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**Healthcare Resource Consumption for Intermittent Urinary Catheterization: Cost-Effectiveness of Hydrophilic Catheters and Budget Impact Analyses**

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## Abstract

**Objectives** – The present study presents a cost-effectiveness analysis comparing hydrophilic-coated to uncoated catheters for patients performing intermittent urinary catheterization. Moreover, a budget impact analysis is included to evaluate the impact on the national healthcare budget of intermittent catheterization for the management of bladder dysfunctions over a period of 1, 3 and 5 years.

**Design** - A Markov model has been designed to project lifetime health outcomes (life years and quality-adjusted life years - QALYs) and economic consequences related to patients performing intermittent catheterization with hydrophilic or uncoated catheters. The clinical effectiveness of the catheters was retrieved from randomized controlled trials, while cost data were estimated based on the healthcare resource consumption derived from an e-survey addressed to a number of key opinion leaders in the field.

**Setting** – The analysis was performed from the Italian Healthcare Service perspective.

**Population** – Patients with spinal cord injury performing intermittent urinary catheterization in the home setting.

**Main outcome measures** – Incremental cost-effectiveness and cost-utility ratios (ICER, ICUR) of hydrophilic vs. uncoated catheters and related healthcare budget impact.

**Results** - The ICER and ICUR resulted 20,949€ and 24,652€, respectively, showing that hydrophilic catheters can be considered a cost-effective choice in comparison to uncoated ones. At 5 years, the estimated healthcare budget for Italy accounted to about 170,000,000€, considering foreseen usages of about 90% and 10% for hydrophilic and uncoated catheters, respectively.

**Conclusions** - Considering a lifetime perspective, hydrophilic catheters seemed a valuable choice in comparison to uncoated ones. These findings can support policy makers to control and coordinate the diffusion of the advanced devices for intermittent catheterization in patients with spinal cord injury.

Strengths and limitations of this study

- This paper presents a cost-effectiveness analysis comparing hydrophilic to uncoated catheters in spinal cord injured patients performing intermittent urinary catheterization. The healthcare resource consumption was derived from an e-survey addressed to a number of key opinion leaders in the field to provide real-world data.
- Our study is the first cost-effectiveness analysis that also includes a budget impact analysis. This kind of analysis may help decision-makers to estimate the impact on healthcare expenditures of introducing new health technologies in regular practice.
- The consumption of healthcare resources is represented in natural units to allow costs adjustment to other countries.
- Data derived from self-reported questionnaire may suffer from inevitable inaccuracies that could be eliminated if a prospective observational multi-centre study would be carried out.
- The findings of the present study are important to support the use of hydrophilic catheters but a broader evaluation which takes into account also costs from a societal perspective would be needed to assess the comprehensive economic sustainability of these innovative devices.

## Introduction

The spinal cord is the part of the central nervous system that performs specific functions such as the conduction of sensory information from the peripheral nervous system to the brain or the conduction of motor information from the brain to various muscles. When the spinal cord is damaged, the ascending and descending pathways are partially or totally interrupted, leading to motor or sensory deficits of a diverse nature and extent. These lesions are mainly caused by spinal cord injuries (SCIs) and multiple sclerosis, but also by cerebrovascular diseases, cancer, infectious diseases, and slipped discs. Numerous lesions result in alterations of bladder motility, with a loss of coordination between the muscles dealing with correct emptying, by configuring the framework of the so-called neurogenic bladder.

In the community setting, the management of a neurogenic bladder, which requires a forced emptying, is performed through Intermittent Catheterization (IC). This technique consists in the temporary placement of a catheter to remove the urine from the body. Patients may use disposable catheters with a hydrophilic polymer surface coating, disposable catheters with pre-packaged water based lubricant (gel reservoir), or non-coated catheters. Non-coated catheters may be discarded after use, or washed and re-used for different days. Determining which material and method represent the best approach is a problem yet with no solution.

One of the major advantages of IC is the significant reduction in the risk of catheter-induced urinary tract infections (UTIs), resulting in the maintenance of urinary tract health in general and in particular of the kidneys. [1, 2] Anyway, UTI risk can be reduced but cannot be eliminated and, as a consequence, UTIs still cause high morbidity and may result in frequent hospitalizations. Moreover, repeated cycles of antibiotic therapy in patients with a recurrent UTI cause the onset of “antibiotic resistance” [3] that in turn increases the need to continuously modify the therapy adopting increasingly expensive new treatments. For these reasons, UTIs entail a relevant economic burden on patients and their families as well as on the healthcare systems. [4]

The studies that tried to estimate the burden of UTIs from the healthcare system perspective reported costs ranging from €523 to €4167, [5-10] where more complicated UTIs are likely to be associated with higher costs.

Moreover, IC performed different times a day poses the individual at risk also for urethral trauma, often causing hematuria. Urethral trauma is associated with an increase in UTI risk [11, 12] even if damage to the urethra is less likely to occur with a lubricated catheter. [13]

A catheter able to lower UTI frequencies and other kinds of complications is advisable to limit the economic burden for the healthcare system and resulting in increased quality of life for the patients. The combination of both economic and quality of life aspects is generally evaluated through a cost-effectiveness analysis (CEA) comparing different types of devices. This analysis could give insights on the choice of a device with good balance between increased costs and improved health outcomes.

To our knowledge only two cost-effectiveness studies [14, 15] compared lifetime quality adjusted life years (QALYs) and costs of different types of catheter from the UK perspective. Although both studies focused on the management of UTIs, the first one [14] considered the number of patients experiencing at least one UTI and their short term consequences, while the second one [15] estimated the mean number of UTI per patient and considered long term sequelae as kidney impairment. Considering a lifetime horizon, the study by Clark and colleagues [15] showed that hydrophilic coated catheters are cost-effective when compared to uncoated ones, while the other study, [14] on the contrary, reported that clean non-coated catheters are the most cost-effective in comparison to all other types of catheters. The divergent results of these studies confirm that the assumptions made and the way the clinical data are chosen and used may highly affect the cost-effectiveness model construction and related results, even for the same country.

The aim of the present study was to perform a CEA comparing hydrophilic-coated to uncoated plastic catheters for patients performing IC, from the Italian Healthcare Service perspective. The analysis focused on these types of catheters since they are the most frequently used in Italy. Moreover, a budget impact analysis (BIA) was conducted to evaluate the impact on the Italian

healthcare budget of IC with hydrophilic catheters for the management of bladder dysfunctions over a period of 1, 3 and 5 years.

## Methods

The clinical effectiveness of each catheter was retrieved from randomized controlled trials published in the literature focusing on community perspective, while cost data were estimated based on the healthcare resource utilization derived from an e-survey addressed to a number of key opinion leaders in the field. Since clinical data were mainly reported for SCI patients, the model considered this kind of population.

### The model

As the management of patients performing IC is an evolving process, Markov multistate models were the choice for this economic evaluation. A decision tree combined with two Markov models has been designed to project lifetime health outcomes (life years and QALYs) and economic consequences related to patients performing IC with hydrophilic or non-hydrophilic urinary catheters. The model focused mainly on UTIs and episodes of hematuria as the former are the most frequent complications in patients performing IC, while the latter occur regularly in one third of patients on a long-term basis. [16] It is acknowledged that other complications that the ones included in the model may be relevant for patients practicing IC. For example, other infections and inflammations such as epididymo-orchitis, urethritis and prostatitis may occur as a complication of IC as well as strictures, false passage and bladder stones. [17] These complications may all increase the general cost why the current model can be regarded as fairly conservative.

The Markov model (Figure 1) includes the following health states: no disease, symptomatic UTI, hematuria and death. A symptomatic UTI can resolve or became an antibiotic-resistant UTI. In this case the model distinguishes among first-line resistant UTI, multi-drug resistant UTI and bacteremia. Multi-drug resistant UTI and bacteremia represent severe UTIs that can eventually lead to patient death.

<Figure 1>

A hypothetical cohort of 40-year-old, 80% male patients enter the Markov process in the no disease state; the population characteristics are the ones reported for SCI patients performing IC in Italy. [18]

Transition probabilities between health states for patients performing IC with hydrophilic and non-hydrophilic catheters have been estimated from the literature. The baseline rate of symptomatic UTIs in patients using uncoated catheters has been retrieved from the study by Clark et al. [15] which reported UTI event rates for community setting. The study reported for uncoated catheters a monthly rate of events of 0.14 and a relative risk of 0.47 for hydrophilic catheters (based on LoFric® catheters) compared to uncoated catheters.

The baseline annual rate of hematuria in patients using uncoated catheters has been estimated from the studies [19, 20] considered by [15] which included information of this type of event. The annual rate was obtained by dividing the total number of events observed in patients using uncoated catheters by the total number of patient years. The annual rate of hematuria resulted equal to 0.33. From the same studies a meta-analysis was conducted to estimate the relative risk of developing hematuria in patients using hydrophilic catheters in comparison to uncoated ones. The analysis was performed using Review Manager (RevMan5) software (Version 5.1. Nordic Cochrane Centre, Cochrane Collaboration, 2011. <http://ims.cochrane.org/revman>). Since the considered studies were performed by researchers working independently, a random-effect model was applied assuming that the true effect size varied among studies. [21] The analysis yielded a relative risk of 1.59 (95%CI 0.81–3.13) of experiencing hematuria using hydrophilic catheters (based on Speedicath® catheters) in comparison to uncoated ones.

The rate of events associated with hydrophilic catheters was calculated by multiplying the baseline risk of symptomatic UTI or hematuria for uncoated catheters by the corresponding relative risk for UTIs (0.47) and hematuria (1.59).

The probability of clinical failure after treatment for symptomatic UTI was estimated to be 15.4% [22] as reported by [14]. For SCI patients, few studies reported an annual probability of multidrug resistant UTI ranging from 4.3% in community dwelling persons performing IC [23] to 9% in acute rehabilitation environments. [24] Considering these estimates, it was assumed that 7% of individuals with catheter-associated UTI are infected with a multidrug resistant pathogen. As a consequence, the remaining patients (8.4%) experience a treatment failure due to first-line antibiotic resistant infections.

Since no transition probability was found in the literature to model the shift from “first-line resistant UTI” to “multidrug resistant UTI”, it has been assumed that “multidrug resistant UTI” state includes also the healthcare resource consumption related to “first-line resistant UTI” state.

As reported by [14], the assumed mortality rate in patients with UTIs caused by multidrug-resistant infection was 2.62%. [25] The pooled estimate for the risk of developing bacteraemia as a result of catheter-associated UTI was assumed 3.6%. [26] A mortality rate of 7.7% related to bacteraemia with a UTI origin has been estimated from the study by Montgomerie and colleagues. [27]

The study by Lidal et al. [28] reported standardized mortality ratios (SMRs) for men and women with SCI equal to 1.8 and 4.9, respectively, showing that life expectancy is reduced in these patients with respect to the normal population. These estimates have been included into the model. Mortality rates were further adjusted for age and gender according to Italian mortality tables (ISTAT).

A 1-year Markov cycle length and a lifetime horizon were chosen for baseline analysis. In order to improve the accuracy of the results a half-cycle correction was performed. The model was developed and analyzed by Microsoft Excel®.

Healthcare resource consumption and costs

The analysis was performed from the Regional Health System (Lombardy) perspective. All costs related to the consumption of direct healthcare resources were estimated and expressed in Euros (2015 value).

The identification of the clinical pathways and healthcare resource consumption for the management of symptomatic UTIs, first-line resistant UTIs, multidrug resistant UTIs, hematuria episode and bacteremia has been performed through the administration of an ad-hoc developed questionnaire to urologists and neuro-urologists. Twenty-six clinicians, most of them belonging to the Italian Continence Foundation [29], were chosen among the spinal units across Italy which treat high volumes of patients.

A web version of the questionnaire has been developed with Qualtrics© software and was made available for filling from 15<sup>th</sup> July 2015 to 15<sup>th</sup> October 2015.

The questionnaire is composed by different sections: 1) introduction, 2) patient's monitoring, 3) management of UTIs, bacteremia and hematuria, 4) future scenarios of catheters use. In the introduction, a case vignette [30] was provided to respondents aimed at identifying the target patients: patients with areflexic bladder or with overactive bladder with good pharmacological response (patients treated with antimuscarinics or with botulinum toxin or with electro-stimulation methods) and good treatment compliance. Target patients shouldn't have been administered prolonged antibiotic treatment, shouldn't be subject to antibiotic resistance and should perform bowel emptying on alternate days. The patient's monitoring section collects information, referred to a period of time of one year, about exams, lab test, visits and drugs performed or administered, including spent inpatient stays. Clinicians were required to indicate, on the basis of their clinical experience, for each healthcare resource, the mean number per year, the percentage of patients involved and the regimen applied (outpatient, day-hospital or inpatient stay). For drugs, active substance, daily dose, duration, percentage of involved patients and hospital cost were required.

As regards the management of UTIs, bacteremia and hematuria, these sections are very similar to the monitoring one, with the difference that clinicians are required to indicate the healthcare resource use for the management of a single episode. The management of UTIs distinguished whether the patient experiences a symptomatic UTI that resolves (with one treatment), a first line resistant UTI or a multidrug resistant UTI. The questionnaire collects the healthcare resource consumption also for severe infections leading to death.

The last section of the questionnaire requires the clinicians to express, on the basis of their clinical experience, a forecast of possible future scenarios (1, 3 and 5 years) of utilization of uncoated and hydrophilic catheters in Italy.

For each healthcare resource, data were estimated as weighted means from the analysis of the questionnaires completed. The monetary quantification of resource consumption for the different events was based on diagnosis-related groups (DRGs) reimbursement rates for hospitalizations, official tariffs for outpatient services and hospital prices for drugs.

Four catheters per day per patient were assumed to be used since this is the number of devices provided by the health local agencies to the patients. The unitary cost was estimated in 1.70€ and 0.25€ for hydrophilic and uncoated catheters, respectively. Since in Italy the lubricant gel for uncoated catheters is paid by the patients, that cost was not included in the model.

The model assumed that during hospital stays the cost of the catheters was included into the DRG reimbursement, so no extra cost for the devices was considered.

#### Quality of life estimates

The search for utility coefficients for patients performing IC was performed through the Cost-Effectiveness Analysis Registry, a comprehensive database of more than 5,000 cost-utility analyses on a wide variety of diseases and treatments. [31] All found values referred to the study

by Bermingham and colleagues. [14] A summary of these values together with 95% CI is presented in Table 1.

The duration of the different events was estimated from the pharmacological treatment duration reported by the questionnaires, with the exception of both multidrug resistant UTI and bacteremia leading to death for which the length of stay threshold of the related DRGs was considered.

Table 1 – Summary of the retrieved utility values for the different health states

Health state	Utility coefficient	95% CI
No symptomatic UTI	0.831	0.809-0.852
Symptomatic UTI	0.782	0.764-0.799
First-line resistant UTI	0.760	0.685-0.834
Multidrug resistant UTI	0.738	0.688-0.787
Bacteraemia	0.716	0.645-0.786
Hematuria	0.738	0.688-0.787

Analyses

Both incremental cost-effectiveness and cost-utility ratios (ICER, ICUR) of hydrophilic versus uncoated catheters were calculated by dividing the incremental cost by the incremental health improvement. Life years, QALYs and costs were discounted at 3.5% yearly rate. [32] Transition probabilities, costs and utilities were entered into the model along with a distribution: beta for utilities and proportions of patients experiencing different kinds of UTIs, log-normal for relative risks and gamma for costs. Deterministic and probabilistic sensitivity analyses (PSA) were performed to test the robustness of the model. Univariate analyses were performed according to the main

parameters; second-order Monte-Carlo analyses (1,000 simulations) were conducted and related acceptability curve was plotted.

Further analyses were performed considering UTI rates for 1) hospital period and 2) combined (hospital plus community) settings as provided by [15]. In the first scenario, 0.64 and 0.79 were considered as the monthly UTI rate for uncoated catheters and the corresponding relative risk for hydrophilic (based on Speedicath® catheters) versus uncoated catheters, respectively. In the second scenario these values were changed to 0.41 and 0.90 (based on Speedicath® and LoFric® catheters), respectively.

### Budget Impact Analysis

Starting from the CEA model, a companion budget impact model [33] has been developed to address the expected changes in the expenditure for the Italian Healthcare Service in the hypothesis of an increased diffusion of hydrophilic catheters.

In order to perform the BIA, a research of epidemiological data focused on SCI patients performing IC was carried out.

The prevalence of SCI patients in Italy resulted in the range 60,000-70,000 according to a national registry [34], while the incidence (data from the Italian registry) showed a decrease from 20-25 to 7.8 per million inhabitants. Based on [35] it was assumed that 60% of patients perform IC.

The total number of prevalent patients with SCI performing IC in Italy was estimated to be about 39,000, while the total number of incident patients was about 285. It was assumed that the distribution of the incident population is the same of the prevalent population (mean age 40 years and 80% men).

The current scenario of patients distribution between the two considered devices was estimated from clinical input as 20% uncoated and 80% hydrophilic catheters; the definition of future

scenarios, in which appropriate increased uses of hydrophilic catheters are considered, were estimated by the key opinion leaders through the questionnaire administration.

The cost of the current or future scenarios was determined by multiplying the cost for each intervention by the proportion of the eligible population using that intervention and by the number of patients in the eligible population, taking into account both prevalent and subsequent yearly incident cohorts. Since in this analysis the interest was focused on the budget expected at each point in time, the financial streams were presented as undiscounted costs. [33]

Results

Model parameters

Nine out of 26 clinicians completed the questionnaire and the estimated healthcare resource consumption for the different events is shown in Table 2. The low participation could be due to the questionnaire administration during the summer period or to the complexity/time required for the completion. Anyway, the nine clinicians who responded refer to institutions around Italy and can be considered representative of the Italian clinical practice.

Table 2 – Healthcare resource consumption for the considered health states

Health state	Category	Type	mean number per pt	dosage (mg)	% patients
Patients' monitoring	Visits	Specialist visit	1.99		
	Exams/procedures	Abdomen ultrasound	0.11		
		Bladder ultrasound	0.81		
		Creatinine	0.20		
		MRI	0.02		
		Pelvic floor examination	0.03		

		Rx	0.06		
		Scintigraphy	0.01		
		Urine culture	3.60		
		Urine exam	2.39		
		Urodynamics	0.46		
		Video-urodynamics	0.17		
	DRGs	313 - Urethral Procedures, Age Greater than 17 without CC	0.01		
		309 - Minor Bladder Procedures without CC	0.01		
		323 - Urinary Stones with CC and/or ESW Lithotripsy	0.03		
		324 - Urinary Stones without CC	0.02		
		325 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 with CC	0.03		
		326 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 without CC	0.14		
		329 - Urethral Stricture, Age Greater than 17 without CC	0.01		
	Drugs	Antimuscarins		465	73%
		Botulinum toxin injection	2		25%
		Antibiotics (prophylaxis)		5,761	16%
<b>Symptomatic UTI</b>	Visits	Specialist visit	0.93		
	Exams/procedures	Creatinine	0.11		
		Bladder ultrasound	0.41		
		Blood culture	0.02		
		CBC	0.11		

		Urine exam	0.78		
		Kidney functionality	0.11		
		Urine culture	1.22		
	DRGs	321 - Kidney and Urinary Tract Infections, Age Greater than 17 without CC	0.52		
	Drugs	Antibiotics		22,411	127%*
First-line resistant UTI (resources in addition to symptomatic UTI)	Visits	Specialist visit	1.17		
	Exams/procedures	Stool culture	0.01		
		Creatinine/glycemia	0.44		
		Abdomen ultrasound	0.11		
		Bladder ultrasound	0.37		
		Blood colture	0.33		
		Urine exam	1.44		
		Video-urodynamics	0.11		
		Lactate	0.11		
		Polymerase Chain Reaction	0.11		
		Urine culture	1.78		
		Erythrocyte sedimentation rate	0.11		
	DRGs	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.07		
	Drugs	Antibiotics		16,278	89%
Multidrug resistant UTI	Visits	Specialist visit	1.2		

(resources in addition to first-line resistant UTI)					
	DH	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.02		
	Exams/procedures	Cystoscopy	0.07		
		Colonscopy	0.11		
		Bladder ultrasound	0.44		
		Bact smear-lower GI	0.11		
		Bowel diagnost proc NEC	0.13		
		CT scan	0.13		
		Urine exam	1.33		
		Urine culture	1.56		
		Video-urodynamics	0.11		
		Blood colture	0.11		
		Intestinal x-ray NEC	0.11		
	DRGs	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.03		
	Drugs	Antibiotics		7,556	34%
<b>Bacteremia</b>	DRGs	576 - Septicemia without mechanical ventilation	0.59		
		320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.03		
	DH	576 - Septicemia without mechanical ventilation	0.22		
	Drugs	Antibiotics		12,311	56%

Infection leading to patient death	DRGs	575 - Septicemia with mechanical ventilation >=96 h	0.45		
	Drugs	Antibiotics		12,225	34%
Hematuria	Visits	Specialist visit	0.71		
	Exams/procedures	Cystoscopy	0.02		
		Bladder ultrasound	0.24		
		Urine exam	0.56		
		Percutaneous cystostomy	0.06		
		Urethroscopy	0.21		
		Urine culture	0.22		
	DRGs	309 - Minor Bladder Procedures without CC	0.002		
		332 - Other Kidney and Urinary Diagnoses, Age Greater than 17 without CC	0.04		
		326 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 without CC	0.01		
	Drugs	Antibiotics		2,557	30%

\* More than one treatment is administered

The estimated event durations resulted 2 days for hematuria, 4 days for symptomatic UTI, additional 8 days for first-line resistant UTI, additional 8 days for multidrug resistant UTI (total 4+8+8=20 days), 35 days for hospitalization for bacteremia (DRG 576) and 65 days for infection leading to death (DRG 575).

In case of bacteremia leading to patient death, only the healthcare resources related to “Infection leading to patient death” in Table 2 are taken into account to avoid double counting (the management of the episode of bacteremia is included in the DRG 575).

Table 3 summarizes the main model parameters with related distributions.

Table 3 – Model parameters and distributions used in PSA

	Base case value	95% CI	Distribution type	Alpha	Beta
<b>Utility coefficients for the health states/events</b>					
Alive no disease	0.831	0.809 - 0.852	beta	969.1	197.1
Symptomatic UTI (4 days)	0.782	0.764 - 0.799	beta	1671.49	465.96
First-line resistant UTI (8 days)	0.76	0.685 - 0.834	beta	95.2	30.1
Multidrug resistant UTI (8 days)	0.738	0.688 - 0.787	beta	222.99	79.16
Bacteremia (37 days or 65 if leading to death)	0.716	0.645 - 0.786	beta	111.82	44.35
Hematuria (2 days)	0.738	0.688 - 0.787	beta	223.0	79.2
<b>Transition probabilities</b>					
First-line resistant UTI	0.083	0.0 - 23.2	beta	1.75	19.36
Multidrug resistant UTI	0.07	5.1 - 9.2	beta	41.6	552.5
Bacteremia	0.036	3.4 - 3.8	beta	1200	32129
Mortality due to multidrug resistant UTI	0.026	1.3 - 5.1	beta	3.1	37.0
Mortality due to UTI associated bacteraemia	0.077	2.9 - 19.2	beta	7.09	263.42
<b>Patients proportions</b>					
Annual proportion, Symptomatic UTI	768%	384% - 1152%	gamma	100.0	0.077
Annual proportion, Hematuria	33%	16.50% - 49.50%	gamma	38	0.009
<b>Relative risks</b>					
RR symptomatic UTI	0.79	0.47 – 0.90	lognormal	0.024*	
RR hematuria	1.59	0.81 – 3.13	lognormal	0.261*	
<b>Costs (€)</b>					
Alive no disease (annual cost)	954.48	477 - 1432	gamma	100.0	9.5
Symptomatic UTI	1,091.86	546 – 1,638	gamma	100.0	10.9
1st line resistant UTI	401.20	201 - 602	gamma	100.0	4.0
Multidrug resistant UTI	775.36	388 – 1,163	gamma	100.0	7.8
Bacteremia	3,664.16	1,832 – 5,496	gamma	100.0	36.6
Hematuria	106.10	53 - 159	gamma	100.0	1.1
Death for bacteremia	6,057.70	3,029 – 9,087	gamma	100.0	60.6

Death for Multidrug res. UTI	9,721.86	4,861 – 14,583	gamma	100.0	97.2
* standard error					

Baseline results

In the base-case scenario, the model estimated an average life expectancy of 17.299 (14.331 QALYs) and 18.284 (15.169 QALYs) years for patients using hydrophilic and uncoated catheters, respectively. The mean costs per patient resulted 83,174€ and 62,530€ for patients using hydrophilic and uncoated catheters, respectively. The ICER and ICUR were 20,949€ and 24,652€, respectively, showing that hydrophilic catheters compare favorably against the commonest threshold values [32, 36] and can therefore be considered a cost-effective choice in comparison to uncoated ones. Moreover, considering a lifetime horizon, hydrophilic catheters may reduce the frequency of UTIs by about 50% (from 48 to 24) in comparison to uncoated devices. Considering the high impact of the management of UTIs, accounting for about 23% to 63% of the total lifetime cost for patients using hydrophilic and uncoated catheters, respectively, the potential for UTIs reduction becomes fundamental.

The model results are summarized in Table 4.

Table 4 – Summary of the model results

Catheter	Cost (€)	Δ Cost (€)	LY	ΔLY	QALYs	ΔQALYs	ICER (€/LY)	ICUR (€/QALY)
Uncoated	€ 62,530		17.299		14.331			
Hydrophilic	€ 83,174	€ 20,644	18.284	0.985	15.169	0.837	€ 20,949	€ 24,652

Sensitivity analyses

One-way sensitivity analyses were performed for ICUR (discounted scenario) on the main model parameters. The results are presented in Table 5. The annual proportion of symptomatic UTIs for uncoated catheters and the relative risk of developing a symptomatic UTI (for hydrophilic catheters vs. uncoated catheters) are the parameters that could mainly influence the ICUR.

Table 5 – One-way sensitivity analyses

Variable	Value			ICUR (€/QALY)		
	Low	Base case	High	Low	Base case	High
Starting age	20	40	60	20,132	24,652	35,924
Proportion of men	40%	80%	100%	25,268	24,652	24,028
Annual proportion, Symptomatic UTI (uncoated catheters)	0.84	1.68	2.52	67,899	24,652	10,573
Annual proportion, Hematuria (uncoated catheters)	0.17	0.33	0.50	24,377	24,652	24,928
Annual proportion, 1st line resistant UTI	0.04	0.08	0.13	24,975	24,652	24,330
Annual proportion, Multidrug resistant UTI	0.04	0.07	0.11	30,105	24,652	21,003
Annual proportion, Bacteremia	0.02	0.04	0.05	34,655	24,652	19,264
Annual risk, Bacteremia to Death	0.04	0.08	0.12	32,747	24,652	20,242
Annual risk, Multidrug resistant UTI to Death	0.01	0.03	0.04	29,430	24,652	21,435
RR symptomatic UTI (hydrophilic vs. uncoated catheters)	0.47	0.47	0.90	24,652	24,652	223,925
RR hematuria (hydrophilic vs. uncoated catheters)	0.81	1.59	3.13	23,987	24,652	25,976
SMR mortality, men	0.90	1.80	2.70	23,588	24,652	25,552
SMR mortality, women	2.45	4.90	7.35	23,952	24,652	25,278
Annual cost, patient monitoring	477	954	1432	24,090	24,652	25,214
Cost per Symptomatic UTI	546	1,092	1,638	34,186	24,652	15,118
Cost per 1st line resistant UTI	201	401	602	24,946	24,652	24,358
Cost per Multidrug resistant UTI	388	775	1,163	25,126	24,652	24,178
Cost per Bacteremia	1,832	3,664	5,496	25,804	24,652	23,500
Cost per Hematuria	53	106	159	24,406	24,652	24,898
Cost per Death for bacteremia	3,029	6,058	9,087	24,801	24,652	24,503
Cost per Death for Multidrug res. UTI	4,861	9,722	14,583	24,810	24,652	24,494
Cost of hydrophilic catheter	0.85	1.70	2.55	dominance	24,652	51,677
Cost of uncoated catheter	0.13	0.25	0.38	28,398	24,652	20,906
Number of catheters per day	2	4	6	1,373	24,652	47,931

Duration of bacteremia hospitalization (days)	18.50	37	55.50	24,703	24,652	24,601
Duration of bacteremia hospitalization (days), leading to death	32.50	65	97.50	24,660	24,652	24,645
Duration of multires UTI-death hospitalization (days)	32.50	65	97.50	24,657	24,652	24,647
Utility, No Disease	0.42	0.83	1.00	65,544	24,652	19,662
Utility, Symptomatic UTI	0.39	0.78	1.00	22,937	24,652	25,725
Utility, 1st line resistant UTI	0.38	0.76	1.00	24,112	24,652	25,006
Utility, Multidrug resistant UTI	0.37	0.75	1.00	24,167	24,652	24,988
Utility, Bacteremia	0.36	0.72	1.00	24,022	24,652	25,176
Utility, Hematuria	0.37	0.74	1.00	24,885	24,652	24,489
Duration, Symptomatic UTI (days)	2.00	4	6.00	24,768	24,652	24,537
Duration, 1st line resistant UTI (days)	4.00	8	12.00	24,680	24,652	24,624
Duration, Multidrug resistant UTI (days)	8.00	16	24.00	24,706	24,652	24,598
Duration, Bacteremia (days)	18.50	37	55.50	24,736	24,652	24,569
Duration, Hematuria (days)	1.00	2.0	3.00	24,623	24,652	24,681
Duration, Bacteremia, if leading to death (days)	32.50	65	97.50	24,664	24,652	24,640
Duration, pre-death multires. UTI hospitalization (days)	32.50	65	97.50	24,660	24,652	24,644
Discount rate, Costs	0.00	0.035	0.05	43,464	24,652	20,287
Discount rate, QALYs	0.00	0.035	0.05	11,366	24,652	32,765

A PSA was performed on the ICUR considering the discounted scenario. The acceptability curve obtained from the Monte Carlo simulation is shown in Figure 2. A threshold of about €50,000/QALY shows the cost-effectiveness of hydrophilic catheters in about 94% of simulations, highlighting the robustness of the model results.

The scenario analyses performed considering hospital period and combined (hospital plus community) settings resulted in ICURs equal to 12,534€/QALY (ICER 10,617€/LY) and 72,468€/QALY (ICER 61,296€/LY), respectively.

<Figure 2>

### Budget impact analysis

A BIA was performed considering increasing hydrophilic coated catheters utilization for people performing IC, as estimated by the filled in questionnaires. Considering only uncoated and hydrophilic coated catheters, the clinicians reported foreseen usages for the latter of 83%, 88% and 89% for 1, 3 and 5 years, respectively.

The yearly total cost for the use of uncoated and hydrophilic coated catheters is presented in Figure 3 together with the total NHS budget. As a consequence of the increasing trend in the utilization of hydrophilic catheters, the total budget also increases over time.

<Figure 3>

### **Discussion**

Intermittent catheterization is considered the method of choice for the management of neurogenic bladder dysfunctions. Although different catheters with various characteristics in terms of medical safety, treatment functionality, patient comfort and environmental performances are available, currently there is no robust consensus on which type of catheter is best. Efforts were made to develop improved catheter materials but the risks of infections and urethral trauma still remain, leading to high morbidity and often resulting in frequent hospitalizations. As a consequence, the management of patients performing IC entails a substantial economic burden on the healthcare system.

The aim of the present study was to conduct a CE and BI analyses in order to support the decision making process as to how to allocate scarce healthcare resources by maximizing patients' health while controlling costs.

Considering a lifetime perspective, hydrophilic catheters resulted cost-effective in comparison to uncoated ones, reporting an ICUR and an ICER of 24,652€/QALY and 20,949€/LY gained, respectively. The results proved to be robust according to one-way and probabilistic sensitivity analyses.

The base-case findings are in line with the ones reported by Clark and colleagues [15] for UK but differ from the results shown in [14], which reported that uncoated catheters are the most cost-effective when compared to all the other types of catheters. Basically, the latter study used data from a meta-analysis that estimated, for the different catheters, the risk of experiencing at least one UTI. Since there could be a great variation in the number of UTIs experienced by each patient, this assumption could have influenced the results, hiding the potential effect of hydrophilic catheters with regard to uncoated ones. In fact, a study [37] evaluating catheter practices and associated problems, through telephone interviews, reported for people mainly performing IC with uncoated catheters a yearly rate for symptomatic UTI treated with an antibiotic of 2.3 (95%CI 1.8-3).

Differently from [15], the present CE model focused only on short-term consequences of symptomatic UTIs excluding their lifetime effects on the renal function. Since the probability of developing UTIs was found to be lower for hydrophilic catheters versus uncoated ones, this means that our results are a conservative estimate of the CE results. As a consequence, the scenario analyses considering community setting and hospital and community settings together reported higher ICERs and ICURs in comparison with the findings of the above cited study.

Another difference is related to the cost of the two devices. While in UK the cost of an uncoated catheter is slightly inferior to the cost of a hydrophilic one, in Italy the cost for uncoated catheters is very low and is about 25% of the cost of the advanced devices. The increased cost for hydrophilic catheters can only be partially compensated by the costs savings due to the management of the lower number of developed UTIs.

Our study is the first cost-effectiveness analysis that also includes a budget impact analysis. To economic rationality, BIA adds an important piece of information for decision-makers who need to

estimate the impact on healthcare expenditures of introducing new health technologies in regular practice.

This study estimated the consumption of healthcare resources by soliciting experts' opinion with the aim of providing real-world costing data. This is important especially for medical devices since their use in regular practice often differs from what established in experimental settings. [38] Also, the fact that the consumption of healthcare resources has been represented in natural units - as suggested by the EUnetHTA guidelines [39] - will allow costs adjustment to other countries. Nevertheless, it must be noted that data derived from self-reported questionnaire may suffer from inevitable inaccuracies that could be eliminated if a prospective observational multi-centre study would be carried out. Observational studies would also serve to confirm clinical evidence on comparative effectiveness of catheters that, for the time being, is drawn from RCTs only.

The findings of the present study are important to support the use of hydrophilic catheters but a broader evaluation which takes into account also costs from a societal perspective would be needed to assess the comprehensive economic sustainability of these innovative devices.

### Corresponding author statement

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**Declaration of competing interests**

All authors have completed the Unified Competing Interest form at [ww.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (1) CeRGAS Bocconi has support from ASBM Srl for the submitted work; (2) CR and RT have no relationships with ASBM Srl that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (4) CR and RT have no non-financial interests that may be relevant to the submitted work.

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## Details of contributors

Carla Rognoni - study concept and design; analysis and interpretation of data; drafting of the manuscript.

Rosanna Tarricone - study supervision; obtained funding; critical revision of the manuscript.

## Transparency declaration

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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## Data Sharing

No additional data available

## References

1. Bakke A, Digraanes A, Høisaeter PA. Physical predictors of infection in patients treated with clean intermittent catheterization: a prospective 7-year study. *Br J Urol*. 1997 Jan;79(1):85-90.

2. Turi MH, Hanif S, Fasih Q, et al. Proportion of complications in patients practicing clean intermittent self-catheterization (CISC) vs indwelling catheter. *J Pak Med Assoc.* 2006 Sep;56(9):401-4.

3. Nicolle LE. Urinary tract infections in patients with spinal injuries. *Curr Infect Dis Rep* 2014 Jan;16(1):390.

4. Ciani O, Grassi D, Tarricone R. An economic perspective on urinary tract infection: the "costs of resignation". *Clin Drug Investig* 2013 Apr;33(4):255-61.

5. Lai KK, Fontecchio SA. Use of silver-hydrogel urinary catheters on the incidence of catheter-associated urinary tract infections in hospitalized patients. *Am J Infect Control* 2002;30(4):221-5.

6. Karchmer TB, Giannetta ET, Muto CA, et al. A randomized crossover study of silver-coated urinary catheters in hospitalized patients. *Arch Intern Med* 2000;160(21):3294-8.

7. McNutt R, Johnson TJ, Odwazny R, et al. Change in MS-DRG assignment and hospital reimbursement as a result of Centers for Medicare & Medicaid changes in payment for hospital-acquired conditions: is it coding or quality? *Qual Manag Health Care* 2010;19(1):17-24.

8. Saint S. Clinical and economic consequences of nosocomial catheter-related bacteriuria. *Am J Infect Control* 2000;28(1):68-75.

9. Tambyah PA, Knasinski V, Maki DG. The direct costs of nosocomial catheter-associated urinary tract infection in the era of managed care. *Infect Control Hosp Epidemiol* 2002;23(1):27-31.

10. Anderson DJ, Kirkland KB, Kaye KS, et al. Underresourced hospital infection control and prevention programs: penny wise, pound foolish? *Infect Control Hosp Epidemiol* 2007;28(7):767-73.

11. Bardsley A. Intermittent Self-Catheterisation in women: reducing the risk of UTIs. *Urology supplements* 2014;22(18).

12. Heard L, Buhrer R. How do we prevent UTI in people who perform intermittent catheterization? *Rehabil Nurs* 2005 Mar-Apr;30(2):44-5,61.
13. Bennett E. Intermittent self-catheterisation and the female patient. *Nurs Stand* 2002;17: 37–42.
14. Bermingham SL, Hodgkinson S, Wright S, et al. Intermittent self catheterisation with hydrophilic, gel reservoir, and non-coated catheters: a systematic review and cost effectiveness analysis. *BMJ* 2013 Jan 8;346:e8639.
15. Clark JF, Mealing SJ, Scott DA, et al. A cost-effectiveness analysis of long-term intermittent catheterisation with hydrophilic and uncoated catheters. *Spinal Cord* 2015 Jul 21.
16. Igawa Y, Wyndaele JJ, Nishizawa O. Catheterization: possible complications and their prevention and treatment. *Int J Urol* 2008 Jun;15(6):481-5.
17. Vahr S, Cobussen-Boekhorst H, Eikenboom J, et al. Catheterisation. Urethral intermittent in adults: dilatation, urethral intermittent in adults. Arnhem (The Netherlands): European Association of Urology Nurses (EAUN); 2013 Mar. 96 p.
18. Euro Mediterranean Rehabilitation Summer School - <http://www.emrss.it/> (accessed 10 Mar 2016).
19. Cardenas DD, Moore KN, Dannels-McClure A, et al. Intermittent catheterization with a hydrophilic-coated. catheter delays urinary tract infections in acute spinal cord injury: a prospective, randomized, multicenter trial. *PM R* 2011 May;3(5):408-17.
20. De Ridder DJ, Everaert K, Fernández LG, et al. Intermittent catheterisation with hydrophilic-coated catheters (SpeediCath). reduces the risk of clinical urinary tract infection in spinal cord injured patients: a prospective randomised parallel comparative trial. *Eur Urol* 2005 Dec;48(6):991-5.
21. Borenstein M, Hedges LV, Higgins JPT, et al. Introduction to Meta-Analysis, 2009, John Wiley & Sons, Ltd.

22. Dow G, Rao P, Harding G, et al. A prospective, randomized trial of 3 or 4 days of ciprofloxacin treatment for acute urinary tract infection in patients with spinal cord injury. *Clinical Infectious Diseases* 2004; 39:658-664.

23. Waites KB, Chen Y, DeVivo MJ, et al. Antimicrobial resistance in gram-negative bacteria isolated from the urinary tract in community-residing persons with spinal cord injury. *Archives of Physical Medicine & Rehabilitation* 2000; 81(6):764-769.

24. Mylotte J, Kahler L, Grahm R, et al. Prospective surveillance for antibiotic-resistant organisms in patients with spinal cord injury admitted to an acute rehabilitation unit. *American Journal of Infection Control* 2000; 28:291-297.

25. Kleven RM, Edwards JR, Gaynes RP. The impact of antimicrobial-resistant health care-associated infections on mortality in the United States. *Clinical Infectious Diseases* 2008; 47:927-930.

26. Saint S. Clinical and economic consequences of nosocomial catheter-related bacteriuria. *Am J Infect Control* 2000;28(1):68-75.

27. Montgomerie JZ, Chan E, Gilmore DS, et al. Low mortality among patients with spinal cord injury and bacteremia. *Rev Infect Dis* 1991 Sep-Oct;13(5):867-71.

28. Lidal IB, Snekkvik H, Aamodt G, et al. Mortality after spinal cord injury in Norway. *J Rehabil Med* 2007 Mar;39(2):145-51.

29. <http://www.contenuti-web.com/continenza/fondazione-0000409.html> (accessed 10 Mar 2016).

30. Fattore G, Torbica A. Cost and reimbursement of cataract surgery in Europe: a cross-country comparison. *Health Econ* 2008 Jan;17(1 Suppl):S71-82.

31. CEA Registry – <https://research.tufts-nemc.org/cear4/SearchingtheCEARegistry> (accessed 10 Mar 2016).

32. National Institute for Clinical Excellence. Guide to the Methods of Technology Appraisal. London: National Institute for Clinical Excellence, 2004.
33. Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health* 2014 Jan-Feb;17(1):5-14.
34. GISEM - Italian Group for the Epidemiological Study of Spinal Cord Injuries - <http://www.istud.it/superabile/lesione.asp> (accessed 10 Mar 2016).
35. Zlatev DV, Shem K, Elliott CS. How many spinal cord injury patients can catheterize their own bladder? The epidemiology of upper extremity function as it affects bladder management. *Spinal Cord* 2016 Jan 19.
36. [http://www.who.int/choice/costs/CER\\_levels/en](http://www.who.int/choice/costs/CER_levels/en) (accessed 10 Mar 2016).
37. Wilde MH, Brasch J, Zhang Y. A qualitative descriptive study of self-management issues in people with long-term intermittent urinary catheters. *J Adv Nurs* 2011 Jun;67(6):1254-63.
38. Drummond M, Griffin A, Tarricone R. Economic evaluation for devices and drugs--same or different? *Value Health* 2009 Jun;12(4):402-4.
39. [www.eunetha.eu](http://www.eunetha.eu) (accessed 10 Mar 2016).

## Figure legends

Figure 1 – Simplified Markov model representation. Patients enter the Markov process in the “Alive no disease” state, where they can remain or move to UTIs or hematuria states. These are transient states since their duration lasts less than one year. From each state, patients can move to the absorbing state death (arrows not shown).

Figure 2 - ICUR acceptability curve

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Figure 3 – Budget impact of uncoated and hydrophilic coated catheters for current (0) and 1, 3, 5-  
years scenarios

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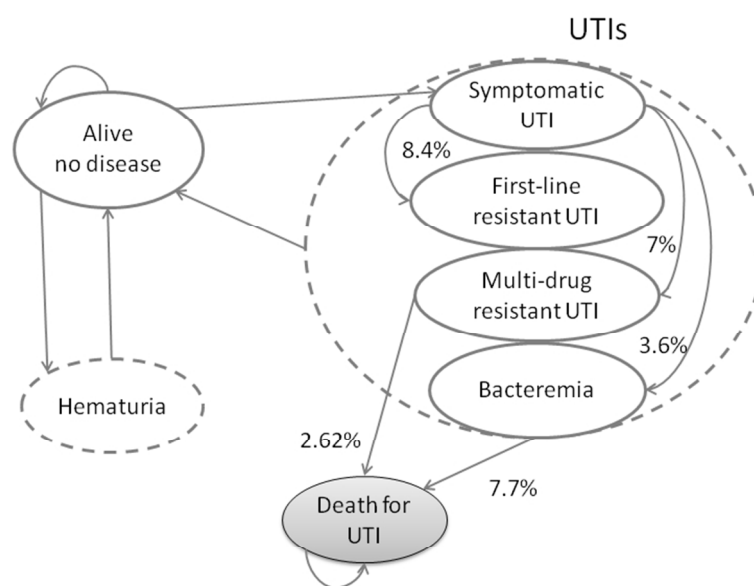


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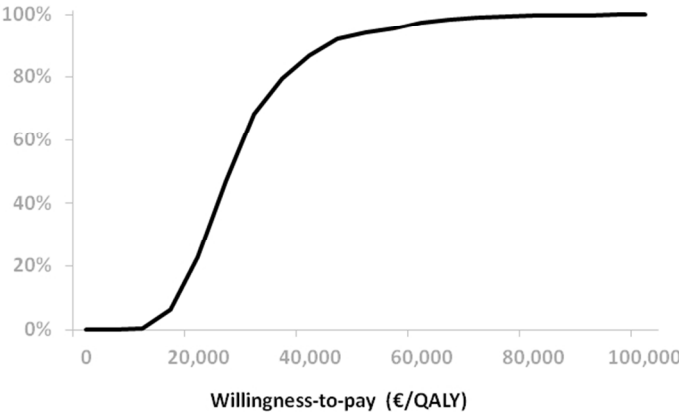


Figure 2 - ICUR acceptability curve  
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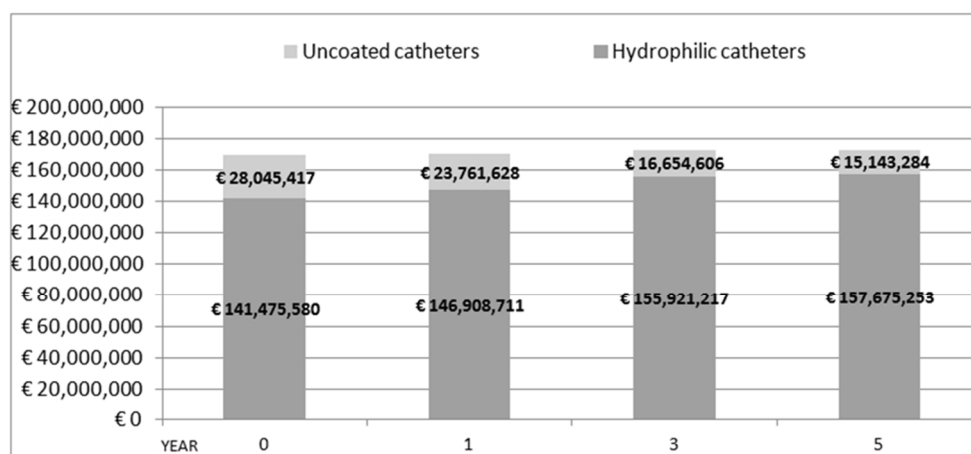


Figure 3 – Budget impact of uncoated and hydrophilic coated catheters for current (0) and 1, 3, 5-years scenarios

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**CHEERS Checklist**  
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The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp>

Section/item	Item No	Recommendation	Reported on page No/line No
<b>Title and abstract</b>			
Title	1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	from page 3
<b>Introduction</b>			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	from page 4
<b>Methods</b>			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	from page 6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	page 9
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	page 9
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	page 6
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	page 6
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	page 11
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	page 6
Measurement of effectiveness	11a	<i>Single study-based estimates:</i> Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	



	11b	<i>Synthesis-based estimates:</i> Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	from page 7
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	pages 11-12
Estimating resources and costs	13a	<i>Single study-based economic evaluation:</i> Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
	13b	<i>Model-based economic evaluation:</i> Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	from page 9
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	page 9
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	page 6
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	pages 6-8
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	pages 8-9
<b>Results</b>			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	page 18
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	page 19
Characterising uncertainty	20a	<i>Single study-based economic evaluation:</i> Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	



		of methodological assumptions (such as discount rate, study perspective).	
	20b	<i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	pages 19-21
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	
<b>Discussion</b>			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	pages 22-24
<b>Other</b>			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	page 25
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

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## Healthcare Resource Consumption for Intermittent Urinary Catheterization: Cost-Effectiveness of Hydrophilic Catheters and Budget Impact Analyses

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Keywords:	intermittent urinary catheterization, hydrophilic catheters, uncoated catheters, Urinary tract infections < UROLOGY, cost-effectiveness analysis, budget impact analysis

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**Healthcare Resource Consumption for Intermittent Urinary Catheterization: Cost-Effectiveness of Hydrophilic Catheters and Budget Impact Analyses**

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## Abstract

**Objectives** – The present study presents a cost-effectiveness analysis comparing hydrophilic-coated to uncoated catheters for patients performing intermittent urinary catheterization. A budget impact analysis is also included to evaluate the impact on a national healthcare budget of intermittent catheterization for management of bladder dysfunctions over a period of 1, 3 and 5 years.

**Design** – The study used a Markov model to project health outcomes (life years and quality-adjusted life years - QALYs) and economic consequences related to patients performing intermittent catheterization with hydrophilic coated or uncoated catheters. The model was populated with clinical efficacy data of catheters, retrieved from randomized controlled trials. Cost data were estimated based on healthcare resource consumption derived from an e-survey addressed to key opinion leaders in the field.

**Setting** – The study used an Italian Healthcare Service perspective.

**Population** – Patients with spinal cord injury performing intermittent urinary catheterization in the home setting.

**Main outcome measures** – Incremental cost-effectiveness and cost-utility ratios (ICER, ICUR) of hydrophilic coated vs. uncoated catheters and associated healthcare budget impact.

**Results** - The ICER and ICUR associated with hydrophilic coated catheters were 20,761€ and 24,405€, respectively. This implies that hydrophilic coated catheters are cost-effective in comparison to uncoated catheters, as Italian threshold values are proposed to range between 25,000-66,400€. The model showed an estimated healthcare budget for Italy of approximately 172 million Euros at 5 years, with 90% and 10% use of hydrophilic coated and uncoated catheters, respectively.

**Conclusions** - Considering a lifetime perspective, hydrophilic coated catheters seem like a cost-effective choice in comparison to uncoated ones. These findings can support policy makers in their evaluation of intermittent catheterization in patients with spinal cord injury.

**Strengths and limitations of this study**

- This paper presents a cost-effectiveness analysis comparing hydrophilic coated to uncoated catheters in spinal cord injured patients performing intermittent catheterization. The healthcare resource consumption was derived from an e-survey addressed to key opinion leaders to provide real-world data.
- The study combines a cost-effectiveness analysis with a budget impact analysis. This kind of analysis may help decision-makers to estimate costs of introducing new health technologies in clinical practice.
- Data derived from self-reported questionnaires may be limited by varying recollection and poor generalizability. Variables derived from a prospective observational multi-centre study would increase the validity of the current model.
- The findings of the present study support the use of hydrophilic coated catheters but are limited to costs from a healthcare perspective. A broader evaluation, also including costs from a societal perspective, would increase the understanding of the economic sustainability of these devices.

## Introduction

The spinal cord is the part of the central nervous system that is responsible for conducting information to/from the brain, i.e. sensory information from the peripheral nervous system and motor information to various muscles. When the spinal cord is damaged, the ascending and descending pathways are partially or totally interrupted, leading to motor or sensory deficits of diverse nature and extent. Damages can be caused by spinal cord injury (SCI), multiple sclerosis, cerebrovascular diseases, cancer, infectious diseases, and slipped discs. Many of these conditions affect the bladder functionality and cause a so-called neurogenic bladder, often characterized by voiding problems.

In the community setting, the management of a neurogenic bladder many times involves Intermittent Catheterization (IC). With this technique, a catheter is temporary used to remove urine from the bladder. As neurogenic bladder is often a permanent condition, IC may be required for a long period of time, often several times a day. There are different catheters available for IC. For example, disposable catheters with a hydrophilic polymer surface coating, disposable catheters with pre-packaged water based lubricant (gel reservoir), or non-coated catheters. Determining on an optimal catheter is today a problem, as there is a lack of strong evidence demonstrating the effectiveness of any particular catheter design, technique or strategy. [1] As a solution, it is proposed to consider economic consequences of using different catheter types, and the existing available evidence of the same, even though it is recognized that the quality of the evidence may be suboptimal. To our knowledge, there are already two cost-effectiveness studies doing this. [2-3] Both studies compare lifetime quality adjusted life years (QALYs) and costs of different types of catheter from the UK perspective, and focus on urinary tract infections (UTIs). The first one, by Bermingham et al., [2] bases its analysis on the annual probability of experiencing at least one UTI for the different catheters considered (without taking into account the mean number of UTIs experienced in the same time by the patients' cohort) and their short term consequences. The second one, by Clark et al., [3] focuses on the average UTI rate per patient and month for hydrophilic coated and uncoated catheters, and considers long term sequelae as kidney

impairment. Considering a lifetime horizon, the study by Clark et al. [3] showed that hydrophilic coated catheters are cost-effective when compared to uncoated ones. The study by Bermingham et al., [2] on the other hand, reported that reuse and cleansing of non-coated catheters is the most cost-effective alternative in comparison to all other catheter types. It should however be noted that reuse and cleansing of non-coated catheter may be regarded as an off-label procedure, not supported by all regulating bodies. The divergent results from previous cost-effectiveness studies confirm that assumptions made, and the way clinical data are chosen, highly affect the model construction and conclusions from the analysis, even when using the same country setting.

One of the major advantages of IC is the significant reduction in the risk of catheter-associated UTIs, ensuring urinary tract health in general and preservation of kidney function in particular. [4-5] Despite of this, UTIs still cause high morbidity and frequent hospitalizations for people with neurogenic bladder. Repeated cycles of antibiotic therapy in patients with recurrent UTIs also contribute to “antibiotic resistance”, [6] which in turn increases the need of new effective treatment options. For these reasons, UTIs entail a significant economic burden for patients, their families, and healthcare systems. [7]

Studies which attempted to estimate the burden of UTIs from the healthcare system perspective reported costs ranging from 523€ to 4,167€, [8-13] where more complicated UTIs were likely to be associated with higher costs. The high variability in costs relates to several aspects. For example, UTI definition (bacteriuria vs. symptomatic UTI), study setting (hospital vs. community), study population (general patients in hospital vs. specific populations) and cost definitions can vary. The latter can for example consider just direct healthcare costs (e.g. medications, therapies) or also indirect costs to society as productivity losses. The use of different payer perspectives (society and/or healthcare system) may also result in different UTI cost values.

In addition to the risk of UTI, IC performed several times a day poses a risk for urethral trauma. Urethral trauma can occur with or without presence of hematuria and it is associated with an increased risk of UTI. [14-15] Damage to the urethra is less likely to occur with a lubricated catheter. [16]

A catheter reducing the risks of urethral trauma and/or UTI, both limits the economic burden for the healthcare system and increases quality of life for patients. A cost-effectiveness analysis (CEA) permits a systematic evaluation of the costs and quality of life consequences of different treatment regimens, highlighting which option would have the highest net benefit.

The aim of the present study was to perform a CEA with an Italian Healthcare Service perspective, comparing the two catheter types most frequently used for IC (i.e. disposable hydrophilic coated or uncoated plastic catheters). This was done to add value to previously conflicting results of cost-effectiveness analyses evaluating different catheter types, and to identify the most cost-effective catheter alternative for the Italian setting. A budget impact analysis (BIA) was also conducted to evaluate the impact on the Italian healthcare budget of IC for management of bladder dysfunctions, over a period of 1, 3 and 5 years.

## Methods

The clinical effectiveness of each catheter was retrieved from randomized controlled trials published in the literature focusing on community perspective. Cost data were estimated based on diagnosis-specific healthcare resource utilization, derived from an e-survey addressed to key opinion leaders in the field. Since clinical data were mainly reported for SCI patients, the model considered these as an applicable study population. The study focused mainly on UTIs and episodes of hematuria as the former are the most frequent complications in patients performing IC, while the latter occur regularly in one third of patients on a long-term basis. [17]

### Systematic literature review and clinical data synthesis

A systematic literature review was performed in June 2016 to retrieve randomized controlled trials (RCTs), comparing hydrophilic coated and uncoated catheters for IC, and reporting outcomes on UTIs and hematuria. A systematic search was conducted on Pubmed, Embase, the Cochrane Library and Web of Science databases to retrieve clinical evidence (see Appendix for detailed search strategy).

In Italy, single-use catheters are considered the standard method for IC and four catheters per day are delivered to users by local health agencies. [18] Reuse of catheters is not present or relevant to the Italian healthcare system, why clinical evidence considering catheter reuse was discarded. Studies not reporting UTIs frequencies per patient were also excluded. The studies by Cardenas et al. [19-20] and Sarica et al. [21] focused on SCI patients and reported data useful for the analysis. Data reported by Clark et al. [3] derived from an internal report of the study conducted by De Ridder et al. [22] were also included.

Table 1 reports UTI rates according to the methods presented in Clark et al. [3], distinguishing the following settings: hospital period, community setting and combined scenario (hospital and community settings).

Table 1 – Urinary tract infection rates (mean number of UTIs per patient per month)

	Study	Patients	N. episodes	Rate per patient per month	Weighted mean	Rate ratio
HOSPITAL PERIOD						
Uncoated catheters	Cardenas 2011 [20]	114		0.68	0.61	0.78
	De Ridder 2005 [22]	61		0.55		
	Sarica 2010 [21]	10	4	0.27		
Hydrophilic coated catheters	Cardenas 2011 [20]	105		0.54	0.48	
	De Ridder 2005 [22]	60		0.44		
	Sarica 2010 [21]	10	1	0.07		
COMMUNITY SETTING						
Uncoated catheters	Cardenas 2009 [19]	23		0.14	0.14	0.47
Hydrophilic coated catheters	Cardenas 2009 [19]	22		0.06	0.06	
COMBINED SCENARIO						
Uncoated catheters	Cardenas 2009 [19]	23		0.14	0.40	

	Cardenas 2011 [20]	114		0.48		<b>0.92</b>
	De Ridder 2005 [22]	61		0.38		
	Sarica 2010 [21]	10	4	0.27		
Hydrophilic coated catheters	Cardenas 2009 [19]	22		0.06	<b>0.37</b>	
	Cardenas 2011 [20]	105		0.48		
	De Ridder 2005 [22]	60		0.34		
	Sarica 2010 [21]	10	1	0.07		

For hematuria, three studies [20-22] reporting useful data were identified by the systematic literature search (Table 2).

Table 2 – Hematuria rates (mean number of hematuria episodes per patient per year)

	Study	Patients	N. episodes	Years	Rate per patient per year	Weighted mean	Rate ratio
Uncoated catheters	Cardenas 2011 [20]	114	6	0.5	0.11	0.29	1.35
	De Ridder 2005 [22]	59	32	1	0.54		
	Sarica 2010 [21]	10	1	0.1151	0.87		
Hydrophilic coated catheters	Cardenas 2011 [20]	105	14	0.5	0.27	0.39	
	De Ridder 2005 [22]	55	38	1	0.69		
	Sarica 2010 [21]	10	0	0.115	0.00		

### The model

As the management of patients performing IC is an evolving process, Markov multistate models were chosen for the health economic evaluation. A decision tree, combined with two Markov models, was designed to project lifetime health outcomes (life years and QALYs) and economic

consequences related to SCI patients performing IC with hydrophilic or non-hydrophilic urinary catheters.

The Markov model (Figure 1) includes the following health states: alive, symptomatic UTI, hematuria and death. A symptomatic UTI can either resolve or become an antibiotic-resistant UTI. In this case the model distinguishes among first-line resistant UTI, multi-drug resistant UTI and bacteremia. Multi-drug resistant UTI and bacteremia represent severe UTIs that can eventually cause patient death.

It is acknowledged that other complications than the ones included in the model health states may be relevant for patients practicing IC. For example, other infections and inflammations such as epididymo-orchitis, urethritis and prostatitis may occur as a complication of IC as well as strictures, false passage and bladder stones. [23] The “alive” state accounts for baseline rates of these kinds of complications, which have been elicited by key opinion leaders in the field and assumed equal for hydrophilic coated and uncoated catheters (see Supplementary Table 1).

<Figure 1>

A hypothetical cohort of 40-year-old, 80% male patients enters the Markov process in the “alive” state. Population characteristics are assumed to be similar as previously reported for SCI patients performing IC in Italy. [24]

The model is mainly based on the structure presented by Bermingham et al. [2] and focuses on short term consequences of UTIs and hematuria. In contrast to Bermingham et al. [2] who used the annual probability of experiencing at least one UTI, the current model incorporates the estimation of the mean number of UTIs per patient and year, which is similar to the approach used by Clark et al., [3] to give a more precise estimate of costs and patients’ quality of life.

A 1-year Markov cycle length and a lifetime horizon were chosen for baseline analysis. In order to improve the accuracy of the results a half-cycle correction was performed. The model was developed and analyzed in Microsoft Excel®.

### Model quantification

As described above, monthly rates of 0.14 and 0.06 were estimated for symptomatic UTIs in patients using uncoated catheters and hydrophilic coated catheters in the community setting, respectively. These data translate into 1.68 and 0.72 events per year and patient, respectively. For hematuria, 0.29 and 0.39 episodes per year and patient were estimated for uncoated and hydrophilic coated catheters, respectively.

The probabilities of clinical failure after treatment for symptomatic UTI reported by Clark et al. [3] were mainly based on expert opinions, why annual transition probabilities as presented by Bermingham et al. [2] were preferred (Figure 1). The annual probabilities of clinical failure, leading to first-line/multidrug resistant UTI or bacteremia, were applied to the mean number of symptomatic UTIs experienced by the patients over 1 year using uncoated or hydrophilic coated catheters.

As no further transition probabilities were found in literature, the model assumed that “multidrug resistant UTI” state also included healthcare resource consumption related to “first-line resistant UTI” state.

Standardized mortality ratios for men and women with SCI were retrieved by Lidal et al. [25] Mortality rates were further adjusted for age and gender according to Italian mortality tables (ISTAT).

A summary of the model parameters is presented in Table 3.

Table 3 – Model parameters with related sources

Parameter	Base case value	Reference
<b>Population</b>		
Start age (years)	40	[24]
Proportion men	80%	[24]
<b>Utility coefficients for the health states/events</b>		
Alive	0.831	[2]
Symptomatic UTI	0.782	[2]

First-line resistant UTI	0.76	[2]
Multidrug resistant UTI	0.738	[2]
Bacteremia	0.716	[2]
Hematuria	0.738	Assumed equal to Multidrug resistant UTI
Annual transition probabilities		
Symptomatic UTI → First-line resistant UTI	0.083	[2]
Symptomatic UTI → Multidrug resistant UTI	0.07	[2]
Symptomatic UTI → Bacteremia	0.036	[2]
Multidrug resistant UTI → Death	0.026	[2]
Bacteremia → Death	0.077	[2]
Standardized mortality ratios for SCI patients	men 1.8, women 4.9	[25]
Mean number of events per patient per year (uncoated catheters)		
Symptomatic UTI	1.68	[19]
Hematuria	0.29	[20-22]
Rate ratios		
Symptomatic UTI (hydrophilic coated vs. uncoated catheters)	0.47	[19]
Hematuria (hydrophilic coated vs. uncoated catheters)	1.35	[20-22]
Costs		
Unit cost, uncoated catheter	0.25€	Tender data for Italy
Unit cost, hydrophilic coated catheter	1.70€	Tender data for Italy
Alive (annual cost)	954.48€	Data processing from e-survey
Symptomatic UTI	1,091.86€	Data processing from e-survey
First-line resistant UTI	401.20€	Data processing from e-survey
Multidrug resistant UTI	775.36€	Data processing from e-survey
Bacteremia	3,664.16€	Data processing from e-survey
Hematuria	106.10€	Data processing from e-survey
Death for bacteremia	6,057.70€	Data processing from e-survey
Death for Multidrug resistant UTI	9,721.86€	Data processing from e-survey
Events duration		
Symptomatic UTI (days)	4	Data processing from e-survey
1st line resistant UTI (days)	8	Data processing from e-survey

Multidrug resistant UTI (days)	16	Data processing from e-survey
Bacteremia (days)	37	DRG 576
Hematuria (days)	2	Data processing from e-survey
Bacteremia, if leading to death (days)	65	DRG 575
Pre-death, Multidrug resistant UTI, hospitalization (days)	65	DRG 575

DRG=Diagnosis Related Group

### Healthcare resource consumption and costs

As the analysis was performed from the Italian Healthcare System perspective, all costs related to the consumption of direct healthcare resources were estimated and expressed in Euros (2015 value).

Clinical pathways and healthcare resource consumption for the management of symptomatic UTIs, first-line resistant UTIs, multidrug resistant UTIs, hematuria episode and bacteremia were estimated by study specific questionnaire to urologists and neuro-urologists. All the clinicians (25) belonging to the NUS team (Italian spinal neuro-urologist group) of Fondazione Italiana Continenza (Italian Continence Foundation),[26] which treat higher volumes of patients across Italy, got access to a web version of the questionnaire (developed with Qualtrics© software) between 15<sup>th</sup> July 2015 to 15<sup>th</sup> October 2015 (a printed version of the questionnaire is available upon request). The questionnaire included four sections: 1) introduction with a case vignette, [27] 2) patient's monitoring (relevant annual exams, lab test, visits, inpatient stay and drugs), 3) management of UTIs, bacteremia and hematuria, and 4) future scenarios of catheters use. On the basis of their clinical experience, clinicians were asked to estimate healthcare utilization. For example, the percentage of patients involved, regimen applied (outpatient, day-hospital or inpatient stay), daily dose, duration and hospital cost of drugs for general management and/or for management of a period of UTI, bacteremia and hematuria (drug costs are generally provided by an administrative office within the Hospital).

The last section of the questionnaire included a forecast of possible future scenarios (1, 3 and 5 years) of utilization of uncoated and hydrophilic coated catheters in Italy.

The results from the questionnaires were summarized to estimate healthcare resource utilization. For each healthcare resource (exam, visit, hospitalization, etc.) reported, a weighted mean was calculated based on the number of responders.

The cost of resource consumption for the different events was calculated by multiplying the quantity of resources consumed by unit costs derived from official sources, i.e. diagnosis-related groups (DRGs) reimbursement for hospitalizations, official tariffs for outpatient services, and hospital prices for drugs. When hospital prices for drugs were missing, a search was performed through the Italian Pharmaceutical Database ([www.federfarma.it](http://www.federfarma.it)), reporting cost data for the national healthcare service.

Four catheters per day and patient were assumed, as this was the reimbursement level provided by the local health agencies. [18] The unit cost was estimated from tender data to 1.70€ and 0.25€ for hydrophilic coated and uncoated catheters, respectively. In Italy, the lubricant gel for uncoated catheters is paid by the patients why this cost was omitted in the model.

During hospital stays, catheter costs are part of the DRG reimbursement excluding the need for additional device costs in the model.

Quality of life estimates

The search for utility coefficients for SCI patients performing IC was performed through Pubmed, Embase, Web of Science databases and the Cost-Effectiveness Analysis Registry. [28] Two studies [29-30] and a review [31] were found reporting utility values for SCI patients experiencing UTIs. The first one [29], reported utility values (estimated by HUI-Mark III health status classification system) of 0.28 and 0.15 for no/mild UTI and moderate/significant UTI, respectively. The second study [30], reported utility values for UTI of 0.58 and 0.60 estimated by SF36 and SF12 questionnaires, respectively. The review [31] included an additional study conducted by Vogel and Zebracki from which utility values of 0.831, 0.782 and 0.738 were estimated for no UTI, UTI and severe UTI, respectively. From the database search no utility values were found for hematuria and bacteremia health states.

Additional utility values were retrieved from Bermingham et al. [2] and Clark et al. [3] All values are summarized in Supplementary Table 1.

The model included utility values referred to the study by Bermingham et al. [2]

For hematuria, a utility value of 0.738 (as for multidrug resistant UTI state) was assumed.

The duration of the different events was estimated from the pharmacological treatment duration reported by the questionnaires, with the exception of both multidrug resistant UTI and bacteremia leading to death for which the length of stay threshold of the related DRGs was considered.

### Analyses

Both incremental cost-effectiveness and cost-utility ratios (ICER, ICUR) of hydrophilic coated versus uncoated catheters were calculated by dividing the incremental cost by the incremental health improvement. Life years, QALYs and costs were discounted with a 3.5% yearly rate.[32] Transition probabilities, costs and utilities were entered into the model along with a distribution: beta for utilities and proportions of patients experiencing different kinds of UTIs, log-normal for relative risks and gamma for costs. Deterministic and probabilistic sensitivity analyses (PSA) were performed to test the robustness of the model. Univariate analyses were performed according to the main parameters; second-order Monte-Carlo analyses (1,000 simulations) were conducted and related acceptability curve was plotted.

Further analyses were performed considering UTI rates for 1) hospital period and 2) combined (hospital plus community) scenario (based on data reported in Table 1).

### Budget Impact Analysis - BIA

Based on the conclusion from the CEA model, a companion budget impact model [33] was developed to address hypothetical changes to the Italian Healthcare Service of an increasing proportion of hydrophilic coated catheters.

In order to perform the BIA, a review of epidemiological data focused on SCI patients performing IC was carried out.

The prevalence of SCI patients in Italy resulted in the range 60,000-70,000 according to a national registry [34], while the incidence (data from the Italian registry) showed a decrease from 20-25 to 7.8 per million inhabitants. Based on the study by Zlatev et al.,[35] it was assumed that 60% of patients perform IC. The total number of prevalent patients with SCI performing IC in Italy was estimated to be about 39,000 (65,000\*60%), while the total number of incident patients was about 285. It was assumed that the distribution of the incident population was the same of the prevalent population (mean age 40 years and 80% men).

The current scenario of patient distribution between the two considered devices was estimated from clinical input as 20% uncoated and 80% hydrophilic coated catheters. The estimation of future scenarios, including an increased proportion of hydrophilic coated catheters, was based on key opinion leaders' replies to the questionnaire.

The cost of the current and future scenarios was determined by multiplying the cost for each intervention by the proportion of the eligible population using it, taking into account both prevalent and subsequent yearly incident cohorts. Financial streams were presented as undiscounted costs as the focus of the analysis was expected budget at each point. [33]

**Results**

Healthcare resource consumption and costs

Nine of 25 clinicians completed the questionnaire, representing institutions with the highest volumes of treated SCI patients in Italy. The estimated healthcare resource utilization is reported

per event in Supplementary Table 2. Reported care pathways were consistent with previous published literature. [36]

The “alive” health state in the model refers to usual patient year including control visits, exams or hospitalizations for causes other than UTIs (e.g. urethral strictures, bladder stones). All other health states consider healthcare resources consumption for management of a single event (e.g. symptomatic UTI, hematuria, bacteremia, etc.). For drugs, the mean dosage per patient was reported together with the proportion of administered patients.

The final estimated event durations were as follows; 2 days for hematuria, 4 days for symptomatic UTI, additional 8 days for first-line resistant UTI, additional 8 days for multidrug resistant UTI (total 4+8+8=20 days), 37 days for hospitalization for bacteremia (DRG 576) and 65 days for infection leading to death (DRG 575).

In case of bacteremia leading to patient death, the healthcare resources related to “Infection leading to patient death” (see Supplementary Table 2) were applied (the management of the episode of bacteremia is included in the DRG 575).

Supplementary Table 3 summarizes the main model parameters (utility coefficients, transition probabilities, event rates and health states associated costs) with related probability distributions.

### Baseline results

The model estimated an average life expectancy of 18.3 years (15.2 QALYs) for a study population using hydrophilic coated catheters and 17.3 years (14.3 QALYs) for a study population using uncoated catheters. The mean lifetime costs per patient were 82,915€ and 62,457€ for hydrophilic coated and uncoated catheters, respectively. For hydrophilic coated catheters this resulted in an ICER of 20,761€ and an ICUR of 24,405€. Although there is no official cost-effectiveness threshold for Italy, the reported proposed thresholds vary between 25,000€–40,000€, [37] 36,500€, [38] 60,000€, [39] and 66,402€ (3 times the Italian gross domestic product per capita as suggested by

the WHO). [40-41] This suggests that the ICER/ICUR for hydrophilic coated catheters is lower than recommended threshold values and thus a cost-effective option.

Considering a lifetime horizon, hydrophilic coated catheters may reduce the frequency of UTIs of about 50% (from 48 to 24) in comparison to uncoated catheters. Considering the significant impact of UTIs, accounting for about 23% to 63% of the total lifetime cost for SCI patients practicing intermittent catheterization, prevention is of high importance.

A PSA was performed on the ICUR considering the discounted scenario. The acceptability curve obtained from the Monte Carlo simulation is shown in Figure 2. Given the varying Italian threshold values of 25,000€–40,000€, 36,500€, 60,000€ and 66,402€, hydrophilic coated catheters have about 47-86%, 77%, 97% and 98% probability of being cost effective, respectively. Considering the the UK-specific threshold value of 20,000-30,000£ recommended by NICE [32] (equal to 26,400€-39,600€ at an exchange rate of 1.32), hydrophilic coated catheters have a 48%-86% probability of being cost effective.

<Figure 2>

The scenario analyses performed considering hospital period and combined (hospital plus community) settings resulted in ICURs equal to 11,908€/QALY (ICER 10,097€/LY) and 97,019€/QALY (ICER 82,188€/LY), respectively.

The model results are summarized in Table 4.

Table 4 – Summary of the model results

Catheter	Cost (€)	Δ Cost (€)	LY	ΔLY	QALYs	ΔQALYs	ICER (€/LY)	ICUR (€/QALY)
Uncoated	€ 62,457		17.299		14.332			
Hydrophilic	€ 82,915	€ 20,459	18.284	0.985	15.170	0.838	€ 20,761	€ 24,405

One-way sensitivity analyses were performed for ICUR (discounted scenario) on the main model parameters. The results are presented in a tornado diagram in Figure 3 for the ten parameters responsible for the main ICUR variations (see Supplementary Table 4 for complete results). The parameters with the greatest impact on ICUR were the relative risk (rate ratio) of developing a symptomatic UTI (for hydrophilic coated catheters vs. uncoated catheters), the mean number of symptomatic UTIs per patient and year for uncoated catheters, the unit cost for hydrophilic catheter and the number of catheters used per day. For example, a rate ratio of developing symptomatic UTI higher than 0.70 would result ICUR values over 60,000€. Hydrophilic coated catheters were the dominant choice when considering a unit cost of 0.85€ or lower but for a unit cost of 2.55€ the ICUR exceeded 50,000€. Also, lowering of the utility value for the “alive” health state to 0.42 resulted in an ICUR higher than 65,000€.

<Figure 3>

### Budget impact analysis

As hydrophilic coated catheters were found to be cost-effective, a BIA was performed to considering future scenarios with an increasing proportion of users among patients performing IC. The proportions for possible future scenarios were estimated by the questionnaires. Focusing on uncoated and hydrophilic coated catheters only, the clinicians reported proportions of hydrophilic coated catheter use of 83%, 88% and 89% after 1, 3 and 5 years, respectively.

Table 5 reports the annual cost for SCI patients performing IC with either uncoated or hydrophilic coated catheters. For both catheter types the total cost per year is weighted according to the proportion of use (i.e. 80% hydrophilic coated and 20% uncoated catheters for current scenario – year 0). The last row summarizes the total national healthcare budget. An increasing use of hydrophilic coated catheters, results in an increase of the total budget from about 169 to about 172 million Euros.

Table 5 – Budget impact analysis

Year	0	1	2	3	4	5
Hydrophilic catheters: % of utilization	80%	83%	83%	88%	88%	89%
Prevalent population	€ 176,295,044	€ 175,162,382	€ 173,997,665	€ 172,799,276	€ 171,558,544	€ 170,267,090
Incident population		€ 1,286,156	€ 1,277,893	€ 1,269,395	€ 1,260,653	€ 1,251,601
Incident population			€ 1,286,156	€ 1,277,893	€ 1,269,395	€ 1,260,653
Incident population				€ 1,286,156	€ 1,277,893	€ 1,269,395
Incident population					€ 1,286,156	€ 1,277,893
Incident population						€ 1,286,156
Weighted cost for hydrophilic catheters	€ 141,036,036	€ 146,452,287	€ 146,546,222	€ 155,436,794	€ 155,454,323	€ 157,185,381
Uncoated catheters: % of utilization	20%	17%	17%	12%	12%	11%
Prevalent population	€ 140,062,430	€ 138,588,340	€ 137,098,619	€ 135,592,327	€ 134,062,925	€ 132,504,223
Incident population		€ 1,021,822	€ 1,011,068	€ 1,000,199	€ 989,210	€ 978,053
Incident population			€ 1,021,822	€ 1,011,068	€ 1,000,199	€ 989,210
Incident population				€ 1,021,822	€ 1,011,068	€ 1,000,199
Incident population					€ 1,021,822	€ 1,011,068
Incident population						€ 1,021,822
Weighted cost for uncoated catheters	€ 28,012,486	€ 23,733,728	€ 23,652,356	€ 16,635,050	€ 16,570,227	€ 15,125,503

TOTAL	€ 169,048,522	€ 170,186,014	€ 170,198,578	€ 172,071,844	€ 172,024,550	€ 172,310,884
HEALTHCARE						
BUDGET						

## Discussion

IC is considered the method of choice for the management of neurogenic bladder dysfunctions. Patients performing IC entail a substantial economic burden on the healthcare system as infections and urethral trauma are common and result in frequent hospitalizations and high morbidity. Although different catheters with various characteristics in terms of medical safety, treatment functionality, patient comfort and environmental performances are available, there is currently no robust consensus on which catheter type is the best. Recent meta-analyses investigating the impact of different catheters types on UTI rate and hematuria reported conflicting results. One study [42] concluded that hydrophilic coated catheters are associated with a significant risk reduction of UTI and hematuria as compared to non-hydrophilic catheters while another study was unable to differentiate between catheter types and techniques. [1]

The aim of the present study was to conduct cost-effectiveness and budget impact analyses of different catheters used for IC. The results were meant to support the decision making process in how to allocate scarce healthcare resources and maximizing patients' health while controlling costs. In Italy, the provision of disposable medical devices for daily repeated use, such as catheters for IC, is currently regulated by the Ministry of Health (MoH), [43] who defines a list of medical devices supplied directly to patients and reimbursed by the Italian NHS. In recent times, the coverage of medical devices has been the object of debates in Italy. The MoH has decided that more information on value contribution of medical devices to both patients and the healthcare systems are necessary. For this reason, a National Health Technology Assessment Programme has been developed that refers to cost-effectiveness analysis as the main decision tool to measure the incremental value of innovative technologies over the standard of care. [44-46]

Considering a lifetime horizon, hydrophilic coated catheters resulted in an ICUR of 24,405€/QALY and an ICER of 20,761€/LY. Accordingly, hydrophilic coated catheters were found to be cost-effective in comparison to uncoated catheters given the available range of thresholds values proposed for Italy (from 25,000€ to about 66,000€). PSA supported this findings, suggesting a cost-effective probability between 50-100% when considering variations and uncertainty of the model.

The base-case findings are in line with conclusions reported by Clark and colleagues [3]. They considered a UK-setting and a cost-effectiveness threshold of 30,000£ (about 40,000€). The results however, differ from the report by Bermingham et al., [2] who concluded that uncoated catheters are the most cost-effective when compared to all the other catheter types. The reason behind this difference is likely related to the difference in selecting studies and data for the underlying meta-analysis investigating UTI risk. Bermingham et al. [2] used data from a meta-analysis that estimated the risk of experiencing at least one UTI for each catheter type. Since there could be a great variation in the number of UTIs experienced by each patient, this assumption could potentially have hidden a risk-reducing efficacy related to hydrophilic coated catheters. A study [47] evaluating self-reported catheter practices and associated problems, for people mainly performing IC with uncoated catheters, found an annual rate of 2.3 (95%CI 1.8-3) symptomatic UTIs treated with an antibiotic.

When a lower cost-effectiveness threshold was considered (i.e. 20,000£ = about 26,400€), the probability that hydrophilic coated catheters may be a cost-effective choice was about 50%, partially supporting the conclusions presented by Bermingham and colleagues. [2]

Differently from Clark et al., [3] the present CE model focused only on short-term consequences of symptomatic UTIs, excluding lifetime effects on renal function. Since the probability of developing UTIs was found to be lower for hydrophilic coated catheters versus uncoated ones, this suggests that results are conservative estimates of the CE results. As a consequence, the scenario analyses considering community setting and hospital and community settings together reported higher ICER and ICUR in comparison with the findings of the above cited study.

Another difference is related to the cost of the two devices. While in UK the cost of an uncoated catheter is slightly inferior to the cost of a hydrophilic coated one, in Italy the cost for uncoated catheters is very low; about 25% of the cost of the hydrophilic coated catheter. The increased cost for hydrophilic coated catheters is partially compensated by the costs savings due to lower number of developed UTIs.

Our study is a cost-effectiveness analysis comparing hydrophilic coated to uncoated catheters that also includes a budget impact analysis. The BIA is considered to add important information for decision-makers who need to estimate the impact on healthcare expenditures of introducing new health technologies in regular practice.

This study estimated the consumption of healthcare resources by soliciting experts' opinion with the aim of providing real-world costing data. This is important especially for medical devices since their use in regular practice often differs from what established in experimental settings. [48] Also, the fact that the consumption of healthcare resources has been represented in natural units - as suggested by the EUnetHTA guidelines [49] - will allow costs adjustment to other countries.

The present study has some limitations. First of all, clinical effectiveness data were derived from few RCTs with less than 50 participants and with variations in length of follow-up and definitions of UTI. Moreover, the model focused mainly on complications as UTI and hematuria, for which different rates were estimated for hydrophilic coated and uncoated catheters. UTIs are recognized as the most frequent complications, while epididymitis and urethritis are relatively rare. [50] To our knowledge there are no randomized controlled data on other complications for different catheter types. However, observational studies reported fewer trauma and urethral inflammation for hydrophilic coated catheters that would potentially increase their cost-effectiveness on a life time perspective. [51-52]

As regards the estimation of the healthcare resources, it must be noted that data derived from self-reported questionnaire may be limited by varying recollection and poor generalizability. Variables derived from prospective observational multi-centre studies would increase the validity of the

current model. Observational studies would also serve to confirm clinical evidence on comparative effectiveness of catheters in addition to RCTs.

Overall, the analysis is based on varying levels of evidence and assumptions and results need to be considered cautiously.

The findings of the present study support the use of hydrophilic coated catheters but are limited to costs from a healthcare perspective. A broader evaluation, also including costs from a societal perspective, would increase the understanding of the economic sustainability of these devices.

**Corresponding author statement**

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### Data sharing

PRISMA statement is available in Appendix.

### Declaration of competing interests

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (1) CeRGAS Bocconi has support from ASBM Srl for the submitted work; (2) CR and RT have no relationships with ASBM Srl that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (4) CR and RT have no non-financial interests that may be relevant to the submitted work.

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### Details of contributors

Carla Rognoni - study concept and design; analysis and interpretation of data; drafting of the manuscript.

Rosanna Tarricone - study supervision; obtained funding; critical revision of the manuscript.

**Transparency declaration**

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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**References**

1. Prieto J, Murphy CL, Moore KN, Fader M. Intermittent catheterisation for long-term bladder management. Cochrane Database Syst Rev 2014 Sep 10;9:CD006008.

2. Bermingham SL, Hodgkinson S, Wright S, et al. Intermittent self catheterisation with hydrophilic, gel reservoir, and non-coated catheters: a systematic review and cost effectiveness analysis. BMJ. 2013 Jan 8;346:e8639.

3. Clark JF, Mealing SJ, Scott DA, et al. A cost-effectiveness analysis of long-term intermittent catheterisation with hydrophilic and uncoated catheters. *Spinal Cord*. 2015 Jul 21.
4. Bakke A, Digraanes A, Høisaeter PA. Physical predictors of infection in patients treated with clean intermittent catheterization: a prospective 7-year study. *Br J Urol*. 1997 Jan;79(1):85-90.
5. Turi MH, Hanif S, Fasih Q, et al. Proportion of complications in patients practicing clean intermittent self-catheterization (CISC) vs indwelling catheter. *J Pak Med Assoc*. 2006 Sep;56(9):401-4.
6. Nicolle LE. Urinary tract infections in patients with spinal injuries. *Curr Infect Dis Rep*. 2014 Jan;16(1):390.
7. Ciani O, Grassi D, Tarricone R. An economic perspective on urinary tract infection: the "costs of resignation". *Clin Drug Investig*. 2013 Apr;33(4):255-61.
8. Lai KK, Fontecchio SA. Use of silver-hydrogel urinary catheters on the incidence of catheter-associated urinary tract infections in hospitalized patients. *Am J Infect Control*. 2002;30(4):221-5.
9. Karchmer TB, Giannetta ET, Muto CA, et al. A randomized crossover study of silver-coated urinary catheters in hospitalized patients. *Arch Intern Med*. 2000;160(21):3294-8.
10. McNutt R, Johnson TJ, Odwazny R, et al. Change in MS-DRG assignment and hospital reimbursement as a result of Centers for Medicare & Medicaid changes in payment for hospital-acquired conditions: is it coding or quality? *Qual Manag Health Care*. 2010;19(1):17-24.
11. Saint S. Clinical and economic consequences of nosocomial catheter-related bacteriuria. *Am J Infect Control*. 2000;28(1):68-75.
12. Tambyah PA, Knasinski V, Maki DG. The direct costs of nosocomial catheter-associated urinary tract infection in the era of managed care. *Infect Control Hosp Epidemiol*. 2002;23(1):27-31.

13. Anderson DJ, Kirkland KB, Kaye KS, et al. Underresourced hospital infection control and prevention programs: penny wise, pound foolish? *Infect Control Hosp Epidemiol.* 2007;28(7):767-73.

14. Bardsley A. Intermittent Self-Catheterisation in women: reducing the risk of UTIs. *Urology supplements.* 2014;22(18).

15. Heard L, Buhrer R. How do we prevent UTI in people who perform intermittent catheterization? *Rehabil Nurs.* 2005 Mar-Apr;30(2):44-5,61.

16. Bennett E. Intermittent self-catheterisation and the female patient. *Nurs Stand* 2002; 17: 37–42.

17. Igawa Y, Wyndaele JJ, Nishizawa O. Catheterization: possible complications and their prevention and treatment. *Int J Urol.* 2008 Jun;15(6):481-5.

18. [http://www.sanita24.ilsole24ore.com/pdf2010/Sanita2/\\_Oggetti\\_Correlati/Documenti/Dal-Governo/Allegato%202%20Ausili%20Monouso%202015\\_Filigrana.pdf](http://www.sanita24.ilsole24ore.com/pdf2010/Sanita2/_Oggetti_Correlati/Documenti/Dal-Governo/Allegato%202%20Ausili%20Monouso%202015_Filigrana.pdf) (accessed 10 Jul 2016).

19. Cardenas DD, Hoffman JM. Hydrophilic catheters versus noncoated catheters for reducing the incidence of urinary tract infections: a randomized controlled trial. *Arch Phys Med Rehabil.* 2009; 90:1668–1671.

20. Cardenas DD, Moore KN, Dannels-McClure A, et al. Intermittent catheterization with a hydrophilic-coated. catheter delays urinary tract infections in acute spinal cord injury: a prospective, randomized, multicenter trial. *PM R.* 2011 May;3(5):408-17.

21. Sarica S, Akkoc Y, Karapolat H, Aktug H. Comparison of the use of conventional, hydrophilic and gel-lubricated catheters with regard to urethral micro trauma, urinary system infection, . and patient satisfaction in patients with spinal cord injury: a randomized controlled study. *Eur J Phys Rehabil Med.* 2010 Dec;46(4):473-9.

22. De Ridder DJ, Everaert K, Fernández LG, et al. Intermittent catheterisation with hydrophilic-coated catheters (SpeediCath). reduces the risk of clinical urinary tract infection in spinal cord

injured patients: a prospective randomised parallel comparative trial. *Eur Urol.* 2005 Dec;48(6):991-5.

23. Vahr S, Cobussen-Boekhorst H, Eikenboom J, et al. Catheterisation. Urethral intermittent in adults: dilatation, urethral intermittent in adults. Arnhem (The Netherlands): European Association of Urology Nurses (EAUN); 2013 Mar. 96 p.

24. Euro Mediterranean Rehabilitation Summer School - <http://www.emrss.it/> (accessed 10 Mar 2016).

25. Lidal IB, Snekkevik H, Aamodt G, et al. Mortality after spinal cord injury in Norway. *J Rehabil Med.* 2007 Mar;39(2):145-51.

26. <http://www.contenuti-web.com/continenza/fondazione-0000409.html> (accessed 10 Jul 2016).

27. Fattore G, Torbica A. Cost and reimbursement of cataract surgery in Europe: a cross-country comparison. *Health Econ.* 2008 Jan;17(1 Suppl):S71-82.

28. CEA Registry – <https://research.tufts-nemc.org/cear4/SearchingtheCEARegistry> (accessed 10 Jul 2016).

29. Craven C, Hitzig SL, Mittmann N. Impact of impairment and secondary health conditions on health preference among Canadians with chronic spinal cord injury. *J Spinal Cord Med.* 2012 Sep;35(5):361-70.

30. Lee BB, King MT, Simpson JM, Haran MJ, Stockler MR, Marial O, Salkeld G. Validity, responsiveness, and minimal important difference for the SF-6D health utility scale in a spinal cord injured population. *Value Health.* 2008 Jul-Aug;11(4):680-8.

31. Bermingham SL, Ashe JF. Systematic review of the impact of urinary tract infections on health-related quality of life. *BJU Int.* 2012 Dec;110(11 Pt C):E830-6.

32. National Institute for Clinical Excellence. Guide to the Methods of Technology Appraisal. London: National Institute for Clinical Excellence, 2004.

33. Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health*. 2014 Jan-Feb;17(1):5-14.

34. GISEM - Italian Group for the Epidemiological Study of Spinal Cord Injuries - <http://www.istud.it/superabile/lesione.asp> (accessed 10 Jul 2016).

35. Zlatev DV, Shem K, Elliott CS. How many spinal cord injury patients can catheterize their own bladder? The epidemiology of upper extremity function as it affects bladder management. *Spinal Cord*. 2016 Jan 19.

36. Biardeau X, Corcos J. Intermittent catheterization in neurologic patients: Update on genitourinary tract infection and urethral trauma. *Ann Phys Rehabil Med*. 2016 Apr;59(2):125-9.

37. Associazione Italiana di Economia Sanitaria (AIES): Proposta di linee guida per la valutazione economica degli interventi sanitari. *PharmacoEconomics–Italian Res Artic*. 2009, 11: 83-93. 10.1007/BF03320660.

38. Lucioni C, Ravasio R. How to evaluate the results of a pharmacoeconomic study? *Pharmacoeconomics – Italian Research Articles*. 2004; 6(3):121–130.

39. Messori A, Santarlasci B, Trippoli S, Vaiani M. Clinical benefit and economic value: methodology and an economic application. *Pharmacoeconomics – Italian Research Articles*. 2003;5(2):53–67.

40. World Health Organization. *World Health Organization: Choosing Interventions that are Cost Effective (WHO-CHOICE)*. Geneva: World Health Organization, 2012.

41. [http://www.who.int/choice/costs/CER\\_levels/en](http://www.who.int/choice/costs/CER_levels/en) (accessed 10 Jul 2016).

42. Li L, Ye W, Ruan H, Yang B, Zhang S, Li L. Impact of hydrophilic catheters on urinary tract infections in people with spinal cord injury: systematic review and meta-analysis of randomized controlled trials. *Arch Phys Med Rehabil*. 2013 Apr;94(4):782-7.

43. Ministerial Decree 27th August 1999, n.332, <http://www.gazzettaufficiale.it/eli/id/1999/09/27/099G0404/sg> (accessed 10 Jul 2016).
44. National Health Pact 2014-2016 (art. 26), [http://www.salute.gov.it/imgs/C\\_17\\_pubblicazioni\\_2309\\_allegato.pdf](http://www.salute.gov.it/imgs/C_17_pubblicazioni_2309_allegato.pdf) (accessed 10 Jul 2016).
45. Law n. 208, 28 December 2015, Stability Law - Legge di stabilità 2016, <http://www.gazzettaufficiale.it/eli/id/2014/12/29/14G00203/sg> (accessed 10 Jul 2016).
46. Law n. 190, 23 December 2014, Stability Law - Legge di stabilità 2015, <http://www.gazzettaufficiale.it/eli/id/2015/12/30/15G00222/sg> (accessed 10 Jul 2016).
47. Wilde MH, Brasch J, Zhang Y. A qualitative descriptive study of self-management issues in people with long-term intermittent urinary catheters. *J Adv Nurs*. 2011 Jun;67(6):1254-63.
48. Drummond M, Griffin A, Tarricone R. Economic evaluation for devices and drugs--same or different? *Value Health*. 2009 Jun;12(4):402-4. .
49. <http://www.eunethta.eu> (accessed 10 Jul 2016).
50. Wyndaele J. Complications of intermittent catheterization: their prevention and treatment. *Spinal Cord*. 2002 Oct;40(10):536-41.
51. Hellström P, Tammela T, Lukkarinen O, Kontturi M. Efficacy and safety of clean intermittent catheterization in adults. *Eur Urol*. 1991;20(2):117-21.
52. Vaidyanathan S, Soni BM, Dundas S, Krishnan KR. Urethral cytology in spinal cord injury patients performing intermittent catheterisation. *Paraplegia*. 1994 Jul;32(7):493-500.

## Figure legends

Figure 1 – Simplified Markov model representation. Patients start the Markov process in the “Alive” state, where they can remain or move to “Symptomatic UTI” or “Hematuria” states. These are

considered sub-states of “Alive” state since their duration lasts less than one year. The model takes into account that patients may die for other causes than for UTI (death of other causes). UC=uncoated catheters, HC=hydrophilic coated catheters, pt=patient.

Figure 2 - ICUR acceptability curve

Figure 3 – Tornado diagram showing one-way sensitivity analyses on ICUR value (24,405€). Upper and lower limits of variables’ values referring to the ICUR extremes are indicated next to the bars.

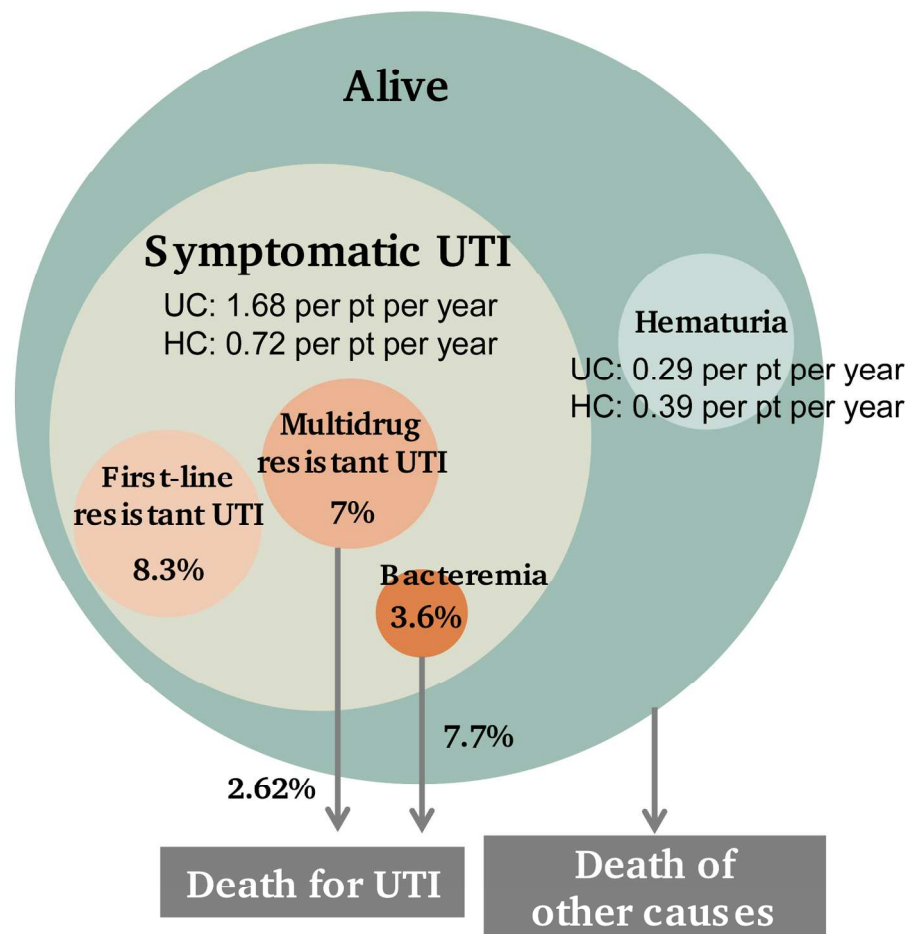


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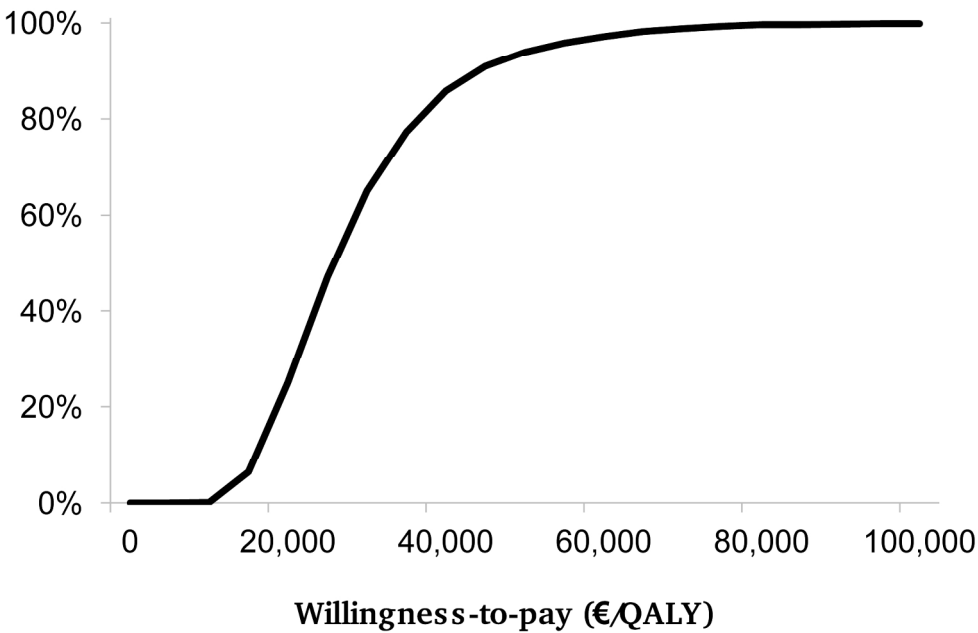


Figure 2 - ICUR acceptability curve  
179x126mm (300 x 300 DPI)

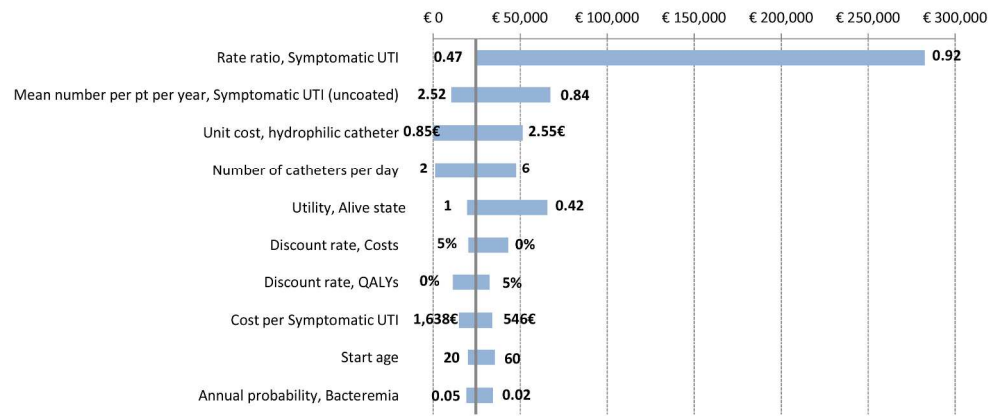


Figure 3 – Tornado diagram showing one-way sensitivity analyses on ICUR value (24,405€). Upper and lower limits of variables' values referring to the ICUR extremes are indicated next to the bars.

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Supplementary Table 1 – Summary of the retrieved utility values for the different health states

Study	no UTI	UTI	Severe UTI	Bacteremia
Craven 2012 [29]		0.28 (SD=0.28)	0.15 (SD=0.18)	
Lee 2008 [30]	0.68-0.70 (SD=0.01)	0.58-0.60 (SD=0.01)		
Birmingham 2013 [2]	0.831 (95%CI 0.809-0.852)	0.782 (95%CI 0.764-0.799)	First-line resistant UTI 0.760 (95%CI 0.685-0.834)  Multidrug resistant UTI 0.738 (95%CI 0.688-0.787)	0.716 (95%CI 0.645-0.786)
Clark 2015 [3]	0.468	disutility 0.060	disutility 0.104 (antibiotic resistant)  disutility 0.160 (UTI not responding to initial treatment)	

CI=confidence interval, SD=standard deviation

Supplementary Table 2 – Healthcare resource consumption for the considered health states/events

Health state	Category	Type	mean number per patient	dosage (mg) per patient	% patients
Alive	Visits	Specialist visit	1.99		
	Exams/procedures	Abdomen ultrasound	0.11		
		Bladder ultrasound	0.81		
		Creatinine	0.20		
		Magnetic resonance imaging	0.02		
		Pelvic floor examination	0.03		
		X-rays	0.06		
		Scintigraphy	0.01		
		Urine culture	3.60		
		Urine exam	2.39		
		Urodynamics	0.46		
		Video-urodynamics	0.17		
	Hospitalization (DRG)	313 - Urethral Procedures, Age Greater than 17 without CC	0.01		
		309 - Minor Bladder Procedures without CC	0.01		
		323 - Urinary Stones with CC and/or ESW Lithotripsy	0.03		
		324 - Urinary Stones without CC	0.02		
		325 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 with CC	0.03		
		326 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 without CC	0.14		
		329 - Urethral Stricture, Age Greater than 17	0.01		

		without CC			
	Drugs	Antimuscarins		465	73%
		Botulinum toxin injection	2		25%
		Antibiotics (prophylaxis): sulfamethoxazole+trimethoprim, amoxicillin, levofloxacin, ciprofloxacin		5,761	16%
Symptomatic UTI	Visits	Specialist visit	0.93		
	Exams/procedures	Creatinine	0.11		
		Bladder ultrasound	0.41		
		Blood culture	0.02		
		Complete blood count	0.11		
		Urine exam	0.78		
		Kidney functionality	0.11		
		Urine culture	1.22		
	Hospitalization (DRG)	321 - Kidney and Urinary Tract Infections, Age Greater than 17 without CC	0.52		
First-line resistant UTI (resources in addition to symptomatic UTI)	Drugs	Antibiotics: amikacin, amoxicillin, ampicillin, cefixime, cefpodoxim, ceftriaxone, ciprofloxacin, imipenem, levofloxacin, meropenem, prulifloxacin, sulfamethoxazole+trimethoprim		22,411	127%*
	Visits	Specialist visit	1.17		
	Exams/procedures	Stool culture	0.01		
		Creatinine/glycemia	0.44		
		Abdomen ultrasound	0.11		
		Bladder ultrasound	0.37		
		Blood culture	0.33		
		Urine exam	1.44		
		Video-urodynamics	0.11		

		Lactate	0.11		
		Polymerase Chain Reaction	0.11		
		Urine culture	1.78		
		Erythrocyte sedimentation rate	0.11		
		Hospitalization (DRG)	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.07	
Multidrug resistant UTI (resources in addition to first-line resistant UTI)	Drugs	Antibiotics: amikacin, ceftazidime, ceftriaxone, gentamicin, imipenem, meropenem, minocycline, piperacillin, thienamycin		16,278	89%
	Visits	Specialist visit	1.2		
		Day-hospital	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.02	
	Exams/procedures	Cystoscopy	0.07		
		Colonscopy	0.11		
		Bladder ultrasound	0.44		
		Bact smear-lower gastro-intestinal	0.11		
		Bowel diagnostic procedure NEC	0.13		
		Computerized tomography scan	0.13		
		Urine exam	1.33		
		Urine culture	1.56		
		Video-urodynamics	0.11		
		Blood culture	0.11		
		Intestinal x-ray NEC	0.11		
	Hospitalization (DRG)	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.03		
	Drugs	Antibiotics: amikacin, imipenem, meropenem, piperacillin		7,556	34%

Bacteremia	Hospitalization (DRG)	576 - Septicemia without mechanical ventilation	0.59		
		320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.03		
	Day-hospital	576 - Septicemia without mechanical ventilation	0.22		
	Drugs	Antibiotics: cefepime, ceftazidime, imipenem, levofloxacin, meropenem, teicoplanin		12,311	56%
Infection leading to patient death	Hospitalization (DRG)	575 - Septicemia with mechanical ventilation >=96 h	0.45		
	Drugs	Antibiotics: amikacin, imipenem, meropenem, vancomycin		12,222	34%
Hematuria	Visits	Specialist visit	0.71		
	Exams/procedures	Cystoscopy	0.02		
		Bladder ultrasound	0.24		
		Urine exam	0.56		
		Percutaneous cystostomy	0.06		
		Urethroscopy	0.21		
		Urine culture	0.22		
	Hospitalization (DRG)	309 - Minor Bladder Procedures without CC	0.002		
		332 - Other Kidney and Urinary Diagnoses, Age Greater than 17 without CC	0.04		
		326 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 without CC	0.01		
	Drugs	Antibiotics: cefepime, ciprofloxacin, levofloxacin		2,556	30%

\* More than one treatment is administered, DRG=Diagnosis Related Group, CC=complications, NEC=not elsewhere classifiable

Supplementary Table 3 – Model parameters and distributions used in PSA (if not otherwise specified, variation ranges refer to +/- 50% of the baseline value)

Parameter	Base case value	Variation range	Distribution type	Alpha	Beta
<b>Utility coefficients for the health states/events</b>					
Alive	0.831	0.809 - 0.852 §	beta	969.1	197.1
Symptomatic UTI (4 days)	0.782	0.764 - 0.799 §	beta	1671.49	465.96
First-line resistant UTI (8 days)	0.76	0.685 - 0.834 §	beta	95.2	30.1
Multidrug resistant UTI (8 days)	0.738	0.688 - 0.787 §	beta	222.99	79.16
Bacteremia (37 days or 65 if leading to death)	0.716	0.645 - 0.786 §	beta	111.82	44.35
Hematuria (2 days)	0.738	0.688 - 0.787 §	beta	223.0	79.2
<b>Annual transition probabilities</b>					
Symptomatic UTI → First-line resistant UTI	0.083	0.0 - 23.2 §	beta	1.75	19.36
Symptomatic UTI → Multidrug resistant UTI	0.07	5.1 - 9.2 §	beta	41.6	552.5
Symptomatic UTI → Bacteremia	0.036	3.4 - 3.8 §	beta	1200	32129
Multidrug resistant UTI → Death	0.026	1.3 - 5.1 §	beta	3.1	37.0
Bacteremia → Death	0.077	2.9 - 19.2 §	beta	7.09	263.42
<b>Mean number of events per patient per year</b>					
Symptomatic UTI	1.68	0.84 - 2.52	gamma	100.0	0.077
Hematuria	0.29	0.14 - 0.49	gamma	38	0.009
<b>Rate ratios</b>					
Symptomatic UTI (uncoated vs. hydrophilic)	0.47	0.47 - 0.92	lognormal	0.024*	
Hematuria (uncoated vs. hydrophilic)	1.35	0.68 - 2.03	lognormal	0.261*	
<b>Costs</b>					
Alive (annual cost)	954.48€	477€ - 1432€	gamma	100.0	9.5
Symptomatic UTI	1,091.86€	546€ - 1,638€	gamma	100.0	10.9
1st line resistant UTI	401.20€	201€ - 602€	gamma	100.0	4.0
Multidrug resistant UTI	775.36€	388€ - 1,163€	gamma	100.0	7.8
Bacteremia	3,664.16€	1,832€ - 5,496€	gamma	100.0	36.6
Hematuria	106.10€	53€ - 159€	gamma	100.0	1.1

Death for bacteremia	6,057.70€	3,029€ – 9,087€	gamma	100.0	60.6
Death for Multidrug resistant UTI	9,721.86€	4,861€ – 14,583€	gamma	100.0	97.2

\* standard error, § values reported are 95%CI

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Supplementary Table 4 - One-way sensitivity analyses

Variable	Value			ICUR (€/QALY)		
	Low	Base case	High	Low	Base case	High
Start age	20	40	60	19,942	24,405	35,525
Proportion men	40%	80%	100%	25,014	24,405	23,789
Mean number per patient per year, Symptomatic UTI	0.84	1.68	2.52	67,340	24,405	10,411
Mean number per patient per year, Hematuria	0.15	0.29	0.44	24,254	24,405	24,557
Annual probability, First line resistant UTI	0.042	0.084	0.126	24,727	24,405	24,084
Annual probability, Multidrug resistant UTI	0.035	0.070	0.105	29,797	24,405	20,797
Annual probability, Bacteremia	0.018	0.036	0.054	34,298	24,405	19,073
Annual probability, Bacteremia to Death	0.039	0.077	0.116	32,395	24,405	20,049
Annual probability, Multidrug resistant UTI to Death	0.013	0.026	0.039	29,122	24,405	21,228
Rate ratio, Symptomatic UTI (uncoated vs. hydrophilic)	0.47	0.47	0.92	24,405	24,405	282,622
Rate ratio, Hematuria (uncoated vs. hydrophilic)	0.68	1.35	2.03	23,900	24,405	24,912
Standardized mortality ratio, men	0.90	1.80	2.70	23,355	24,405	25,294
Standardized mortality ratio, women	2.45	4.90	7.35	23,714	24,405	25,023
Annual cost, "alive" health state	€ 477	€ 954	€ 1,432	23,844	24,405	24,966
Cost per Symptomatic UTI	€ 546	€ 1,092	€ 1,638	33,929	24,405	14,881
Cost per First-line resistant UTI	€ 201	€ 401	€ 602	24,699	24,405	24,111
Cost per Multidrug resistant UTI	€ 388	€ 775	€ 1,163	24,879	24,405	23,932
Cost per Bacteremia	€ 1,832	€ 3,664	€ 5,496	25,556	24,405	23,255

Cost per Hematuria	€ 53	€ 106	€ 159	24,270	24,405	24,541
Cost per Death for bacteremia	€ 3,029	€ 6,058	€ 9,087	24,554	24,405	24,257
Cost per Death for multidrug resistant UTI	€ 4,861	€ 9,722	€ 14,583	24,563	24,405	24,248
Unit cost, hydrophilic catheter	€ 0.85	€ 1.70	€ 2.55	dominance	24,405	51,402
Unit cost, standard catheter	€ 0.13	€ 0.25	€ 0.38	28,147	24,405	20,663
Number of catheters per day	2	4	6	1,151	24,405	47,660
Duration of bacteremia hospitalization (days)	19	37	56	24,456	24,405	24,355
Duration of bacteremia hospitalization (days), leading to death	33	65	98	24,413	24,405	24,398
Duration of multidrug resistant UTI-death hospitalization (days)	33	65	98	24,410	24,405	24,400
Utility, Alive	0.416	0.831	1	65,598	24,405	19,440
Utility, Symptomatic UTI	0.391	0.782	1	22,709	24,405	25,466
Utility, 1st line resistant UTI	0.380	0.760	1	23,871	24,405	24,755
Utility, Multidrug resistant UTI	0.375	0.749	1	23,926	24,405	24,737
Utility, Bacteremia	0.358	0.716	1	23,782	24,405	24,923
Utility, Hematuria	0.369	0.738	1	24,532	24,405	24,316
Duration, Symptomatic UTI (days)	2	4	6	24,520	24,405	24,292
Duration, First-line resistant UTI (days)	4	8	12	24,433	24,405	24,377
Duration, Multidrug resistant UTI (days)	8	16	24	24,459	24,405	24,352
Duration, Bacteremia (days)	19	37	56	24,488	24,405	24,323
Duration, Hematuria (days)	1	2	3	24,389	24,405	24,421
Duration, Bacteremia, if leading to death (days)	33	65	98	24,417	24,405	24,393
Duration, pre-death multidrug resistant UTI	33	65	98	24,413	24,405	24,397

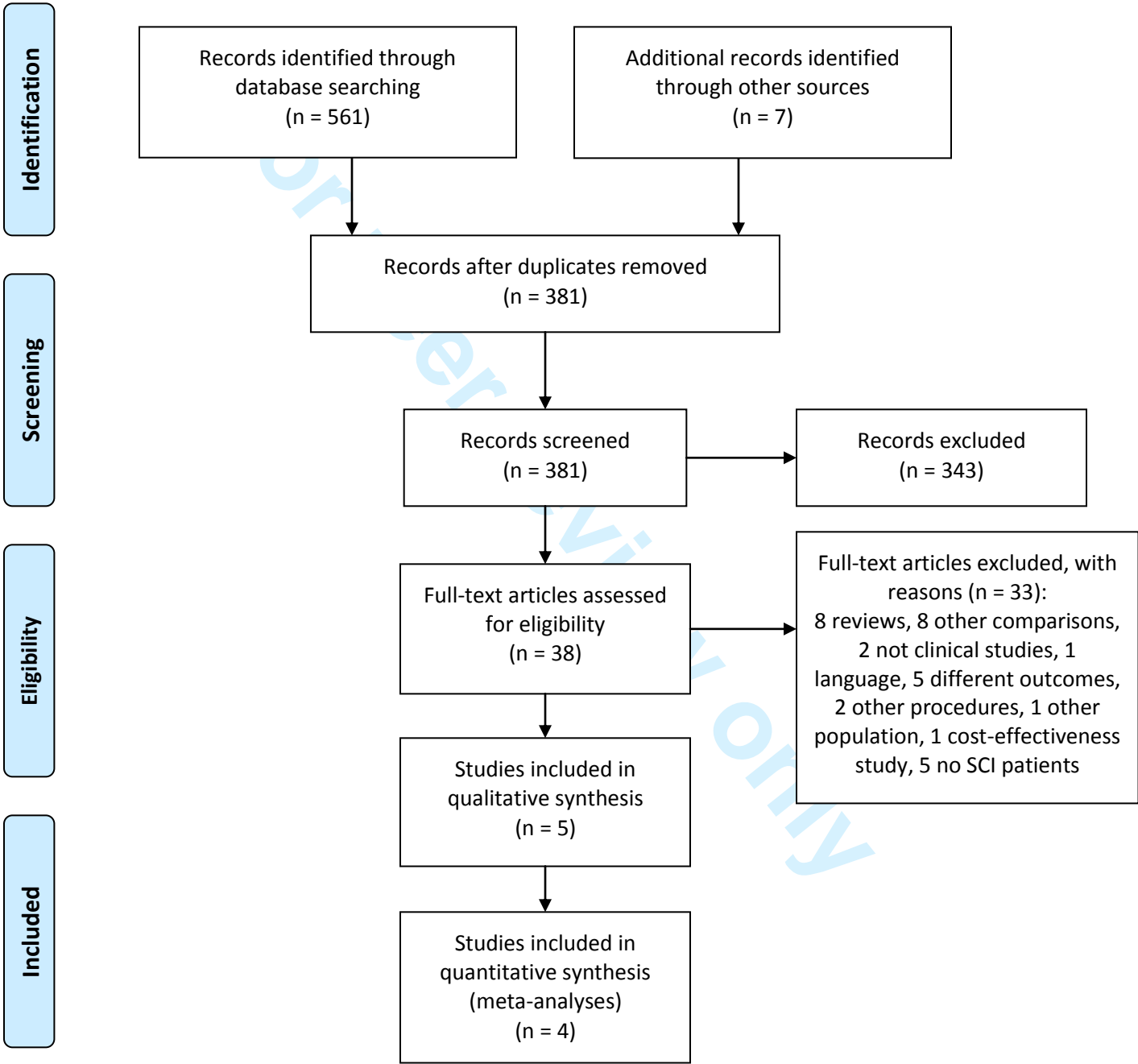
hospitalization (days)						
Discount rate, Costs	0	3.5%	5%	43,046	24,405	20,081
Discount rate, QALYs	0	3.5%	5%	11,255	24,405	32,433

\* Catheters cost not included

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Appendix

PRISMA 2009 Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).

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## CHEERS Checklist

### Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp>

Section/item	Item No	Recommendation	Reported on page No/line No
<b>Title and abstract</b>			
Title	1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	page 2
<b>Introduction</b>			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	from page 4
<b>Methods</b>			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	from page 6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	page 12
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	page 12
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	page 6
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	page 8
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	page 14
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	page 8
Measurement of effectiveness	11a	<i>Single study-based estimates:</i> Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	



1		11b	<i>Synthesis-based estimates:</i> Describe fully the methods used for	
2			identification of included studies and synthesis of clinical	
3			effectiveness data.	pages 6-8
4				
5	Measurement and	12	If applicable, describe the population and methods used to	
6	valuation of preference		elicit preferences for outcomes.	pages 13-14
7	based outcomes			
8	Estimating resources	13a	<i>Single study-based economic evaluation:</i> Describe approaches	
9	and costs		used to estimate resource use associated with the alternative	
10			interventions. Describe primary or secondary research methods	
11			for valuing each resource item in terms of its unit cost.	
12			Describe any adjustments made to approximate to opportunity	
13			costs.	
14				
15		13b	<i>Model-based economic evaluation:</i> Describe approaches and	
16			data sources used to estimate resource use associated with	
17			model health states. Describe primary or secondary research	
18			methods for valuing each resource item in terms of its unit	
19			cost. Describe any adjustments made to approximate to	
20			opportunity costs.	pages 12-13
21				
22				
23	Currency, price date,	14	Report the dates of the estimated resource quantities and unit	
24	and conversion		costs. Describe methods for adjusting estimated unit costs to	
25			the year of reported costs if necessary. Describe methods for	
26			converting costs into a common currency base and the	
27			exchange rate.	page 12
28				
29	Choice of model	15	Describe and give reasons for the specific type of decision-	
30			analytical model used. Providing a figure to show model	
31			structure is strongly recommended.	page 8
32				
33	Assumptions	16	Describe all structural or other assumptions underpinning the	
34			decision-analytical model.	pages 6-10
35	Analytical methods	17	Describe all analytical methods supporting the evaluation. This	
36			could include methods for dealing with skewed, missing, or	
37			censored data; extrapolation methods; methods for pooling	
38			data; approaches to validate or make adjustments (such as half	
39			cycle corrections) to a model; and methods for handling	
40			population heterogeneity and uncertainty.	pages 6-9
41				
42				
43	<b>Results</b>			
44	Study parameters	18	Report the values, ranges, references, and, if used, probability	
45			distributions for all parameters. Report reasons or sources for	
46			distributions used to represent uncertainty where appropriate.	
47			Providing a table to show the input values is strongly	
48			recommended.	Suppl. Table 3
49				
50	Incremental costs and	19	For each intervention, report mean values for the main	
51	outcomes		categories of estimated costs and outcomes of interest, as well	
52			as mean differences between the comparator groups. If	
53			applicable, report incremental cost-effectiveness ratios.	pages 16-17
54				
55	Characterising	20a	<i>Single study-based economic evaluation:</i> Describe the effects	
56	uncertainty		of sampling uncertainty for the estimated incremental cost and	
57			incremental effectiveness parameters, together with the impact	
58				
59				
60				

		of methodological assumptions (such as discount rate, study perspective).	
	20b	<i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	pages 17-18
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	
<b>Discussion</b>			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	pages 19-22
<b>Other</b>			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	page 24
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp>

The citation for the CHEERS Task Force Report is:

Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. *Value Health* 2013;16:231-50.



# BMJ Open

## Healthcare Resource Consumption for Intermittent Urinary Catheterisation: Cost-Effectiveness of Hydrophilic Catheters and Budget Impact Analyses

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**Healthcare Resource Consumption for Intermittent Urinary Catheterisation: Cost-Effectiveness of Hydrophilic Catheters and Budget Impact Analyses**

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## Abstract

**Objectives** – This study presents a cost-effectiveness analysis comparing hydrophilic coated to uncoated catheters for patients performing urinary intermittent catheterisation. A national budget impact analysis is also included to evaluate the impact of intermittent catheterisation for management of bladder dysfunctions over a period of 5 years.

**Design** – A Markov model (lifetime horizon, 1 year cycle length) was developed to project health outcomes (life years and quality-adjusted life years – QALYs) and economic consequences related to patients using hydrophilic coated or uncoated catheters. The model was populated with catheter-related clinical efficacy data retrieved from randomised controlled trials and quality-of-life data (utility weights) from the literature. Cost data (EUR, 2015) were estimated on the basis of healthcare resource consumption derived from an e-survey addressed to key opinion leaders in the field.

**Setting** – Italian Healthcare Service perspective.

**Population** – Patients with spinal cord injury performing intermittent urinary catheterisation in the home setting.

**Main outcome measures** – Incremental cost-effectiveness and cost-utility ratios (ICER, ICUR) of hydrophilic coated vs. uncoated catheters and associated healthcare budget impact.

**Results** – The base-case ICER and ICUR associated with hydrophilic coated catheters were €20,761 and €24,405, respectively. This implies that hydrophilic coated catheters are likely to be cost-effective in comparison to uncoated ones, as proposed Italian threshold values range between €25,000 and €66,400. Considering a market share at year 5 of 89% hydrophilic catheters and 11% uncoated catheters, the additional cost for Italy is approximately €12 million in the next 5 years (current market share scenario for year 0: 80% hydrophilic catheters, 20% uncoated catheters).

**Conclusions** – Considered over a lifetime, hydrophilic coated catheters are potentially a cost-effective choice in comparison to uncoated ones. These findings can assist policymakers in evaluating intermittent catheterisation in patients with spinal cord injury.

**Strengths and limitations of this study**

- This paper presents a cost-effectiveness analysis comparing hydrophilic coated to uncoated catheters in spinal cord-injured patients performing intermittent catheterisation. Healthcare resource consumption was derived from an e-survey addressed to key opinion leaders to provide real-world data.
- The study combines a cost-effectiveness analysis with a budget impact analysis. The addition of the budget impact analysis gives further evidence as to the overall impact of adopting the device for decision-makers to review.
- Data derived from self-reported questionnaires may be limited by varying recollection and poor generalisability. Variables derived from prospective observational multi-centre studies would increase the validity of the current model.
- The findings of this study support the use of hydrophilic coated catheters but are limited to costs from a healthcare perspective. A broader evaluation, also including costs from a societal perspective, would increase the understanding of the economic sustainability of these devices.

## Introduction

Injuries to the spinal cord (SCI) affect bladder functionality and cause motor or sensory deficits of a diverse nature and extent. Many of these conditions affect bladder functionality and cause what is known as a neurogenic bladder, often characterised by voiding problems. This clinical condition has a negative impact on health-related quality of life, and the associated economic costs can be overwhelming for patients already hampered with neurological problems. Healthcare utilisation may be excessive for these patients, including emergency department visits and subsequent hospitalisations. [1]

In the community setting, the management of a neurogenic bladder frequently involves Intermittent Catheterisation (IC). With this technique, a catheter is temporary used to remove urine from the bladder. As neurogenic bladder is often a permanent condition, IC may be required for a long period of time, often several times a day. There are different catheters available for IC. For example, disposable catheters with a hydrophilic polymer surface coating, disposable catheters with pre-packaged water based lubricant (gel reservoir), and uncoated catheters. While there is a lack of strong evidence demonstrating the effectiveness of any particular catheter design, technique or strategy, [2] the use of different kinds of catheters in the community may have different economic consequences. To our knowledge, two cost-effectiveness studies [3-4] have compared lifetime quality adjusted life years (QALYs) and costs of different types of catheter from the UK perspective. Although both studies focused on the management of urinary tract infections (UTIs), the first [3] based its analysis on the annual probability of experiencing at least one UTI for the different catheters considered (without taking into account the mean number of UTIs experienced in the same time by the patients' cohort) and their short-term consequences. The second study [4] focused on the average UTI rate per patient and month for hydrophilic coated and uncoated catheters, and considered long-term sequelae such as kidney impairment. Considering a lifetime horizon, the study by Clark et al. [4] showed that hydrophilic coated catheters are cost-effective when compared to uncoated catheters. Conversely, the study by Bermingham et al. [3] reported that the reuse and cleansing of uncoated catheters is the most cost-effective alternative in

comparison to all other catheter types. It should however be noted that reuse and cleaning of uncoated catheters may be regarded as an off-label procedure not supported by all regulating bodies. The divergent results from previous cost-effectiveness studies confirm that assumptions made, and the manner in which clinical data are chosen, highly affect the model construction and conclusions from the analysis, even in the same country setting.

One of the major advantages of IC is the significant reduction in the risk of catheter-associated UTIs, ensuring urinary tract health in general and preservation of kidney function in particular. [5-6] Despite the efforts in reducing the risk of UTIs, they still cause high morbidity and frequent hospitalisations for people with neurogenic bladder. Repeated cycles of antibiotic therapy in patients with recurrent UTIs also contribute to “antibiotic resistance”, [7] which in turn increases the need for new effective treatment options. For these reasons, UTIs entail a significant economic burden for patients, their families and healthcare systems. [8]

Studies which attempted to estimate the burden of UTIs from the healthcare system perspective report costs ranging from €523 to €4,167, [9-14] with more complicated UTIs likely to be associated with higher costs. The high variability in costs relates to several aspects. For example, UTI definition (bacteriuria vs. symptomatic UTI), study setting (hospital vs. community), study population (general patients in hospital vs. specific populations) and cost definitions can vary. The latter may consider direct healthcare costs only (e.g. medications, therapies), or include indirect costs to society as productivity losses. The use of different payer perspectives (society and/or healthcare system) may also result in different UTI cost values.

In addition to the risk of UTI, IC performed several times a day poses a risk for urethral trauma. Urethral trauma can occur with or without the presence of haematuria and is associated with an increased risk of UTI. [15-16] Damage to the urethra is less likely to occur with a lubricated catheter. [17]

A catheter reducing the risks of urethral trauma and/or UTI may limit the economic burden for the healthcare system and may increase quality of life for patients. A cost-effectiveness analysis (CEA)

permits a systematic evaluation of the costs and quality-of-life consequences of different treatment regimens, highlighting the option that would have the highest net benefit.

The aim of this study was to perform a CEA from an Italian Healthcare Service perspective, comparing the two catheter types most frequently used for IC (i.e. disposable hydrophilic coated or uncoated plastic catheters). This was done to add value to previously conflicting results of cost-effectiveness analyses evaluating different catheter types, and to identify the most cost-effective catheter alternative for the Italian setting. A budget impact analysis (BIA) was also conducted to evaluate the impact on the Italian healthcare budget of IC for management of bladder dysfunctions, over a period of 5 years.

## Methods

The clinical effectiveness of each catheter was retrieved from randomised controlled trials focusing on the community perspective that were published in the literature. Cost data were estimated on the basis of diagnosis-specific healthcare resource utilisation, derived from an e-survey addressed to key opinion leaders in the field. Since clinical data were mainly reported for SCI patients, the model considered these as an applicable study population. The study focused mainly on UTIs and episodes of haematuria, as the former are the most frequent complications in patients performing IC, while the latter occur regularly in one-third of patients on a long-term basis. [18]

### Systematic literature review and clinical data synthesis

A systematic literature review was performed in June 2016 to retrieve randomised controlled trials (RCTs), comparing hydrophilic coated and uncoated catheters for IC, and reporting outcomes on UTIs and haematuria. A systematic search was conducted on Pubmed, Embase, the Cochrane Library and Web of Science databases to retrieve clinical evidence (see Appendix for detailed search strategy).

In Italy, single-use catheters are considered the standard method for IC, and four catheters per day are delivered to users by local health agencies. [19] Reuse of catheters is not present or relevant to the Italian healthcare system, so clinical evidence considering catheter reuse was discarded. Studies not reporting UTIs frequencies per patient were also excluded. The studies by Cardenas et al. [20-21] and Sarica et al. [22] focused on SCI patients and reported data useful for the analysis. Data reported by Clark et al. [4] derived from an internal report of the study conducted by De Ridder et al. [23] were also included.

Table 1 reports UTI rates according to the methods presented in Clark et al., [4] distinguishing the following settings: hospital period, community setting and combined scenario (hospital and community settings).

Table 1 – Urinary tract infection rates (mean number of UTIs per patient per month)

	Study	Patients	Number of events	Rate per patient per month	Weighted mean	Rate ratio	
HOSPITAL PERIOD							
Uncoated	Cardenas 2011 [21]	114		0.68	0.61	0.78	
	De Ridder 2005 [23]	61		0.55			
	Sarica 2010 [22]	10	4	0.27			
Hydrophilic	Cardenas 2011 [21]	105		0.54	0.48		
	De Ridder 2005 [23]	60		0.44			
	Sarica 2010 [22]	10	1	0.07			
COMMUNITY SETTING							

Uncoated	Cardenas 2009 [20]	23		0.14	<b>0.14</b>	<b>0.47</b>
Hydrophilic	Cardenas 2009 [20]	22		0.06	<b>0.06</b>	
COMBINED SCENARIO						
Uncoated	Cardenas 2009 [20]	23		0.14	<b>0.40</b>	<b>0.92</b>
	Cardenas 2011 [21]	114		0.48		
	De Ridder 2005 [23]	61		0.38		
	Sarica 2010 [22]	10	4	0.27		
Hydrophilic	Cardenas 2009 [20]	22		0.06	<b>0.37</b>	
	Cardenas 2011 [21]	105		0.48		
	De Ridder 2005 [23]	60		0.34		
	Sarica 2010 [22]	10	1	0.07		

For haematuria, three studies [21-23] reporting useful data were identified by the systematic literature search (Table 2).

Table 2 – Haematuria rates (mean number of haematuria episodes per patient per year)

	Study	Patients	Number of events	Years	Rate per patient per year	Weighted mean	Rate ratio
--	-------	----------	------------------	-------	---------------------------	---------------	------------

Uncoated	Cardenas 2011 [21]	114	6	0.5	0.11	0.29	1.35
	De Ridder 2005 [23]	59	32	1	0.54		
	Sarica 2010 [22]	10	1	0.1151	0.87		
Hydrophilic	Cardenas 2011 [21]	105	14	0.5	0.27	0.39	
	De Ridder 2005 [23]	55	38	1	0.69		
	Sarica 2010 [22]	10	0	0.115	0.00		

The model

As the management of patients performing IC is an evolving process, Markov multistate models were chosen for the health economic evaluation. A decision tree, combined with two Markov models, was designed to project lifetime health outcomes (life years and QALYs) and economic consequences related to SCI patients performing IC with hydrophilic or non-hydrophilic urinary catheters.

The Markov model (Figure 1) includes the following health states: Alive, Symptomatic UTI, Haematuria and Death. A symptomatic UTI can either resolve or become an antibiotic-resistant UTI. In this case, the model distinguishes between first-line-resistant UTI, multidrug-resistant UTI and bacteraemia. Multidrug-resistant UTI and bacteraemia represent severe UTIs that can eventually cause patient death.

It is acknowledged that complications other than the ones included in the model health states may be relevant for patients practicing IC. For example, other infections and inflammations such as epididymo-orchitis, urethritis and prostatitis may occur as a complication of IC as well as strictures, false passage and bladder stones. [24] The “Alive” state accounts for baseline rates of these kinds

of complications, which have been elicited by key opinion leaders in the field and assumed equal for hydrophilic coated and uncoated catheters (see details in the Results section – Healthcare resource consumption and costs).

<Figure 1>

A hypothetical cohort of 40-year-old, 80% male patients enters the Markov process in the “Alive” state. Population characteristics are assumed to be similar to those previously reported for SCI patients performing IC in Italy. [25]

The model is mainly based on the structure presented by Bermingham et al. [3] and focuses on short term consequences of UTIs and haematuria. In contrast to Bermingham et al., [3] who use the annual probability of experiencing at least one UTI, the current model incorporates the estimation of mean number of UTIs per patient and month as reported for Clark et al. [4] to give a more precise estimate of costs and patients’ quality of life.

A 1-year Markov cycle length and a lifetime horizon were chosen for baseline analysis. To improve the accuracy of the results, a half-cycle correction was performed. The model was developed and analysed in Microsoft Excel®.

### Model quantification

As described above, monthly rates of 0.14 and 0.06 were estimated for symptomatic UTIs in patients using uncoated catheters and hydrophilic coated catheters in the community setting, respectively. These data translate into 1.68 and 0.72 events per year and patient, respectively. For haematuria, 0.29 and 0.39 episodes per year and patient were estimated for uncoated and hydrophilic coated catheters, respectively.

The probabilities of clinical failure after treatment for symptomatic UTI reported by Clark et al. [4] were mainly based on expert opinions, so annual transition probabilities as presented by

Bermingham et al. [3] were preferred. The annual probabilities of clinical failure, leading to first-line/multidrug-resistant UTI or bacteraemia, were applied to the mean number of symptomatic UTIs experienced by the patients over 1 year using uncoated or hydrophilic coated catheters.

As no further transition probabilities were found in literature, the model assumed that “Multidrug-resistant UTI” state also included healthcare resource consumption related to “First-line-resistant UTI” state.

Standardised mortality ratios for men and women with SCI were retrieved by Lidal et al. [26]. Mortality rates were further adjusted for age and gender according to Italian mortality tables (ISTAT).

A summary of transition probabilities and model parameters is presented in Tables 3 and 4, respectively (for cost data and event durations, see the details in the Results section – Healthcare resource consumption and costs).

Table 3 – Transition probabilities matrix

Health state	Transition to:	Annual transition probability	Reference
Symptomatic UTI	First-line-resistant UTI	0.083	[3]
Symptomatic UTI	Multidrug-resistant UTI	0.07	[3]
Symptomatic UTI	Bacteraemia	0.036	[3]
Multidrug-resistant UTI	Death from UTI	0.026	[3]
Bacteraemia	Death from UTI	0.077	[3]

Table 4 – Model parameters with related sources

Parameter	Base-case value	Reference
Population		
Start age (years)	40	[25]

Proportion men	80%	[25]
<b>Utility coefficients for the health states/events</b>		
Alive	0.831	[3]
Symptomatic UTI	0.782	[3]
First-line-resistant UTI	0.76	[3]
Multidrug-resistant UTI	0.738	[3]
Bacteraemia	0.716	[3]
Haematuria	0.738	Assumed equal to Multidrug-resistant UTI
<b>Mean number of events per patient per year</b>		
Symptomatic UTI	1.68	[20]
Haematuria	0.29	[21-23]
<b>Rate ratios</b>		
Symptomatic UTI (uncoated vs. hydrophilic)	0.47	[20]
Haematuria (uncoated vs. hydrophilic)	1.35	[21-23]
Standardised mortality ratios for SCI patients	men 1.8, women 4.9	[26]
<b>Costs</b>		
Unit cost, standard catheter	0.25€	Tender data for Italy
Unit cost, hydrophilic catheter	1.70€	Tender data for Italy
Alive (annual cost)	954.48€	E-survey and official tariffs
Symptomatic UTI	1,091.86€	E-survey and official tariffs
First-line-resistant UTI	401.20€	E-survey and official tariffs
Multidrug-resistant UTI	775.36€	E-survey and official tariffs
Bacteraemia	3,664.16€	E-survey and official tariffs
Haematuria	106.10€	E-survey and official tariffs
Death for bacteraemia	6,057.70€	E-survey and official tariffs
Death for Multidrug-resistant UTI	9,721.86€	E-survey and official tariffs
<b>Events duration (days)</b>		
Symptomatic UTI	4	E-survey
First-line-resistant UTI	8	E-survey
Multidrug-resistant UTI	16	E-survey
Bacteraemia	37	DRG 576

Haematuria	2	E-survey
Bacteraemia, if leading to death	65	DRG 575
Pre-death Multidrug-resistant UTI hospitalisation	65	DRG 575

Healthcare resource consumption and costs

As the analysis was performed from the Italian Healthcare System perspective, all costs related to the consumption of direct healthcare resources were estimated and expressed in euro (2015 value).

Clinical pathways and healthcare resource consumption for the management of symptomatic UTIs, first-line-resistant UTIs, multidrug-resistant UTIs, haematuria episodes and bacteraemia were estimated by study-specific questionnaire to urologists and neuro-urologists. All the clinicians (N=25) belonging to the NUS team (Italian spinal neuro-urologist group) of Fondazione Italiana Continenza (Italian Continence Foundation), [27] which treat the highest volumes of patients across Italy, received access to a web version of the questionnaire (developed with Qualtrics© software) between July 15<sup>th</sup>, 2015 and October 15<sup>th</sup>, 2015 (a printed version of the questionnaire is available upon request). The questionnaire included four sections: 1) introduction with a case vignette, [28] 2) patient monitoring (relevant annual exams, lab tests, visits, inpatient stays and drugs – irrespective of catheter type), 3) management of UTIs, bacteraemia and haematuria, and 4) future scenarios of catheter use. On the basis of their clinical experience, clinicians were asked to estimate healthcare utilisation. For example, the percentage of patients involved, regimen applied (outpatient, day-hospital or inpatient stay), daily dose and duration of drugs for general management and/or for management of an episode of UTI, bacteraemia and haematuria (drug costs are generally provided by an administrative office within the Hospital).

The last section of the questionnaire included a forecast of possible future scenarios (1, 3 and 5 years) of utilisation of uncoated and hydrophilic coated catheters in Italy.

The results from the questionnaires were summarised to estimate healthcare resource utilisation. For each healthcare resource (exam, visit, hospitalisation, etc.) reported, a weighted mean was calculated on the basis of the number of responders.

The cost of resource consumption for the different events was calculated by multiplying the quantity of resources consumed by unit costs derived from official sources, i.e. diagnosis-related groups' (DRGs) reimbursement for hospitalisations, official tariffs for outpatient services, and hospital prices for drugs. When hospital prices for drugs were missing, a search was performed through the Italian Pharmaceutical Database ([www.federfarma.it](http://www.federfarma.it)) reporting cost data for the National Healthcare Service.

Four catheters per day and patient were assumed, as this was the reimbursement level provided by the local health agencies. The unit cost was estimated from tender data at €1.70 and €0.25 for hydrophilic coated and uncoated catheters, respectively. In Italy, the lubricant gel for uncoated catheters is paid for by the patients, so this cost was omitted in the model.

During hospital stays, catheter costs are assumed included in the DRG reimbursement, excluding the need for additional device costs in the model.

### Quality-of-life estimates

The search for utility coefficients for SCI patients performing IC was performed through Pubmed, Embase, Web of Science databases and the Cost-Effectiveness Analysis Registry. [29] Two studies [30-31] and a review [32] were found that reported utility values for SCI patients experiencing UTIs. The first one [30] reported utility values (estimated by HUI-Mark III health status classification system) of 0.28 and 0.15 for no/mild UTI and moderate/significant UTI, respectively. The second study [31] reported utility values for UTI of 0.58 and 0.60 estimated by SF36 and SF12 questionnaires, respectively. The review [32] included an additional study conducted by Vogel and Zebracki from which utility values of 0.831, 0.782 and 0.738 were estimated for no UTI, UTI and

severe UTI, respectively. From the database search, no utility values were found for haematuria and bacteraemia health states.

Additional utility values were retrieved from Bermingham et al. [3] and Clark et al. [4] All values are summarised in Supplementary Table 1.

The model included utility values referred to in the study by Bermingham et al. [3] (see Table 4).

For haematuria, a utility value of 0.738 (as for multidrug-resistant UTI state) was assumed.

The duration of the different events was estimated from the pharmacological treatment duration reported by the questionnaires, with the exception of both multidrug-resistant UTI and bacteraemia leading to death for which the length-of-stay threshold of the related DRGs was considered.

Analyses

Both incremental cost-effectiveness and cost-utility ratios (ICER, ICUR) of hydrophilic coated versus uncoated catheters were calculated by dividing the incremental cost by the incremental health improvement. Life years, QALYs and costs were discounted with a 3.5% yearly rate. [33] Transition probabilities, costs and utilities were entered into the model along with a distribution: beta for utilities and proportions of patients experiencing different kinds of UTIs, log-normal for relative risks and gamma for costs. Deterministic and probabilistic sensitivity analyses (PSA) were performed to test the robustness of the model. Univariate analyses were performed according to the main parameters; second-order Monte-Carlo analysis (1,000 simulations) was conducted and the related acceptability curve was plotted.

Further analyses were performed that considered UTI rates for 1) hospital period and 2) combined (hospital plus community) scenario (based on data presented in Table 1). Since UTI rates per patient per month vary across the retrieved studies, different scenario analyses were performed that considered data input from each study separately to evaluate heterogeneity. The same was performed for episodes of haematuria (based on data presented in Table 2).

## Budget Impact Analysis – BIA

Based on the conclusion from the CEA model, a companion budget impact model [34] was developed to address hypothetical changes to the Italian Healthcare Service budget considering an increased utilisation of hydrophilic coated catheters.

In order to perform the BIA, a review of epidemiological data focused on SCI patients performing IC was carried out.

The prevalence of SCI patients in Italy resulted in the range 60,000-70,000 according to a national registry, [35] while the incidence (data from the Italian registry) showed a decrease from 20-25 to 7.8 per million inhabitants. Based on the study by Zlatev et al., [36] it was assumed that 60% of patients perform IC. The total number of prevalent patients with SCI performing IC in Italy was estimated to be about 39,000 (65,000 x 60%), while the total number of incident patients was about 285. It was assumed that the distribution of the incident population was the same as that of the prevalent population (mean age of 40 years, 80% men).

The current scenario of patient distribution between the two devices under consideration was estimated from clinical input as 20% uncoated and 80% hydrophilic coated catheters. The estimation of the new scenario, including an increased proportion of hydrophilic coated catheters in the years, was based on key opinion leaders' replies to the questionnaire.

The cost of the current and new scenarios was determined by multiplying the cost for each intervention by the proportion of the eligible population using it, taking into account both prevalent and subsequent yearly incident cohorts. Financial streams were presented as undiscounted costs, since the focus of the analysis was expected budget at each point. [34]

## **Results**

### Healthcare resource consumption and costs

Nine of 25 clinicians completed the questionnaire, representing institutions with the highest volumes of treated SCI patients in Italy. The estimated healthcare resource utilisation is reported in Supplementary Table 2. Reported care pathways were consistent with previous published literature. [37]

The “Alive” health state in the model refers to usual patient year including control visits, exams or hospitalisations for causes other than UTIs (e.g. urethral strictures, bladder stones). All other health states consider healthcare resources consumption for management of a single event (e.g. symptomatic UTI, haematuria, bacteraemia, etc.). For drugs, the mean dosage per patient was reported together with the proportion of administered patients.

Unit costs related to the healthcare resource consumption are summarised in Supplementary Table 3.

The estimated event durations were 2 days for haematuria, 4 days for symptomatic UTI, additional 8 days for first-line-resistant UTI, additional 8 days for multidrug-resistant UTI (total 4+8+8=20 days), 37 days for hospitalisation for bacteraemia (DRG 576) and 65 days for infection leading to death (DRG 575).

In case of bacteraemia leading to patient death, the healthcare resources related to “Infection leading to patient death” (see Supplementary Table 2) were applied (the management of the episode of bacteraemia is included in the DRG 575).

Summaries of event durations and costs estimated for the different health states/events are included in Table 4.

Baseline results

Deterministic and probabilistic results were obtained from the model. It estimated an average life expectancy of 18.3 years (15.2 QALYs) for a study population using hydrophilic coated catheters and 17.3 years (14.3 QALYs) for a study population using uncoated catheters. The mean lifetime

costs per patient were €82,915 and €62,457 for hydrophilic coated and uncoated catheters, respectively. For hydrophilic coated catheters, this resulted in an ICER of €20,761 and an ICUR of €24,405 (Table 5 – deterministic results). Although there is no official cost-effectiveness threshold for Italy, the reported proposed thresholds vary between €25,000–€40,000, [38] €36,500, [39] €60,000, [40] and €66,400 (three times the Italian gross domestic product per capita according to the WHO). [41-42] This suggests that the ICER/ICUR for hydrophilic coated catheters is lower than recommended threshold values and thus could be considered a cost-effective option.

Table 5 – Summary of the model results

Results	Catheter	Cost (€)	Δ Cost (€)	LY	ΔLY	QALYs	ΔQALYs	ICER (€/LY)	ICUR (€/QALY)
Deterministic	Uncoated	€ 62,457		17.299		14.332			
	Hydrophilic	€ 82,915	€ 20,459	18.284	0.985	15.170	0.838	€ 20,761	€ 24,405
Probabilistic	Uncoated	€ 62,357		17.300		14.329			
	Hydrophilic	€ 82,971	€ 20,614	18.276	0.977	15.158	0.830	€ 21,110	€ 24,840

Considering a lifetime horizon, hydrophilic coated catheters may reduce the frequency of UTIs by about 50% (from 48 to 24) in comparison to uncoated catheters. Considering the significant impact of UTIs, which account for about 23% to 63% of the total lifetime cost for SCI patients practicing intermittent catheterisation, prevention is of high importance.

A PSA was performed to account for uncertainty in cost-effectiveness calculations (Supplementary Table 4 summarises the main model parameters with related probability distributions). Probabilistic model results are included in Table 5.

The acceptability curve obtained from the Monte Carlo simulation is shown in Figure 2 for the ICUR. Given the varying Italian threshold values of €25,000–40,000, €36,500, €60,000 and €66,400, hydrophilic coated catheters have about a 47-86%, 77%, 97% and 98% probability of being cost-effective, respectively. Considering the UK-specific threshold value of £20,000–£30,000

recommended by NICE [33] (equal to €26,400-€39,600 at an exchange rate of 1.32), hydrophilic coated catheters have a 48%-86% probability of being cost-effective.

<Figure 2>

The scenario analyses performed considering weighted UTIs rates for hospital period and combined (hospital plus community) settings resulted in ICURs equal to €11,908/QALY (ICER €10,097/LY) and €97,019/QALY (ICER €82,188/LY), respectively.

The additional scenario analyses conducted considering UTI rates from single studies, as reported in Table 1, showed ICUR values for the hospital period that were equal to €11,240/QALY and €17,368/QALY, based on data from Cardenas 2011 [21] and De Ridder 2005, [23] respectively. Concerning the combined scenario, ICURs obtained were €21,184/QALY and €68,979/QALY based on data from Cardenas 2009 [20] and De Ridder 2005, [23] respectively. Only data from Cardenas 2011 [21] showed the dominance of uncoated catheters, while data from Sarica 2010 [22] showed hydrophilic catheter dominance for both hospital and hospital-plus-community settings.

Scenario analyses considering haematuria rates from single studies, as reported in Table 2, showed limited variations in the ICUR, which ranged from €22,000/QALY (data from Sarica 2010 [22]) to €24,569/QALY (data from De Ridder 2005 [23]), respectively.

One-way sensitivity analyses were performed for the ICUR on the main model parameters. The results for the ten parameters responsible for the main ICUR variations are presented in a tornado diagram in Figure 3 (see Supplementary Table 5 for complete results). The parameters with the greatest impact on ICUR were the relative risk (rate ratio) of developing a symptomatic UTI (for hydrophilic catheters vs. uncoated catheters), the mean number of symptomatic UTIs per patient and year for uncoated catheters, the unit cost for hydrophilic catheters and the number of catheters used per day. For example, a rate ratio higher than 0.70 for developing a symptomatic UTI would result in ICUR values over €60,000. Hydrophilic coated catheters are the dominant choice if the

unit cost is €0.85 or lower, but if the unit cost is €2.55, the ICUR exceeds €50,000. Also, lowering the utility value for the “Alive” health state to 0.42 results in an ICUR above €65,000.

<Figure 3>

### Budget impact analysis

As hydrophilic coated catheters are likely to be a cost-effective strategy, a BIA was performed to consider a new scenario with an increasing proportion of users of these advanced devices among patients performing IC in the next years. The proportions for possible future usages were estimated by the questionnaires. Focusing on uncoated and hydrophilic coated catheters only, the clinicians reported possible proportions of hydrophilic coated catheter use of 83%, 88% and 89% after 1, 3 and 5 years, respectively.

Table 6 reports the mean yearly cost per patient for both uncoated and hydrophilic coated catheters as calculated from the CEA model. Costs are presented for the following four sub-categories: patient monitoring (i.e. control visits/exams, etc.), management of UTIs, management of haematuria episodes, and catheters. The highest costs for uncoated catheters are related to the management of UTIs, while the highest costs for hydrophilic coated catheters are reported for the catheters themselves.

Table 6 – Detailed mean costs per patient for uncoated and hydrophilic coated catheters for the first five years

	Uncoated catheters (UC)					Hydrophilic coated catheters (HC)				
Year	UC Patient monitoring	UC UTIs	UC Haematuria	UC Catheters	UC TOT Cost	HC Patient monitoring	HC UTIs	HC Haematuria	HC Catheters	HC TOT Cost
0	€950	€2,250	€31	€361	<b>€3,591</b>	€951	€1,060	€41	€2,468	<b>€4,520</b>
1	€940	€2,227	€30	€357	<b>€3,554</b>	€945	€1,053	€41	€2,452	<b>€4,491</b>

2	€929	€2,203	€30	€353	<b>€3,515</b>	€939	€1,046	€41	€2,436	<b>€4,461</b>
3	€919	€2,179	€30	€349	<b>€3,477</b>	€933	€1,039	€41	€2,419	<b>€4,431</b>
4	€909	€2,154	€29	€345	<b>€3,438</b>	€926	€1,031	€40	€2,401	<b>€4,399</b>
5	€898	€2,129	€29	€341	<b>€3,398</b>	€919	€1,024	€40	€2,383	<b>€4,366</b>

Table 7 reports the annual cost for SCI patients performing IC with either uncoated or hydrophilic coated catheters with related number of users (year 0: prevalent cohort, following years: incident cohorts), for both current and new scenarios. For both catheter types, the total cost per year has been weighted according to the proportion of use (i.e. 80% hydrophilic coated and 20% uncoated catheters for all years in the current scenario and increasing percentage of use of hydrophilic catheters in the years in the new scenario). The last two columns summarise the total national healthcare budget and the yearly incremental cost. An increasing use of hydrophilic coated catheters results in an increase of the total budget of about €12 million in the next 5 years.

Table 7 – Budget impact analysis

Current scenario																
Uncoated catheters (UC)								Hydrophilic coated catheters (HC)								
Year	UC Market share	UC Users cohort	UC Patients' monitoring	UC UTIs	UC Haematuria	UC Catheters	UC TOT Cost	HC Market share	HC Users cohort	HC Patients' monitoring	HC UTIs	HC Haematuria	HC Catheters	HC TOT Cost	TOT budget impact	
0	20%	7,800	€7,406,202	€17,553,353	€238,749	€2,814,182	€28,012,486	80%	31,200	€29,685,875	€33,066,569	€1,291,904	€76,991,688	€141,036,036	€169,048,522	
1	20%	57	€7,382,273	€17,496,692	€237,978	€2,805,089	€27,922,032	80%	228	€29,711,701	€33,095,438	€1,293,028	€77,058,664	€141,158,831	€169,080,863	
2	20%	57	€7,356,951	€17,436,723	€237,162	€2,795,467	€27,826,302	80%	228	€29,730,740	€33,116,734	€1,293,856	€77,108,040	€141,249,370	€169,075,672	
3	20%	57	€7,330,174	€17,373,319	€236,298	€2,785,292	€27,725,083	80%	228	€29,742,674	€33,130,139	€1,294,376	€77,138,987	€141,306,176	€169,031,259	
4	20%	57	€7,301,592	€17,305,645	€235,377	€2,774,431	€27,617,045	80%	228	€29,746,001	€33,133,978	€1,294,520	€77,147,612	€141,322,112	€168,939,157	
5	20%	57	€7,270,867	€17,232,905	€234,387	€2,762,756	€27,500,915	80%	228	€29,739,259	€33,126,624	€1,294,227	€77,130,119	€141,290,230	€168,791,145	
New scenario																
Uncoated catheters (UC)								Hydrophilic coated catheters (HC)								
Year	UC Market share	UC Users cohort	UC Patients' monitoring	UC UTIs	UC Haematuria	UC Catheters	UC TOT Cost	HC Market share	HC Users cohort	HC Patients' monitoring	HC UTIs	HC Haematuria	HC Catheters	HC TOT Cost	TOT budget impact	Incremental cost in comparison to current scenario
0	20%	7,800	€7,406,202	€17,553,353	€238,749	€2,814,182	€28,012,486	80%	31,200	€29,685,875	€33,066,569	€1,291,904	€76,991,688	€141,036,036	€169,048,522	€0
1	17%	48	€6,274,932	€14,872,189	€202,281	€2,384,326	€23,733,728	83%	237	€30,825,890	€34,336,517	€1,341,516	€79,948,364	€146,452,287	€170,186,014	€1,105,151
2	17%	48	€6,253,408	€14,821,214	€201,587	€2,376,147	€23,652,356	83%	237	€30,845,643	€34,358,612	€1,342,376	€79,999,592	€146,546,222	€170,198,578	€1,122,906
3	12%	34	€4,398,104	€10,423,991	€141,779	€1,671,175	€16,635,050	88%	251	€32,716,942	€36,443,153	€1,423,813	€84,852,886	€155,436,794	€172,071,844	€3,040,584
4	12%	34	€4,380,955	€10,383,387	€141,226	€1,664,659	€16,570,227	88%	251	€32,720,602	€36,447,376	€1,423,972	€84,862,373	€155,454,323	€172,024,550	€3,085,393
5	11%	31	€3,998,977	€9,478,098	€128,913	€1,519,516	€15,125,503	89%	254	€33,084,926	€36,853,369	€1,439,828	€85,807,258	€157,185,381	€172,310,884	€3,519,739
Total incremental cost																€11,873,774

Discussion

IC is considered the method of choice for the management of neurogenic bladder dysfunctions. Patients performing IC entail a substantial economic burden on the healthcare system, as infections and urethral trauma are common and result in frequent hospitalisations and high morbidity. Although different catheters are available with various characteristics in terms of medical safety, treatment functionality, patient comfort and environmental performance, there is currently no robust consensus as to which catheter type is the best. Recent meta-analyses investigating the impact of different catheters types on UTI rate and haematuria reported conflicting results. One study [43] concluded that hydrophilic coated catheters are associated with a significant reduction in the risk of UTI and haematuria compared to non-hydrophilic catheters while another study was unable to differentiate between catheter types and techniques. [2]

The aim of this study was to conduct cost-effectiveness and budget impact analyses of different catheters used for IC. The results were meant to support the process for deciding how to allocate scarce healthcare resources and maximise patients' health while controlling costs. In Italy, the provision of disposable medical devices for daily repeated use, such as catheters for IC, is currently regulated by the Ministry of Health (MoH), [44] which defines a list of medical devices supplied directly to patients and reimbursed by the Italian NHS. In recent times, the coverage of medical devices has been the subject of debates in Italy. The MoH has decided that more information is needed on the value contribution of medical devices both to patients and to the healthcare systems. For this reason, a National Health Technology Assessment Programme has been developed that refers to cost-effectiveness analysis as the main decision tool in measuring the incremental value of innovative technologies in comparison to the standard of care. [45-47]

Considering a lifetime perspective, hydrophilic coated catheters resulted in an ICUR of €24,405/QALY and an ICER of €20,761/LY. Accordingly, hydrophilic coated catheters were likely to be considered cost-effective in comparison to uncoated catheters, given the available range of thresholds values proposed for Italy (from €25,000 to €66,400). PSA supported this findings: considering the Italian threshold values of €25,000–€40,000, €36,500, €60,000 and €66,400,

hydrophilic coated catheters showed about a 47-86%, 77%, 97% and 98% probability of being cost-effective, respectively.

The base-case findings are in line with conclusions reported by Clark and colleagues [4], who considered a UK setting and a cost-effectiveness threshold of £30,000 (about €40,000). However, the results differ from the report by Bermingham et al. [3], who concluded that uncoated catheters are the most cost-effective when compared to all the other catheter types. This discrepancy is likely related to the difference in selecting studies and data for the underlying meta-analysis investigating UTI risk. Bermingham et al. [3] used data from a meta-analysis that estimated the risk of experiencing at least one UTI for each catheter type. Since there could be a great variation in the number of UTIs experienced by each patient, this assumption could potentially have hidden a risk-reducing efficacy related to hydrophilic coated catheters. A study [48] evaluating self-reported catheter practices and associated problems for people mainly performing IC with uncoated catheters found an annual rate of 2.3 (95%CI 1.8-3) symptomatic UTIs treated with an antibiotic.

When a lower cost-effectiveness threshold was considered (i.e. £20,000 = about €26,400), the probability that hydrophilic coated catheters may be a cost-effective choice was about 50%, partially supporting the conclusions presented by Bermingham et al. [3]

Differently from [4], the present CE model focused only on short-term consequences of symptomatic UTIs, excluding lifetime effects on renal function. Since the probability of developing UTIs was found to be lower for hydrophilic coated catheters versus uncoated ones, this suggests that results are conservative estimates of the CE results. As a consequence, the scenario analyses considering community setting and hospital-plus-community settings together reported higher ICERs and ICURs in comparison to the findings of the study cited above.

Another difference is related to the cost of the two devices. While in UK the cost of an uncoated catheter is slightly lower than the cost of a hydrophilic coated one, in Italy the cost of uncoated catheters is very low: about 25% of the cost of the hydrophilic coated catheter. The increased cost of hydrophilic coated catheters is partially offset by the cost savings due to the lower number of UTIs that develop.

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Our study is a cost-effectiveness analysis comparing hydrophilic coated to uncoated catheters that also includes a budget impact analysis. The BIA is considered to add important information for decision-makers who need to estimate the impact on healthcare expenditures of introducing new health technologies in regular practice.

This study estimated the consumption of healthcare resources by soliciting expert opinions with the aim of providing real-world costing data. This is especially important for medical devices, since their use in regular practice often differs from that established in experimental settings. [49] Also, the fact that the consumption of healthcare resources has been represented in natural units – as suggested by the EUnetHTA guidelines [50] – will allow cost adjustment to other countries.

This study has some limitations. First of all, clinical effectiveness data were derived from few RCTs with fewer than 50 participants and with variations in length of follow-up and definitions of UTI. Moreover, the rates of events per patient per month varied across the studies and the calculated weighted means may not be fully representative of the Italian scenario.

The model focused mainly on complications such as UTI and haematuria, for which different rates were estimated for hydrophilic coated and uncoated catheters. UTIs are recognised as the most frequent complications, while epididymitis and urethritis are relatively rare. [51] To our knowledge, there are no randomised controlled data on other complications for different catheter types. However, observational studies reported fewer traumas and urethral inflammations for hydrophilic coated catheters that would potentially increase their cost-effectiveness on a life time perspective. [52-53]

As regards the estimation of the healthcare resources, it must be noted that data derived from self-reported questionnaires may be limited by varying recollection and poor generalisability. Variables derived from prospective observational multi-centre studies would increase the validity of the current model. Observational studies would also serve to confirm clinical evidence of the comparative effectiveness of catheters in addition to RCTs.

Overall, the analysis is based on varying levels of evidence and assumptions, and the results need to be considered cautiously.

The findings of this study support the use of hydrophilic coated catheters but are limited to costs from a healthcare perspective. A broader evaluation, also including costs from a societal perspective, would increase the understanding of the economic sustainability of these devices.

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### Data sharing

PRISMA statement is available in Appendix.

**Declaration of competing interests**

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (1) CeRGAS Bocconi has support from ASBM Srl for the submitted work; (2) CR and RT have no relationships with ASBM Srl that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (4) CR and RT have no non-financial interests that may be relevant to the submitted work.

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**Details of contributors**

Carla Rognoni – study concept and design; analysis and interpretation of data; drafting of the manuscript.

Rosanna Tarricone – study supervision; acquisition of funding; critical revision of the manuscript.

**Transparency declaration**

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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## References

1. Cardarelli WJ. Managed care aspects of managing neurogenic bladder/neurogenic detrusor overactivity. *Am J Manag Care*. 2013;19(10 Suppl):s205-8.
2. Prieto J, Murphy CL, Moore KN, Fader M. Intermittent catheterisation for long-term bladder management. *Cochrane Database Syst Rev* 2014 Sep 10;9:CD006008.
3. Bermingham SL, Hodgkinson S, Wright S, et al. Intermittent self catheterisation with hydrophilic, gel reservoir, and non-coated catheters: a systematic review and cost effectiveness analysis. *BMJ*. 2013 Jan 8;346:e8639.
4. Clark JF, Mealing SJ, Scott DA, et al. A cost-effectiveness analysis of long-term intermittent catheterisation with hydrophilic and uncoated catheters. *Spinal Cord*. 2015 Jul 21.
5. Bakke A, Digraanes A, Høisaeter PA. Physical predictors of infection in patients treated with clean intermittent catheterization: a prospective 7-year study. *Br J Urol*. 1997 Jan;79(1):85-90.

6. Turi MH, Hanif S, Fasih Q, et al. Proportion of complications in patients practicing clean intermittent self-catheterization (CISC) vs indwelling catheter. *J Pak Med Assoc.* 2006 Sep;56(9):401-4.

7. Nicolle LE. Urinary tract infections in patients with spinal injuries. *Curr Infect Dis Rep.* 2014 Jan;16(1):390.

8. Ciani O, Grassi D, Tarricone R. An economic perspective on urinary tract infection: the "costs of resignation". *Clin Drug Investig.* 2013 Apr;33(4):255-61.

9. Lai KK, Fontecchio SA. Use of silver-hydrogel urinary catheters on the incidence of catheter-associated urinary tract infections in hospitalized patients. *Am J Infect Control.* 2002;30(4):221-5.

10. Karchmer TB, Giannetta ET, Muto CA, et al. A randomized crossover study of silver-coated urinary catheters in hospitalized patients. *Arch Intern Med.* 2000;160(21):3294-8.

11. McNutt R, Johnson TJ, Odwazny R, et al. Change in MS-DRG assignment and hospital reimbursement as a result of Centers for Medicare & Medicaid changes in payment for hospital-acquired conditions: is it coding or quality? *Qual Manag Health Care.* 2010;19(1):17-24.

12. Saint S. Clinical and economic consequences of nosocomial catheter-related bacteriuria. *Am J Infect Control.* 2000;28(1):68-75.

13. Tambyah PA, Knasinski V, Maki DG. The direct costs of nosocomial catheter-associated urinary tract infection in the era of managed care. *Infect Control Hosp Epidemiol.* 2002;23(1):27-31.

14. Anderson DJ, Kirkland KB, Kaye KS, et al. Underresourced hospital infection control and prevention programs: penny wise, pound foolish? *Infect Control Hosp Epidemiol.* 2007;28(7):767-73.

15. Bardsley A. Intermittent Self-Catheterisation in women: reducing the risk of UTIs. *Urology supplements.* 2014;22(18).

16. Heard L, Buhner R. How do we prevent UTI in people who perform intermittent catheterization? *Rehabil Nurs.* 2005 Mar-Apr;30(2):44-5,61.

17. Bennett E. Intermittent self-catheterisation and the female patient. *Nurs Stand* 2002; 17: 37–42.
18. Igawa Y, Wyndaele JJ, Nishizawa O. Catheterization: possible complications and their prevention and treatment. *Int J Urol*. 2008 Jun;15(6):481-5.
19. [http://www.sanita24.ilsole24ore.com/pdf2010/Sanita2/\\_Oggetti\\_Correlati/Documenti/Dal-Governo/Allegato%20%20Ausili%20Monouso%202015\\_Filigrana.pdf](http://www.sanita24.ilsole24ore.com/pdf2010/Sanita2/_Oggetti_Correlati/Documenti/Dal-Governo/Allegato%20%20Ausili%20Monouso%202015_Filigrana.pdf) (accessed 10 Jul 2016).
20. Cardenas DD, Hoffman JM. Hydrophilic catheters versus noncoated catheters for reducing the incidence of urinary tract infections: a randomized controlled trial. *Arch Phys Med Rehabil*. 2009; 90:1668–1671.
21. Cardenas DD, Moore KN, Dannels-McClure A, et al. Intermittent catheterization with a hydrophilic-coated catheter delays urinary tract infections in acute spinal cord injury: a prospective, randomized, multicenter trial. *PM R*. 2011 May;3(5):408-17.
22. Sarica S, Akkoc Y, Karapolat H, Aktug H. Comparison of the use of conventional, hydrophilic and gel-lubricated catheters with regard to urethral micro trauma, urinary system infection, . and patient satisfaction in patients with spinal cord injury: a randomized controlled study. *Eur J Phys Rehabil Med*. 2010 Dec;46(4):473-9.
23. De Ridder DJ, Everaert K, Fernández LG, et al. Intermittent catheterisation with hydrophilic-coated catheters (SpeediCath). reduces the risk of clinical urinary tract infection in spinal cord injured patients: a prospective randomised parallel comparative trial. *Eur Urol*. 2005 Dec;48(6):991-5.
24. Vahr S, Cobussen-Boekhorst H, Eikenboom J, et al. Catheterisation. Urethral intermittent in adults: dilatation, urethral intermittent in adults. Arnhem (The Netherlands): European Association of Urology Nurses (EAUN); 2013 Mar. 96 p.
25. Euro Mediterranean Rehabilitation Summer School - <http://www.emrss.it/> (accessed 10 Mar 2016).

26. Lidal IB, Snekkvik H, Aamodt G, et al. Mortality after spinal cord injury in Norway. *J Rehabil Med*. 2007 Mar;39(2):145-51.

27. <http://www.contenuti-web.com/continenza/fondazione-0000409.html> (accessed 10 Jul 2016).

28. Fattore G, Torbica A. Cost and reimbursement of cataract surgery in Europe: a cross-country comparison. *Health Econ*. 2008 Jan;17(1 Suppl):S71-82.

29. CEA Registry – <https://research.tufts-nemc.org/cear4/SearchingtheCEARegistry> (accessed 10 Jul 2016).

30. Craven C, Hitzig SL, Mittmann N. Impact of impairment and secondary health conditions on health preference among Canadians with chronic spinal cord injury. *J Spinal Cord Med*. 2012 Sep;35(5):361-70.

31. Lee BB, King MT, Simpson JM, Haran MJ, Stockler MR, Marial O, Salkeld G. Validity, responsiveness, and minimal important difference for the SF-6D health utility scale in a spinal cord injured population. *Value Health*. 2008 Jul-Aug;11(4):680-8.

32. Bermingham SL, Ashe JF. Systematic review of the impact of urinary tract infections on health-related quality of life. *BJU Int*. 2012 Dec;110(11 Pt C):E830-6.

33. National Institute for Clinical Excellence. Guide to the Methods of Technology Appraisal. London: National Institute for Clinical Excellence, 2004.

34. Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health*. 2014 Jan-Feb;17(1):5-14.

35. GISEM - Italian Group for the Epidemiological Study of Spinal Cord Injuries - <http://www.istud.it/superabile/lesione.asp> (accessed 10 Jul 2016).

36. Zlatev DV, Shem K, Elliott CS. How many spinal cord injury patients can catheterize their own bladder? The epidemiology of upper extremity function as it affects bladder management. *Spinal Cord*. 2016 Jan 19.

37. Biardeau X, Corcos J. Intermittent catheterization in neurologic patients: Update on genitourinary tract infection and urethral trauma. *Ann Phys Rehabil Med*. 2016 Apr;59(2):125-9.
38. Associazione Italiana di Economia Sanitaria (AIES): Proposta di linee guida per la valutazione economica degli interventi sanitari. *PharmacoEconomics–Italian Res Artic*. 2009, 11: 83-93. 10.1007/BF03320660.
39. Lucioni C, Ravasio R. How to evaluate the results of a pharmacoeconomic study? *Pharmacoeconomics – Italian Research Articles*. 2004; 6(3):121–130.
40. Messori A, Santarlasci B, Trippoli S, Vaiani M. Clinical benefit and economic value: methodology and an economic application. *Pharmacoeconomics – Italian Research Articles*. 2003;5(2):53–67.
41. World Health Organization. World Health Organization: Choosing Interventions that are Cost Effective (WHO-CHOICE). Geneva: World Health Organization, 2012.
42. [http://www.who.int/choice/costs/CER\\_levels/en](http://www.who.int/choice/costs/CER_levels/en) (accessed 10 Jul 2016).
43. Li L, Ye W, Ruan H, Yang B, Zhang S, Li L. Impact of hydrophilic catheters on urinary tract infections in people with spinal cord injury: systematic review and meta-analysis of randomized controlled trials. *Arch Phys Med Rehabil*. 2013 Apr;94(4):782-7.
44. Ministerial Decree 27th August 1999, n.332, <http://www.gazzettaufficiale.it/eli/id/1999/09/27/099G0404/sg> (accessed 10 Jul 2016).
45. National Health Pact 2014-2016 (art. 26), [http://www.salute.gov.it/imgs/C\\_17\\_pubblicazioni\\_2309\\_allegato.pdf](http://www.salute.gov.it/imgs/C_17_pubblicazioni_2309_allegato.pdf) (accessed 10 Jul 2016).
46. Law n. 208, 28 December 2015, Stability Law - Legge di stabilità 2016, <http://www.gazzettaufficiale.it/eli/id/2014/12/29/14G00203/sg> (accessed 10 Jul 2016).
47. Law n. 190, 23 December 2014, Stability Law - Legge di stabilità 2015, <http://www.gazzettaufficiale.it/eli/id/2015/12/30/15G00222/sg> (accessed 10 Jul 2016).

48. Wilde MH, Brasch J, Zhang Y. A qualitative descriptive study of self-management issues in people with long-term intermittent urinary catheters. *J Adv Nurs*. 2011 Jun;67(6):1254-63.

49. Drummond M, Griffin A, Tarricone R. Economic evaluation for devices and drugs--same or different? *Value Health*. 2009 Jun;12(4):402-4.

50. <http://www.eunethta.eu> (accessed 10 Jul 2016).

51. Wyndaele J. Complications of intermittent catheterization: their prevention and treatment. *Spinal Cord*. 2002 Oct;40(10):536-41.

52. Hellström P, Tammela T, Lukkarinen O, Kontturi M. Efficacy and safety of clean intermittent catheterization in adults. *Eur Urol*. 1991;20(2):117-21.

53. Vaidyanathan S, Soni BM, Dundas S, Krishnan KR. Urethral cytology in spinal cord injury patients performing intermittent catheterisation. *Paraplegia*. 1994 Jul;32(7):493-500.

**Figure legends**

Figure 1 – Simplified Markov model representation. Patients start the Markov process in the “Alive” state, where they can remain or move to the “Symptomatic UTI” or “Haematuria” states. These are considered sub-states of the “Alive” state since they last less than one year. The model accounts for the possibility of patients dying from causes other than UTI (death from other causes).

UC=uncoated catheters, HC=hydrophilic coated catheters, pt=patient.

Figure 2 – ICUR acceptability curve

Figure 3 – Tornado diagram showing one-way sensitivity analyses on ICUR value (€24,405). Upper and lower limits of variables’ values referring to the ICUR extremes are indicated next to the bars.

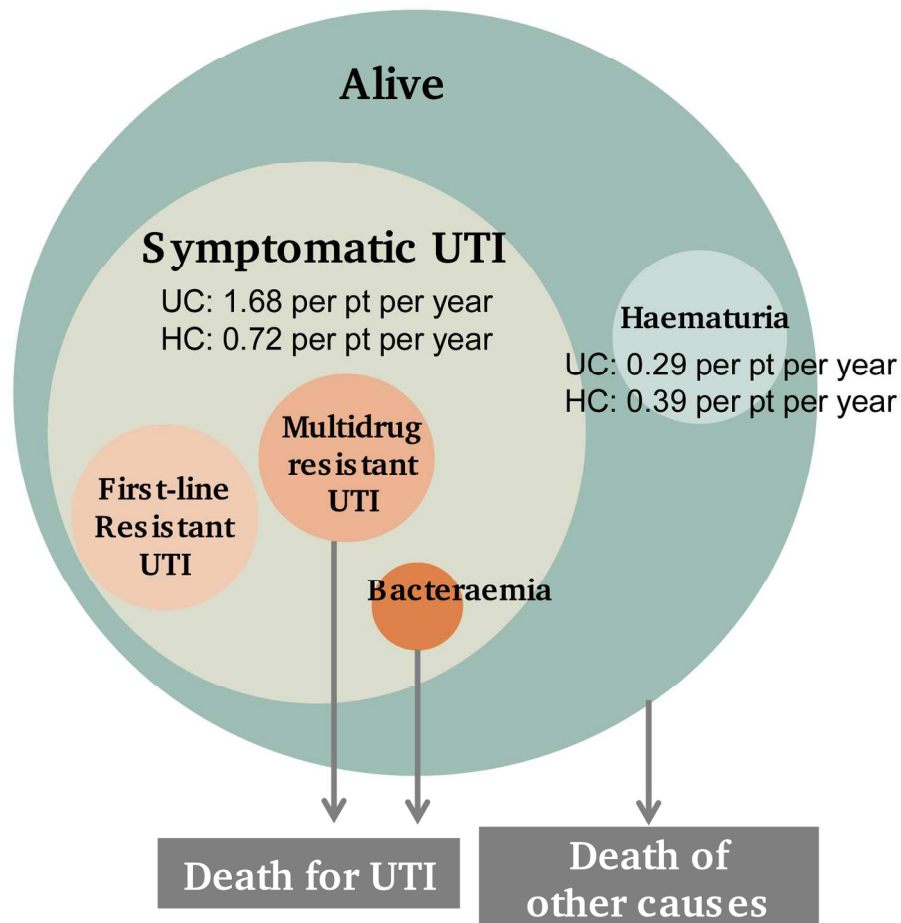


Figure 1 – Simplified Markov model representation. Patients start the Markov process in the "Alive" state, where they can remain or move to the "Symptomatic UTI" or "Haematuria" states. These are considered sub-states of the "Alive" state since they last less than one year. The model accounts for the possibility of patients dying from causes other than UTI (death from other causes). UC=uncoated catheters, HC=hydrophilic coated catheters, pt=patient.

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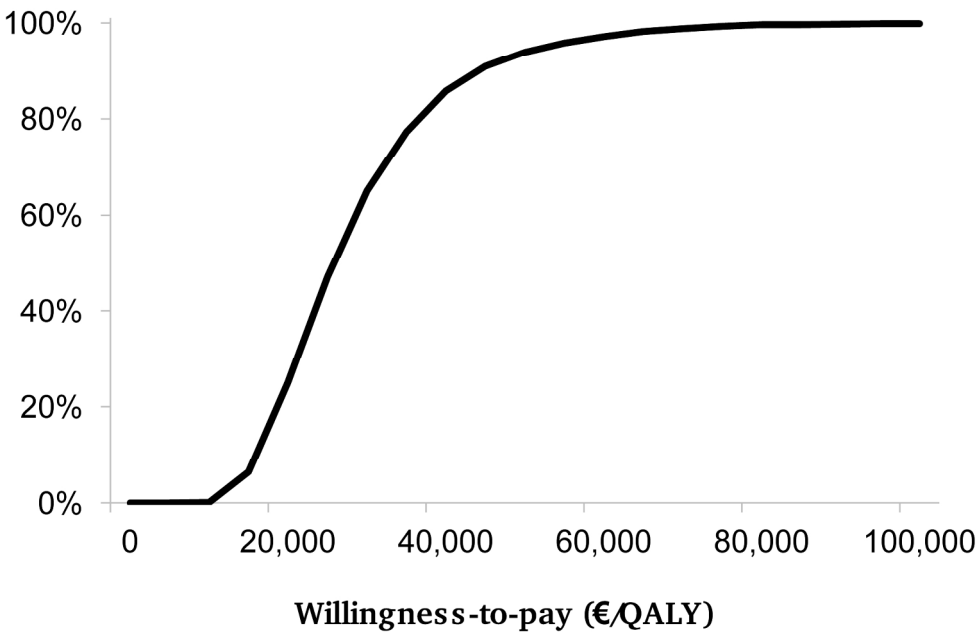


Figure 2 – ICUR acceptability curve  
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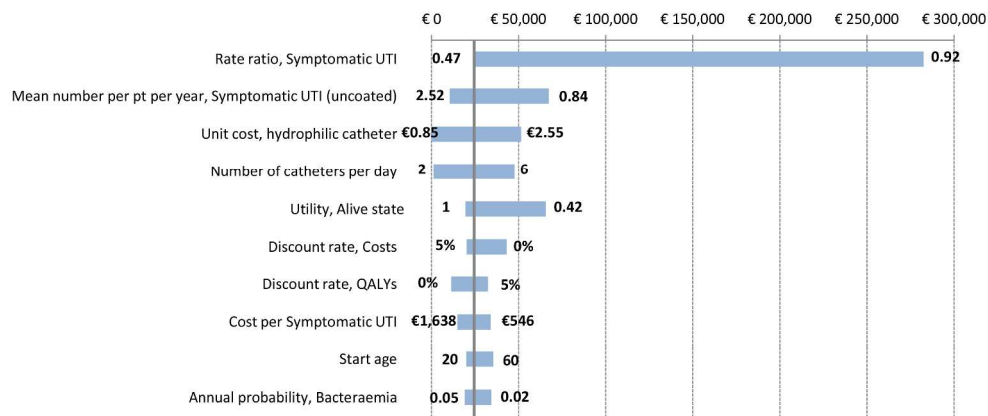


Figure 3 – Tornado diagram showing one-way sensitivity analyses on ICUR value (€24,405). Upper and lower limits of variables' values referring to the ICUR extremes are indicated next to the bars.

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Supplementary Table 1 – Summary of the retrieved utility values for the different health states

Study	no UTI	UTI	Severe UTI	Bacteraemia
Craven 2012 [30]		0.28 (SD=0.28)	0.15 (SD=0.18)	
Lee 2008 [31]	0.68-0.70 (SD=0.01)	0.58-0.60 (SD=0.01)		
Birmingham 2013 [3]	0.831 (95%CI 0.809-0.852)	0.782 (95%CI 0.764-0.799)	First-line-resistant UTI 0.760 (95%CI 0.685-0.834)  Multidrug-resistant UTI  0.738 (95%CI 0.688-0.787)	0.716 (95%CI 0.645-0.786)
Clark 2015 [4]	0.468	disutility 0.060	disutility 0.104 (antibiotic resistant)  disutility 0.160 (UTI not responding to initial treatment)	

CI=confidence interval, SD=standard deviation

Supplementary Table 2 – Healthcare resource consumption for the considered health states/events

Health state	Category	Type	mean number per patient	dosage (mg) per patient	% patients
Alive (1 year)	Visits	Specialist visit	1.99		
	Exams/procedures	Abdomen ultrasound	0.11		
		Bladder ultrasound	0.81		
		Creatinine	0.20		
		Magnetic resonance imaging	0.02		
		Pelvic floor examination	0.03		
		Cystography	0.06		
		Renal scintigraphy	0.01		
		Urine culture	3.60		
		Urine exam	2.39		
		Urodynamics	0.46		
		Video-urodynamics	0.17		
	Hospitalisation (DRG)	313 - Urethral Procedures, Age Greater than 17 without CC	0.01		
		309 - Minor Bladder Procedures without CC	0.01		
		323 - Urinary Stones with CC and/or ESW Lithotripsy	0.03		
		324 - Urinary Stones without CC	0.02		
		325 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 with CC	0.03		
		326 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 without CC	0.14		
		329 - Urethral Stricture, Age Greater than 17	0.01		

		without CC			
	Drugs	Antimuscarins		5,576	73%
		Botulinum toxin injection	2		25%
		Antibiotics (prophylaxis): sulfamethoxazole+trimethoprim, amoxicillin, levofloxacin, ciprofloxacin		69,127	16%
Symptomatic UTI	Visits	Specialist visit	0.93		
	Exams/procedures	Creatinine	0.11		
		Bladder ultrasound	0.41		
		Blood culture	0.02		
		Complete blood count	0.11		
		Urine exam	0.78		
		Kidney functionality	0.11		
		Urine culture	1.22		
	Hospitalisation (DRG)	321 - Kidney and Urinary Tract Infections, Age Greater than 17 without CC	0.52		
	Drugs	Antibiotics: amikacin, amoxicillin, ampicillin, cefixime, cefpodoxim, ceftriaxone, ciprofloxacin, imipenem, levofloxacin, meropenem, prulifloxacin, sulfamethoxazole+trimethoprim		22,411	127%*
First-line-resistant UTI (resources in addition to symptomatic UTI)	Visits	Specialist visit	1.17		
	Exams/procedures	Stool culture	0.01		
		Creatinine/glycaemia	0.44		
		Abdomen ultrasound	0.11		
		Bladder ultrasound	0.37		
		Blood culture	0.33		
		Urine exam	1.44		
		Video-urodynamics	0.11		

		Lactate	0.11		
		Polymerase Chain Reaction	0.11		
		Urine culture	1.78		
		Erythrocyte sedimentation rate	0.11		
Multidrug-resistant UTI (resources in addition to first-line-resistant UTI)	Hospitalisation (DRG)	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.07		
	Drugs	Antibiotics: amikacin, ceftazidime, ceftriaxone, gentamicin, imipenem, meropenem, minocycline, piperacillin, thienamycin		16,278	89%
	Visits	Specialist visit	1.2		
		Day-hospital	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.02	
	Exams/procedures	Cystoscopy	0.07		
		Colonoscopy	0.11		
		Bladder ultrasound	0.44		
		Bact smear-lower gastro-intestinal	0.11		
		Bowel diagnostic procedure NEC	0.13		
		Computerised tomography scan	0.13		
		Urine exam	1.33		
		Urine culture	1.56		
		Video-urodynamics	0.11		
		Blood culture	0.11		
		Intestinal x-ray NEC	0.11		
	Hospitalisation (DRG)	320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.03		
	Drugs	Antibiotics: amikacin, imipenem, meropenem, piperacillin		7,556	34%

Bacteraemia	Hospitalisation (DRG)	576 - Septicaemia without mechanical ventilation	0.59		
		320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	0.03		
	Day-hospital	576 - Septicaemia without mechanical ventilation	0.22		
	Drugs	Antibiotics: cefepime, ceftazidime, imipenem, levofloxacin, meropenem, teicoplanin		12,311	56%
Infection leading to patient death	Hospitalisation (DRG)	575 - Septicaemia with mechanical ventilation >=96 h	0.45		
	Drugs	Antibiotics: amikacin, imipenem, meropenem, vancomycin		12,222	34%
Haematuria	Visits	Specialist visit	0.71		
	Exams/procedures	Cystoscopy	0.02		
		Bladder ultrasound	0.24		
		Urine exam	0.56		
		Percutaneous cystostomy	0.06		
		Urethroscopy	0.21		
		Urine culture	0.22		
	Hospitalisation (DRG)	309 - Minor Bladder Procedures without CC	0.002		
		332 - Other Kidney and Urinary Diagnoses, Age Greater than 17 without CC	0.04		
		326 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 without CC	0.01		
	Drugs	Antibiotics: cefepime, ciprofloxacin, levofloxacin		2,556	30%

\* More than one treatment is administered, DRG=Diagnosis Related Group, CC=complications, NEC=not elsewhere classifiable

Supplementary Table 3 – Costs references related to the healthcare resource consumption

Visits/exams	Official tariff/cost
Specialist visit	€20.66
Abdomen ultrasound	€32.02
Bact smear-lower gastro-intestinal	€2.53
Bladder ultrasound	€32.02
Blood culture	€26.44
Bowel diagnostic procedure NEC	€51.65
Colonoscopy	€86.80
Complete blood count	€3.17
Computerised tomography scan	€126.90
Creatinine	€1.13
Creatinine/glycaemia	€1.17
Cystography	€48.29
Cystoscopy	€79.52
Erythrocyte sedimentation rate	€1.95
Intestinal x-ray NEC	€51.65
Kidney functionality	€18.84
Lactate	€4.84
Magnetic resonance imaging	€120.08
Pelvic floor examination	€90.00
Percutaneous cystostomy	€32.76

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Polymerase Chain Reaction	€3.87
Renal scintigraphy	€56.81
Stool culture	€12.01
Urethroscopy	€38.22
Urine culture	€8.31
Urine exam	€2.17
Urodynamics	€56.81
Video-urodynamics	€104.07
<b>DRGs</b>	
309 - Minor Bladder Procedures without CC	€3,397.00
313 - Urethral Procedures, Age Greater than 17 without CC	€3,059.00
320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	€2,701.00
321 - Kidney and Urinary Tract Infections, Age Greater than 17 without CC	€1,883.00
323 - Urinary Stones with CC and/or ESW Lithotripsy	€1,372.00
324 - Urinary Stones without CC	€935.00
325 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 with CC	€1,878.00
326 - Kidney and Urinary Tract Signs and Symptoms, Age Greater than 17 without CC	€1,075.00
329 - Urethral Stricture, Age Greater than 17 without CC	€781.00
332 - Other Kidney and Urinary Diagnoses, Age Greater than 17 without CC	€1,008.00
575 - Septicaemia with mechanical ventilation >=96 h	€21,349.00
576 - Septicaemia without mechanical ventilation	€5,493.00
<b>Day-hospitals</b>	

320 - Kidney and Urinary Tract Infections, Age Greater than 17 with CC	€216.00
576 - Septicaemia without mechanical ventilation	€247.00
<b>Drugs</b>	
Botulinum toxin injection	€658.00
Antimuscarins (mean cost per mg)	€0.032
Antibiotics (prophylaxis): sulfamethoxazole+trimethoprim, amoxicillin, levofloxacin, ciprofloxacin (mean cost per mg)	€0.003
Antibiotics mix - Symptomatic UTI: amikacin, amoxicillin, ampicillin, cefixime, cefpodoxim, ceftriaxone, ciprofloxacin, imipenem, levofloxacin, meropenem, prulifloxacin, sulfamethoxazole+trimethoprim (mean cost per mg)	€0.002
Antibiotics mix - First-line-resistant UTI: amikacin, ceftazidime, ceftriaxone, gentamicin, imipenem, meropenem, minocycline, piperacillin, thienamycin (mean cost per mg)	€0.008
Antibiotics mix - Multidrug-resistant UTI: amikacin, imipenem, meropenem, piperacillin (mean cost per mg)	€0.05
Antibiotics mix - Bacteraemia: cefepime, ceftazidime, imipenem, levofloxacin, meropenem, teicoplanin (mean cost per mg)	€0.04
Antibiotics mix - Infection leading to patient death: amikacin, imipenem, meropenem, vancomycin (mean cost per mg)	€0.04
Antibiotics mix - Haematuria: cefepime, ciprofloxacin, levofloxacin (mean cost per mg)	€0.01

DRG=Diagnosis Related Group, CC=complications, NEC=not elsewhere classifiable

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Supplementary Table 4 – Model parameters and distributions used in PSA (unless otherwise specified, variation ranges refer to +/- 50% of the baseline value)

Parameter	Base case value	Variation range	Distribution type	Alpha	Beta
<b>Utility coefficients for the health states/events</b>					
Alive	0.831	0.809 - 0.852 §	beta	969.1	197.1
Symptomatic UTI (4 days)	0.782	0.764 - 0.799 §	beta	1671.49	465.96
First-line-resistant UTI (8 days)	0.76	0.685 - 0.834 §	beta	95.2	30.1
Multidrug-resistant UTI (8 days)	0.738	0.688 - 0.787 §	beta	222.99	79.16
Bacteraemia (37 days or 65 if leading to death)	0.716	0.645 - 0.786 §	beta	111.82	44.35
Haematuria (2 days)	0.738	0.688 - 0.787 §	beta	223.0	79.2
<b>Annual transition probabilities</b>					
Symptomatic UTI → First-line-resistant UTI	0.083	0.0 - 23.2 §	beta	1.75	19.36
Symptomatic UTI → Multidrug-resistant UTI	0.07	5.1 - 9.2 §	beta	41.6	552.5
Symptomatic UTI → Bacteraemia	0.036	3.4 - 3.8 §	beta	1200	32129
Multidrug-resistant UTI → Death	0.026	1.3 - 5.1 §	beta	3.1	37.0
Bacteraemia → Death	0.077	2.9 - 19.2 §	beta	7.09	263.42
<b>Mean number of events per patient per year</b>					
Symptomatic UTI	1.68	0.84 - 2.52	gamma	100.0	0.077
Haematuria	0.29	0.14 - 0.49	gamma	38	0.009
<b>Rate ratios</b>					
Symptomatic UTI (uncoated vs. hydrophilic)	0.47	0.47 – 0.92	lognormal	0.024*	
Haematuria (uncoated vs. hydrophilic)	1.35	0.68 – 2.03	lognormal	0.261*	
<b>Costs</b>					
Alive (annual cost)	954.48€	477€ - 1432€	gamma	100.0	9.5
Symptomatic UTI	1,091.86€	546€ – 1,638€	gamma	100.0	10.9
First-line-resistant UTI	401.20€	201€ - 602€	gamma	100.0	4.0
Multidrug-resistant UTI	775.36€	388€ – 1,163€	gamma	100.0	7.8
Bacteraemia	3,664.16€	1,832€ – 5,496€	gamma	100.0	36.6
Haematuria	106.10€	53€ - 159€	gamma	100.0	1.1

Death for bacteraemia	6,057.70€	3,029€ – 9,087€	gamma	100.0	60.6
Death for Multidrug-resistant UTI	9,721.86€	4,861€ – 14,583€	gamma	100.0	97.2

\* standard error, § values reported are 95%CI

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Supplementary Table 5 – One-way sensitivity analyses

	Value			ICUR (€/QALY)		
Variable	Low	Base case	High	Low	Base case	High
Start age	20	40	60	19,942	24,405	35,525
Proportion men	40%	80%	100%	25,014	24,405	23,789
Mean number per patient per year, Symptomatic UTI	0.84	1.68	2.52	67,340	24,405	10,411
Mean number per patient per year, Haematuria	0.15	0.29	0.44	24,254	24,405	24,557
Annual probability, First line resistant UTI	0.042	0.084	0.126	24,727	24,405	24,084
Annual probability, Multidrug-resistant UTI	0.035	0.070	0.105	29,797	24,405	20,797
Annual probability, Bacteraemia	0.018	0.036	0.054	34,298	24,405	19,073
Annual probability, Bacteraemia to Death	0.039	0.077	0.116	32,395	24,405	20,049
Annual probability, Multidrug-resistant UTI to Death	0.013	0.026	0.039	29,122	24,405	21,228
Rate ratio, Symptomatic UTI (uncoated vs. hydrophilic)	0.47	0.47	0.92	24,405	24,405	282,622
Rate ratio, Haematuria (uncoated vs. hydrophilic)	0.68	1.35	2.03	23,900	24,405	24,912
Standardised mortality ratio, men	0.90	1.80	2.70	23,355	24,405	25,294
Standardised mortality ratio, women	2.45	4.90	7.35	23,714	24,405	25,023
Annual cost, "Alive" health state	€ 477	€ 954	€ 1,432	23,844	24,405	24,966

Cost per Symptomatic UTI	€ 546	€ 1,092	€ 1,638	33,929	24,405	14,881
Cost per First-line-resistant UTI	€ 201	€ 401	€ 602	24,699	24,405	24,111
Cost per Multidrug-resistant UTI	€ 388	€ 775	€ 1,163	24,879	24,405	23,932
Cost per Bacteraemia	€ 1,832	€ 3,664	€ 5,496	25,556	24,405	23,255
Cost per Haematuria	€ 53	€ 106	€ 159	24,270	24,405	24,541
Cost per Death for bacteraemia	€ 3,029	€ 6,058	€ 9,087	24,554	24,405	24,257
Cost per Death for multidrug-resistant UTI	€ 4,861	€ 9,722	€ 14,583	24,563	24,405	24,248
Unit cost, hydrophilic catheter	€ 0.85	€ 1.70	€ 2.55	dominance	24,405	51,402
Unit cost, standard catheter	€ 0.13	€ 0.25	€ 0.38	28,147	24,405	20,663
Number of catheters per day	2	4	6	1,151	24,405	47,660
Duration of bacteraemia hospitalisation (days)	19	37	56	24,456	24,405	24,355
Duration of bacteraemia hospitalisation (days), leading to death	33	65	98	24,413	24,405	24,398
Duration of multidrug-resistant UTI-death hospitalisation (days)	33	65	98	24,410	24,405	24,400
Utility, Alive	0.416	0.831	1	65,598	24,405	19,440
Utility, Symptomatic UTI	0.391	0.782	1	22,709	24,405	25,466
Utility, First-line-resistant UTI	0.380	0.760	1	23,871	24,405	24,755
Utility, Multidrug-resistant UTI	0.375	0.749	1	23,926	24,405	24,737
Utility, Bacteraemia	0.358	0.716	1	23,782	24,405	24,923
Utility, Haematuria	0.369	0.738	1	24,532	24,405	24,316
Duration, Symptomatic UTI (days)	2	4	6	24,520	24,405	24,292

Duration, First-line-resistant UTI (days)	4	8	12	24,433	24,405	24,377
Duration, Multidrug-resistant UTI (days)	8	16	24	24,459	24,405	24,352
Duration, Bacteraemia (days)	19	37	56	24,488	24,405	24,323
Duration, Haematuria (days)	1	2	3	24,389	24,405	24,421
Duration, Bacteraemia, if leading to death (days)	33	65	98	24,417	24,405	24,393
Duration, pre-death multidrug-resistant UTI hospitalisation (days)	33	65	98	24,413	24,405	24,397
Discount rate, Costs	0	3.5%	5%	43,046	24,405	20,081
Discount rate, QALYs	0	3.5%	5%	11,255	24,405	32,433

\* Catheters cost not included

## Appendix

### SEARCH QUERY:

(spinal OR SCI OR SCIs OR neurogenic OR bladder OR urinary OR urethral OR dysfunction)

AND

(hydrophilic OR LoFric OR coated OR POBE OR polyolefin based elastomer OR polyolefin-based elastomer OR PVC free OR PVC-free OR Speedicath OR Easicath)

AND

(standard OR conventional OR plastic OR polyethylene OR PVC OR polyvinyl OR nonhydrophilic OR non hydrophilic OR non-hydrophilic OR non coated OR non-coated)

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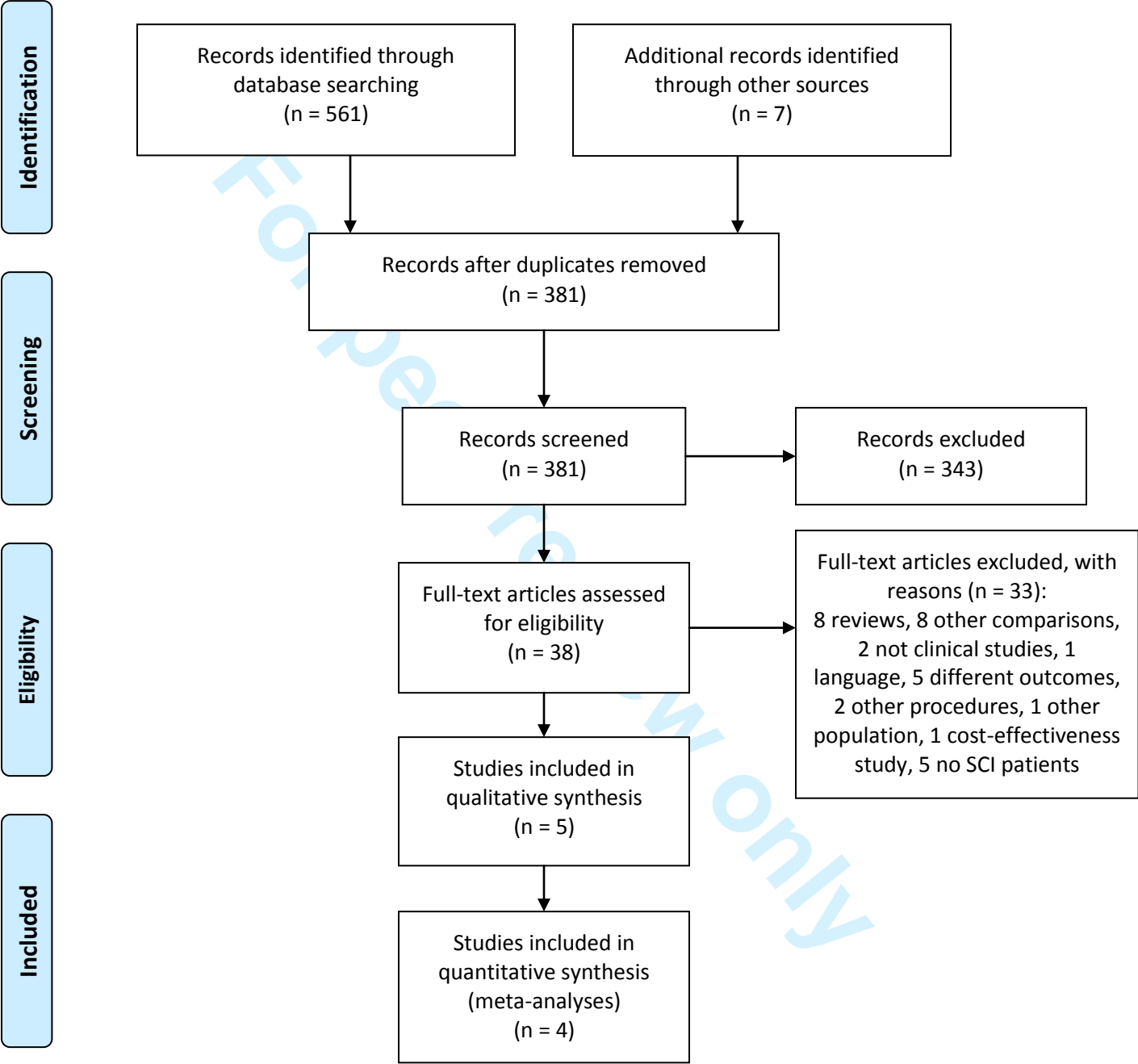
(intermittent OR catheter\*)

AND

(urinary tract infection\* OR UTI OR UTIs OR infection\* OR urethral trauma OR stricture\* OR hematuria OR quality of life OR QOL OR QALY OR QALYs)



PRISMA Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

## CHEERS Checklist

### Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp>

Section/item	Item No	Recommendation	Reported on page No/line No
<b>Title and abstract</b>			
Title	1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	pages 2-3
<b>Introduction</b>			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	from page 4
<b>Methods</b>			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	from page 6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	page 13
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	page 13
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	page 6
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	page 9
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	page 15
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	page 9
Measurement of effectiveness	11a	<i>Single study-based estimates:</i> Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	



	11b	<i>Synthesis-based estimates:</i> Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	pages 6-9
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	pages 14-15
Estimating resources and costs	13a	<i>Single study-based economic evaluation:</i> Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
	13b	<i>Model-based economic evaluation:</i> Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	pages 13-14
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	page 13
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	pages 9-10
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	pages 9-15
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	pages 6-9, 15
<b>Results</b>			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	page 15 and Suppl. Table 4
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	pages 17-18
Characterising uncertainty	20a	<i>Single study-based economic evaluation:</i> Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	

		of methodological assumptions (such as discount rate, study perspective).	
	20b	<i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	pages 18-20
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	
<b>Discussion</b>			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	pages 23-26
<b>Other</b>			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	page 27
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp>

The citation for the CHEERS Task Force Report is:

Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. *Value Health* 2013;16:231-50.

