;0-7), moderate to severe (IPSS: 8 -35)*

Table 3. *Univariate associations of patient determinants with general practitioner's management in men's first GP visit for LUTS*

	Treatment versus watchful waiting (n=68)		
	OR	**P-value**	**C.I.$^{95\%}$**
General			
Age	0.99	0.52	0.95-1.02
Living together†	0.47	0.59	0.57-1.92
Higher educationEducational level†	1.03	0.96	0.34-3.13
Symptoms and diseases			
IPSS	1.05	0.31	0.96-1.15
Co-morbidity†	0.38	0.10**	0.12-1.20
Quality of Life			
Mini-ISH	0.97	0.31	0.91-1.03
SIP Social	0.96	0.11***	0.91-1.01
SIP Emotion	0.93	0.09**	0.86-1.01
SIP Recreation	1.00	0.50	0.98-1.01
IPSS_QOL	1.47	0.11***	0.91-2.29
BII	0.97	0.83	0.70-1.32
Coping styles			
Active problem solving (A)	1.00	0.97	0.84-1.20
Palliative reaction (P)	0.93	<0.0001*	0.89-0.97
Avoidance and passive expectancy (AV)	0.99	0.83	0.91-1.07
Seeking social support (S)	1.02	0.77	0.88-1.20
Passive reaction (PR)	0.85	0.002*	0.79-0.91
Expression of emotions and anger (E)	0.87	0.17	0.71-1.06
Reassuring thoughts (R)	0.98	0.84	0.84-1.15

† Dichotomous variable

** Variable with a p value < 0.05 to be entered in the multivariate model*

*** Variable with a p value < 0.10 to be entered in the multivariate model*

**** Variable with a p value < 0.15 to be entered in the multivariate model*

Table 4. *Multivariate model of patient determinants associated with general practitioner's management in men's first GP visit for LUTS*

	Treatment versus watchful waiting (n=68)	
	$OR^{adjusted}$	$C.I._{95\%}$
IPSS_QOL	8.80	3.94-19.49
Passive reaction (PR)	1.11	0.95-1.30
IPSS_QOL*Passive reaction (PR)	0.86	0.82-0.90

DISCUSSION

The present study shows that in more than half of the men first visiting their GP with LUTS the GP prescribed pharmacological treatment. The GP's initial management was highly related to the disease specific QOL of the patient in interaction with coping.

In the Krimpen study 50% of the invited men responded. A questionnaire was sent to those that did not participate at baseline to investigate the characteristics of this group. As the prevalence of men with IPSS > 7 was lower in the non-participants [11], we have to conclude that the prevalence and incidence of men with LUTS in fact must be slightly lower than measured in the present study. However, because this study reports about the relationship between patient characteristics and GP's initial treatment decision and the relation with the coping styles of the patient this bias has not influenced our results. In this type of epidemiological research the reliability of the electronic medical record is a problem because the information entered by the physician is often variable. However, because of the large number of keywords (N=82) used in the search our concerns about missing hits are minimal.

Data on coping behaviour were only collected in the third follow-up round, which could have narrowed the sample size of men we used in the analyses. No loss of follow up (missing files) occurred in the GP data. The 68 men with data on coping behaviour with a first GP visit for LUTS, can be seen as a core group completing all the follow-up rounds: they are slightly younger, have less co-morbidity, a lower IPSS and a better QOL than the remainder. Nevertheless, this small sample was sufficiently large to yield significant relationships and the small confidence limits around the estimates strengthen our findings. Since the UCL regard coping as a personal disposition the moment of the data collection on coping (only at third follow up) does not limit our results.

The participants themselves and their GPs enrolled in our study were not exposed to information about prostate volume, flow, IPSS and QOL scores. Only the value of the PSA was given to the GP, in relation to the need to detect prostate cancer and not initially for the GP's management in men with LUTS. In the present study, fear of prostate cancer does not play a role in the GP's management, because men with prostate cancers have already been filtered out of the study population. To check this assumption we entered 'the level on PSA' in the analyses, which did not change the presented results; PSA was not significantly related to the treatment. As information on digital rectal examination (DRE) was mostly missing in the medical records of the men visiting their GP for LUTS, we were not able to add information about prostate volume in our analyses.

Other studies have also investigated GP management in men with LUTS. Similar to our results, Verhamme et al. also reported that almost 50% of their study group received pharmacological treatment.[17] In addition, two theoretical studies addressed the intention to treat in men with LUTS: Wolters et al. [18] and Hees [19] used a hypothetical case of a man, aged 50 and 65 respectively, with LUTS to determine the GP's initial management. Both studies showed a higher percentage of pharmacological treatment and referral than in our study. Thus, there seems to be a remarkable difference between the GP's intention to treat a man with LUTS and what happens in 'real life' practice. Both Verhamme et al [17] and Hees[19] report a positive relationship between treatment and the following patient characteristics: age, type of urological symptoms at diagnosis, co-morbidity and bother. The present study also contained data on the generic QOL and coping styles of the patient. Coping seemed highly relevant in the GP's initial treatment management. To our knowledge ours is the first study that has shown and quantified the relation between coping of the patient and the initial management of GPs in men with LUTS.

The present study showed that men with a bad disease specific QOL received treatment more often. This result is in line with the guidelines[9, 20] which recommend treatment to improve the patient's QOL. Our multivariate model showed that in the group of men with a bad disease-specific QOL those with a high passive reaction pattern were treated less frequently than those with a low passive reaction pattern.

This finding suggests a large influence of this specific coping style on the GP's initial management in men with LUTS. It seems that men which disease specific QOL deteriorates and using the coping style PR get overwhelmed by their voiding problems and thereby cause the GP to decide not to treat but to choose for watchful waiting initially. However, based on this single study we do not want to speculate on the (non) importance of the other coping styles. These styles could be of importance if they interact with factors not determined in our study, e.g. the coping style of the GP. We conclude that this quantitative study confirms the hypothesis that different coping styles of patients may result in different GP behaviour regarding treatment.

This study provides a starting point to elucidate and quantify the influence of the coping style of the patient on the GP's initial treatment policy. Further studies on the influence of coping styles on the GP's initial policy for LUTS, and into the relationship between coping style and the development of QOL is needed before practical advice on these matters can be given to GPs.

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Coping style of GPs do not influence their treatment decision in men with lower urinary tract symptoms

Submitted

ABSTRACT

Objective

GPs do not always respond identically in the same situation because they differ in their medical knowledge, experience and gender. In men with LUTS it has not yet been investigated before whether the coping style of the GP influences the decision to treat. Therefore, this study explored GP characteristics associated with their treatment decisions for men with LUTS, and tested the hypothesis that the different coping styles of GPs result in different treatment decisions.

Materials and Methods

Sixteen hypothetical patient-cases were developed for a 68-year-old man but differing with regard to the severity of LUTS, the duration of LUTS, the perceived bother of LUTS, and the way the patient copes with problems in general. GPs (n=86) from the greater Rotterdam area were asked to complete the 16 cases and answer additional questions about their own age, gender, experience, estimations of the possibility for and severity of treatment for LUTS, and their own general coping behaviour. After reading all cases the GPs had to make a choice between: 1) watchful waiting, 2) pharmaceutical treatment, or 3) referral to an urologist.

Results

The final multivariate model of the logistic regression analysis of the determinants influencing GP's management showed that severity of LUTS, duration of LUTS, patient's perceived bother of LUTS, and patient's coping behaviour with problems in general have a significant association with treatment less frequently. Conversely, the expected efficacy of medication is significantly associated with prescribing treatment more often.

Conclusion

This quantitative study rejects the hypothesis that different coping styles of GPs may result in different GP behaviour regarding treatment in patients with LUTS. This finding suggests that different GPs are prone to treat identical patients equally. Since treatment decisions depend on the severity of LUTS, the perceived bother of LUTS and the coping style of the patient, the correct estimation of these items is important.

INTRODUCTION

In the Netherlands, men with lower urinary tract symptoms (LUTS) that seek health care initially visit their general practitioner (GP). Dependent on the patient's situation, the GP can advise for watchful waiting (close follow-up of the patient without an active therapy), decide to prescribe drugs (5α-reductase inhibitors or α-blockers), or refer the patient to a urologist for possible surgical intervention. It has been shown that the initial management of men with LUTS depends on the GP's estimation of the patient's quality of life combined with the level of specific coping styles of the patient [1]. This is not surprising, since it is well known that medical practitioners in general make judgements about the coping abilities of their patients [2].

Different GPs do not always act identically in the same situation because they differ in their medical knowledge, experience and gender. Even the coping style of the GP could play a role in the decision to treat; this aspect has not yet been studied in men with LUTS. Therefore, this study aims to identify GP characteristics associated with the GP's treatment decisions (watchful waiting versus pharmacological treatment/referral) in men with LUTS, and to test the hypothesis that different coping styles of the GPs result in different treatment decisions.

MATERIALS AND METHODS

Based on a sample size calculation (with alpha = 0.05 and power = 0.80) a minimum of 25 GPs and 10 patient-cases were needed to obtain representative data to determine the influence of GP characteristics on treatment choice in men with LUTS. The GPs were divided into those with a high score on a coping style and those with a low score on a coping style. The matching fractions are as follows: p_{low} : 0.4 (in GPs with a low score) and p_{high}: 0.6 (in GPs with a high score).

Two GPs developed 16 different cases based on their own experience and the literature on LUTS. After this first, all 16 cases were individually checked for feasibility by a researcher, another GP and a urologist. GPs (n=86) from the greater Rotterdam area were asked to complete the 16 cases and additional questions about their own age, gender, practical experience and estimations of the possibility for and severity of treatment for LUTS. They were also asked to complete a questionnaire about their own general coping behaviour.

Refusal of the GP to enter the study was accepted without any further attempt to persuade the GP to join the study.

Cases

Case 1: *"Mr A, 68 years, visits you for LUTS. You have known him for many years. Most of the time he has to strain to void and he feels that his bladder has not emptied completely. He wakes up to urinate three times each night. There is no history of prostatic carcinoma in his family. His* *prostate seems to be symmetric, slightly enlarged but without any palpable nodules. After examination it becomes clear that neither of you suspect prostate cancer. Then, you concentrate on the symptoms. For 5 months the patient has suffered from LUTS and has been bothered by LUTS. This man generally does not cope easily with problems".*

After reading all 16 cases the GP has to make a choice between: 1) watchful waiting, 2) pharmaceutical treatment or 3) referral to a urologist.

The remaining 15 cases were also based on the hypothetical 68-years-old man but differed with regard to the following factors:

- The severity of LUTS of the patient: <u>Most of the time</u> he had to strain to void and his bladder did not feel completely emptied. <u>Three times a night</u> he had to wake up to urinate ***versus*** <u>sometimes</u> he had to strain to void and felt his bladder was not emptied completely. There is <u>no nocturia</u>
- The duration of the LUTS history: 5 months ***versus*** 11 months
- Patient's perceived bother of LUTS: no bother ***versus*** bother
- Patient's coping behaviour in general: copes easily with problems ***versus*** does not cope not easily with problems

Coping Style

To assess the coping style of the GP the Utrecht Coping List (UCL) was used[3]. In the UCL, coping behaviour is regarded as a personal disposition, e.g. a trait. The respondent is asked to imagine his reaction to 'problems in general'. The UCL consists of 47 items describing a specific coping behaviour. Answers are given on a 4-point scale ranging from 'seldom or never' to 'very frequently'. The instrument has been validated for use in a Dutch population[3]. The UCL consists of seven coping scales representing different coping styles. The names of the styles and examples of items (between brackets) are: **A**: active problem solving ('putting things in a row', 'seeking a way to solve a problem'), **P**: palliative reaction ('looking for distraction', and 'looking for good company'), **AV**: avoidance ('avoiding difficult situations' and ' letting things go'), **S**: seeking social support ('discussing the problem with friends or family' and 'asking somebody for help'), **PR**: passive reaction ('being overwhelmed by problems'), **E**: expression of emotions ('showing anger to the person who is responsible for the problem'), and **R**: Reassuring thoughts ('imagining that things could be worse'). A higher score on a coping style represents a higher level of use of this style. Note that there are no abnormal styles or normal values for the frequency that a specific style is used.

Statistical Analysis

The determinants of the GP's management (watchful waiting versus pharmacological treatment/referral) were evaluated by means of logistic regression (SAS PROC GENMOD). The following factors were analysed: age, gender, experience, expected efficacy and outcomes of therapy for LUTS, the seven coping styles separately, severity of LUTS, duration of LUTS, patient's perceived bother due to LUTS and patient's coping behaviour with problems in general. To correct for within-GP correlation the GP was entered in the analysis as a 'repeated measure'. Analyses were performed in univariate and multivariate models. Variables with a p-value ≤ 0.20 in the univariate analyses were entered into the multivariate model. After backward stepwise elimination of the non-significant variables, only the significant variables remained in the model ($p \leq 0.05$). Final analysis was performed using statistically significant variables only. The SAS (version 8.2) program was used for all analyses.

RESULTS

Of the 86 invited GPs, 39 (45%) completed all the cases and returned the questionnaires. However, 5 GPs were excluded because their data on age, gender, and/or experience were missing, leaving 34 GPs for analysis.

Table 1 presents the baseline characteristics of the GPs and their responses concerning expected outcomes of therapy for LUTS. The mean age of the GPs was 47 years and 65% was male. The scores on the seven coping styles of the responding GPs did not differ from the mean scores of Dutch reference groups [3]. About 50% of the GPs did expect a high rate of serious complications of transurethral electro-resection of the prostate (TURP).

Table 2 gives the results of the univariate logistic regression analyses of the determinants influencing GP's management in men with LUTS. The severity of LUTS, the duration of LUTS, patient's perceived bother of LUTS, and patient's coping behaviour with complaints in general were significantly negatively associated with treatment ($p<0.001$). A high-expected efficacy of medication seems to result in treatment more often ($p<0.001$).

Table 3 gives data on the final multivariate model of the logistic regression analysis of the determinants influencing GP's management. The severity of LUTS, the duration of LUTS, patient's perceived bother of LUTS, and patient's coping behaviour with problems in general have a significant association with treatment less frequently. Conversely, the expected efficacy of medication is significantly associated with prescribing treatment more often. The univariate significant association between the coping style 'Reassuring thoughts' and GP's management disappeared after adjusting for other significant variables in the multivariate model. The GP's treatment choice seems to be independent of their personal characteristics or coping style.

Table 1. *Characteristics of the GPs and their expected outcome of therapy*

	Study population (n = 34)
Gender	**Percentages**
Men	65
Women	35
Age (years)	**Percentages**
30 - 39	24
40 - 49	38
50 - 59	24
60 >	14
Experience	**Mean (sd)**
Number of years	18.3 (10.3)
Coping style of GP	**Mean (sd)**
Active problem solving [7-28]	20.2 (2.1)
Palliative response [8-32]	17.1 (2.8)
Avoidance and passive expectancy [8-32]	16.2 (2.9)
Seeking social support [8-32]	15.4 (2.3)
Passive reaction [7-28]	10.9 (2.4)
Expression of emotion and anger [3-12]	6.2 (1.1)
Reassuring Thoughts [5-20]	11.7 (1.9)
Expected efficacy of therapy [0-10]	**Mean (sd)**
5 α-reductase inhibitors	5.4 (1.9)
α-blockers	6.5 (1.1)
Transurethral Electro-Resection of the Prostate (TURP)	7.1 (1.0)
Expected chance of complications of therapy	**Percentages**
Watchful waiting	
Low chance	94
High chance	6
Medication	
Low chance	87
High chance	13
TURP	
Low chance	53
High chance	47

[Numbers between brackets represent the scale]; Mark for the efficacy [0-10], in which 10 is highest

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Expected severity of complications of therapy	**Percentages**
Watchful waiting	
Not serious	88
Serious	12
Medication	
Not serious	97
Serious	3
TURP	
Not serious	42
Serious	58

DISCUSSION

In the present study we were interested to learn whether GP's background characteristics and especially his coping style influenced their management in hypothetical patients with uncomplicated LUTS. GP's management was highly related to GP's expected efficacy of medication, the duration of the LUTS history, patient's perceived bother of LUTS and the way patients cope with problems in general. The coping style of the GP did not influence GP's treatment choice.

The response rate among GPs to the cases and questionnaires was relatively low (45%), so we cannot exclude selection bias in the results. However, the characteristics of the study population seem not to differ with demographic data of the overall GP population in the Netherlands [4]. The number of GPs (n=34) and the number of cases (n=16) entered in the study was sufficient according the sample size calculation. Our sample was also sufficiently large to yield significant relationships and the small confidence limits around the estimates strengthen our findings. The questionnaire contained 16 differing cases of a 68-year-old man with uncomplicated LUTS. This cannot reflect the tailor-made approach of daily practice, and the results have to be judged with respect to this limitation.

Most studies on variation of GP practice are studies focussed on referral rates and characteristics of the GP rather than on the management of LUTS [5-12]. Moreover, LUTS and coping were not the subjects of these studies. Our previous results showed that in the group of men with a bad disease-specific QOL those with a high passive reaction pattern were treated less frequently than those with a low passive reaction pattern. So, different coping styles of patients may result in different GP behaviour regarding treatment [1]. This is in line with the present study that also showed that the way a man copes with problems in general plays a role in GP's management in men with LUTS. Also Kahn et al.[2] reported that medical practitioners take into account the coping abilities of patients in daily practice. However, to our knowledge this is the first study that showed that GP's management in men with LUTS is independent of GP's coping style and other characteristics as age, gender, and practical experience. GP's seems to

Table 2. *Univariate associations of GP determinants with GPs' management pharmaceutical treatment/ referral versus watchful waiting) in men's first GP visit for LUTS (based on 34 * 16 = 544 consults)*

	Treatment versus watchful waiting	
	OR#	***P-value***
GP characteristics		
Age† (years)	0.99	0.50
Male (versus female)	0.99	0.96
Experience† (in years)	0.99	0.55
Coping styles of GPs†		
Active problem solving	0.96	0.55
Palliative reaction	0.95	0.14*
Avoidance and passive expectancy	1.03	0.56
Seeking social support	0.99	0.88
Passive reaction	0.85	0.27
Expression of emotions and anger	0.93	0.65
Reassuring thoughts	0.85	0.04*
Patients & their complaints		
Severity of LUTS (low versus high)	0.52	0.0003*
Duration of LUTS (small versus large)	0.50	< 0.0001*
Perceived bother of LUTS (no versus yes)	0.16	< 0.0001*
Coping with complaints in general (easily versus not easily)	0.45	< 0.0001*
Expected efficacy † [0-10]		
Medication (5 α-reductase inhibitors and α-blockers)	1.61	< 0.0001*
Transurethral Electro-Resection of the Prostate (TURP)	1.28	0.08*
Chance of expected complications		
Watchful waiting		
Low (versus high)	0.50	0.17*
Medication		
Low (versus high)	1.55	0.49
TURP		
Low (versus high)	0.86	0.64
Expected severity of complications		
Watchful waiting		
Not serious (versus serious)	0.64	0.16*
Medication		
Not serious (versus serious)	0.98	0.93
TURP		
Not serious (versus serious)	0.85	0.61

† Continuous variable

** Variable with a p-value < 0.20 to be entered in the multivariate model*

N.A; not applicable

 # An odds ratio > 1 favours treatment

Table 3. *Multivariate model of GP determinants associated with GPs' management in men's first GP visit for LUTS (based on 34 * 16 = 544 consults)*

	Treatment versus watchful waiting	
	OR ^{adjusted}	***C.I.*** $_{95\%}$
Expected efficacy of medication[†]	1.91	1.43-2.56
Severity of LUTS (low versus high)	0.26	0.16-0.79
Duration of LUTS (small versus large)	0.51	0.33-0.73
Perceived bother of LUTS (no versus yes)	0.10	0.06-0.17
Coping with problems in general (easily versus not easily)	0.44	0.28-0.68

[†] *Continuous variable; Mark for the efficacy [0-10], in which 10 is highest.*

practice as advocated by the guidelines that recommend treating patients to improve their quality of life, and state that treatment decisions depends on the severity of LUTS [13, 14]. We also found that the treatment choice of the GP was strongly related to GP's knowledge on the expected efficacy of medication. Remarkably, this (significant) association indicates a large variance in GP's knowledge of the expected efficacy of medication. So, GPs expecting medication not being effective will probably unjustly decide not to treat a patient, and the opposite may also occur. This finding stresses the importance of a good continuous medical education (CME) on the efficacy of new and existing pharmaceuticals.

We conclude that this quantitative study rejects the hypothesis that different coping styles of GPs may result in different GP behaviour regarding treatment in patients with LUTS. This finding suggests that different GPs are prone to treat identical patients equally. Since treatment decisions depend on the severity of LUTS, the quality of life of the patient and the coping style of the patient, correct estimation of these items is important. The correctness of these estimations will be an interesting topic for further research.

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The validation of the International Prostate Symptoms Score for use in economic evaluations

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ABSTRACT

Objective

Lower Urinary Tract Symptoms (LUTS) suggestive of Benign Prostatic Obstruction (BPO) cause a reduction in quality of life, but the magnitude of that reduction cannot be estimated empirically. This is because survey instruments currently available merely sum the symptoms found, but do not value their impact on quality of life. It is therefore difficult to determine whether the effects of treatments for LUTS suggestive of BPO justify the costs. This complicates economic evaluations.

Materials and Methods

We valued the impact on quality of life of patients with LUTS suggestive of BPO, by valuing health states defined by the International Prostate Symptom Score (IPSS) using the time trade-off technique (TTO). TTO values range from 1.0 for perfect health to 0.0 for the value of death, and can be used to calculate Quality Adjusted Life Years (QALYs), the preferred outcome measure in health economics.

Results

We reduced the number of health states defined by the IPSS using factor analysis. The resulting 9 health states were valued by a representative sample of the general public (N = 170) using TTO. The worst IPSS health state was valued at 0.87.

Conclusion

The values for health states defined by the IPSS revealed that LUTS suggestive of BPO has a mild impact on quality of life. The valuation of the IPSS facilitates economic evaluations of treatments for LUTS suggestive of BPO, because QALYs (the preferred outcome measure in health economics) can be determined empirically.

INTRODUCTION

In clinical sciences, it is common to begin a clinical report with a description of the magnitude of the health problem to emphasize the relevance of the study objectives. Often, such remarks inadequately describe the magnitude of the problem, however, as in most cases the impact of heath problems on the quality of life of the patients is not based on validated measurement. For instance, in Lower Urinary Tract Symptoms (LUTS) suggestive of Benign Prostatic Obstruction (BPO), authors often refer to the high prevalence of the condition in older males, but the relative impact of LUTS suggestive of BPO on quality of life compared to other health problems is unknown. Quality of life instruments used in economic evaluation are especially suitable to estimate the impact of a condition on quality of life, because their outcome is the value or "utility" people attach to health states. These utilities have a standardized range of 1.0 for perfect health and 0.0 for death, which allows for relative statements about the impact of quality of life. A simple multiplication of the utilities with the life years gives the number of "Quality Adjusted Life Years" or QALYs. Because QALYs allow for comparisons and relative statements across very different conditions, interventions and diseases, they have become the preferred outcome in health economics [1].

Health state utilities are elicited in interviews with members of the general public using techniques such as "Time Trade-Off" (TTO). Questionnaires such as the EQ-5D have been validated using TTO, so that outcome can be used directly to estimate QALYs. Nevertheless, the use of these instruments in urology is rare, probably because urologists do not expect these instruments to be very sensitive for the very specific urinary problems associated with LUTS [2]. If a disease specific questionnaire like the International Prostate Symptom Score (IPSS) could be validated using TTO, urologists would have a sensitive tool for utility measurement and QALY-analysis in LUTS suggestive of BPO. Such measurement would allow us to describe the impact of LUTS suggestive of BPO on quality of life and facilitate a state-of-the-art economic evaluation of various treatment options. The purpose of this article is to describe how the IPSS, in a context of LUTS suggestive of BPO, was valued, and how these values should be interpreted.

MATERIALS AND METHODS

In this study, we valued the impact on quality of life of patients with LUTS suggestive of BPO, by valuing health states defined by the IPSS using TTO. In order to facilitate the administration of TTO, we reduced the number of health states defined by the IPSS using factor analysis.

Basically the study involved two steps: the first step was the reduction of the number of health states of the IPSS using factor analysis and merging of answer levels, and the second step contained the determination of the values of the remained health states using TTO.

Time trade-off

The methodology of the TTO interview technique is described in detail in Drummond, O' Brien & Stoddart et al (1997) [3]. Briefly, interviewees are asked to imagine that they will live for the rest of their lives in a specified health state. They are then told that a complete and permanent cure is available, but at the cost of reduced survival. In this way 'time' is traded off for an increase in quality of life. By accepting or rejecting various time trade-offs, the 'point of indifference' is reached, i.e. the loss of time, which 'equals' the gain in quality of life. The point of indifference determines the "utility" for the health state: the higher the trade-off of time, the lower the utility.

In the present study, subjects had to imagine that they were in a health state describing voiding and filling problems caused by LUTS suggestive of BPO. The health states were based on outcomes of the IPSS. Because we wanted to validate the IPSS for use in economic evaluation, representatives of the general public were asked to value the health states of the IPSS. This is to ensure that the TTO values for the IPSS health states represent the societal perspective, the preferred perspective in health economics 1. Before the valuation task using the IPSS states, the respondents gained experience with TTO using general health states as defined by the EuroQol EQ-5D questionnaire. This administration protocol was based on the work of Bleichrodt & Johannesson and Stolk et al. [4-6.]

IPSS

The IPSS is a widely used tool for assessing symptom severity in LUTS suggestive of BPO and includes 7 questions about both voiding and filling, and one question on the impact of the symptoms on the quality of life. All questions are answered on a scale of 0 to 5. There are 279,936 possible combinations of scores: 7 items with 6 response levels give 6^7 unique health states. We wished to attribute TTO values to each of these health states. However, this was complicated by the very large number of health states, which is far too many to present to subjects for valuation. Therefore, the number of health states had to be reduced. We applied factor analysis to achieve this.

Factor analysis

Factor analysis is often employed to reduce the dimensionality of the data by summarising the data in a small number of factors (typically much smaller than the original number of variables) with little loss of information. Factor analysis is a generic term for a number of related statistical models which have a number of objectives. First, it aims to study the correlation of a large number of variables by clustering these into factors so that variables within each cluster are highly correlated [7]. Weights (or loadings) on each factor are calculated for each variable: the nature of each factor can be interpreted from the variables with high loading. The structure of the factors found can often be simplified by 'rotating' them so that the loadings for each factor are either large on just a few variables (and essentially zero on the rest).

Rotation may be oblique or orthogonal. Orthogonal rotation produces factors which are not correlated with each other. While this may appear desirable, there is generally little reason to assume that factors in a population are not correlated. In oblique rotations, the factors are assumed to be possibly correlated. Oblique rotations often produce simpler loadings than an orthogonal rotation.The data used in the factor analysis was elicited from a study of 1414 consecutive male patients, newly referred to a urologist, from a selection of 12 practices, situated in 13 hospitals in the Netherlands. All the patients were older than 50 years [8]. All 1414 patients filled in the IPSS.

Respondents

After reducing the number of health states using factor analysis, the health states were valued by a sample of the general public from Rotterdam and its surroundings. The age of the respondents was restricted to the range 18 to 70 years to ensure the cognitive abilities necessary to complete the TTO task. In former research[5, 6] for example, elderly people were found to give too many invalid responses.

The respondents were invited by telephone to attend a session during which a number of health states would be valued and they were offered a small honorarium plus travel expenses. Quota sampling was applied to elicit a representative sample in terms of gender and age (within the age range of 18 to 70 years). We further analysed whether age and gender influenced the values of the general public. If such effects occurred it would be appropriate to further adjust the TTO values by using weighted factors for age and gender based on the distribution of the factors in the general population.

Interview protocol

The respondents valued the health states of the IPSS using TTO. The subjects had to imagine that they were in an IPSS defined chronic health state. In this way, subjects gave values to the IPSS health states from their own personal perspective: young / old, male / female, etc. The subjects were informed about the symptoms associated with LUTS suggestive of BPO. Subjects were told that Benign Prostatic Hyperplasia (BPH) is defined histologically, but clinically the condition is characterised by lower urinary tract symptoms (urinary frequency, urgency, a weak and intermittent stream, needing to strain, a sense of incomplete emptying, and nocturia) and can lead to complications, including acute urinary retention. [9]. The health states were presented on cards in random order but subjects were allowed to reshuffle the cards. Subjects were also allowed to return to a response if they had changed their mind during the interview. The time frame for the time trade-off was the remaining life expectancy of the subject. Life expectancy was truncated at 80 years for all respondents younger than 64, and 85 for respondents older than 65. TTO responses were considered invalid if the respondents showed a lexicographic response to the EQ-5D states, had too much missing data either on the IPSS or EQ-5D states, or clearly did not understand the task. A lexicographic response means that when a respondent is faced with an option, he will always choose one particular alternative, no matter how favourable the other might be. A similar protocol was used to value the International Index of Erectile Functioning (IIEF) [5, 6].

RESULTS

Factor analysis

The factor analysis separated the 7 symptom scores of the IPSS into 2 factors which could be interpreted as obstructive symptoms (incomplete emptying, intermittency, weak stream and hesitancy) and irritative symptoms (frequency, urgency and nocturia). Similar results were found in the studies of Welch [10] and Yu [11]. As table 1 shows, the three types of factor analysis reflect the same correlation structure.

Following the factor analysis, the 6 response categories (from "not at all" to "almost always") of the two remaining factors, obstructive and irritative, were merged into 3 categories. For the obstructive factor, we combined the scores 0 and 1 to the category "seldom/never", the scores 2, 3 and 4 to the category "about half the time or sometimes" and score 5 to the category "almost always". For the irritative factor, the scores 0 and 1 belong to the category "seldom/never", the scores 2 and 3 to the category "about half the time/ sometimes" and score 4 and 5 to the category "almost always". In this way 9 (3^2) IPSS states remained after factor analysis (figure 1 and 2).

Valuation

A sample of 191 subjects of the general public valued the 9 IPSS states (figure 2). The age of the subjects ranged from 20 to 68 years (mean age of 42,9 (SD 12,9) years). A total of 170 (89%) responses was judged valid and was included in the analysis. Most exclusions were because of lexicographic responses to the EQ-5D states (9%) and 2% were excluded because these subjects clearly did not understand the task. The valid responses where made by 73 men (42,9%) and 97 women.

Figure 1 gives the mean utilities that were calculated for the 8 health states described by the 2 factors. The 9th health state (no voiding or filling problems) was the reference state and had a theoretical value 1.0. The utilities for the other IPSS states ranged from 0.87 for the worst IPSS state to 0.97 for the best IPSS state. The factor 'irritative' appeared to be rated as more severe than the factor 'obstructive', which is in line with results found in the literature [10, 11].

Men considered LUTS suggestive of BPO symptoms as more of a problem than women and older subjects gave lower values than younger subjects ($p < .01$). When the values were adjusted with weighted factors for gender and age, the mean utilities did not differ noticeably: the maximum deviation between the utilities was equal to 0,68%. This suggests that the representativeness of our sample was sufficient.

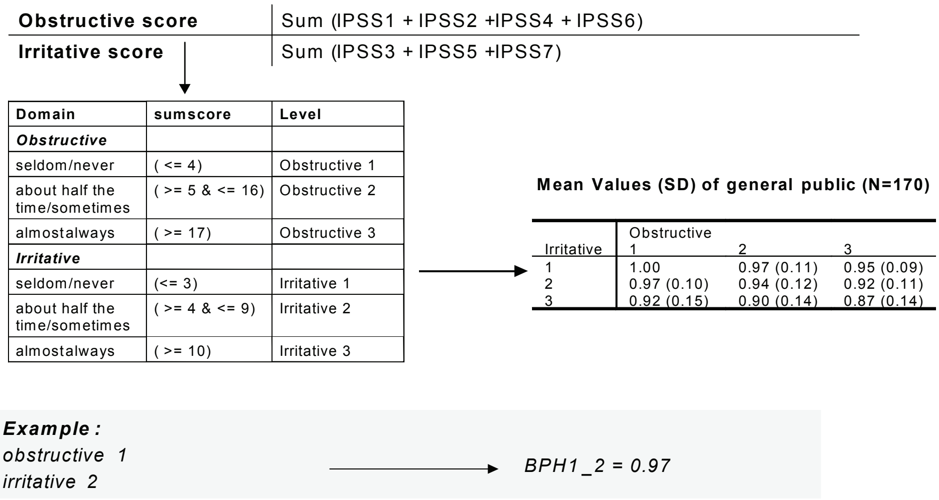
Table 1. *The factor structure of the IPSS for 1414 men newly referred to an urologist [8]*

	Obstructive scores				**Irritative scores**		
	Hesitancy	**Incomplete emptying**	**Intermittency**	**Weak stream**	**Frequency**	**Urgency**	**Nocturia**
PCA*							
Factor 1	0.653	0.750	0.720	0.625	0.606	0.579	0.413
Factor 2	-0.412	-0.255	-0.312	-0.239	0.526	0.479	0.575
Varimax							
Factor 1	0.771	0.763	0.771	0.651	0.204	0.208	0.017
Factor 2	0.028	0.213	0.149	0.165	0.776	0.722	0.708
Oblimin							
Factor 1	0.765	0.788	0.785	0.668	0.331	0.327	0.135
Factor 2	0.154	0.799	0.272	0.260	0.799	0.747	0.701

**PCA = principal components analysis. Obstructive factor alpha = 0.8; Irritative factor alpha = 0.7*

DISCUSSION

We determined values for the health states of the IPSS in a context of LUTS suggestive of BPO. The values for the IPSS health states in this context, as described by the questionnaire, are relatively high; they are located at the top of the utility scale, where 1.0 stands for the value of perfect health. Other conditions affect quality of life to a larger extent. For example, Patients with moderate rheumatoid arthritis have a quality of life between 0.60 and 0.70 and patients with disseminated prostate cancer score between 0.35 and 0.50. This has consequences for



Obstructive score	Sum (IPSS1 + IPSS2 +IPSS4 + IPSS6)
Irritative score	Sum (IPSS3 + IPSS5 +IPSS7)

Domain	**sumscore**	**Level**
Obstructive		
seldom/never	(<= 4)	Obstructive 1
about half the time/sometimes	(>= 5 & <= 16)	Obstructive 2
almostalways	(>= 17)	Obstructive 3
Irritative		
seldom/never	(<= 3)	Irritative 1
about half the time/sometimes	(>= 4 & <= 9)	Irritative 2
almostalways	(>= 10)	Irritative 3

Mean Values (SD) of general public (N=170)

Irritative	Obstructive 1	2	3
1	1.00	0.97 (0.11)	0.95 (0.09)
2	0.97 (0.10)	0.94 (0.12)	0.92 (0.11)
3	0.92 (0.15)	0.90 (0.14)	0.87 (0.14)

Example :
obstructive 1
irritative 2 → *BPH1 _2 = 0.97*

Figure 1. *The 9 resulting IPSS health states and their mean values (SD).*

I experience about half of the time problems with:

- To push or strain to begin urinating
- Complete emptying the bladder
- Urinating without stopping and starting again several times
- A reduction in the strength and force of the urinary stream

Sometimes, I have:

- To urinate again, less than two hours after finishing urinating
- Difficulty to hold back urinating after felt the need
- To get up from bed twice or three times to urinate during the night

Figure 2. *IPSS health state 2_2*

the assumption that LUTS suggestive of BPO has a large impact on quality of life. Given the high prevalence of LUTS suggestive of BPO, the reduction in quality of life is felt by a great number of people, but the magnitude of the individual reduction is modest. It should be noted that interventions in LUTS suggestive of BPO could still attribute considerably to the health status of populations; a small increase in QALYs in a large number of patients might well outweigh a large increase in QALYs in a small number of patients.

We quantified the impact of LUTS suggestive of BPO using the IPSS. The validity of our results is therefore first of all dependent on the quality of this instrument. Usually, the IPSS is found to have a high level of sensitivity and specificity for the effects of treatment, which supports at large the validity of our choice to quantify the impact of LUTS suggestive of BPO using the IPSS score. If the IPSS is used in a different context, however, the utility weights found may not be fully adequate. After all, the utility weights for the IPSS were determined within the context of LUTS suggestive for BPO, and one cannot simply assume that the results will be valid as well in a different context were the IPSS may be used (for example in women with LUTS). Furthermore, it could be recognized that an indirect measure of quality of life, such as this new scoring algorithm for the IPSS provides, is validated at the group level. The relative weights that an individual patient attributes to different aspects of the LUTS suggestive of BPO may deviate from the average weight given by the group. Our results only predict average responses at the group level, but not at the individual level. Application of this scoring algorithm is directed at the macro- or meso level, not at the level of individual treatment decisions.

The question then becomes if the utility weights themselves validly represent quality of life of BPO patients. Our results were generally in line with previously published findings, which supports the validity of our findings. The two-factor structure found, was also reported by Welch and Yu [10, 11]. In addition, our study confirmed the importance of the irritative factor over the obstructive factor for a patient's quality of life. The values for health states of LUTS suggestive of BPO found in this investigation tend to be the same or a little higher than values made by expert panels. For instance, based on several expert opinions in the literature, Baladi et al. valued the most severe health state at 0.79 [12]. It is important to note however that the values elicited here represent societal values, which sometimes deviate from the experts' perspective and the patients' perspective. For instance, compared to the general public and patients, experts tend to put more emphasis on functional limitations, and less on emotional problems and pain.[1] Such emphasis would indeed explain why the values of the experts are lower than those of the general public elicited in this investigation. In an investigation of Ackerman[13], a group of patients valued health states of LUTS suggestive of BPO. The patients gave on average, slightly higher values than the values elicited in our investigation. This is in line with other research that shows that patients report higher values (a lower burden of the disease) than those not affected by the disease. The higher values of the patients are attributed to coping mechanisms in patients.[1] Thus the values of our investigation could be considered as falling between patient values and expert values. Theoretically this is where we expect values from the general public to be, therefore providing support for the construct validity of our data.

The general public are the payers and consumers of care, they are therefore seen as representing the societal perspective in economic evaluations.[1] Our investigation is the first study whereby the societal perspective is used to validate a questionnaire that classifies patients into health states of LUTS suggestive of BPO. This facilitates an economic evaluation in patients with LUTS suggestive of BPO, because the widely used IPSS questionnaire can now also be used to make QALY calculations from a societal perspective (the preferred analysis and perspective in economic evaluations). The influence of background variables of the general public on TTO values is often found to be limited, unlike the results found here [6, 14]. We are uncertain what caused the gender and age differences. The nature of the disease might partially explain these findings. Men and women have a different daily voiding routine that might result in a different attitude to voiding problems. Furthermore, LUTS suggestive of BPO is an age specific condition. Older men therefore might be more aware of this problem, which may result in different values. One might criticize our study for eliciting values in a relative young population, under the age of 70. Whether one should use the values of a subgroup or the values of the general public as a group, is a subject still under debate [1, 15]. In any case, the adjustment of the original values for the influences of the background variables age and gender demonstrated minimal differences in the mean values, which supports the generalizability of the societal values found in this study.

The values of the IPSS in this investigation represent symptom specific utilities. The IPSS is not expected to be sensitive for other symptoms. This means that in patients with co-morbidity, the overall utility will be lower. This will not be a problem if the treatment to be evaluated has little influence on co-morbidity and does not have significant side effects. If it has, generic instruments like the EQ-5D will be more suitable to evaluate the overall gain (or loss) of the utility of quality of life. This typically represents the down side of symptom specific measurement in quality of life: specific measurement will be sensitive in one aspect of health, but will be unable to pick up changes in unrelated dimensions. This disadvantage will not be manifest though in the evaluation of most treatments in patients with LUTS suggestive of BPO, because these treatments typically produce few side effects. An exception might be TURP, where perioperative death is a possible outcome. However, QALY-analysis can take account of this and other well defined events. [12].

A limitation for international studies might be that only Dutch values were determined. It is often hypothesised that different nationalities produce different values for different health states. However, there is no evidence to support this hypothesis. The few international comparisons in which utility measures such as TTO were applied, revealed only small national differences [4, 16].

In conclusion, we valued the impact of LUTS suggestive of BPO, as represented by the IPSS, on quality of life. The impact of LUTS suggestive of BPO on quality of life was found to be mild, but nevertheless clearly measurable. IPSS scores therefore have the potential to be used in QALY calculations, thus facilitating an economic evaluation. This will be carried out in the forthcoming TRIUMPH investigation: a large-scale international study to measure the impact and cost-effectiveness of different interventions in BPH in a naturalistic setting [17]. Such economic evaluations will give urologists an opportunity to justify the money spent in this field of medicine. This justification will become increasingly important, as medical opportunities continue to exceed the available budget. National health authorities have already started to demand not only clinical evidence of an intervention before reimbursement is considered, but also proof of cost-effectiveness. The validation of the IPSS provides urology with a tailor-made instrument to participate actively in the search for evidence for cost-effective medicine.

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APPENDIX

Appendix 1. *Member of the Pan-European Expert Panel*

Name	City	Country	Discipline
W. Atribani	Verona	Italy	Urology
B. Begaud	Bordeaux	France	Pharmaco-epidemiology
R. Berges	Herne	Germany	Urology
A. Borkowski	Warsaw	Poland	Urology
C.R. Chapple	Sheffield	UK	Urology
A. Costello	Melbourne	Australia	Urology
P. Dobronski	Warsaw	Poland	Urology
R.D.T. Farmer	Guildford	UK	Pharmaco-epidemiology
F. Jiménez Cruz	Valencia	Spain	Urology
U. Jonas	Hannover	Germany	Urology
K. MacRae	London	UK	Biostatistics
L. Pientka	Bochum	Germany	Geriatrics
F.F.H. Rutten	Rotterdam	The Netherlands	Pharmaco-economics
C.P. van Schayck	Maastricht	The Netherlands	Primary care medicine
M.L. Speakman	Taunton	UK	Urology
M.C. Sturkenboom	Rotterdam	The Netherlands	Pharmaco-epidemiology
P. Teillac	Paris	France	Urology
A. Tubaro	L'aquila	Italy	Urology
G. Vallancien	Paris	France	Urology
R. Vela Navarrete	Madrid	Spain	Urology

General discussion

The main focus of this thesis was to establish the relationship between changes in LUTS and changes in quality of life, taking into account the impact of coping behaviour, in men with new and increasing LUTS. To further explore the clinical relevance of these factors the relationships with GP consultation and GP policy was also studied. In this chapter, the most important findings are summarized and discussed in a broader perspective. In addition, implications of this research for daily clinical practice and the potential for future research within the domain of LUTS are discussed.

QUALITY OF LIFE AND LUTS IN A LONGITUDINAL STUDY DESIGN (CHAPTER 4)

Earlier conclusions of studies, including the Krimpen Study, based on cross-sectional data suggested that LUTS largely influenced the perceived quality of life (QOL) of men[1-3]. However, after analysing the longitudinal data of the population-based Krimpen Study in men aged 50 to 78 years, the relationship between LUTS and QOL has to be reconsidered. We conclude that a change in LUTS (defined as a change in symptom frequencies as measured by the IPSS) during a follow-up period of 4.2 years has on average only a small impact on the disease-specific QOL, and hardly any impact on the generic QOL. The differences between results based on cross-sectional data and on longitudinal data may be attributable to differences in study design, but may also be related to co-morbidity that occurs more frequently in patients with LUTS. Because LUTS are likely to be associated with other morbidity, it follows that the relationship between LUTS and QOL may be confounded by such co-morbidity. This methodological problem is not present when measuring the relationship between changes in LUTS and changes in QOL over time.

Normally, one would expect the reported QOL to deteriorate with ageing; however, in the present study we found the opposite. The overall health status of our participants (as measured by the generic QOL questionnaires) improved during follow-up. The better generic QOL might be explained by reaching retirement age during the study period, more spare time, less work-related stress and/or other kinds of daily activities; however, due to a lack of suitable data on these factors we could not confirm these assumptions. We did find that the positive change in generic QOL could not be attributed to improvement in LUTS. Contrary to the generic QOL, the disease-specific QOL of men deteriorates with increasing IPSS. The average IPSS-QOL score after 4.2 years of follow-up of every subgroup indicated at least “mixed, about equally satisfied and dissatisfied” (bother score ‘3’). Therefore, most men did not perceive their LUTS to be bothersome after an increasing IPSS. The generic- and disease-specific QOL-instruments were found to be sensitive, and in most of the study population the IPSS changes with 4 or more points. However, the magnitude of this change in IPSS may be too small to cause a measurable effect on generic questionnaires.

The relationship between changes in QOL and changes in LUTS implies that men in the community suffering from LUTS do not perceive a considerable influence of these symptoms on their general well-being. This in turn, could suggest the need for more restraint in the intervention policy for men with mild LUTS. Obviously, there are small populations or patient subgroups with more extreme changes in the severity of LUTS that may show larger effects on QOL and for whom direct therapy is preferred.

QUALITY OF LIFE AND LUTS IN RELATION TO COPING BEHAVIOUR (CHAPTER 5)

On average the relationship between changes in LUTS and changes in QOL is weak. Therefore, we hypothesized that in a specific subgroup this relationship could be stronger depending on the patient personal characteristics, such as his coping behaviour (the way one manages stressful situations and circumstances). Coping behaviour could also explain the discrepancy found between the increase in LUTS and deteriorated disease-specific QOL on the one hand, and the improved generic QOL on the other. Previous studies have shown that coping behaviour affects psychological, physical and social well-being[4, 5]; however, LUTS were not the subject of these studies. The Utrecht Coping List (UCL) considers the coping style to be a personality trait[6]. To test this assumption we checked whether there was a relationship between coping style and LUTS in our data. But no relationship between new and increasing LUTS and coping style was found. This is consistent with the assumption underlying the UCL (coping as a personality trait). Inasmuch as we do not assume a causal relationship between LUTS and coping, the interaction between coping, LUTS and QOL may be the result of a causal relationship between coping and QOL.

Our multivariate linear regression analysis showed that a change in LUTS alone was not significantly associated with a change in generic QOL. However, it seems that changes in LUTS in combination with the use of specific coping styles did affect generic QOL. Based on these analyses we conclude that a change in LUTS is significantly positively associated with a change in QOL when men use the coping style 'active problem solving' and negatively associated 'with reassuring thoughts'. For example, a man with new or increasing LUTS who always wants to solve a problem efficiently (coping style: active problem solving) may seek care more readily thus resulting in a better QOL. But denying LUTS, which is treatable, by thinking that it is not really a serious problem and that it will disappear in time (coping style reassuring thoughts) can negatively affect generic QOL. Thus, the way QOL changes due to new and increasing LUTS also depend on a man's coping style.

The impact of LUTS (adjusted for other factors such as age and co-morbidity) on generic QOL in men using a specific coping style seems to be large enough to be detected by generic QOL instruments, implying a large impact on QOL. To test this assumption we compared the influence of new and increasing LUTS in combination with the use of specific coping styles with the impact on generic QOL of, for example, getting a new chronic disease. It appears that the impact of new and increasing LUTS on QOL in men using the coping style 'active problem solving' or 'reassuring thoughts' was in this subgroup of men larger than the impact of getting a new chronic disease in men not selected on their coping style (diabetes mellitus, Parkinson's disease, chronic inflammation of the urinary tract, or heart problems).

GP CONSULTATION IN MEN WITH NEW AND INCREASING LUTS (CHAPTERS 3 AND 6)

The current opinion is that with the ageing of the population LUTS will become more prevalent and that the number of men consulting their physician with LUTS will increase. However, we have to conclude that the number of older men in the community first visiting the GP for LUTS within 2 years after baseline is still very low (about 10%). The small number of men seeking primary care for LUTS suggests that GP consultation does not only depend on symptom severity, which is consistent with Norby et al. who reported that other factors than symptom severity must influence the health care-seeking behaviour[7].

The participants themselves and their GPs enrolled in our study did not receive any information about the tests results of the Krimpen Study. In the Krimpen Study, about 25% of the first GP visits for LUTS in men within two years after baseline can be predicted by the multivariate model combining prostate volume, postvoid residual urine volume, IPSS and social generic QOL (Social domain of the Sickness Impact Profile). Measurements (anatomical and physiological urological parameters) and self-reported items (symptom severity and quality of life) contribute almost equally to the GP consultation rate in these men. The urologic measurements (prostate volume and post-void residual urine volume) and self-reported information about symptoms and QOL can help to select those who will benefit most from medical care, and help to reassure those men that are not likely to need help for LUTS in the near future.

Until now, the condition clinical benign prostatic hyperplasia (BPH) is considered to incorporate three parameters: 1) LUTS, 2) prostate enlargement, and 3) bladder outflow obstruction. In older men, LUTS are considered to be the result of the interaction between age-related morphological changes in the bladder wall, functional subvesical obstruction and bladder changes secondary BPH and non-urinary tract related factors [8]. There is no consensus about a case definition of clinical BPH that can be readily used in epidemiological studies. In particular, there is no agreement about the choice of possible parameters to be included in such a definition, or about the cut-off point between normal and abnormal values for such parameters. Therefore, we postulated that the case definition that would predict GP consultation best would be the one most appropriate for use in epidemiological studies. We tested 5 case definitions for their predictive potential of GP consultation and found the case definition of clinical BPH “IPSS>7” had the best predictive value for a first GP visit for LUTS. This case definition complied with the highest number of men and had the best sensitivity and the best positive predictive value.

We would like to emphasize that the values of all baseline parameters were not communicated to GPs of the participants in this epidemiological study. The men themselves were also not informed about the total scores or the interpretation of such scores.

It seems that an “IPSS greater than 7” is the most appropriate and simple case definition for clinical BPH for use in epidemiological studies. Other studies showed that a poor maximum urinary flow rate (Qmax) and baseline serum prostate specific antigen (PSA) are two of the major risk factors for overall clinical progression in men that already consulted the GP for LUTS [9-11].

GP POLICY IN MEN WITH NEW AND INCREASING LUTS (CHAPTERS 7 AND 8)

Treatment of LUTS includes watchful waiting, pharmacological treatment, and referral for possible surgical interventions. Previous studies mainly focused on referral rather than on the management of new and increasing LUTS. Factors such as the length of the GP’s vocational training [12], gender [13] and psycho-social orientation [14] are known to influence the GP’s decision to refer a patient to a specialist. Furthermore, some studies suggest that referral rates increase with patient’s age[15] or socio-economic status[16, 17], but other studies suggest no effect of these factors[14, 18, 19] To our knowledge our study is the first that has quantified and shown the relationship between coping of the patient and the initial management of GPs, and between coping of the GP and the initial management of GPs in men with LUTS.

Similar to Verhamme et al. we also found that almost 50% of our study group received pharmacological treatment [20]. Two theoretical studies that addressed the intention-to-treat of men with LUTS using hypothetical patient cases showed a higher percentage of pharmacological treatment and referral than we did[21],[22] . A remarkable difference seemed to exist between the GP’s intention to treat a man with LUTS and what happens in ‘real life’ practice. However, the use of hypothetical patients in the other studies makes it difficult to compare study results and supports the fact that studies including hypothetical patients cannot reflect the tailor-made approach of daily practice.

In agreement with the guidelines recommending treatment to improve the patient’s QOL[23, 24] our study confirmed that men with a poor disease-specific QOL received treatment more often. We want to emphasize that in the group of men with a poor disease-specific QOL those with a ‘high passive reaction pattern’ were treated less frequently than those with a low ‘passive reaction pattern’. This might be explained by the consideration that men with deteriorated disease specific QOL who used the coping style ‘passive reaction pattern’ became overwhelmed by their voiding problems that may have resulted in a pessimistic view on their own health. In this situation the patient and GP may have agreed not to treat but to choose for watchful waiting initially. In our model we could not enter the interaction between the coping style of the patient and the coping style of the GP because the Krimpen Study has no data on the GP's coping style. Based on this single study we do not want to speculate on the (non) importance of the coping styles other than 'passive reaction pattern'. These styles could be of importance if they interact with factors not determined in our study, e.g. the coping style of the GP.

The influence of the patient's coping style on GP's initial management also raises interest in the possible influence of the coping style of the GP on treatment decisions. Unfortunately, the Krimpen study does not include information on the coping style of the GP. Therefore, we designed a separate study, which includes 16 hypothetical patient cases with uncomplicated LUTS, to determine whether the GP's characteristics, and especially their coping style, influenced their management. It appears that GP's management was highly related to the duration of LUTS history, the perceived bother of LUTS, and the way patients cope with problems in general. The coping style of the GP did not influence the GP's treatment choice. We also found that the treatment choice of the GP was strongly related to the GP's knowledge on the expected efficacy of medication, indicating a large variance in GPs' knowledge on the expected efficacy of medication. This implies that GPs who expect medication not to be effective will probably unjustly decide not to treat a patient; the opposite may also occur. This finding stresses the importance of a good continuous medical education on the efficacy of existing and new drugs.

We reject the hypothesis that different coping styles of GPs may result in different treatment decisions. The fact that the coping style of the GP and personal characteristics do not influence their management in men with LUTS suggests that different GPs are prone to treat identical patients equally.

VALIDATION OF THE INTERNATIONAL PROSTATE SYMPTOM SCORE (IPSS) FOR THE USE IN ECONOMIC EVALUATIONS (CHAPTER 9)

LUTS cause a reduction in disease-specific QOL, but the magnitude of that reduction cannot be estimated empirically. It is also impossible to estimate the impact of LUTS on QOL compared to the impact of other conditions and diseases. This is because available survey instruments merely quantity the symptoms found, but do not estimate their impact on QOL. Thus it is difficult to determine whether the effects of treatments for LUTS justify the costs; this complicates economic evaluations.

We determined the impact of LUTS on QOL, the so-called 'values' (utilities) people attach to health states, of the various possible health states of the IPSS in a context of LUTS suggestive of BPH. The values for the IPSS health states in this context, as described by the questionnaire, are relatively high; they are located at the top of the utility scale, where 1.0 stands for the value of perfect health. This is in line with the results of the Krimpen Study showing that on average changes in LUTS has a small impact on changes in QOL (chapter 4). Given the high prevalence of LUTS suggestive of BPH, this change in QOL is perceived by a large number of people, but the magnitude of the individual reduction is modest. However, it should be noted that interventions in LUTS suggestive of BPH could still contribute considerably to the health status of populations; a small increase in quality-adjusted life years (QALYs) in a large number of patients might well outweigh a large increase in QALYs in a small number of patients.

The values elicited in this study represent societal values, which sometimes deviate from the experts' perspective and the patients' perspective. For instance, compared to the general public and patients, experts tend to put more emphasis on functional limitations, and less on emotional problems and pain. Patients often report higher values (a lower burden of the disease) than those not affected by the disease. The higher values of the patients are attributed to coping mechanisms in patients[25]. Thus the values of our investigation could be considered as falling between patient values and expert values. Theoretically, this is where we expect values from the general public to be.

The IPSS scores can be used in QALY calculations, and as such can facilitate an economic evaluation[26]. Such economic evaluations give urologists and the society an opportunity to justify the amount of money spent on this clinical problem. This justification will become increasingly important, as medical opportunities continue to exceed the available budget. The validation of the IPSS now provides us with an instrument to participate in the search for evidence of cost-effective medication. A limitation that has to be reported is that the utiliites for the IPSS have been acquired in the context of symptoms of LUTS suggestive of BPH. If the IPSS is used in another context, for instance in women with LUTS, the values may not be fully adequate.

ADVANTAGES AND DISADVANTAGES OF THE KRIMPEN STUDY AND THE GP DATA

In the Krimpen study 50% of the initially invited men responded. Given that several invasive measurements were performed in these men (transrectal ultrasound of the prostate (TRUS) and venapuncture in all men) this is a good respond rate, and comparable to the response rate of the Olmsted County Study which performed TRUS in only limited subgroups of men. In the Krimpen Study, a questionnaire was sent to those who did not participate at baseline to investigate the characteristics of this group. As the prevalence of men with IPSS>7 was slightly lower in the non-participants [27], we have to conclude that the prevalence and incidence of the first GP visit for LUTS must be slightly lower than actually measured in the present study. However, because this study reports on the relationship between determinants and GP consultation, this bias is not likely to have influenced our results.

None of the participants themselves or their GPs enrolled in our study received information about the tests results of the Krimpen Study; therefore, our findings are also not biased by this knowledge. Only the PSA value was given to the GP, in case of the need to detect prostate cancer. Had the PSA value not been communicated to participant's GP the GP's initial management could have differed from the management we reported, because the GP's management would then also be related to the detection of prostate cancer. However, in the current study, most probably, possible fear of prostate cancer does not play a role in GP consultation for LUTS, because men with prostate cancer have already been filtered out of the study population.

In this type of epidemiological research the reliability of the electronic medical record is a problem because the information entered by the physician is often variable. However, because of the large number of keywords (n=82) used in the search to determine GP visits for signs of LUTS, our concerns about missing hits are minimal.

Data on coping behaviour, aiming to determine the influence of coping on QOL or GP's initial management, were only collected in the third follow-up round. This narrowed the sample size of the men we used in the analyses. No loss to follow-up (missing files) occurred in the GP data. The 68 men with data on coping behaviour with a first GP visit for LUTS, can be seen as a group completing all the follow-up rounds: they are slightly younger, have less co-morbidity, a lower IPSS and a better QOL than the remainder. Nevertheless, this small sample was sufficiently large to yield significant relationships; and the small confidence limits around the estimates strengthen our findings. Since the Utrecht Coping LIST (UCL) considers coping to be a personal trait we assume that the time point of the data collection on coping (i.e. only at third follow-up) does not bias our results.

In our separate study on a hypothetical patient population (n=16 cases), which was presented to selected GPs, the response rate among GPs to the cases and questionnaires was relatively low (45%). Therefore, we cannot exclude selection bias in the results. However, the characteristics of the study population do not seem to differ from demographic data of the overall GP population in the Netherlands [28]. The number of responding GPs (n=34) and the 16 cases entered in the study were sufficient according to the sample size calculation. Our sample was sufficiently large to yield significant relationships and the small confidence limits around the estimates strengthen our findings. Moreover, as this study also reports on relationships and not on the number of GPs using a specific coping style, this small sample size is not likely to have influenced our results. The questionnaire contained 16 differing cases based on a hypothetical 68-year-old man with uncomplicated LUTS. This cannot of course reflect the tailor-made approach of daily practice, thus the results have to be judged with regard to this limitation.

IMPLICATIONS FOR CLINICAL PRACTICE AND SUGGESTIONS FOR FURTHER RESEARCH

We suggest to use "IPSS greater than 7" as the case definition of clinical BPH for use in epidemiological studies.

Men suffering from LUTS on average do not perceive a considerable influence of these symptoms on their general well-being. Therefore, we suggest the need for more restraint (watchful waiting) in the intervention policy for men with mild LUTS. Obviously, there are small populations or patient subgroups with more extreme changes in the severity of LUTS that may exert greater effects on QOL and for whom direct therapy is preferred.

Our study showed that the treatment choice of the GP was strongly related to the GP's knowledge on the expected efficacy of medication. This finding stresses the importance of a good continuous medical education on the efficacy of new and existing pharmaceuticals. It has to be noted that the medication used (α-blockers) has a limited effect on symptoms (IPSS) and urodynamic parameters compared to placebo and invasive therapies[29].

In this population no attention is paid to the impact of potential treatments on QOL, because the aim of the Krimpen Study was to describe the natural history of BPH. Therefore, treatments were neither encouraged nor randomised. The influence of treatment for LUTS in relation to changes in QOL could be a topic of future research. However, we have determined that only 10.6% of the men at risk in our study (n=1506) consulted their GP for the first time for LUTS during the total study period, of which 50.6 % (n=81) received pharmacological treatment and 12.5% (n=20) was initially referred to a urologist.

We have validated the International Prostate Symptom Score (IPSS) for use in economic evaluations and to make comparisons and relative statements across different conditions, interventions and diseases. Further research has to demonstrate the impact of LUTS on QOL compared to the impact of other conditions on QOL.

The associations found between a change in LUTS and different coping styles (such as 'active problem solving' and 'reassuring thoughts') in relation to generic QOL are interesting for physicians. For example, it may be advisable to stimulate effective coping styles in patients and to discourage non-effective styles. Because we found that the influence of the coping style 'active problem solving' is positively related to a change in QOL in men with new LUTS, GPs could encourage men to handle the problem (i.e. the LUTS) efficiently. Furthermore, when the GP knows that his patient generally uses the coping style 'reassuring thoughts' (thinking that most problems are not really serious and will disappear with time) he could inform the man about the prevalence of LUTS and the treatment options for these symptoms, which may positively affect his QOL. This may imply that physicians should take the coping style of the patient into consideration. However, this needs further study in which an intervention is introduced to discover the coping style of the patient, with the aim to influence the outcome QOL.

The present study provides a starting point to elucidate and quantify the influence of the coping style of the patient on the GP's initial treatment policy. Further studies on the influence of coping styles on the GP's initial policy for LUTS, and on the relationship between coping style and the development of QOL, are needed before definite advice on these matters can be given to GPs. Our findings also emphasize the importance of further study on the influence of coping on QOL, in relation to GP consultation and policy, in populations with disorders or diseases other than LUTS.

The management of the GP in men with LUTS does not depend of the coping style of the GP. Discussing the coping style with the patient may be an effective way to influence QOL in chronic diseases like LUTS, which have relatively limited treatment options. Although a validated research instrument is available to determine the coping style of the patient, further studies are needed to develop simple methods to detect coping style for use in daily clinical practice.

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Summary

During the past decades, a lot of knowledge about the epidemiology and natural history of lower urinary tract symptoms (LUTS) and the efficacy and safety of treatment approaches was gained from research published in the international literature. Worldwide the prevalence of men with LUTS is known, and the attention on the impact of LUTS on quality of life (QOL) is growing strongly. Remarkably, the most studies upon which this knowledge is based are cross sectional in study design. The Krimpen Study offers the opportunity to study factors associated with LUTS in a longitudinal study design. The aim of this thesis is to study the relationship between LUTS, QOL and coping styles. To study the clinical relevance of these factors also the relationship with general practitioner consultation and – policy was determined.

Chapter 2 presents the study design of the Krimpen Study. In this study, all eligible men, 50 to 78 years living in Krimpen aan den IJssel, were invited to complete a 113-item questionnaire, a three-day-frequency-volume chart and to visit the health centre and the urology outpatient department of the Erasmus MC for additional measurements, including blood pressure, urinalyses, body height and weight, digital rectal examination, transrectal ultrasound of the prostate, uroflowmetry, post-void residual volume, and serum prostate specific antigen. After the baseline study three consecutive rounds of follow-up were performed with an average follow-up period of 2.1, 4.2 and 6.5 years. In each of these rounds all measurements were repeated. The visit to the health centre in Krimpen aan den IJssel was only at baseline. Men who did not respond at first or second-follow up and did not meet the exclusion criteria were nevertheless also re-invited for participation in the third follow-up round. After the last follow-up round data is assembled of the medical GP files of the participants and the pharmacy database.

In **chapter 3** we determined which case-definition of clinical benign prostatic hyperplasia (BPH) has the best predictive value for a first GP visit for lower urinary tract symptoms (LUTS) suggestive of BPH in the near future. In relation, the incidence and prevalence rates of first GP visits for LUTS were estimated. These incidence and prevalence rates of the men at risk were 19.6% and 14.0% in the total study period, respectively; these rates increase with age. With regard to the sensitivity and the positive predictive value, the simple case-definition of clinical BPH "IPSS >7" has the best predictive value for first GP visit for LUTS within two years after baseline. Measurements of prostate volume and Q_max have no additional value to the estimation of symptoms (IPSS) only in predicting which men will seek care for LUTS in the near future.

Chapter 4 focuses on the relationship between changes in LUTS and changes in QOL (disease-specific and generic). Data were collected through self-administered questionnaires, including the Sickness Impact Profile (SIP, three domains), the Inventory of Subjective Health (ISH), the International Prostate Symptom Score (IPSS) and the BPH Impact Index (BII). Although mean IPSS increased over time, the average generic quality of life improved and almost one third of the men reported a better disease-specific quality of life. Multiple linear regressions revealed that disease-specific quality of life was associated with IPSS at baseline, changes in IPSS between baseline and follow up, and age; however, the generic quality of life scores were not associated with these parameters. We concluded that changes in the severity of LUTS have on average little impact on the disease-specific quality of life of men aged 50 to 78 years old and on average hardly no impact on their generic quality of life during a follow-up period of 4.2 years.

In **chapter 5** we explored whether the relationship between changes in LUTS and changes in QOL is influenced by factors, such as personal characteristics e.g. age, co-morbidity and coping style. Data were collected through self-administered questionnaires, including the Sickness Impact Profile (SIP, three domains), Inventory of Subjective Health (ISH), International Prostate Symptom Score (IPSS), BPH Impact Index (BII) and the Utrecht Coping List (UCL). Using multiple linear regressions overall no significant association is found between changes in LUTS with a change in QOL. However, a positive change in QOL is significantly associated with a change in LUTS when men use the coping style 'active problem solving' and a negative relationship exists with coping style 'reassuring thoughts'. Different coping styles have a different impact on the relationship between a change in LUTS and a change in generic QOL in community-dwelling elderly men. The change in generic QOL determined by a change in LUTS in combination with the use of these coping styles is large compared to the influence of, for example, getting a new chronic disease. This makes a future exploration of the clinical treatment possibilities warranted.

Chapter 6 reports the factors that predict seeking of primary care for LUTS for the first time in community-dwelling men aged between 50 – 78 years. Information on primary care seeking during 2 years of follow-up of all participants was collected from the general practitioners (GP) record using a computerised search engine, and an additional manual check of the electronically selected files. Prostate volume, post-void residual volume, IPSS and social generic QOL (SIP Social) are important determinants of first GP consultation in men with LUTS. Measurements (physical urological parameters) and self-reported items (symptom-severity and quality of life) contribute almost equally to GP consultation in these men. Both measurements of prostate volume and post-void residual urine volume as self-reported information about symptoms or QOL can help to select those who will benefit from medical care and help to reassure those men that are not likely to need near future help.

In **chapter 7** we identified patient characteristics associated with general practitioner's (GP) initial treatment decision in men with LUTS and we tested the hypothesis that a different coping style of patients results in different GP behaviour regarding treatment. Data were collected on quality of life, symptom severity based on the International-Prostate-Symptom-Score (IPSS) and coping. Information on primary care seeking and GP's initial management during 2 years of follow-up of all participants was collected from the GP's records. Data were obtained of 68 men having data on coping behaviour, without a history of LUTS, who had a first GP visit for LUTS during the study period. In the group of men with a bad disease-specific QOL those with a high 'passive reaction pattern' were treated less frequently than those with a low 'passive reaction pattern'. This quantitative study confirms the hypothesis that different coping styles of patients may result in different GP behaviour regarding treatment. The use of the coping style 'passive reaction pattern' has a large influence on GP's initial management in men with LUTS.

Chapter 8 reports about our interest to learn whether GP's background characteristics and especially his coping style influenced his management in hypothetical patients with uncomplicated LUTS. In a separate study design 39 GPs completed 16 differing hypothetical patient-cases and additional questions. Moreover, they completed questions about their coping behaviour in general (UCL). After reading all cases the GPs had to make a choice between 1) watchful waiting, 2) pharmaceutical treatment or 3) referral to urologist. Multivariate logistic regression analyses yielded that GP's management was highly related to GP's expected efficacy of medication, the duration of the LUTS history, patient's perceived bother of LUTS and the way patients cope with problems in general. The coping style of the GP did not influence GP's treatment choice. This finding suggests that different GPs are prone to treat identical patients equally in men with LUTS.

In **chapter 9** we describe the validation of the International Prostate Symptom Score (IPSS) for use in economic evaluations. Quality of life instruments used in economic evaluation are suitable to estimate the impact of a condition on quality of life and to make comparisons and relative statements across different conditions, interventions and diseases. To make the IPSS suitable for use in economic evaluation we valued the impact on quality of life of patients with LUTS suggestive of BPH, by valuing health states defined by the International Prostate Symptom Score (IPSS) using the time trade-off technique (TTO). TTO values range from 1.0 for perfect health to 0.0 for the value of death, and can be used to calculate Quality Adjusted Life Years (QALYs), the preferred outcome measure in health economics. We reduced the number of health states defined by the IPSS using factor analysis. The resulting 9 health states were valued by a representative sample of the general public (N = 170) using TTO. The worst IPSS health state was valued at 0.87. The values for health states defined by the IPSS revealed that LUTS suggestive of BPH has a mild impact on quality of life. The valuation of the IPSS facilitates economic evaluations of treatments for LUTS suggestive of BPH, because QALYs can be determined empirically.

Chapter 10 discuss the main topics addressed in this thesis. The relationship between changes in LUTS and changes in QOL and the influence of coping on this relationship is addressed. The discussion also focuses on patient– and GP characteristics, especially their coping style, in relation to GP consultation and GP management in men with LUTS. Finally, implications for daily practice are described and recommendations are made for future research.

Samenvatting

Gedurende de laatste decennia is internationaal veel onderzoek verricht naar zowel de epidemiologie en het natuurlijk beloop van klachten van de lagere urinewegen (Lower urinary tract symptoms (LUTS)) als naar de werkzaamheid en veiligheid van therapie bij mannen. Wereldwijd is de prevalentie van mannen met LUTS bekend en is de aandacht voor de impact van LUTS op de kwaliteit van leven sterk toegenomen. Opvallend is echter dat de meeste studies waarop deze kennis is gebaseerd cross-sectioneel zijn opgezet.

De Krimpen Studie maakt het mogelijk om de aan LUTS gerelateerde factoren te bestuderen in een longitudinale studie-opzet. Het doel van dit proefschrift is om de relatie te bestuderen tussen LUTS, kwaliteit van leven en copinggedrag. Om de klinische relevantie van deze factoren te bepalen is tevens de relatie met het bezoek aan de huisarts en diens beleid bepaald.

Hoofdstuk 2 beschrijft de studie-opzet van de Krimpen Studie. In deze studie werden alle mannen tussen de 50 en 78 jaar oud woonachtig in Krimpen aan den IJssel uitgenodigd om een 113-item vragenlijst en een driedaags plasdagboek in te vullen en het gezondheidscentrum en de polikliniek urologie van het Erasmus MC te bezoeken voor aanvullende metingen. Bloeddruk, lengte en gewicht werden gemeten, urine geanalyseerd, een rectaal toucher, transrectale echografie van de prostaat, uroflowmetrie en residu-bepaling uitgevoerd en het prostaat specifiek antigen (PSA) gehalte bepaald. Na de baseline studie zijn vervolgens drie follow-up rondes uitgevoerd met een gemiddelde follow-up periode van 2,1 en, 4,2 en 6,5 jaar vanaf de eerste meting. Tijdens elke follow-up ronde werden genoemde metingen herhaald. Het bezoek aan het gezondheidscentrum in Krimpen aan den IJssel vond enkel plaats tijdens de eerste meting. Mannen die niet hadden deelgenomen aan de eerste of tweede follow-up ronde en niet aan de exclusiecriteria voldeden werden opnieuw uitgenodigd om deel te nemen aan de derde follow-up ronde. Daarnaast werden na de laatste ronde gegevens verzameld uit de dossiers van de huisarts en apotheek.

In **hoofdstuk 3** hebben we bepaald welke definitie van de conditie klinische benigne prostaat hypertrofie (BPH) het best voorspellend is voor een eerste huisartsbezoek voor LUTS in de nabije toekomst. Tevens is de incidentie en prevalentie van het eerste huisartsbezoek voor LUTS bepaald. De incidentie en prevalentie voor een eerste huisartsbezoek voor LUTS voor de mannen “at risk” was respectievelijk 19,6% en 14,0 % gedurende de gehele studieperiode; deze waarden namen toe met de leeftijd. Met betrekking tot de sensitiviteit en de positief voorspellende waarde heeft de eenvoudige case-definitie van de conditie klinische BPH “IPSS>7” de beste voorspellende waarde voor een eerste huisartsbezoek voor LUTS in een periode van twee jaar na baseline. Metingen van prostaatvolume en maximale urineflow (Q_max) bleken geen toegevoegde waarde te hebben boven enkel de bepaling van de klachten (IPSS) in de voorspelling welke mannen in de nabije toekomst hun huisarts voor de eerste keer met LUTS zullen bezoeken.

Hoofdstuk 4 focust op de relatie tussen veranderingen in LUTS en veranderingen in kwaliteit van leven (ziektespecifiek en generiek). De data zijn verzameld met behulp van vragenlijsten, namelijk de Sickness Impact Profile (SIP, drie domeinen), de vragenlijst over ervaren gezondheid (mini-VOEG), de International Prostate Symptom Score (IPSS) en de BPH Impact Index (BII). Alhoewel de gemiddelde IPSS toenam in de tijd, verbeterde de gemiddelde generieke kwaliteit van leven en rapporteerde bijna een derde van de mannen een betere ziekte-specifieke kwaliteit van leven. Multiple lineaire regressie analyses toonden aan dat de ziektespecifieke kwaliteit van leven was gerelateerd aan de IPSS tijdens baseline, veranderingen in IPSS tussen baseline en follow-up en leeftijd; de generieke kwaliteit van leven was echter niet gerelateerd aan deze parameters. Wij concluderen dat veranderingen in de ernst van de plasklachten (LUTS) gemiddeld genomen maar een kleine invloed heeft op de ziektespecifieke kwaliteit van leven van mannen tussen de 50 en 78 jaar oud en bijna geen impact hebben op de generieke kwaliteit van leven van deze mannen gedurende een follow-up periode van 4.2 jaar.

In **hoofdstuk 5** is bestudeerd of de relatie tussen veranderingen in LUTS en veranderingen in kwaliteit van leven wordt beïnvloed door andere factoren zoals bijvoorbeeld persoonlijke kenmerken of karaktereigenschappen zoals leeftijd, comorbiditeit en copingstijl. Opnieuw werd gebruik gemaakt van verschillen vragenlijsten: de Sickness Impact Profile (SIP, drie domeinen), de vragenlijst over ervaren gezondheid (mini-VOEG), de International Prostate Symptom Score (IPSS), de BPH Impact Index (BII) en de Utrechtse Coping Lijst (UCL). Met gebruik van multiple lineaire regressie analyses werd in het algemeen geen significante relatie gevonden tussen veranderingen in LUTS en veranderingen in kwaliteit van leven. Een positieve verandering in kwaliteit van leven is echter wel gerelateerd aan een verandering in LUTS bij mannen die de copingstijl ‘actief aanpakken’ gebruikten en een negatieve relatie bestond bij mannen die de copingstijl ‘geruststellende gedachten’ gebruikten. Verschillende copingstijlen hebben een verschillende impact op de relatie tussen veranderingen in LUTS en veranderingen in generieke kwaliteit van leven bij oudere mannen. De verandering in generieke kwaliteit van leven door een verandering in LUTS in combinatie met het gebruik van de copingstijlen ‘geruststellende gedachten’ en ‘actief aanpakken’ is groot in vergelijking met de impact van, bijvoorbeeld, het krijgen van een chronische ziekte. Deze bevinding opent een weg naar onderzoek naar andere behandelmogelijkheden voor LUTS.

Hoofdstuk 6 rapporteert over de factoren die een eerste huisartsbezoek voor LUTS bij oudere mannen voorspellen. Informatie over huisartsbezoek van alle participanten gedurende twee jaar na baseline werd verzameld uit de huisartsendossiers met gebruik van een elektronische zoekprocedure en een extra handmatige controle van alle elektronisch geselecteerde dossiers. Belangrijke factoren voor de voorspelling van een eerste huisartsbezoek voor LUTS zijn het prostaat volume, het residu, de IPSS en de sociale generieke kwaliteit van leven (SIP sociaal). De metingen (urologische parameters) en de zelf gerapporteerde items (ernst van de plasklachten en kwaliteit van leven) dragen in bijna gelijke mate bij aan de voorspelling van een eerste huisartsbezoek voor LUTS bij deze mannen. Zowel metingen van de prostaat en het residu als de zelf gerapporteerde items kunnen helpen om die mannen te selecteren die kunnen profiteren van medische hulp en die mannen te selecteren aan wie verzekerd kan worden dat zij waarschijnlijk geen medische zorg voor LUTS nodig hebben in de nabije toekomst.

In **hoofdstuk 7** hebben wij de patiëntkenmerken vastgesteld die gerelateerd zijn aan het beleid van de huisarts bij een eerste consult voor LUTS en hebben wij de hypothese getest dat verschillende copingstijlen van de patiënt resulteren in verschillend huisartsgedrag met betrekking tot het beleid bij mannen met LUTS. De data zijn verzameld met behulp van vragenlijsten, inbegrepen de Sickness Impact Profile (SIP, drie domeinen), de vragenlijst over ervaren gezondheid (mini-voeg), de International Prostate Symptom Score (IPSS) en de Utrechtse Coping Lijst (UCL). Informatie over huisartsbezoek van alle participanten is verzameld uit de huisartsendossiers. De analyse betreft 68 mannen, zonder een voorgeschiedenis van LUTS, maar met data over hun copinggedrag, die een eerste huisartsbezoek hadden voor LUTS gedurende de studieperiode. In de groep mannen met een slechte ziektespecifieke kwaliteit van leven zijn diegenen met een hoge score op de copingstijl 'passief reactiepatroon' minder vaak behandeld (medicatie of verwijzen naar uroloog) dan diegene met een lage score op deze copingstijl. Deze kwantitatieve studie bevestigt de hypothese dat verschillende copingstijlen van patiënten resulteren in verschillend beleid van de huisarts bij mannen met LUTS. Het gebruik van de copingstijl 'passief reactiepatroon' heeft een grote invloed op het beleid van de huisarts bij mannen die voor de eerste keer de huisarts met LUTS consulteren.

Hoofdstuk 8 rapporteert over ons onderzoek of de persoonskenmerken en karaktereigenschappen, met name de copingstijl, van de huisarts zelf van invloed zijn op zijn beleid bij hypothetische mannen met ongecompliceerde LUTS. In een afzonderlijke studie-opzet hebben 39 huisartsen 16 verschillende casussen van hypothetische patiënten en aanvullende vragen beantwoord. Bovendien hebben zij de Utrechte coping lijst ingevuld om te achterhalen hoe de huisarts zelf in het algemeen in problematische situaties reageert. Na het lezen van de casussen moest de huisarts zijn beleidskeuze maken: 1) afwachten (watchful waiting), 2) medicatie voorschrijven of 3) verwijzen naar de uroloog. Multivariate logische regressie analyses toonden aan dat het beleid van de huisarts bij mannen met ongecompliceerde LUTS afhing van de kennis van de huisarts over de verwachte werkzaamheid van medicatie, de duur van de LUTS geschiedenis, de ervaren hinder van de LUTS door de patiënt en de manier waarop de patiënt in het algemeen met problemen omgaat (coping). De copingstijl van de huisarts zelf had geen invloed op zijn therapiekeuze. Dit suggereert dat verschillende huisartsen in staat zijn identieke patiënten met LUTS op een zelfde wijze te behandelen.

In **hoofdstuk 9** beschrijven wij de validering van de International Prostate Symptom Score (IPSS) voor het gebruik in economische evaluaties. De instrumenten die in een economische evaluatie worden gebruikt voor het meten van kwaliteit van leven zijn geschikt om de invloed van een ziekte op de kwaliteit van leven weer te geven en kunnen gebruikt worden om relatieve vergelijkingen te maken tussen de invloed van verschillende aandoeningen op kwaliteit van leven. Om de IPSS hiervoor geschikt te maken hebben wij de invloed van LUTS op kwaliteit van leven vastgesteld door middel van het waarderen van de gezondheidstoestanden van de IPSS met de time trade-off interview techniek (TTO). De TTO waarderingen variëren tussen de 1,0 voor 'perfecte gezondheid' en 0,0 voor de waarde van 'dood' en kunnen worden gebruikt voor de berekening van Quality Adjusted Life Years (QALYs), de geprefereerde uitkomstmaat in de gezondheidseconomie. Het aantal gezondheidstoestanden van de IPSS is met behulp van een factor analyse gereduceerd. De overgebleven 9 gezondheidstoestanden zijn door een representatieve steekproef uit de algemene bevolking (N = 170) gewaardeerd met behulp van TTO. De slechtste IPSS gezondheidstoestand is gewaardeerd op 0,87. De waardering van de gezondheidstoestanden van de IPSS tonen aan dat LUTS op verdenking van benigne prostaat obstructie (BPO) een geringe invloed heeft op de kwaliteit van leven. De waardering van de gezondheidstoestanden van de IPSS maakt economische evaluaties voor behandelingen van LUTS mogelijk, aangezien nu QALYs empirisch bepaald kunnen worden.

Hoofdstuk 10 bediscussieert de belangrijkste onderwerpen van dit proefschrift. De relatie tussen een verandering in LUTS en een verandering in kwaliteit van leven, rekening houdend met de invloed van copinggedrag komt aan de orde. De discussie richt zich tevens op de persoonskenmerken en karaktereigenschappen van zowel de patiënt als de huisarts, met name hun copingstijl, in relatie tot huisartsbezoek en het beleid van de huisarts bij mannen met LUTS. Tenslotte worden de implicaties van onze bevindingen voor de dagelijkse huisartspraktijk beschreven en geven wij adviezen voor toekomstig onderzoek.

Dankwoord

DANKWOORD

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Lieve kleine Olle, als jij eens wist hoe groot jouw bijdrage is aan onze Q*olle*ty of life!

Esther

CURRICULUM VITAE

Esther Tanja Kok werd op 1 februari 1976 geboren te Haarlem. Na het behalen van het gymnasiumdiploma aan het Mendelcollege te Haarlem in 1994 studeerde zij een jaar Kunst en Cultuurwetenschappen aan de Erasmus Universiteit Rotterdam. In 1995 haalde zij het propedeutisch examen van die studie en maakte de overstap naar de studie Beleid en Management van de Gezondheidszorg (BMG) aan dezelfde universiteit. Tijdens haar afstudeeronderzoek onderzocht zij het algemeen welbevinden en de mate van zorggebruik van Nederlandse overwinteraars in Benidorm (Spanje). In 1999 haalde zij het doctoraal examen. In 2000 trad zij in dienst van het institute for Medical Technology Assessment (iMTA) waar zij gedurende 2 jaar werkte aan verschillende projecten met betrekking tot kwaliteit van leven, kosten-effectiviteit, richtlijnen en de breedte van het geneesmiddelenpakket. Vanaf maart 2002 deed zij voor een jaar ervaring op als beleidsmedewerker bij het Zorgkantoor DWO/NWN (Zorgverzekeraar DSW). Sinds maart 2003 werkt zij als onderzoeker binnen de Krimpen Studie op de afdeling huisartsgeneeskunde van het Erasmus MC. Zij volgde het Nihes-programma Epidemiologie en sloot dit in juni 2006 af met het behalen van het Master of Science-diploma Epidemiologie.

Op 2 augustus 2002 huwde zij met Ytzen van der Werf met wie zij een zoon heeft (Olle, 4 mei 2004).