

Health economic analysis of a urinary catheter which reduce the frequency of urinary tract infections (UTIs)

Research questions: a) What is the willingness-to-pay (WTP) in Sweden - from a patient perspective - for a urinary catheter which reduce the annual frequency of urinary tract infections by 25% and 50%, respectively, and (b) is the WTP dependent on the annual frequency of UTIs and gender?

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Abstract

Objective: To investigate the preference for urinary catheters that can reduce the frequency of urinary tract infections (UTIs), among Swedish patients practicing clean intermittent catheterization (CIC), and analyze if the preference is affected by the frequency of UTIs and gender.

Methods: The preference for a clinically more effective catheter was expressed as a monetary value by investigating the patients' willingness-to-pay (WTP) to switch catheters. The results were stratified on annual frequency of UTIs and gender.

An electronic questionnaire was sent by e-mail to 144 Swedish users of intermittent catheters. The participants were asked to assume a situation in which they use their current catheter but had the choice to switch to a similar catheter, which hypothetically would reduce the frequency of UTIs including possible complications. Either every fourth or every second UTI could be avoided.

The participants were asked to report their frequency of UTIs and their willingness-to-pay for the new catheter was collected by letting them choose to spend either one of eleven explicit monthly amounts from 0–1000 SEK or any other amount in an open answer. Only individuals stating that they were 'certain' or 'very certain' regarding their answers were included in the analyses. Statistical analyses were performed with non-parametric testing methods.

Results: 96 individuals returned the questionnaire, of which 42 males and 28 females were certain or very certain regarding their answers. The proportion of respondents with ≤ 1 UTI/year and ≥ 2 UTI/year was 74% and 26%, respectively. The respondents were willing to spend on average 120 SEK each month to avoid every fourth UTI and 174 SEK each month to avoid every second UTI. The results to avoid every fourth and every second UTI, respectively, showed no difference between men and women but having ≥ 2 UTI/year reached statistical significance.

Conclusion The CIC users in this study, who practice intermittent catheterization on a daily basis, expressed a preference for catheters that could help to decrease the frequency of urinary tract infections as expressed by a willingness to pay for more effective catheters. The result was dependent on the annual frequency of UTIs but not gender.

Introduction

Clean intermittent catheterization¹ (CIC) was introduced in the early 1970s and has since then proved to be an efficient method in the management of neuropathic bladders to solve problems with incontinence and dysuria. There are many indications for CIC, for instance in spinal cord injured (SCI) patients as a mode of voiding at the initial phase in an intensive care unit after an injury, during the period of the bladder retraining and as a long-term solution to empty the bladder.²

Complications of intermittent catheterization

Even though intermittent catheterization is an efficient method for SCI patients, there are complications associated with the procedure. A retrospective study of 159 SCI patients investigated the overall rate of complications of CIC.³ Ninety-two of the patients used CIC only temporarily for the mean length of 3.5 months. Sixty-seven of the patients continued to use CIC in the medium and long term for a mean period of 2 years and 8 months. The study showed that 60% of the patients had an asymptomatic cytobacteriological infection. Twenty-eight percent (28%) developed a symptomatic lower urinary tract infection (UTI).⁴ Ten percent (10%) of the men had epididymitis. In addition, strictures occurred in 5.3% of the male population with a mean delay of 2 years and 6 months. Bladder stones were seen in 2% of the patients.

A literature review investigating the complications of intermittent catheterization, found that infections in the urinary tract is the most common complication, but the prevalence of UTIs varies. To prevent UTIs, a non-infecting technique is needed.⁵

In a study where 302 CIC treated patients were followed for a mean time of 13 months, approximately 3 out of 4 patients experienced urinary tract infections. 58.3% of the patients had minor symptoms, 14.3% had more comprehensive or frequent symptoms and 2.6% major symptoms.⁶

¹ Clean intermittent catheterization involves the passing of a hollow tube through the urethra several times per day to empty the bladder

² Perrouin-Verbe B, Labat JJ, Richard I, et al. 'Clean intermittent catheterisation from the acute period in spinal cord injury patients. Long term evaluation of urethral and genital tolerance. *Paraplegia* vol. 33, 1994, pp. 619-624

³ Perrouin-Verbe, *Paraplegia*, pp. 619-624

⁴ UTI is defined as positive urine culture with pyuria and one or more systemic symptoms as fever, loin pain, dysuria, urgency, hematuria

⁵ Wyndaele JJ, Complications of intermittent catheterization: their prevention and treatment. *Spinal Cord*, vol. 40, 2002, pp. 536-541.

⁶ Bakke A, Vollset SE, Høisæter PÅ, et al. Physical complications in patients treated with clean intermittent catheterization. *Scand J Urol Nephrol*, vol. 27, 1993, pp. 55-61.

In 77 CIC patients completing a 5 year study, 81% were treated for UTI at least once. Twenty-two percent (22%) had 2-3 UTIs per year and 12% four or more UTIs per year.⁷

A recent cost utility study evaluated the cost effectiveness of different catheter types.⁸ The health economic model incorporated clinical data into a probabilistic Markov Model consisting of key health states between which the patients moved with certain transition probabilities. The development of UTI and difficulties to treat the infection was central to the model. The annual transition probability for UTI was 67.7%. It was 8.3% for UTI resistant to first line antibiotic, 7% for multidrug resistant UTI and lastly 3.6% for UTI associated bacteremia. Not only do the UTIs and associated complications impose a substantial cost to any health care system, but they also affect the patients' quality of life.

Impact of UTIs on quality of life

In a national survey performed in Canada, 912 SCI patients responded to a 36 item questionnaire to collect information on clinical demographic data, techniques and use of IC, occurrence of UTIs and consequences of having UTIs. The mean frequency of self-reported UTIs in the past 12 months was 2.6. Females had more UTIs than men, 3.2 and 2.4 respectively. Twenty-three percent (23%) felt ill for an average of 4 days or longer with a UTI, 15% had missed work or school and 34% had refrained from social activities because of UTIs. Seventy-one percent (71%) of the respondents said that UTIs negatively impacted their quality of life. There was a positive relationship between the number of UTIs and the impact of UTIs on quality of life.⁹

The cost utility analysis by Bermingham et al. (2013) assumed a relationship between individuals' quality of life and the health outcomes achieved as a consequence of each intervention. The authors also meant that where preferences have implications for the costs and outcomes, it is important to include these in the models. Although important, it is unfortunately difficult to find data on patient preferences to include in health economic models.¹⁰

⁷ Biering-Sorensen F, Nielans HM, Dorflinger T, et al. Urological situation five years after spinal cord injury. *Scand J Urol Nephrol*, vol. 33, 1999, pp. 157-161.

⁸ Bermingham S, Hodgkinson S, Wright S, et al. Intermittent self-catheterization with hydrophilic, gel reservoir, and non-coated catheters: a systematic review and cost effectiveness analysis. *British Medical Journal*, 2013, pp. 1-16.

⁹ Woodbury MG, Hayes KC, Askes HK. Intermittent catheterization practices following spinal cord injury: a national survey. *The Canadian Journal of Urology*, vol. 15(3), June 2008, pp. 4065-4071

¹⁰ Bermingham, *BMJ*, 2013, p. 6.

Catheters for intermittent catheterization

In a Cochrane review from 2007, long-term bladder management by intermittent catheterization in adults and children was discussed.¹¹ Different intermittent catheterization methods and catheter types were compared regarding their ability to reduce the incidence of urinary tract infections (UTIs), hematuria, other infections and which method the patients' prefer. Fourteen studies met the inclusion criteria. With the available data it was not possible to support a favorable catheter type in a mixed group of patients in need to empty their bladder for various reasons. The authors mean patient satisfaction, acceptability and preferences are important secondary outcome variables which need to be included in clinical trials evaluating urinary catheters. These parameters are particularly important in assessing the cost-effectiveness of single-use products such as urinary catheters.

A recent review article which compared two types of catheters, coated catheters and non-coated, found a difference regarding reported UTIs and hematuria events. There were significantly less reported UTIs in the group receiving coated catheters, 50% versus 72%. There were also less hematuria cases among the patients with coated catheters, 46% versus 55%.¹²

Infections have an impact on patients' quality of life and they are costly to the health care system. A reduction in the frequency of catheter-associated UTIs will benefit the patients, the health care organizations and payers of health care.

Purpose and research questions

This health economic analysis focused on the patient perspective of UTIs. The patients in need for intermittent catheters evaluated a hypothetical situation where they could experience less UTIs and associated complications by switching to a similar urinary catheter as the one they already used.

The preference for a clinically more effective catheter was expressed as a monetary value by investigating the patients' willingness-to-pay (WTP) to switch catheters. The results were stratified on annual frequency of UTIs and gender.

¹¹ Moore KN, Fader M, Getliffe K. Long-term bladder management by intermittent catheterization in adults and children. *Cochrane Database of Systematic Reviews* 2007, Issue 4.

¹² Li L, Wenqin Y, Hong R, et al. Impact of hydrophilic catheters on urinary tract infections in people with spinal cord injury: systematic review and meta-analysis of randomized controlled trials. *Archives of Physical Medicine and Rehabilitation*, vol. 94, 2013, pp. 782-787.

This study investigated the following questions:

- What is the willingness-to-pay in Sweden - from a patient perspective - for a urinary catheter which reduces the annual frequency of urinary tract infection by 25% and 50%, respectively?
- Is the patients' willingness-to-pay for a more effective catheter dependent on the annual frequency of UTIs or gender?
- What is the additional value of a more effective catheter from a healthcare perspective?

Hypotheses

The null hypotheses tested in the study were:

- (1) Probability that willingness-to-pay is 0 SEK at p-level 0.05.
- (2) Probability of no difference in willingness-to-pay between men and women.
- (3) Probability of no difference in willingness-to-pay between UTI frequency $\leq 1/\text{year}$ and UTI frequency $\geq 2/\text{year}$.

Methods

Health economics is a discipline that analyzes the economic aspects of health and health care and usually focuses on the costs and the consequences of health care interventions, using methods and theories from economics and medicine. A health economic evaluation is a tool to facilitate decision-making in the healthcare system and to improve the welfare.¹³

All economic evaluations have a common structure which involves explicit measurements of inputs ('costs') and outcomes ('benefits'). At least two comparators are needed to be able to perform an economic evaluation and to say something about the cost-effectiveness of the investigated medical intervention. There are four types of analyses to consider when the cost-effectiveness of an intervention should be assessed (table 1).¹⁴

ANALYSIS	COST MEASURE	OUTCOMES MEASURE
Cost-minimization	SEK	No
Cost-effectiveness	SEK	Life-years gained, symptom-free days, clinical endpoint
Cost-utility	SEK	Quality-adjusted life-years (QALYs)
Cost-benefit	SEK	SEK

Table 1. Health economic analyses for assessing the cost-effectiveness of an intervention.

All analyses share the same input, which are all costs associated with the interventions. These costs can be either direct as for instance the cost of the medical interventions, hospital care, physician visits and rehabilitation or indirect such as sick leave, early retirement and family support.¹⁵

¹³ Ferraz-Nunes J, Karlberg I and Bergström G. Ekonomi, sjukvård och hälsa. In: *Hälsoekonomi – begrepp och tillämpningar*. 79-82. Malmö: Studentlitteratur. 2007

¹⁴ Drummond MF, O'Brien B., Stoddart GL. and Torrance GW. Basic types of economic evaluation. In *Methods for the Economic Evaluations of Health*. 6-26. Oxford: Oxford University Press. 1997

¹⁵ In addition to the four health economic analyses, it is also possible to investigate how the intervention affects the health care budget in a Budget Impact Analysis. In such an analysis the cost for the health care payer is in focus.

When two interventions with the same efficacy are compared, a cost-minimization analysis can be chosen. In most situations there is a difference in outcomes between the comparative interventions and a different type of analysis is needed. Often a cost-effectiveness or cost-utility analysis is performed, which are methods of economic evaluation where the value of the resources spent on an intervention is compared with the quantity of health gained as a result.

The value of a medical intervention must be identified and quantified to be able to perform a health economic analysis. A challenge for MedTech companies and their products is to define the meaningful value of the device. The value can for instance be described from the patients' perspective or the healthcare perspective. It can depend on the learning curve and if the medical device is integrated in a complex procedure or not. In the case of intermittent urinary catheters, which are used 4-6 times per day, not only the clinical outcome or quality of life gains are important. Also, the convenience factors experienced by the patients constitute a value which needs to be investigated.

Assessing patient preferences¹⁶

The Dental and Pharmaceutical Benefits Board (TLV) in Sweden is a central government agency which regularly evaluate pharmaceuticals and dental products with regard to their cost effectiveness and determines if the products should be subsidized by the state. Recently the government mandated TLV to also investigate how MedTech products could be evaluated from an economical perspective. Guidelines on how to perform a health economic analysis – for instance for single use products such as urinary catheters – were released 2011 within the so called 'Medical Device Project'.

For new products with a proposed added benefit in comparison to one or more comparators, a health economic assessment showing an acceptable cost per benefit should be provided. Thereby, TLV can assess the new product's cost effectiveness. TLV suggests Medtech companies to perform either a cost benefit or cost utility analysis.

A cost-benefit analysis is useful when the relative risks and benefits of a new product are known to the patient and have a direct and episodic effect. It is appropriate when an added value, as experienced by the patient, is not easily measured with a quality of life instrument to support a cost-utility analysis.

¹⁶ Tandvårds- och läkemedelsförmånsverket, *Handbok till Tandvårds- och läkemedelsförmånsverkets föreskrifter (TLVFS 2011:3) om ansökan om pris och subvention för förbrukningsartiklar*, Sept. 2011, viewed on 28 Aug. 2013, <http://www.tlv.se/Upload/Foretag/Handbok-TLVFS2011-3-subvention-forbrukningsartiklar-sept-2011.pdf>

In a cost-benefit analysis, the benefit is measured as the average willingness-to-pay (WTP) and the cost effectiveness assessed as the net monetary benefit.

The value of specific products with various product features can be assessed by letting the patients reveal their willingness-to-pay (WTP) for the compared alternatives. If the difference in WTP between a new product and a comparator exceeds the difference in cost between the products, the new product can be considered cost effective.

Patients are the primary source when asking questions regarding the willingness-to-pay for a product. It is important to ask questions, which measure the same behaviour as when the patients purchase ordinary consumer goods. A WTP-study can either use interviews or questionnaires. Personal interviews normally generate more reliable results. Web questionnaires are generally not suitable unless a random sample from a relevant population can be assured.

Study design

The method chosen to answer the research questions was a quantitative research approach where data was collected through a questionnaire and the answers analyzed with a non-parametric statistical method. The questionnaire was sent electronically to users of intermittent catheterization. The patients had previously given their permission to be registered in a global database called TellUs, which is a database of intermittent catheter users held by Wellspect Healthcare in Mölndal.

Wellspect Healthcare is a company developing catheters for intermittent use. The company is using the TellUs database to interact with users of intermittent urinary catheters, primarily users of the LoFric® catheter assortment. At the time of the study, the database included approximately 1000 users from the following countries: Denmark, Germany, Italy, Norway, Sweden, United Kingdom and USA.

The patient preferences for catheters, which can reduce the frequency of UTIs, were investigated by sending the questionnaire to 144 TellUS participants from Sweden, who could be reached with an email.

Patient selection

This study focused on the Swedish TellUs users - both men and women – in need of intermittent urinary catheters for any medical reason.

An analysis of the whole cohort of TellUs patients from the markets in Europe and in the USA, showed that the recruitment of users to the database for market surveys, have generated a mixed group of individuals, both with respect to gender, age and reasons for using urinary catheters. The characteristics of the Swedish patients included in the study were comparable to the other countries (see attachment 2). The selected TellUS cohort was therefore likely a representative sample of intermittent catheter users and suitable to participate in the study.

The patients in the Swedish TellUs database are primarily users of a specific catheter brand belonging to the category hydrophilic catheters. On the other hand, well above 90% of the Swedish market consists of hydrophilic catheters.

Ethical consideration

The users' participation in the electronic survey was voluntary. A request to participate in the survey was sent to them via e-mail, where they also found the login details to get access to the questions. The collected individual answers were anonymized and transferred to an excel file for statistical analysis, which occurred at a group level where each respondent received a serial number. All survey data in the database was deleted after the completion of the analysis to make it impossible to search for individual answers as the survey contained questions related to health.

Description of survey

The participants were asked to assume a situation in which they use their current catheter but had the choice to switch to a similar catheter, which hypothetically would reduce the frequency of UTIs including possible complications (see attachment 1). Either every fourth or every second UTI could be avoided.

The participants' willingness-to-pay for the new catheter was collected by letting them choose to spend either one of eleven explicit monthly amounts from 0 SEK–1000 SEK or any other amount in an open answer. The participants also reported their UTI frequency.

The validity and reliability must be taken into consideration, when choosing an instrument or designing a survey. Validity means to what extent a measurement tool, for instance a survey, measures what it is expected to measure. The reliability of an investigatory experiment or statistical test means that the same or comparable results can be generated in repeated experiments.¹⁷

The survey was designed to answer the research questions in the purpose. To avoid conflicting answers and answers difficult to interpret, free text options were avoided and defined lists of answers chosen when possible. In addition, few questions were included and only those relevant for the purpose of the study. The explicit amounts to measure the willingness-to-pay were derived from the cost of treating a UTI in the healthcare setting.

Before initiating the study, the complicating fact to ask for out-of-pocket payment to receive treatment in a tax-financed healthcare system, was considered. The situation was therefore explained to the respondents, that they had to answer to an imaginary situation and that the explicit amounts reflected a value they experienced from having fewer UTIs and associated complications. Nevertheless, there might be a resistance among some respondents to pay anything at all for treatments that normally are for free. In such a case, the WTP would be an underestimation of the true value brought to the patients from having fewer UTIs and complications. To limit the amount of protest votes and to avoid uncertainties regarding the assessment of WTP, only respondents who were certain of their answer were included in the statistical analyses.¹⁸

Statistical testing¹⁹

Both descriptive and analytical statistics were performed. The descriptive statistics was used to present the mean UTI frequency and the distribution of the WTP testing and proceeded the significance testing. All statistical tests which were used for significance testing required that the individuals in each group had been selected randomly and were independent from each other, which was the case with the survey used in this study. The survey was sent to all accessible individuals in the Swedish TellUS database and the participation was voluntary and no selection occurred. Thereafter the patients were split in groups defined by gender and self-reported annual frequency of UTIs.

¹⁷ Gunnarson R. Validitet och reliabilitet. [Dept. of Prim Health Care Göteborg University - Research methodology web site]. May 8, 2010. Available at: <http://infovoice.se/fou>. Accessed November 20, 2014.

¹⁸ Tandvårds- och läkemedelsförmånsverket, sid 16. (2013)

¹⁹ Gunnarson R. Att välja statistisk metod. [Dept. of Prim Health Care Göteborg University - Research methodology web site]. May 8, 2010. Available at: <http://infovoice.se/fou>. Accessed November 25, 2014.

Non parametric tests

The investigated WTP parameter was quantitative. The study population and each group were relatively small and the WTP-values not normally distributed, as expected in a tax financed system where patients unwilling to spend anything at all could be proportionally large. As a consequence, non-parametric tests were chosen to investigate the hypotheses.

Wilcoxon rank sum test²⁰

The Wilcoxon one sample signed rank sum test is a non-parametric test. It can be used for significance testing where one group is compared to a fixed value, for instance 0, and when the quantitative parameter has a skewed distribution. In this study, the Wilcoxon signed rank sum test was useful as the willingness-to-pay answers were tested against the null hypothesis that there is no willingness-to-pay for a better urinary catheter.

Mann-Whitney test²¹

The Mann-Whitney test is used to compare the mean between two non-matched groups of individuals. It is the non-parametric equivalent to the parametric test called Student t-test. To perform a Mann-Whitney test, the distributions of values in the comparative groups are equal but skewed. There is no need for the values to be normally distributed. The Mann-Whitney test was used to test if there were any differences in WTP between men and women and if it was dependent on the UTI frequency, respectively.

Kruskal-Wallis one-way analysis of variance²²

The Kruskal-Wallis method is the same as the Mann-Whitney test, but with the essential difference that more than two non-matched groups of individuals can be compared. It is the non-parametric equivalent to the parametric test one-way ANOVA. Also for Kruskal-Wallis, the distributions of values in each group are equal but skewed. The Kruskal-Wallis one-way analysis of variance was used to test if there was a significant difference between the subgroups of men and women with no more than

²⁰ Gunnarson R. Översikt över signifikansanalys. [Dept. of Prim Health Care Göteborg University - Research methodology web site]. Jan 2, 2003. Available at: <http://infovoice.se/fou>. Accessed November 26, 2014

²¹ Gunnarson R. Rangsummetest (Mann-Whitney's Test). [Dept. of Prim Health Care Göteborg University - Research methodology web site]. Jan 1, 2002. Available at: <http://infovoice.se/fou>. Accessed November 24, 2014

²² Gunnarson R. Kruskal-Wallis one way analysis of variance. [Dept. of Prim Health Care Göteborg University - Research methodology web site]. Jan 1, 2002. Available at: <http://infovoice.se/fou>. Accessed November 24, 2014

one UTI per year or two or more UTIs. Mann-Whitney tests were thereafter performed to see which subgroup contributed the most to the results.

Results

Descriptive statistics

The electronic survey was sent by e-mail to 144 Swedish users of intermittent catheters. 96 users responded to the survey which gave a response rate of 67% (fig. 1). 26 of them were excluded due to uncertain and very uncertain answers. The willingness-to-pay analyses were performed on the 42 males and 28 females who were certain or very certain of their answers (fig. 2).

Figure 1. Total number of survey respondents

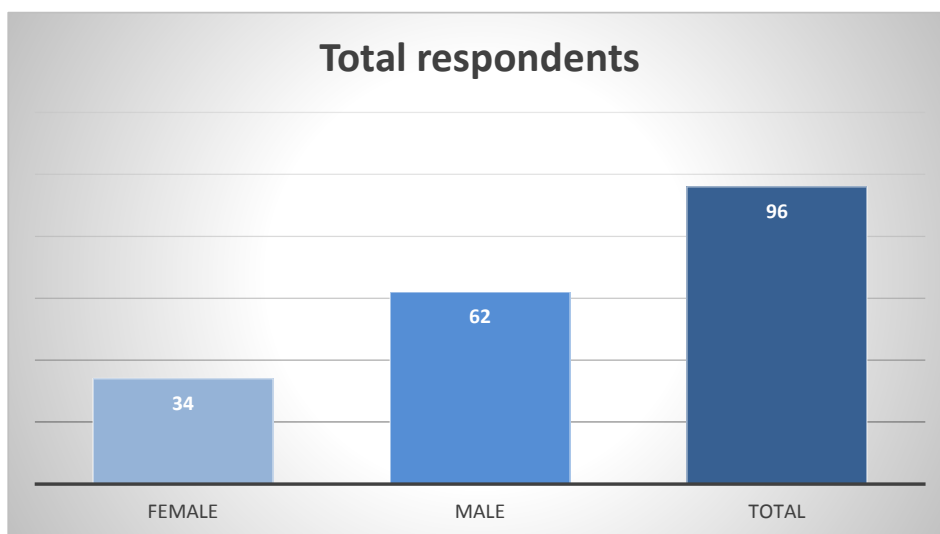
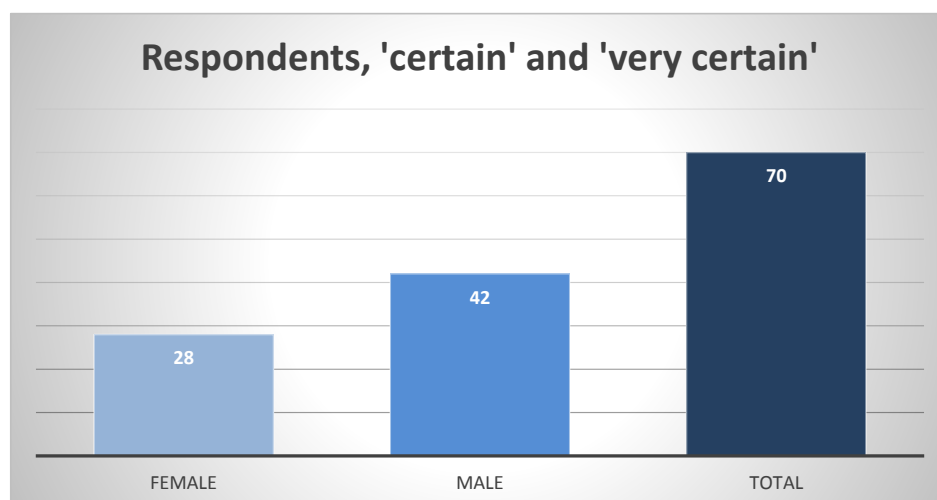
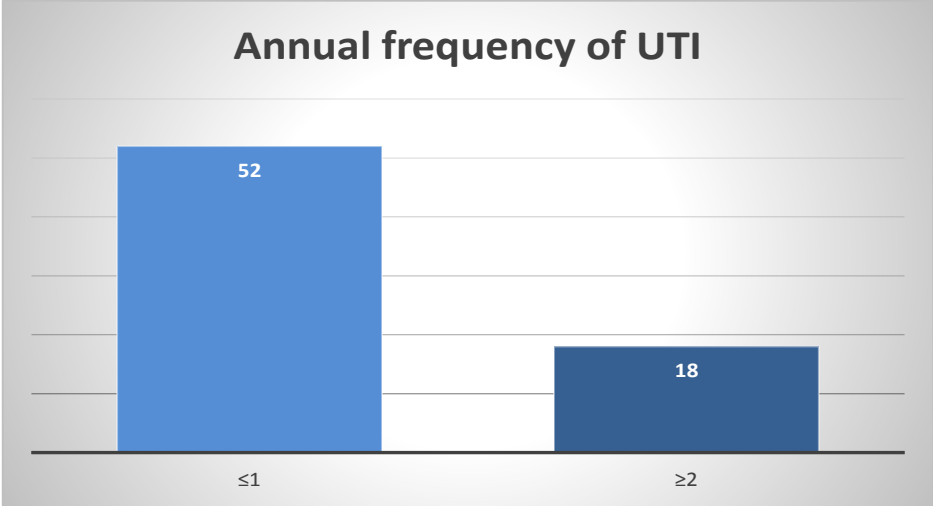


Figure 2. Number of certain and very certain answers



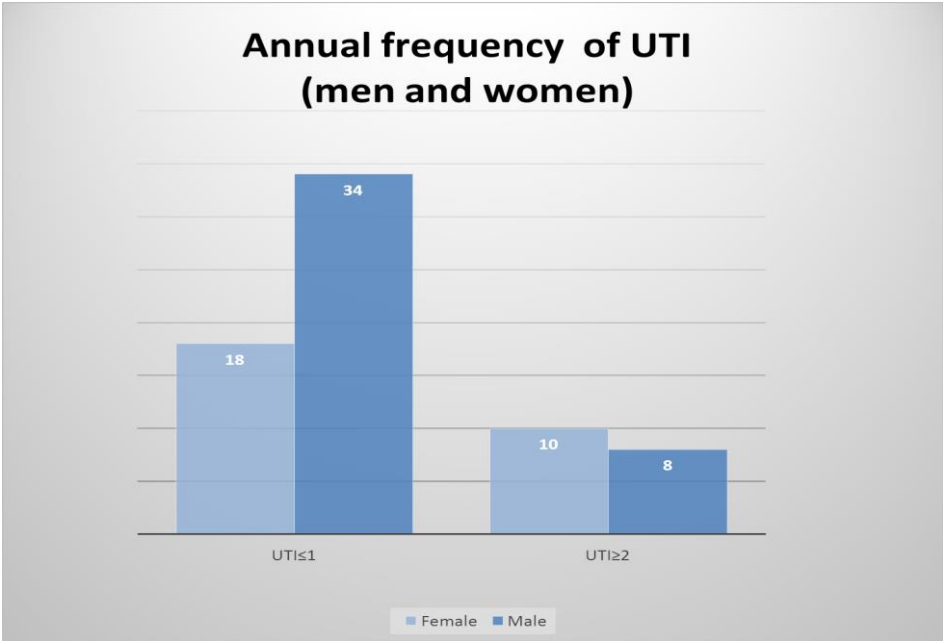
Seventy-four percent (74%, n=52) of the respondents included in the analyses had one or no urinary tract infection per year. Thirty-nine percent (39%) had no UTIs. Twenty-six (26%, n=18) of them had two or more UTIs (fig. 3). The two groups were compared to investigate whether the willingness-to-pay differed depending on the frequency of UTIs.

Figure 3. The number of respondents included in the analyses with $UTI \leq 1$ and $UTI \geq 2$, respectively



Eighty-one percent (81%, n=34) of the male respondents had one or no urinary tract infection. Nineteen percent (19%) had more than one urinary tract infection. The corresponding frequencies for the female respondents were 64% (n=18) and 36% (n=10), respectively (fig. 4).

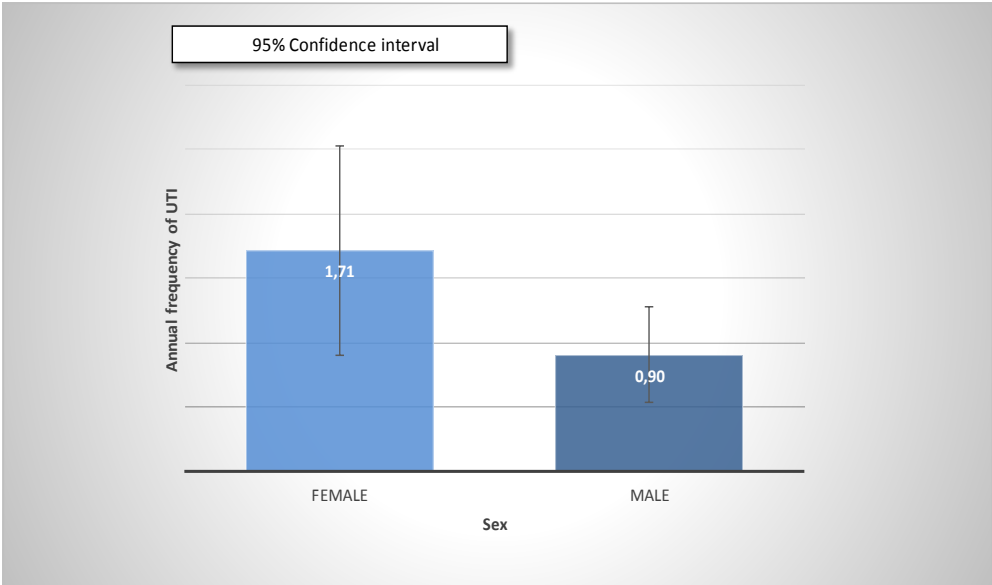
Figure 4. The number of men and women included in the analyses with $UTI \leq 1$ and $UTI \geq 2$, respectively



The mean annual number of UTIs among the respondents in the study was 1.23. Women had more UTIs per year than men, 1.71 versus 0.90 (fig. 5).

Figure 5. The mean number of UTIs among the respondents in the analysis

	N	Mean	95% Conf. (±)	Std.Error	Std.Dev.
Female	28	1,71	0,81	0,39	2,09
Male	42	0,90	0,37	0,18	1,19
Entire sample	70	1,23	0,39	0,20	1,64

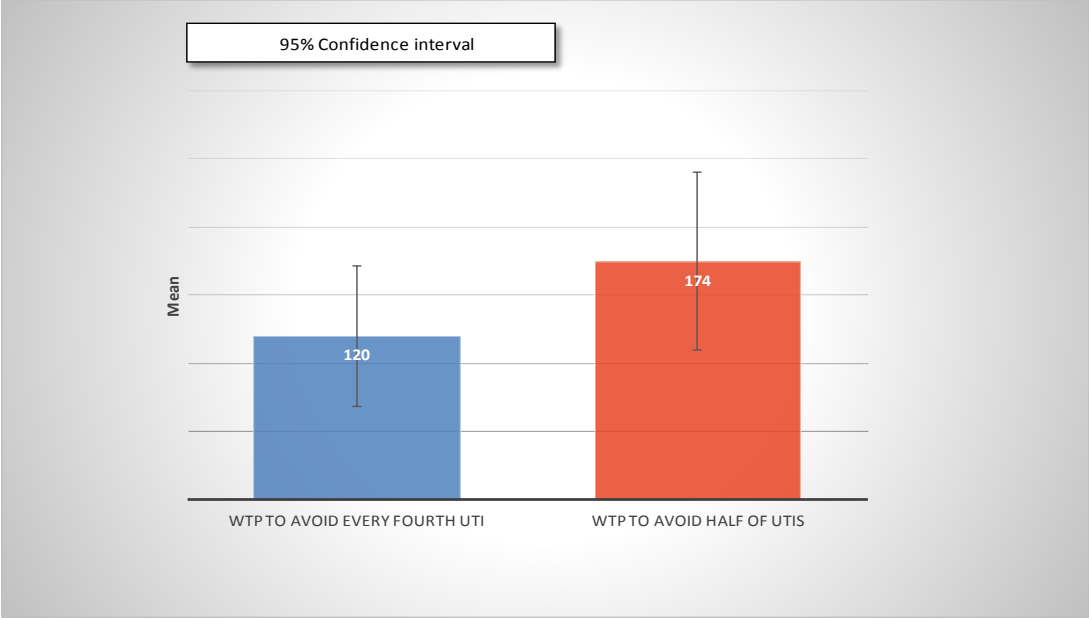


Willingness to pay results for the whole sample

The willingness-to-pay to avoid every fourth UTI, for all the respondents, was 120 SEK and to avoid half of the UTIs 174 SEK (fig. 6).

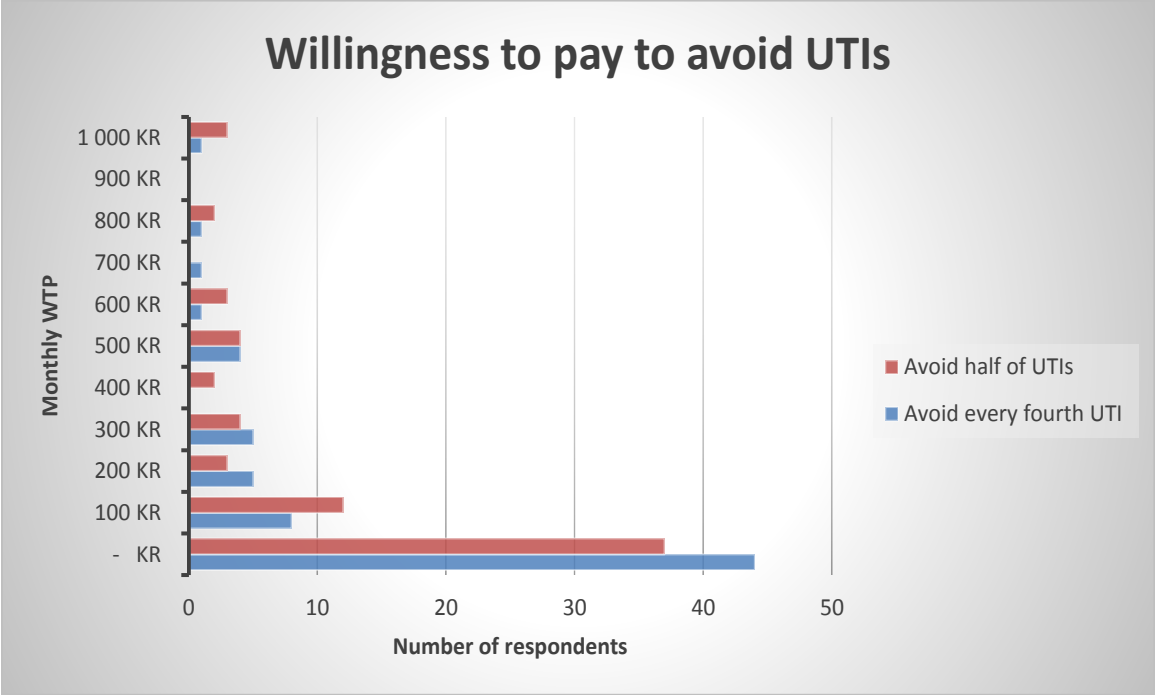
Figure 6. Willingness-to pay (WTP) to avoid UTIs (SEK)

	N	Mean	95% Conf. (±)	Std.Error	Std.Dev.
WTP to avoid every fourth UTI	70	120	51	26	216
WTP to avoid half of UTIs	70	174	65	33	273



A substantial proportion of the respondents did not want to spend any money out-of-pocket for the prevention of UTIs and associated complications (fig. 7).

Figure 7. The distribution of the answers about willingness-to-pay to avoid UTIs

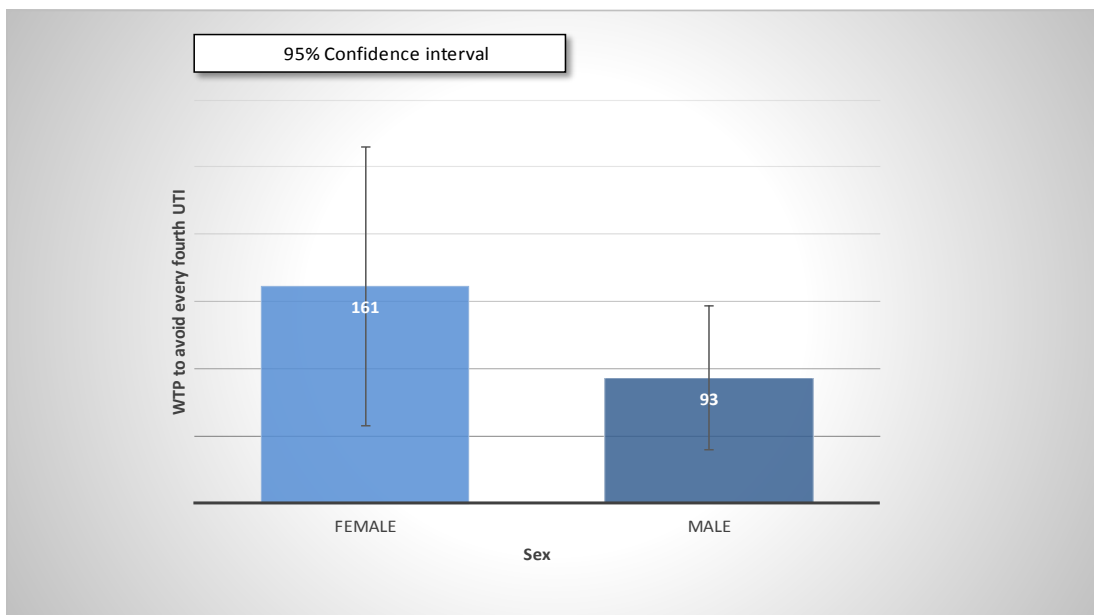


Willingness to pay results to avoid every fourth UTI for men and women

The willingness-to-pay to avoid every fourth UTI for the men was 93 SEK. It was higher for women, 161 SEK (fig. 8).

Figure 8. Willingness-to pay (WTP) to avoid every fourth UTI (SEK) for men and women

	N	Mean	95% Conf. (±)	Std.Error	Std.Dev.
Female	28	161	104	50	267
Male	42	93	53	26	172
Entire sample	70	120	51	26	216

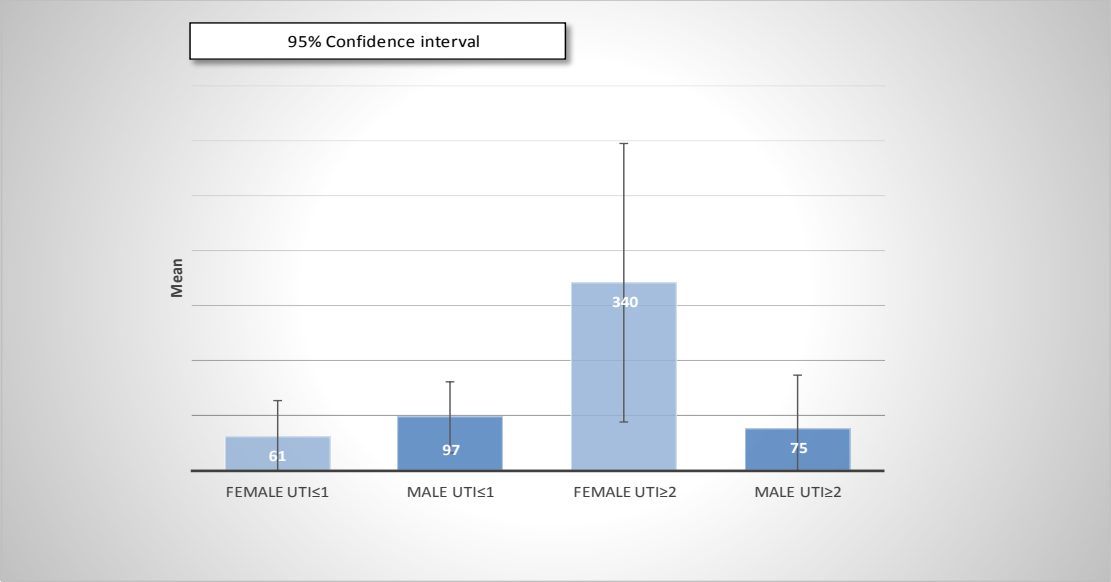


When the female respondents were divided into groups dependent on the number of UTIs, the women with $UTIs \geq 2$ were willing to spend more than five times as much as the women with few UTIs. The willingness-to-pay to avoid every fourth UTI was 340 SEK versus 61 SEK, respectively. For

the male respondents the situation was the opposite. The men with $UTIs \geq 2$ were willing to spend 75 SEK and those with few UTIs 97 SEK (fig. 9).

Figure 9. Willingness-to pay to avoid UTIs (SEK) for men and women and stratified according to the annual number of UTIs

	N	Mean	95% Conf. (±)	Std.Error	Std.Dev.
Female $UTI \leq 1$	18	61	66	31	133
Male $UTI \leq 1$	34	97	64	31	183
Female $UTI \geq 2$	10	340	253	112	353
Male $UTI \geq 2$	8	75	97	41	116

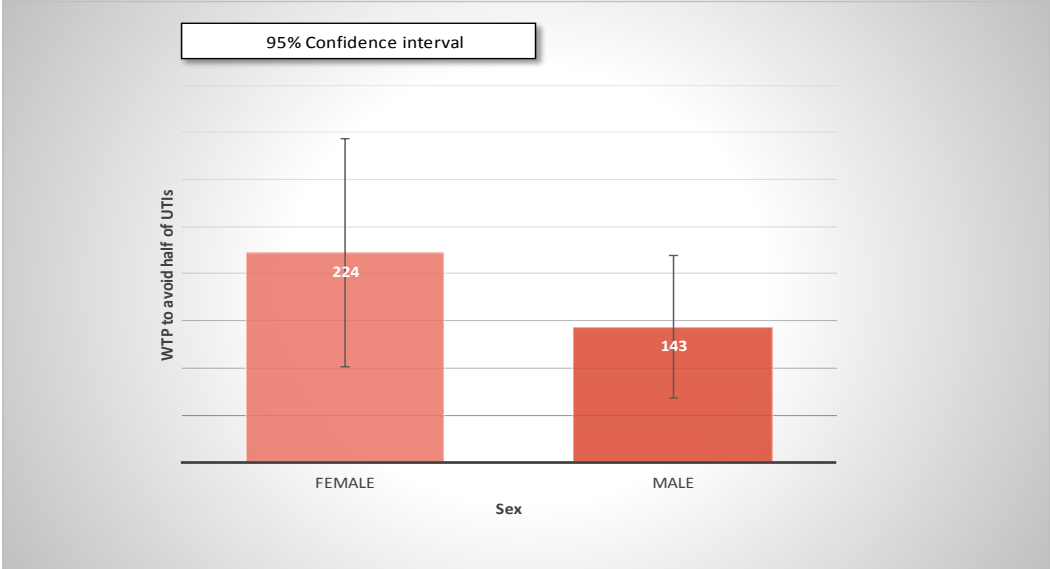


Willingness to pay results to avoid half of the UTIs for men and women

The willingness-to-pay to avoid half of the UTIs for the men was 143 SEK, which was 54% more than the WTP to avoid every fourth UTI. It was higher for women, 224 SEK, which was 39% more than to avoid every fourth UTI (fig. 10).

Figure 10. Willingness-to pay (WTP) to avoid half of the UTIs (SEK) for men and women

	N	Mean	95% Conf. (±)	Std.Error	Std.Dev.
Female	28	221	121	59	312
Male	42	143	76	38	243
Entire sample	70	174	65	33	273

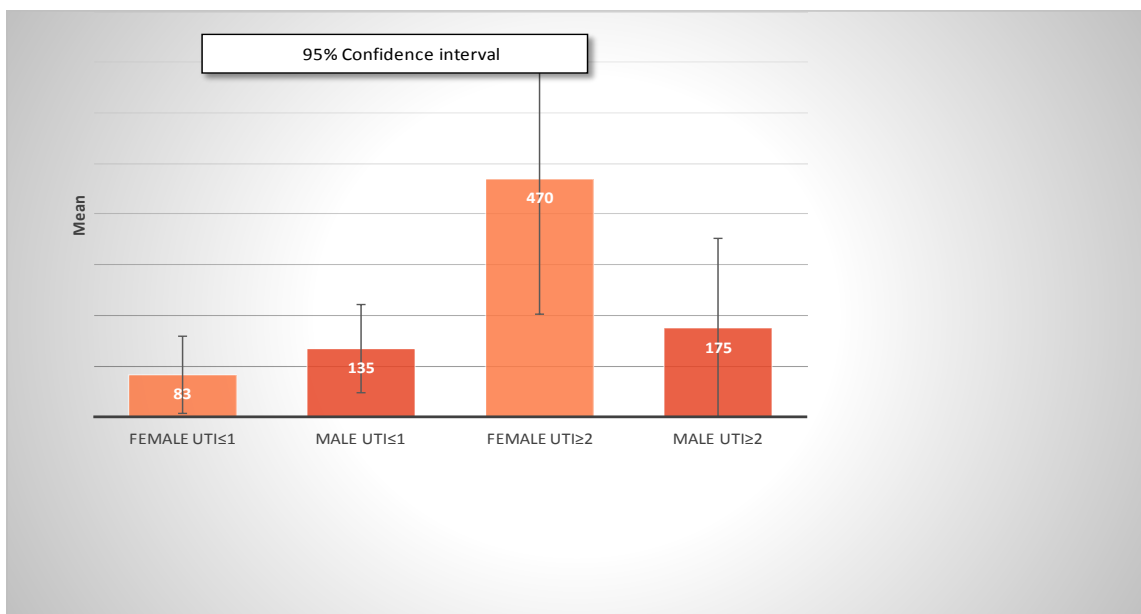


When the female respondents were divided into groups dependent on the number of annual UTIs, the women with UTIs \geq 2 were willing to spend more than five times as much as the women with few UTIs. The willingness-to-pay to avoid half of the UTIs was 470 SEK versus 83 SEK, respectively. Also

the male respondents with more UTIs were willing to spend more money on the prevention, 175 SEK versus 135 SEK (fig. 11).

Figure 11. Willingness-to pay to avoid UTIs (SEK) for men and women and stratified according to the annual number of UTIs

	N	Mean	95% Conf. (±)	Std.Error	Std.Dev.
Female UTI≤1	18	83	77	36	154
Male UTI≤1	34	135	88	43	252
Female UTI≥2	10	470	268	118	374
Male UTI≥2	8	175	177	75	212



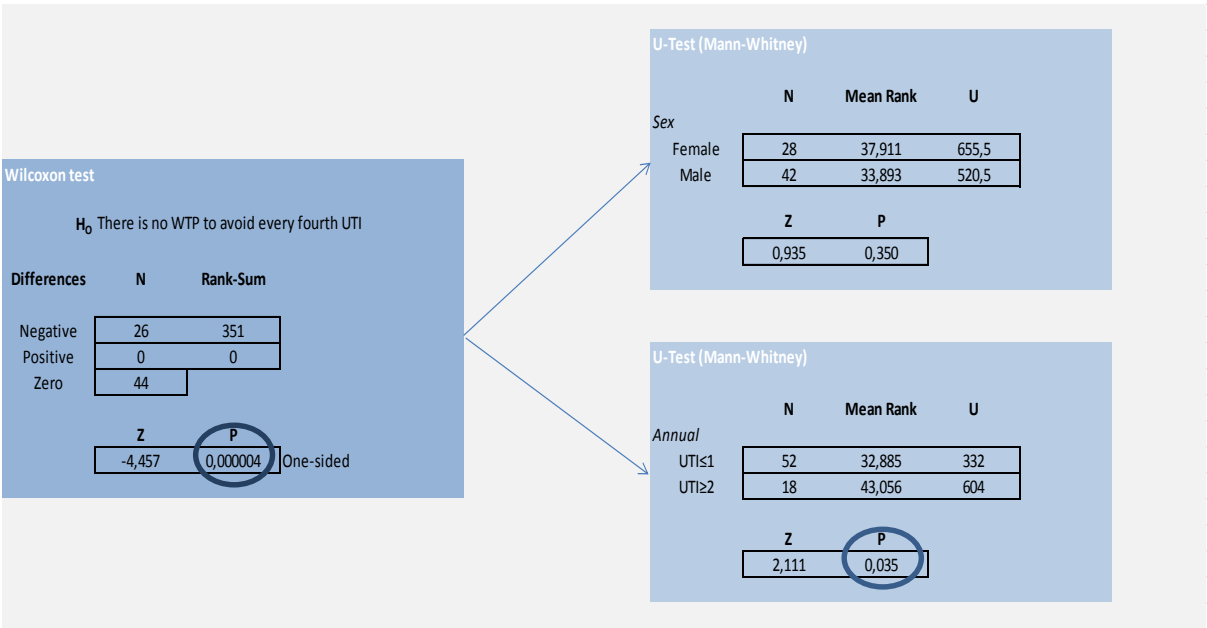
Analytical statistics

Avoid every fourth UTI

A Wilcoxon signed rank test was performed to test the null hypothesis of a probability of a willingness-to-pay to avoid every fourth UTI equal to 0 SEK at the p-level 0.05. The test confirmed the alternative hypothesis and showed there is a significant willingness-to-pay ($p=0.000004$) (fig. 12).

Mann-Whitney’s tests to compare two independent samples were run to investigate if the significant willingness-to-pay to avoid every fourth UTI was dependent on sex and annual frequency of UTI. The results showed no difference between men and women ($p=0.35$), but having more than one UTI per year reached statistical significance ($p=0.035$) (fig. 12).

Figure 12. Significance testing of the probability of WTP equal to 0 SEK to avoid every fourth UTI, no difference between men and women and no difference due to annual UTI frequency

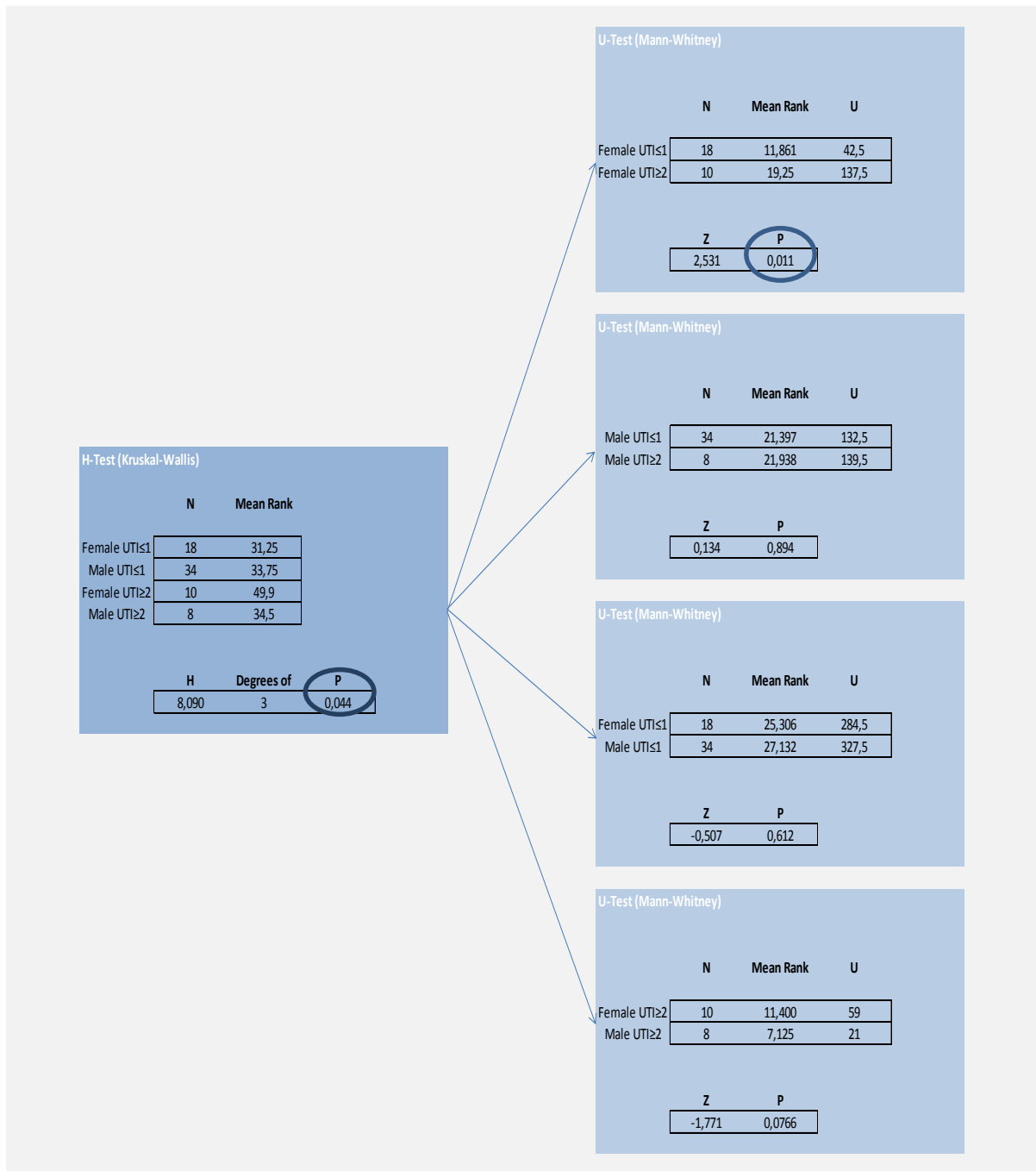


Additional analyses were performed to investigate if there were any differences between the following subgroups: (1) men and $UTI \leq 1$, (2) men and $UTI \geq 2$, (3) women and $UTI \leq 1$ and (4) women and $UTI \geq 2$.

A Kruskal-Wallis one-way analysis of variance was chosen to compare many unpaired samples. It discovered a significant difference in the willingness-to-pay to avoid every fourth UTI between the

groups. Mann-Whitney's tests followed and showed that the difference between women with more or less UTIs contributed most to the significant result (fig. 13).

Figure 13. Significance testing of the probability of WTP equal to 0 SEK to avoid every fourth UTI between the subgroups (1) men and UTI≤1, (2) men and UTI≥2, (3) women and UTI≤1 and (4) women and UTI≥2

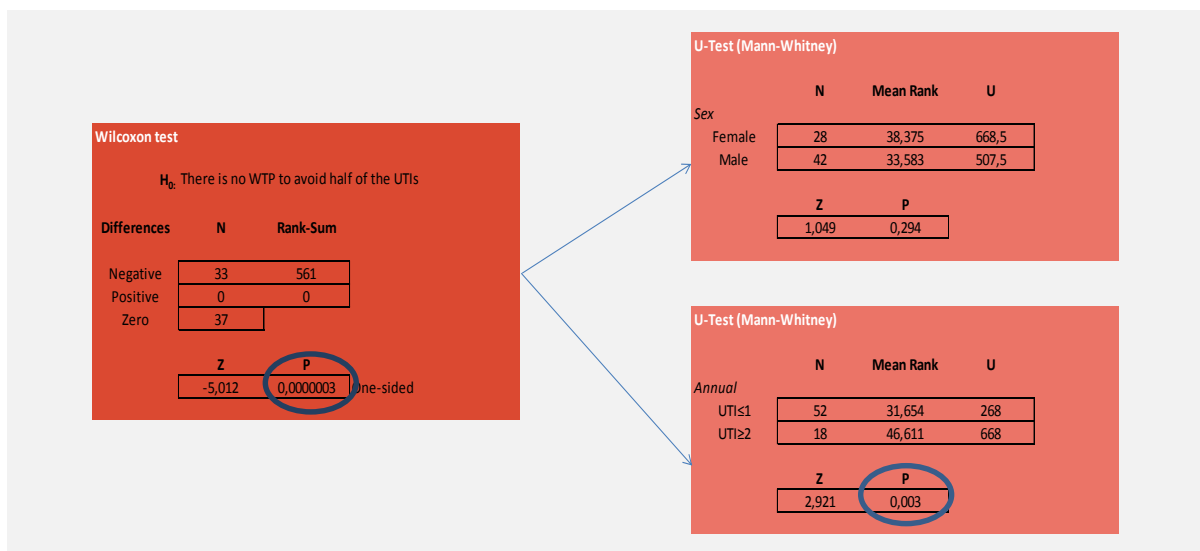


Avoid half of the UTIs

A Wilcoxon signed rank test was performed to test the null hypothesis of a probability of a willingness-to-pay to avoid half of the UTIs equal to 0 SEK at the p-level 0.05. The test confirmed the alternative hypothesis and showed there is a significant willingness-to-pay ($p=0.0000003$) (fig. 14).

Mann-Whitney's tests to compare two independent samples were run to investigate if the significant willingness-to-pay to avoid half of the UTIs was dependent on sex or annual frequency of UTIs. The results showed no difference between men and women ($p=0.35$), but having more than one UTI/year reached statistical significance ($p=0.003$) (fig. 14).

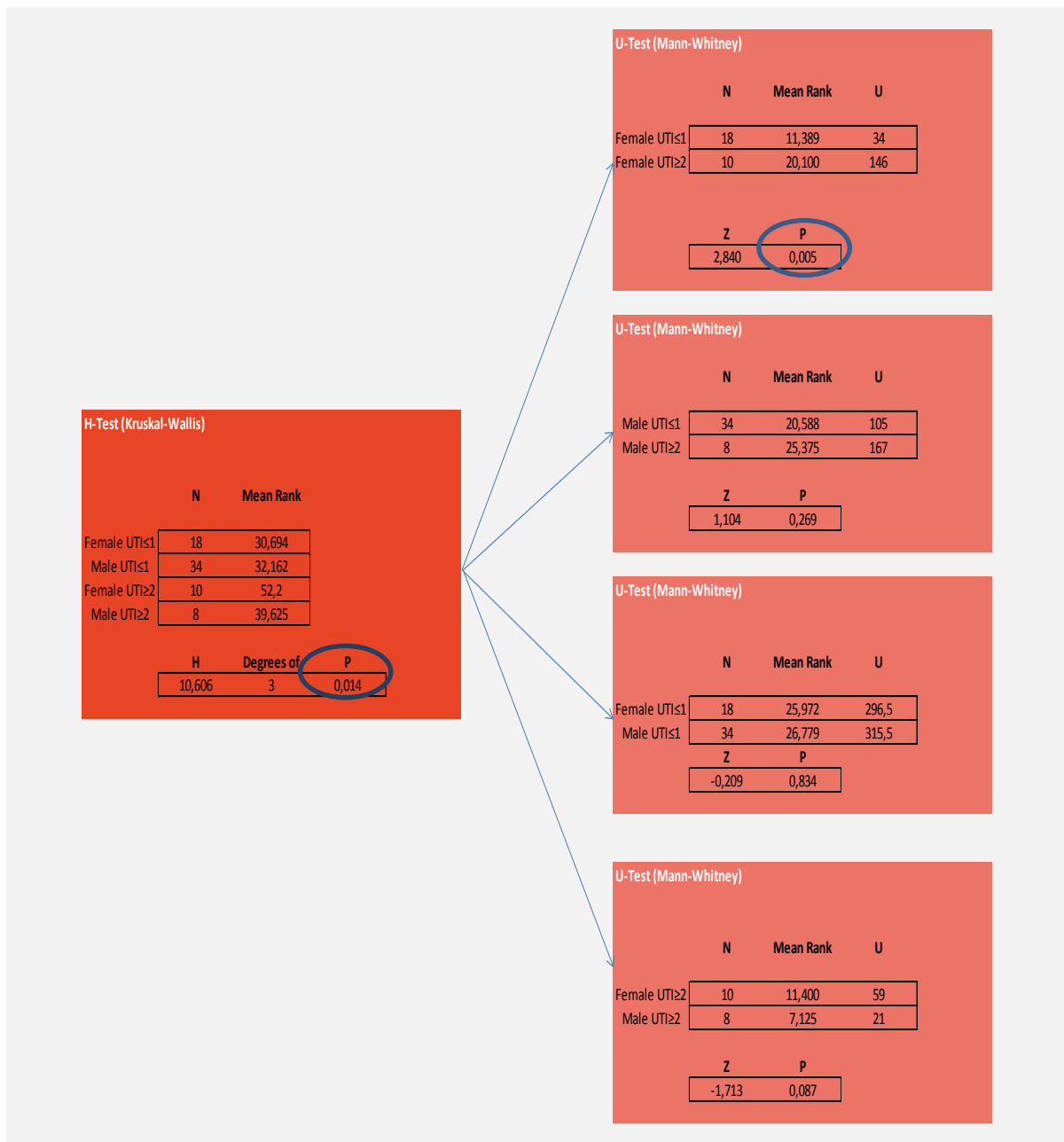
Figure 14. Significance testing of the probability of WTP equal to 0 SEK to avoid half of the UTIs, no difference between men and women and no difference due to annual UTI frequency



Additional analyses were performed to investigate if there were any differences between the following subgroups: (1) men and $UTI \leq 1$, (2) men and $UTI \geq 2$, (3) women and $UTI \leq 1$ and (4) women and $UTI \geq 2$.

A Kruskal-Wallis one-way analysis of variance was chosen to compare many unpaired samples. It discovered a significant difference in the willingness-to-pay to avoid half of the UTIs between the groups. Mann-Whitney's tests followed and showed that the difference between women with more or less UTIs contributed most to the significant result (fig. 15).

Figure 15. Significance testing of the probability of WTP equal to 0 SEK to avoid half of the UTIs between the subgroups (1) men and UTI \leq 1, (2) men and UTI \geq 2, (3) women and UTI \leq 1 and (4) women and UTI \geq 2



Conclusion

This study confirms that urinary tract infection is a common complication among users of intermittent urinary catheters, but the annual frequency of UTIs of 1.23 was only half as many as reported by Woodbury et al. (2008) where the annual frequency was 2.6. Both studies show that the UTI incidence is higher among women.

Approximately every fourth respondent in the study population reported they have two or more UTIs per year. The share of patients with two or more UTIs is smaller than reported in the study by Biering-Sorensen et al. (1999) where approximately every third patient had 2 or more infections per year.

An explanation to the difference discovered in this survey, can be the development of urinary catheters that has occurred the last decade. Nevertheless, since UTI is still a frequent problem associated with intermittent catheterization, there is a need to develop more effective catheters or find other solutions to reduce the frequency of this complication.

The request for better catheters was reflected in the survey respondents' willingness-to-pay for a switch from the existing catheter to a hypothetically more effective one of the same quality. As expected, the wish for a better catheter was dependent on the frequency of urinary tract infections. The respondents' readiness to spend money to get a more effective catheter reveals their concern about urinary tract infections.

Surprisingly, there was a large share of respondents who were not willing to spend any money at all. A possible explanation can be that the users normally get their catheters for free in a healthcare system financed by taxes as in Sweden. The contribution of out-of-pocket payment is not an issue to consider and difficult to even imagine.

The overall willingness-to-pay results were higher for the women than for the men, both to avoid every fourth and every second UTI (161 versus 93 SEK and 224 versus 143 SEK, respectively). This gender difference is difficult to explain. Perhaps there is a difference in the UTI severity between women and men and hence, in the subjective experience of this complication associated with intermittent catheterization. It needs to be investigated further.

There was an expected difference in the willingness-to-pay for more effective catheters depending on the annual frequency of UTIs and the patients with one UTI or less versus those with more than one UTI per year. Also here, the difference was larger among the women which further emphasize the need to understand if women with many infections have a stronger need for solutions to reduce the frequency of UTIs.

This study wanted to investigate if there is willingness-to-pay (WTP) - from a patient perspective - for a urinary catheter which reduces the annual frequency of urinary tract infection by 25% and 50%, respectively. In both situations there were a significant WTP and the null hypothesis was rejected. The statistical testing showed that in both situations the difference between women with more or less UTIs contributed most to the significant results.

Reduction in the frequency of catheter-associated UTIs will benefit the users of intermittent urinary catheters by improving their quality of life. It will also benefit the health care organization and payers of health care when lesser resources are spent on treating the infections and other complications. A focus on solutions to treat the patients with the most frequent problems appears to be most valuable.

Example: The value of a more effective urinary catheter in the group with UTI ≥ 2

The cost utility analysis of intermittent urinary catheters by Bermingham et al. (BMJ, 2013), uses assumptions regarding costs and complications to UTIs²³. If the same transition probabilities to have a 1st line antibiotic resistant UTI, multidrug resistant UTI or to develop bacteremia are applied to the results, a simplified cost-of-illness calculation which only focuses on UTIs can be performed. In the study, 8.3% of the users with UTI ≥ 2 are resistant to the first line antibiotic treatment, 7% of them have a multidrug resistant UTI, 3.6% develop bacteremia. The costs are 738 SEK, 23.428 SEK and 34.610 SEK, respectively. A non-complicated symptomatic UTI costs 531 SEK.²⁴

The group of men and women with more than one UTI per year (n=18) causes the following costs related to urinary tract infections when the input from Bermingham et al. is used:

²³Bermingham, *BMJ*, 2013

²⁴ Pound conversion to SEK, www.valuta.se, 2014-04-07

- Symptomatic UTI: (18-1,5-1,3-0,6) x 531 SEK
- 1st line antibiotic resistant UTI: n=1,5 x 739 SEK (*n is rounded up*)
- Multidrug resistant UTI: n=1,3 x 23.428 SEK (*n is rounded up*)
- Bacteremia: n=0,6 x 34.610 SEK (*n is rounded down*)

This equals a cost of approximately 60.000 SEK per year or 3300 SEK per patient.

As previously mentioned, urinary tract infections and complications are also associated with lower quality of life. In the WTP analysis, which focused on the prevention of UTIs with better catheters, the possible quality-of-life gains were not measured. In an electronic survey with a recall period of one year, it is also difficult to accurately share information of the quality of life decrements at the time of the infection or infections. As a proxy variable, the patients' preference for a more efficacious catheter was measured by the patient responses on how much they were willing to pay per month using explicit amounts from 0 SEK to 1000 SEK in 100 SEK increments. The monthly willingness-to-pay to avoid every fourth UTI was 222 SEK²⁵ and to avoid half of the UTIs 339 SEK²⁶ in the group with more than one UTI per year. The WTP for a year is:

- 222 SEK x 12 months = 2664 SEK for every fourth UTI avoided
- 339 SEK x 12 months = 4068 SEK for every second UTI avoided

If the value of a new hypothetical catheter, or catheter plus support package, is a combination of the (1) value experienced by the patient and (2) the savings for the health care system for avoiding infections, then the total value per patient with more than one infection per year is:

- $825^* + 2664 = \mathbf{3489 \text{ SEK to avoid every fourth UTI}}$ (*3300 SEK/4 =825 SEK)
- $1650^{**} + 4068 = \mathbf{5718 \text{ SEK to avoid half of the UTIs}}$ (**3300 SEK/2 = 1650 SEK)

In summary, this survey study suggests that any new intermittent catheter with or without another solution such as educational support, which reduce the UTI frequency by 25%, can cost 3500 SEK more per year than the current alternative to be cost neutral to the Swedish health care system when also the value experienced by the patient is included in the evaluation. If the UTI frequency is reduced by 50%, it can cost 5700 SEK more per year.

²⁵ $((n=10 \times 340 \text{ SEK}) + (n=8 \times 75))/18$

²⁶ $((n=10 \times 470 \text{ SEK}) + (n=8 \times 175))/18$

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Attachment 1 - Questionnaire

Initial input data

male female

Sex

Estimate the number of catheters you normally use per day:

Estimate the number of urinary tract infections you normally have per year:

Catheter brand/type you use today:

Introduction:

The purpose of this study is to try to capture the value of a hypothetical catheter type, which presumably reduces the frequency of urinary tract infections including possible complications of such an event. Either every fourth urinary tract infection is avoided (situation 1) or half of the urinary tract infections are avoided (situation 2). We ask you to imagine - for this study only - a situation where you would have to pay for this new catheter type yourself, even though this would not be the situation in real life.

Description of catheter types:

In the table below, two different catheters are described. Assume that you are using catheter A. You have the choice to switch to catheter B. A very similar catheter, but this one reduces the frequency of urinary tract infections including possible complications.

Situation 1:

	Catheter A	Catheter B
Reduction of urinary tract infections including possible complications:	Same frequency of urinary tract infections including possible complications per year as with the catheter you currently use	Every fourth urinary tract infection including possible complications which you experience with your current catheter will be avoided

1. How much are you willing to pay **each month** for catheter B, if this catheter can help you avoid every fourth urinary tract infection including possible complications? (Check one box only)

- SEK 0
- SEK 100
- SEK 200
- SEK 300
- SEK 400
- SEK 500

- SEK 600
- SEK 700
- SEK 800
- SEK 900
- SEK 1000
- Other amount: _____

=====

Situation 2:

	Catheter A	Catheter B
Reduction of urinary tract infections including possible complications:	Same frequency of urinary tract infections including possible complications per year as with the catheter you currently use	You will avoid half of the urinary tract infections including possible complications which you experience with your current catheter

2. How much are you willing to pay **each month** for catheter B, if this catheter can help you avoid half of your urinary tract infections including possible complications? (Check one box only)

- SEK 0
- SEK 100
- SEK 200
- SEK 300
- SEK 400
- SEK 500

- SEK 600
- SEK 700
- SEK 800
- SEK 900
- SEK 1000
- Other amount: _____

=====

3. How certain are you regarding your answers? (check one box only)

- Very uncertain Uncertain Certain Very certain

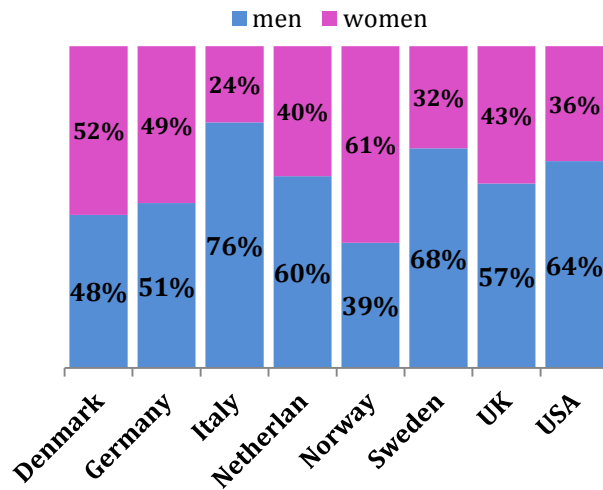
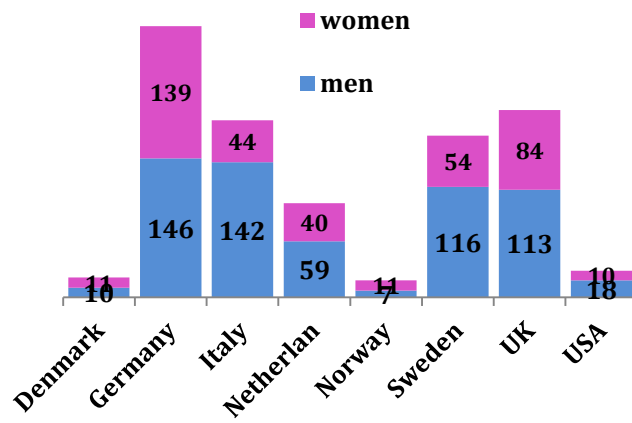
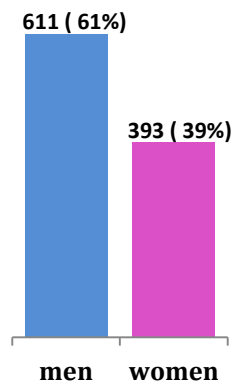
Attachment 2 – Patient database (TellUS)

Wellspect HealthCare had at the time of the study more than 1000 European and US catheter users registered in the TellUS database. The database is used to perform various surveys, for instance in the fields of marketing and health economics. Background data is presented below to describe the patient cohort and to illustrate how representative it is for the patients using intermittent urinary catheters on a daily basis.

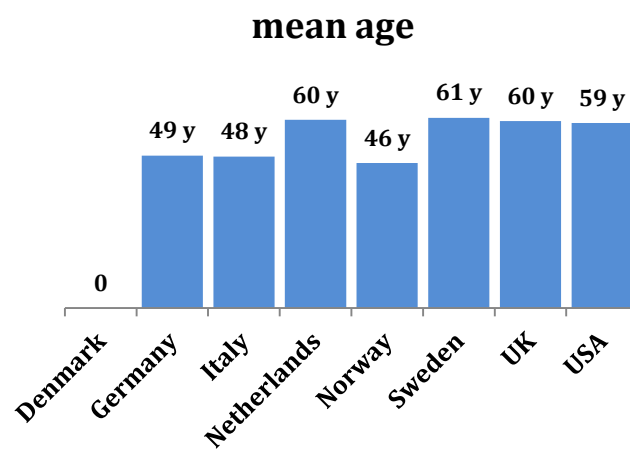
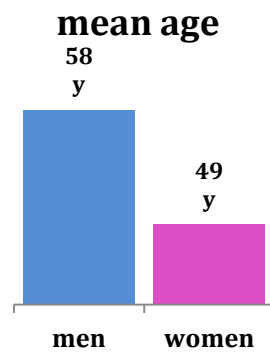
In the study only the patients from Sweden were included. Please note that some individuals have not entered all background data and the data set contains missing values. Hence, the patient numbers in the graphs vary depending on the parameters. The parameters included here are:

- (1) sex
 - (2) age
 - (3) years of CIC
 - (4) numbers of catheters per day
 - (5) diagnosis
-

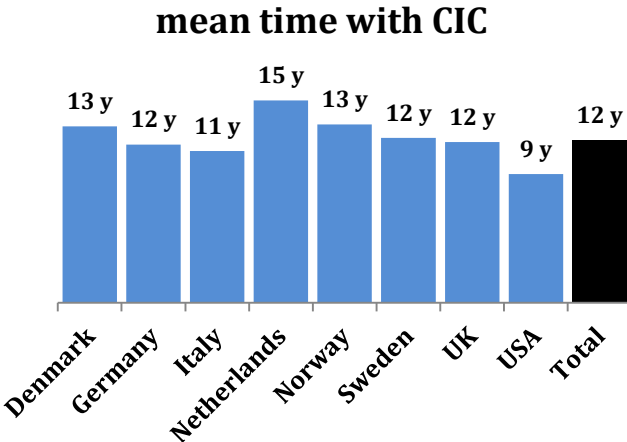
(1) Men/Women



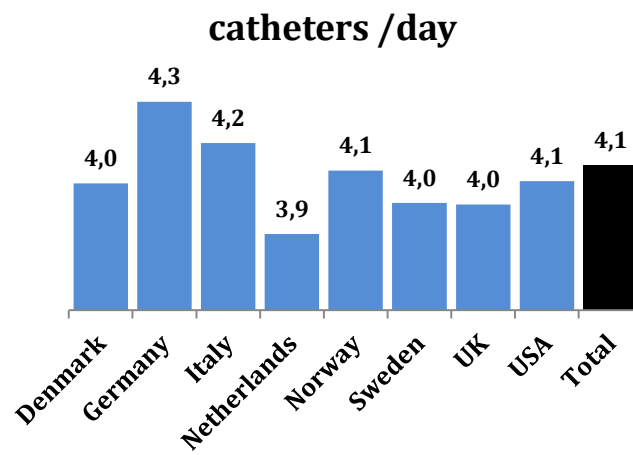
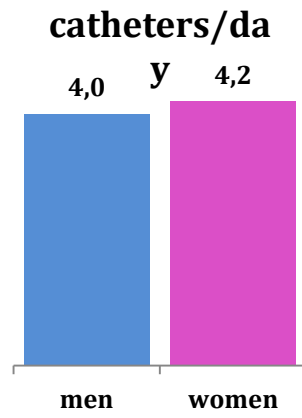
(2) Age



(3) Years of CIC



(4) Catheters per day



(5) Diagnosis

BPH	3,9%
MS	11,9%
PD	0,3%
SB	9,0%
SCI para	23,2%
SCI tetra	4,5%
cancer	2,7%
diabetes	0,7%
other	40,4%
post op	3,5%

