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ORIGINAL RESEARCH

Artificial Urinary Sphincters as a Treatment for Post-Prostatectomy Severe Urinary Incontinence in Italy: A Cost-Utility Analysis

Francesco Saverio Mennini [1,2], Daniele Rossi [1], Andrea Marcellusi [1]

1 Economic Evaluation and HTA (EEHTA), CEIS, DEF Department, Faculty of Economics, University of Rome "Tor Vergata", Rome, Italy

2 Institute for Leadership and Management in Health - Kingston University London, London, UK

ABSTRACT

Objective: This study aimed at evaluating the cost-utility of artificial urinary sphincter (AUS) in men affected by post-prostatectomy severe urinary incontinence and identifying the most cost-effective alternative among the various devices analyzed in Italy.

Methods: A 5-year cycles Markov model was developed to simulate the disease evolution. The analysis compared conservative therapy, ZSI 375®, single-cuff (SC) AMS 800™, and double-cuff (DC) AMS 800™. A Probabilistic Sensitivity Analysis (PSA) was performed. One thousand Monte Carlo simulations were conducted to generate the Cost-Effectiveness Acceptability Curve for each intervention strategy. A sensitivity analysis on the price of the device was conducted.

Results: From the Italian National Health Service perspective, DC AMS 800™ was the most cost-effective alternative in comparison with conservative therapy, with an Incremental Cost-Effectiveness Ratio (ICER) value equal to € 12,893. From the NHS + patient perspective, both the AMS 800™ devices (SC and DC) were dominant in comparison with conservative therapy. From the societal perspective, ICER was dominant for all the alternatives considered in terms of cost-effectiveness. The PSA showed that DC AMS 800™ had a greater probability to be cost-effective with respect to the other strategies considered in the analysis. The sensitivity analysis on the price of the device showed that in all the cases analyzed the incremental cost per QALY gained would be below € 25,000.

Conclusions: This cost-utility analysis confirms that AUSs are cost-effective options in the Italian context with respect to conservative therapy. Among AUSs, DC AMS 800™ has the greatest probability to be cost-effective.

Keywords

Cost-utility; Artificial Urinary Sphincters; AMS 800; Prostatectomy; Urinary Incontinence; Conservative Therapy

INTRODUCTION

Post-prostatectomy incontinence affects a variable proportion of patients undergoing this type of surgery, from < 5% to 70% [1].

In Italy, according with expert opinion, 80% of patients suffer from post-prostatectomy incontinence, but conservative therapy resolves symptoms within 12 months from surgery in 90% of these patients [2]. Conservative therapy consists mainly of duloxetine, pelvic floor muscle training, and lifestyle changes, such as caffeine reduction, physical exercise, fluid intake, diet, and smoking cessation [3].

Men with persistent moderate-to-severe post-prostatectomy incontinence may be offered artificial urinary sphincters (AUSs) [3,4].

The first externally worn urethral cuff was described by Foley in 1949 [5]. Afterwards, other increasingly improved devices were developed, and a completely internalized AUS has been used since 1973 [6]. Less than 10 years after, a new version, namely AMS 800™ model (Boston Scientific Corporation, Marlborough, Massachusetts, USA), allowed to reduce mechanical malfunction and erosion rates [7,8]. Little changed since then and AUS became, and still remains, the gold standard for the treatment of post-prostatectomy incontinence [8].

AMS 800™ models are composed of:

- one cuff, but an additional cuff may be implanted. Therefore, two arrangements are possible: single-cuff (SC) AMS 800™ and double-cuff (DC) AMS 800™;

Corresponding author
Francesco Saverio Mennini
f.mennini@uniroma2.it

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- pressure regulating baloon;
- control pump.

Other AUSs had been developed, among which Zephyr artificial sphincter device (Zephyr ZSI 375®; Zephyr Surgical Implants, Geneva, Switzerland), that needs no remote reservoir balloon and consists of an adjustable inflatable cuff [8].

In the Italian panorama, AMS 800™ and ZSI 375® are the main available AUSs. Data about a third device, which is VICTO® (Promedon, Kolbermoor, Germania) are scarce due to the recent approval: this is why it was not considered in the present analysis.

The analysis of hospital discharge records 2016 [9] highlights that in Italy around 240 AUS implantations are performed, whilst about 1,000 patients live with unresolved incontinence in conservative therapy. Therefore, AUS implantation is underused, mainly because of scarce information to patients, poor availability of qualified personnel, with long waiting lists, and inadequate reimbursement, which are unable to cover all the costs incurred by NHS.

Further evidence about the cost-effectiveness of these procedures is required.

Cost-Utility Analysis (CUA) is a method aimed at evaluating healthcare investment projects. It comes of a particular kind of cost-effectiveness analysis using Quality-Adjusted Life Years (QALYs), which measures the increase in the mean life expectancy corrected for the quality and aims at quantifying the effects coming from using or not a therapy to treat a pathology.

This study aimed at evaluating the cost-utility of AUS in men affected by post-prostatectomy severe urinary incontinence and identifying the most cost-effective alternative among the various devices which were analyzed.

METHODS

Perspectives

The outcome evaluated was the Incremental Cost-Effectiveness Ratio (ICER). ICER values were calculated from two perspectives:

1. ICER: evaluation of the cost-effectiveness of every device analyzed in comparison with the alternative with the lowest effectiveness among all the alternatives considered (conservative therapy);
2. ICER vs. best alternative**:** cost-effectiveness evaluation of every device analyzed in comparison with the alternative with a strictly lower effectiveness. In particular, the following comparisons were described:
   - ZSI 375® vs. conservative therapy;
   - SC AMS 800™ vs. ZSI 375®;
   - DC AMS 800™ vs. SC AMS 800™.

Markov model

With the aim of simulating various cohorts of patients undergone implantations with the devices in analysis, a Markov model was developed to simulate the disease evolution in pa-

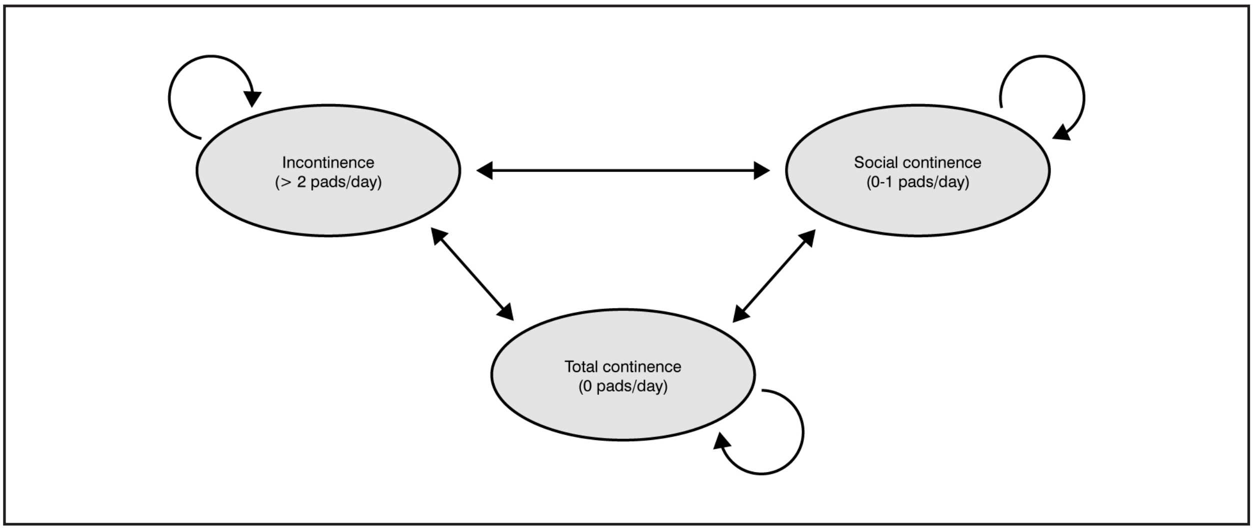

Figure 1. *Model scheme*

tients affected by urinary incontinence. The model was built considering a 5-year time horizon (60 months).

In particular, Markov process is based on three mutually exclusive health statuses that reflect the evolution of the patients in the study (Figure 1):
1. incontinence (> 2 pads/day);
2. social continence (0-1 pads/day);
3. total continence (0 pads/day).

Epidemiological parameters

Table I shows the risk parameters considered in the analysis and coming from the calculations already performed for budget impact analysis, as reported by our group [10].

Utility

Table II shows the impact of urinary incontinence on patients' quality of life by means of QALY. In particular, in this study, the article by Lee et al. [11] is taken into account. They quantified and demonstrated that the incontinence severity has a clinically significant impact on the patients' quality of life (QoL) and is associated with the increase in the weekly cost of drug therapy for incontinence, the reduction in working hours, and the increased interference with daily activities.

Also, the study by Currie et al. was considered [12], where, after standardization for other potential confounders, urological symptoms particularly reduced the utility and the QoL in the affected patients.

Therefore, as utilities differed between the abovementioned studies, we used the mean of the two utilities for every item (Table II).

Risk parameters (%)	SC AMS 800™	DC AMS 800™	ZSI 375®
12 months			
Incontinence	12.44	0.00	19.00
Total continence	61.24	71.95	26.00
Social continence (0-1 pads)	26.32	28.05	55.00
24 months			
Incontinence	13.89	0.00	22.00
Total continence	59.81	70.28	25.00
Social continence (0-1 pads)	26.30	29.72	53.00
36 months			
Incontinence	14.72	0.03	24.00
Total continence	59.00	69.31	24.00
Social continence (0-1 pads)	26.28	30.66	52.00
48 months			
Incontinence	15.31	0.72	25.00
Total continence	58.42	68.64	24.00
Social continence (0-1 pads)	26.27	30.64	51.00
60 months			
Incontinence	15.76	1.25	26.00
Total continence	57.92	68.12	24.00
Social continence (0-1 pads)	26.32	30.63	50.00

Table I. *Transition probability per year and per device*

	Min	Source	Max	Source	Mean
Incontinence	0.564	Lee et al., 2015 [11]	0.742	Currie et al., 2006 [12]	0.653
Total continence	0.746		0.848		0.797
Social continence (0-1 pads)	0.689		0.784		0.737

Table II. *Impact of urinary incontinence on the quality of life*

Cost parameters

Table III shows the cost parameters considered in the CUA model [10]. In particular:

- the cost of total continence was equal to € 41 [13] by assuming that continent patients had just 2 control visits/year;
- the cost of social continence: the use of just one pad/day, which is borne by NHS, is hypothesized. The expected expenditure is equal to € 121.6, which takes into account 2 visits/year + 1 pad/day incurred by NHS;
- the cost of incontinent subjects: following the analysis perspectives, the model assumes a cost equal to € 842.5 in the perspective of NHS (coming from the use of 4 devices paid by NHS at the price of € 0.22 [14], the cost of 2 control visits/year, and the need to administer further drugs). In the perspective of the patient, also the cost for 3 further pads/day to be borne by him/herself at the mean price of € 0.92 must be added [14].

	Incontinence	Social continence	Total continence
NHS cost (€)	842.5	121.6	41.3
NHS + patient cost (€)	1,849.92	121.6	41.3

Table III. *Estimation of the cost items considered in the analysis*

Sensitivity Analysis

With the aim of considering the variability of results according with the parameters that make up the model, a Probabilistic Sensitivity Analysis (PSA) was performed.

In this analysis, all the parameters considered in the model vary according with a certain probability distribution to capture the uncertainty that characterizes the parameters of interest. The probabilistic distribution was attributed by applying what is generally reported for the development of the probabilistic models in the economic evaluations, distinguishing between cost parameters (gamma distribution) and epidemiologic parameters (beta distribution) [11]. One thousand Monte Carlo simulations were conducted to generate the Cost-Effectiveness Acceptability Curve (CEAC) for each intervention strategy. This curve expresses the cost-effectiveness probability of each strategy (in comparison with the conservative therapy) on the grounds of the NHS Willingness To Pay. In addition, the cost-effectiveness plan was reported, showing all ICER values that were generated by the 1,000 Monte Carlo simulations.

Furthermore, a specific sensitivity analysis was carried out on the price of the device, based on the assumption that a growing number of devices purchased by the NHS may ensure discounts on the cost of SC or DC AMS 800™. The results of this sensitivity analysis are reported from the perspective of NHS only, as we assume that the same improvements in the results may be proportionally identified even from the other perspectives.

RESULTS

Deterministic results from the NHS perspective

Table IV shows the results about patients with urinary incontinence after radical prostatectomy from the NHS perspective.

Figure 2 shows the projection of ICER estimates compared with conservative therapy on the cost-effectiveness plane.

Year 5	NHS costs	QALYs	Incremental cost (vs. conservative therapy)	Incremental QALYs (vs. conservative therapy)	NHS ICER vs. conservative therapy	Incremental cost (vs. worst alternative)	Incremental QALYs (vs. worst alternative)	ICER best alternative
Conservative therapy	€ 421,260	326.50						
ZSI 375®	€ 1,825,062	366.00	€ 1,403,802	39.50	€ 35,535	€ 1,403,802	39.50	€ 35,535
SC AMS 800™	€ 1,151,036	380.16	€ 729,776	53.66	€ 13,601	-€ 674,025	14.15	Dominant vs. ZSI 375®
DC AMS 800™	€ 1,218,826	388.36	€ 797,566	61.86	€ 12,893	€ 67,790	8.21	€ 8,260

Table IV. *Cost-effectiveness from the NHS perspective*

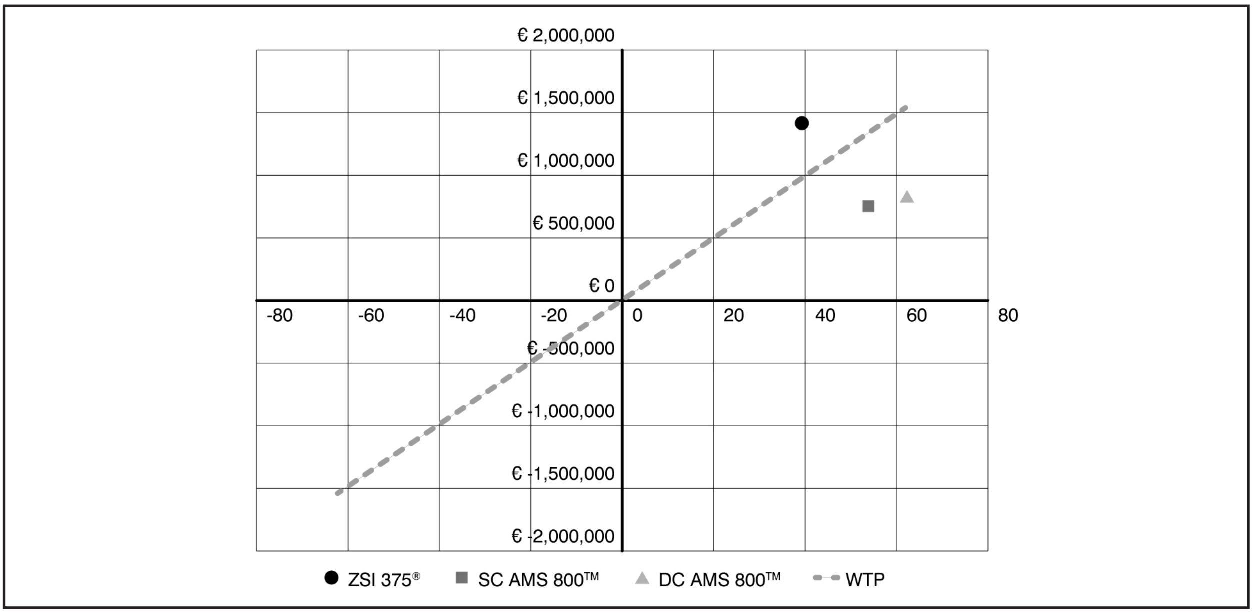

Figure 2. *Cost-effectiveness plane from the NHS perspective with Willingness To Pay = € 25,000 per QALY gained*

Year 5	NHS + patient costs	QALYs	Incremental cost (vs. conservative therapy)	Incremental QALYs (vs. conservative therapy)	NHS + patient ICER vs. conservative therapy	Incremental cost (vs. worst alternative)	Incremental QALYs (vs. worst alternative)	ICER best alternative
Conservative therapy	€ 421,260	326.50						
ZSI 375®	€ 1,825,062	366.00	€ 693,442	39.50	€ 17,553	€ 693,442	39.50	€ 17,553
SC AMS 800™	€ 1,151,036	380.16	-€ 61,676	53.66	Dominant	-€ 755,118	14.15	Dominant vs. ZSI 375®
DC AMS 800™	€ 1,218,826	388.36	-€ 106,134	61.86	Dominant	-€ 44,458	8.21	Dominant vs. SC AMS 800™

Table V. *Cost-effectiveness from the NHS + patient perspective*

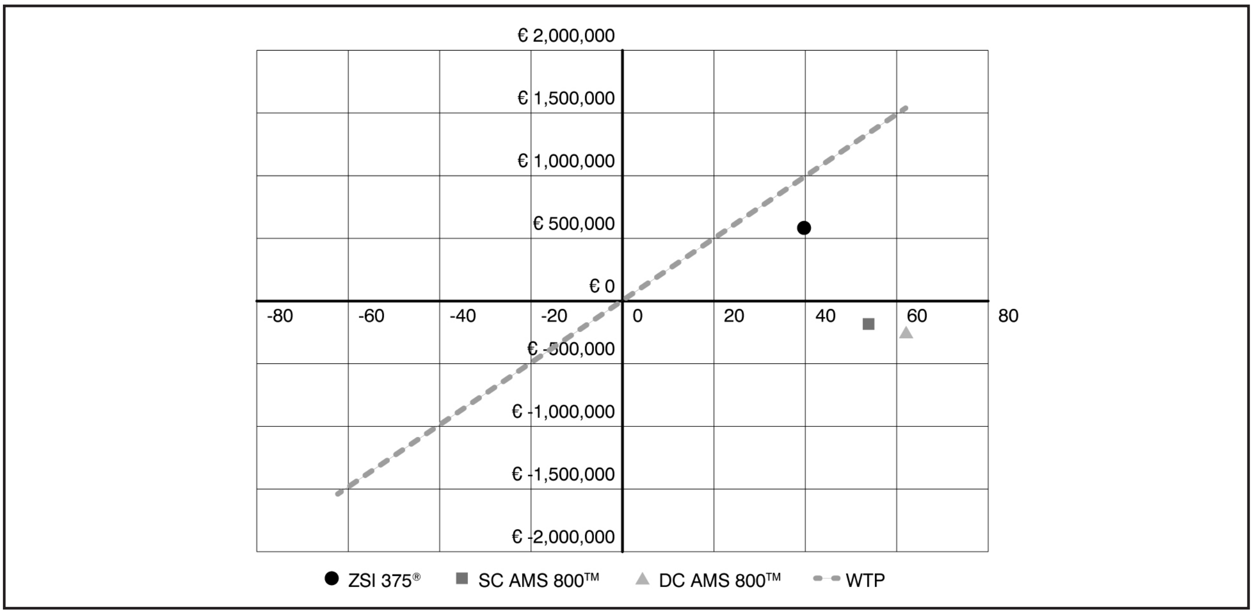

Figure 3. *Cost-effectiveness plane from the NHS + patient perspective with Willingness To Pay = € 25,000 per QALY gained*

Results from the NHS + patient perspective

Table V shows the results about patients with urinary incontinence after radical prostatectomy from the NHS + patient perspective.

Figure 3 shows the projection of ICER estimates compared with conservative therapy on the cost-effectiveness plane: the ICER of ZSI 375® is below the Willingness To Pay—WTP (dashed line) (see Methods section), whilst the ICERs of SC and DC AMS 800™ are both in the IV quadrant, thus in the plane area where the alternative is less costly and more effective.

Results from the societal perspective

Table VI shows the results about patients with urinary incontinence after radical prostatectomy from the societal perspective.

Figure 4 shows the projection of ICER estimates compared with conservative therapy on the cost-effectiveness plane.

Results of the probabilistic sensitivity analysis

CEACs obtained by means of 1,000 Monte Carlo simulations showed that DC AMS 800™ has a greater probability to be cost-effective with respect to the other strategies considered in the analysis (Figure 5). Figure 6 shows the cost-effectiveness plane with all the combinations of QALY differentials (abscissa axis) and costs (ordinate axis).

Year 5	Societal costs	QALYs	Incremental cost (vs. conservative therapy)	Incremental QALYs (vs. conservative therapy)	Societal ICER vs. conservative therapy	Incremental cost (vs. worst alternative)	Incremental QALYs (vs. worst alternative)	ICER best alternative
Conservative therapy	€ 3,286,220	326.50						
ZSI 375®	€ 2,562,097	366.00	-€ 724,123	39.50	Dominant	-€ 724,123	39.50	Dominant vs. conservative therapy
SC AMS 800™	€ 1,600,987	380.16	-€ 1,685,233	53.66	Dominant	-€ 961,109	14.15	Dominant vs. ZSI 375®
DC AMS 800™	€ 1,323,533	388.36	-€ 1,962,687	61.86	Dominant	-€ 277,454	8.21	Dominant vs SC AMS 800™

Table VI. *Cost-effectiveness from the societal perspective*

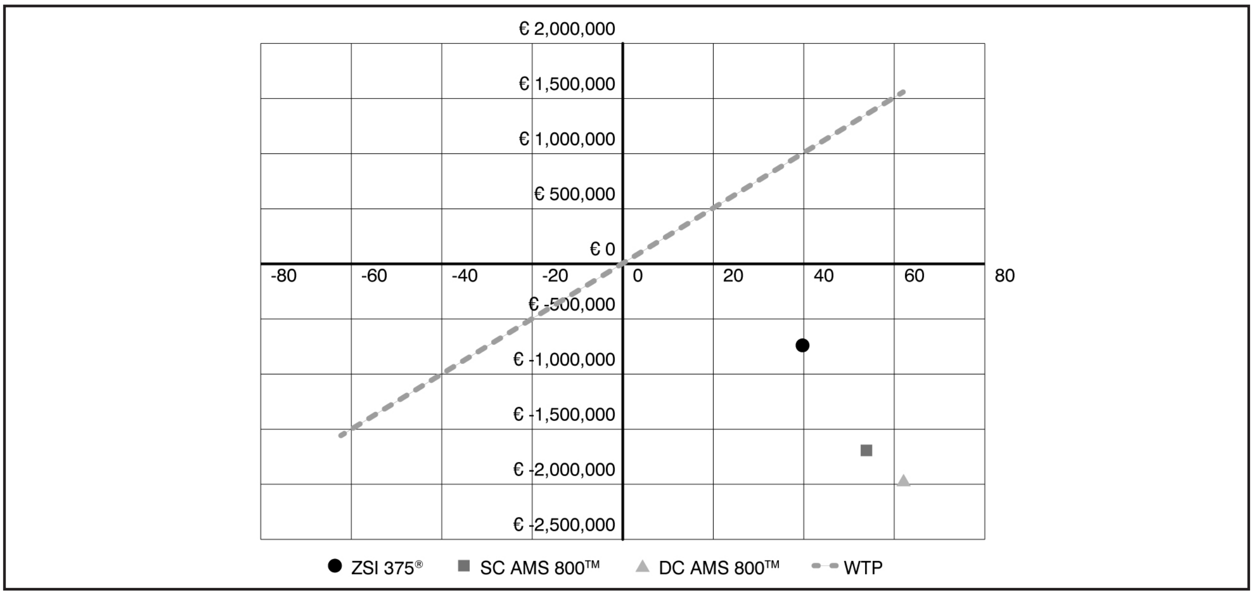

Figure 4. *Cost-effectiveness plane from the societal perspective with Willingness To Pay = € 25,000 per QALY gained*

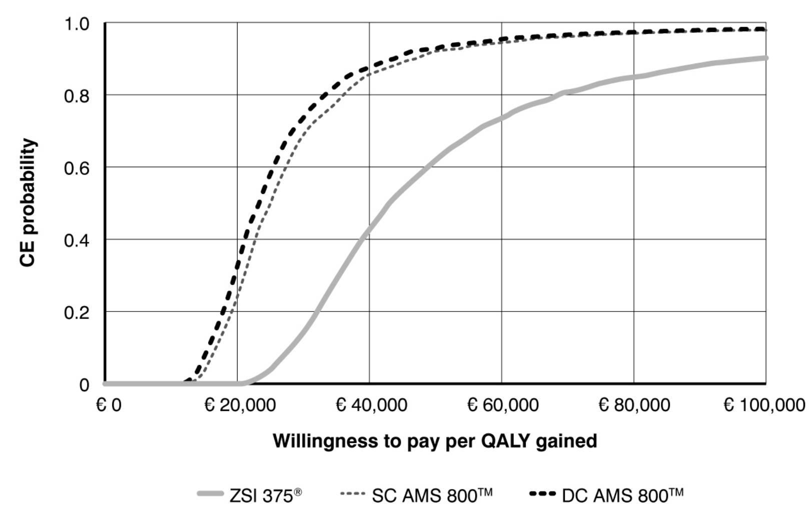

Figure 5. *Cost-Effectiveness Acceptability Curve – CEAC*

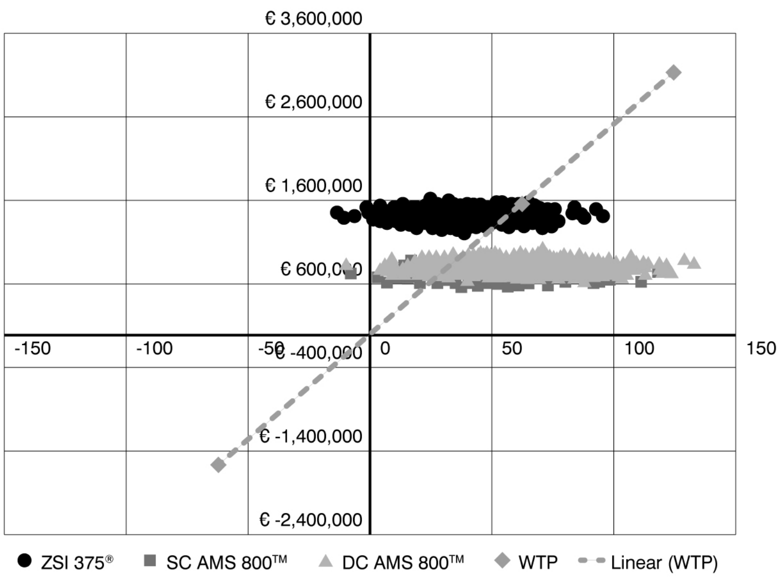

Figure 6. *Cost-effectiveness plane with all the combinations of QALY differentials and costs*

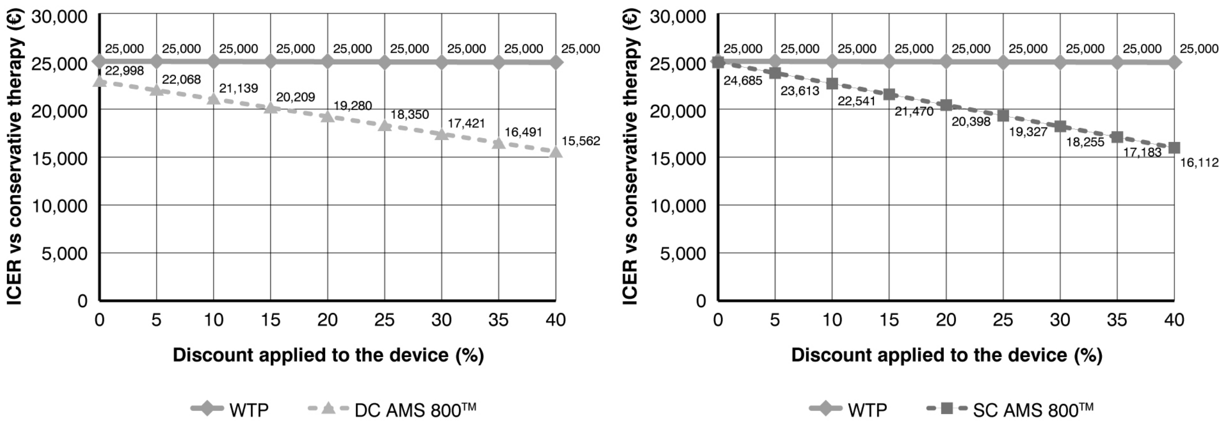

Figure 7. *ICER results hypothesizing discounts on the device with Willingness To Pay = € 25,000 per QALY gained*

The cost-effectiveness plane confirms that DC AMS 800™ is the most cost-effective alternative, because in 57% of the simulations ICER values were below the WTP.

Sensitivity analysis on the price of the device

Finally, a sensitivity analysis was conducted for the ICER value per QALY gained of SC and DC AMS 800™ vs. conservative therapy from the NHS perspective considering the various discounts proposed for the two devices in analysis (Figure 7).

DISCUSSION

To our knowledge, this is the first cost-utility analysis evaluating the use of AUS in Italy.

In order to provide readers with a complete overview, we analyzed the expenditures coming from the various methods of managing post-prostatectomy severe urinary incontinence from three different perspectives: NHS perspective, NHS + patient perspective, and societal perspective.

The main indicator in the cost-utility analyses is the ICER, i.e., the incremental cost required to obtain one additional unit of the measure of effect with the treatment in analysis in comparison with the standard therapy. To date, no ICER threshold is considered internationally acceptable. However, in Italy, values in the acceptability range included in the interval € 20,000-40,000 have been proposed. In this analysis, ICER values below € 25,000 per QALY gained were considered cost-effective.

From the NHS perspective, DC AMS 800™ was the most cost-effective alternative in comparison with conservative therapy, with an ICER value equal to € 12,893. Observing the estimated ICER values in comparison with the alternative with strictly lower effectiveness, thereby comparing ZSI 375® with the conservative therapy, SC AMS 800™ with ZSI 375®, and DC AMS 800™ with SC AMS 800™, SC AMS 800™ was dominant compared with ZSI 375®, i.e., more effective and less costly (Table 4). The ICER of DC and SC AMS 800™ was below the WTP (Figure 2).

From the NHS + patient perspective, both AMS 800™ devices (SC and DC) were dominant in comparison with conservative therapy. When comparing the various devices with each other, SC AMS 800™ was again dominant with respect to ZSI 375®, whilst DC AMS 800™ was dominant if compared with SC AMS 800™ (Table V). The ICER of ZSI 375® was below WTP, whilst the ICERs of both SC and DC AMS 800™ are both in the IV quadrant, thus in the plane area where the alternative is less costly and more effective (Figure 3).

From the societal perspective, ICERs of both SC and DC AMS 800™ were dominant for all the alternatives considered, both in comparison with conservative therapy and the worst alternative in terms of cost-effectiveness (Table 6). ICER estimates were in the IV quadrant (Figure 4).

The probabilistic sensitivity analysis showed that DC AMS 800™ had a greater probability to be cost-effective with respect to the other strategies considered in the analysis: in fact, considering a WTP per QALY gained equal to € 25,000, the cost-effectiveness probability of DC AMS 800™ in comparison with the conservative therapy was 57%, whilst the cost-effectiveness probability of SC AMS 800™ and ZSI 375® with respect to conservative therapy were equal to 50% and 5%, respectively (Figure 5). The confirmation of the greatest cost-effectiveness of DC AMS 800™ came from the Monte Carlo simulations, 57% of which were below the WTP in the cost-effectiveness plane (Figure 6).

The sensitivity analysis on the price of the device was based on the assumption that a growing number of devices purchased by the NHS may ensure discounts on the cost of SC or DC AMS 800™. The analysis for the ICER value per QALY gained of SC and DC AMS 800™ vs. conservative therapy from the NHS perspective showed that ICER value may range from a maximum of about € 22,000 considering a 5% discount to a minimum of around € 15,500 with a 40% discount for both the devices. However, in all the cases analyzed, the incremental cost per QALY gained would be below € 25,000 (Figure 7).

This CUA confirms that AUSs are cost-effective options in the Italian context with respect to conservative therapy. Among AUSs, DC AMS 800™ had the greatest probability to be cost-effective.

In the Italian context, in the light of this analysis, a regulatory intervention that recognizes dignity and value of the implantation of AUS post-radical prostatectomy in the patient in whom conservative therapy failed would be desirable.

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Conflicts of interests

The authors declare they have no further competing interests in addition to the funding for the analysis provided by Boston Scientific Corporation.

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