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HTA Report

Sling operation for urinary incontinence in women and men

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Caruso Orlando declares that in the last three years he received congressional Reimbursement from Astellas.

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Abstract

Background: Stress urinary incontinence (SUI) is the most common type of UI among women but less common in men and mainly secondary to radical prostatectomy. Non-surgical approaches are recommended as first-line treatment. Surgery is generally performed when these strategies have failed.

Aim: This HTA report focuses on the impact of sling operation in women (compared to Burch colposuspension or autologous vaginal tapes) and men (compared to Artificial Urinary Sphincter – AUS – or adjustable continence therapy) with SUI. Conservative therapy with diapers was considered a comparator for both populations.

Methods: We performed searches of the national hospital discharge database to describe the level of use of sling insertion versus its comparators. We included evidence synthesis assessing comparative evidence on effectiveness, safety and the economics of sling use.

Results: As of today, 17 manufacturers of slings for women and 9 manufacturers of male slings are present on the Italian market. National hospital discharge data for the period 2010–2014 show that sling operations represent 95.9% of all interventions for SUI in women and 36.3% in men. While in women the figures are stable, in men the proportion has increased from 26.7% to 38.1% (intervention rate of 123.2/1,000,000 women per year and 6.1/1,000,000 men per year). The evidence from a Cochrane review supports sling compared to Burch procedure in women, but the studies are affected by methodological problems and no specific device models are identified. Measures of Quality of Life (QoL) were rarely reported. No studies comparing sling insertion with AUS or adjustable continence therapy in men were identified. Only one ongoing trial (to be completed in August 2019) comparing sling insertion with AUS was identified.

We found economic evidence from two studies for female sling and none for males. The mean total cost of tension-free vaginal tape (TVT) was lower than the other intervention mainly due to the shorter hospital stay and operating time. Another reported that sling operation was more cost effective than the Burch procedure.

Conclusions: Only devices supported by robust clinical data should be used in women. Comparative clinical data are insufficient to support the use of male slings. All sling devices should be tested in prospective multicentre comparative studies before marketing and current legislation should be changed accordingly. Such studies should include prospective economic evaluation with reproducible measures of QoL.

Sintesi in italiano

Introduzione

Il presente report di HTA tratta la procedura chirurgica che prevede l'impianto di una benderella in materiale sintetico, nota come sling, in donne e uomini affetti da incontinenza urinaria da stress (IUS) per ripristinare o migliorare il supporto uretrale e prevenire la perdita involontaria di urina. Le differenze tra le due popolazioni in oggetto hanno reso necessario un approccio distinto per strutturare l'analisi e la definizione di due diversi set di comparatori: colposospensione di Burch o sling vaginale autologa nelle donne; sfintere urinario artificiale (AUS) o *adjustable continence therapy* (ACT) negli uomini.

Obiettivi

Il report di HTA è stato sviluppato al fine di rispondere al seguente quesito di ricerca: "Quali sono gli effetti dell'intervento di sling su donne e uomini con IUS in termini di efficacia clinica, rischi e costo-efficacia?"

Metodi

Il presente report di HTA è stato costruito utilizzando un adattamento della versione 2.0 dell'applicazione *"Medical and surgical procedures"* del Core Model® di EUnetHTA. Le specifiche aree d'indagine, denominate domini e suddivise in quesiti denominati *Assessment Elements (AE)*, sono presentate sequenzialmente nei diversi capitoli del documento.

Sono stati sviluppati i seguenti domini:

- Problema sanitario e uso corrente della tecnologia (CUR)
- Descrizione e caratteristiche della tecnologia (TEC)
- Aspetti regolatori (REG)
- Efficacia clinica (EFF) e Sicurezza (SAF);
- Costi e valutazione economica (ECO).

I relativi AE sono stati sviluppati, secondo pertinenza, effettuando ricerche su banche dati nazionali, indagini dirette presso i produttori della tecnologia in esame e loro siti web, revisione sistematica della letteratura clinica ed economica.

Risultati

Problema sanitario e uso corrente della tecnologia (CUR)

L'incontinenza urinaria è una condizione comune tra le donne e gli uomini. Tra i tre sottotipi principali di incontinenza urinaria, la IUS rappresenta la più comune tra le donne (10-39% dei casi) mentre sembra essere meno comune tra gli uomini (meno del 10% dei casi). La diagnosi inizia con un'accurata storia clinica seguita dall'esame fisico e dalla valutazione ecografica del volume residuo post-minzionale, pad test ed eventuali studi urodinamici di approfondimento. Tuttavia, la gravità della condizione deve essere sempre valutata contestualmente al fastidio percepito dal/dalla paziente e al suo impatto sulle attività della vita quotidiana. Opzioni di trattamento non-chirurgiche sono raccomandate come prima linea, mentre gli approcci chirurgici vengono generalmente proposti quando le strategie conservative hanno fallito.

I dati italiani hanno mostrato che la maggior parte degli interventi chirurgici per IUS vengono effettuati nel Nord Italia (66% del totale dimissioni tra le donne; 77,6% tra gli uomini). La procedura di sling è effettuata con maggiore frequenza nelle donne (95,5% rispetto a 36,3% negli uomini). La durata media della degenza tra le donne è molto più breve per l'intervento di sling che per la procedura di Burch (rispettivamente 3 e 4,9 giorni). Tra gli uomini, la durata media della degenza non presenta differenze rilevanti tra le procedure (3,6 giorni per l'intervento di sling, 3,7 giorni per l'inserimento di AUS). La correzione chirurgica della IUS appare in diminuzione tra le donne, mentre negli uomini si evidenzia un leggero incremento nel periodo di osservazione (2010–2014). Dalla loro introduzione sul mercato italiano, sono state vendute circa 30.000 sling femminili e 3.000 sling maschili. Nel 2015, il prezzo medio di un kit (sling più introduttori) è stato di € 520 (range: € 360–730) per le sling femminili standard e di € 700 (range: € 450–920) per le mini-sling. Nello stesso anno, il prezzo medio di un kit di sling maschile è stato di € 2,650 (€ 2,300–3,300).

Descrizione e caratteristiche della tecnologia (TEC)

La procedura di sling viene eseguita in anestesia generale, spinale o locale dall'uro-ginecologo o dall'urologo. Le sling sono in genere disponibili in kit specifici, che comprendono gli strumenti per effettuare l'impianto (aghi introduttori specifici per i diversi approcci chirurgici attraverso i quali l'impianto della sling può essere effettuato). Sul mercato italiano sono stati individuati 17 produttori di sling femminili per un totale di 33 prodotti diversi. Le sling maschili sono invece offerte da 9 produttori per un totale di 10 prodotti.

Aspetti regolatori (REG)

Le sling per l'incontinenza urinaria sono dispositivi medici appartenenti alla classe di rischio IIb e sono disponibili sul mercato italiano da diversi anni. Diversi modelli di sling hanno ricevuto anche l'approvazione dalla FDA americana. In Italia, la procedura può essere rimborsata secondo tre

diversi codici DRG con una tariffa nazionale massima di rimborso di € 4.693, € 3.397 e € 2.901 rispettivamente per i codici 308, 309, e 356.

Efficacia clinica (EFF) e Sicurezza (SAF)

Sling per incontinenza urinaria nelle donne

È stata individuata una revisione sistematica di 22 studi (2.343 donne). Nonostante i limiti nel disegno degli studi inclusi e nel reporting di metodi e risultati, l'evidenza sembra supportare l'utilizzo delle sling femminili rispetto alla colposospensione di Burch. Nel periodo post-intervento, la procedura di sling sembra essere associata ad una minore incidenza di eventi di prolasso pelvico ma ad una maggiore incidenza di disfunzioni minzionali rispetto alla colposospensione. Solo 2 studi si sono concentrati sull'impatto degli interventi sulla qualità della vita delle pazienti, nonostante questo aspetto sia riconosciuto come uno dei maggiori determinanti nel processo decisionale. La qualità metodologica generale degli studi è stata giudicata moderatamente bassa.

Sling per incontinenza urinaria negli uomini

Non sono stati identificati studi in cui l'intervento di sling fosse stato comparato con AUS, ACT o approcci conservativi. Tra gli studi in corso, è stato identificato uno studio che si propone di comparare l'efficacia dell'intervento di sling rispetto a AUS in 360 uomini. I risultati potrebbero essere disponibili entro Agosto 2019.

Costi e valutazione economica (ECO)

L'evidenza da studi economici sull'utilizzo delle sling è molto limitata. Solo 2 studi sull'intervento di sling nelle donne sono stati inclusi nella presente revisione sistematica. Nessuno studio sull'intervento di sling negli uomini è stato individuato. Tra i due studi inclusi, uno studio di costo-utilità ha mostrato la dominanza dell'intervento di sling rispetto alla colposospensione di Burch mentre una analisi dei costi ha evidenziato un minor costo medio totale dell'intervento di sling rispetto ad altri interventi tra cui la colposospensione di Burch. Tale differenza è stata collegata al minor tempo operatorio e di degenza.

Conclusioni

Mentre l'uso delle sling per l'incontinenza urinaria femminile rispetto alla colposospensione di Burch sembra essere supportato da studi di efficacia comparativi, la provenienza di dati a supporto dell'uso delle sling maschili rispetto a AUS e ACT rimane al momento limitata a studi non comparativi e opinioni di esperti. A seguito di questo scenario, ad esempio, il NICE ha formulato raccomandazioni precauzionali che restringono l'uso delle sling a incisione singola (mini-sling) nelle donne e l'uso delle sling maschili entro percorsi atti a generare evidenza. Inoltre, le conclusioni estratte dai soli due studi economici disponibili non possono essere considerate definitive.

Altri elementi di criticità nella valutazione delle sling per incontinenza urinaria sono sicuramente rappresentati dalla vastità di dispositivi e varianti offerti sul mercato, dalla potenziale inadeguatezza dell'attuale sistema di certificazione e dal sistema di codifica degli interventi che, non essendo aggiornato alla pratica corrente, non permette di distinguere interventi molto diversi in termini di risorse impiegate e complessità chirurgica.

Raccomandazioni

Nelle donne, l'intervento di sling dovrebbe essere effettuato solo utilizzando quei dispositivi per i quali siano stati generati dati di efficacia comparativa. Negli uomini, l'intervento di sling dovrebbe essere limitato a quei contesti clinici all'interno dei quali sia possibile generare evidenze comparative di efficacia e sicurezza. La codifica delle procedure per il trattamento dell'incontinenza urinaria dovrebbe essere aggiornata e rivista per riflettere maggiormente la pratica clinica corrente. Tutte le sling per incontinenza urinaria dovrebbero essere oggetto di studi prospettici comparativi multicentrici prima della loro immissione in commercio e la normativa di riferimento dovrebbe essere aggiornata di conseguenza. Gli studi clinici futuri dovrebbero includere elementi per valutazione economiche e parametri per la misura dell'impatto della procedura sulla qualità della vita.

Introduction

This document was developed following the EUnetHTA Core Model® application for "Medical and surgical procedures" version 2.0. The Core Model is divided into domains representing each a specific area of technology impact that have to be assessed. Each domain contains a series of research questions or Assessment Elements (AEs) identified by a capital letter and number. To test the Core Model applicability, an adapted model was elaborated by Agenas (see Appendix 1 for a full description). The use of the Core Model is mirrored in the structure of this report, where each chapter corresponds to a domain and reports the AEs considered for the assessment.

The present HTA report focuses on the surgical procedure entailing the insertion of a mesh tape, known as sling, in women and men with stress urinary incontinence (SUI). The structure of the chapters reflects the facts that the condition, as well as the technology, present some peculiarities for the two populations and, in the same way, two different sets of comparators were necessary to develop the assessment.

1. Report's objectives: policy and research questions

A HTA report was developed to answer the following:

Policy Question: What is the impact of sling insertion in the treatment of stress urinary incontinence (SUI) in women and men?

Research Question: What are the effects of sling operation in women and men, in terms of effectiveness, harms and cost-effectiveness?

The following domains were developed within the present rapid HTA report:

- Health problem and current use of technology (CUR)
- Description and technical characteristics of technology (TEC)
- Regulatory aspects (REG)
- Clinical effectiveness (EFF) and Safety (SAF);
- Costs and economic evaluation (ECO).

For each investigated domain, the selected Assessment Elements (AEs) are listed in Appendix 2. Each included AE is listed in the relevant text in bold.

2. Health problem and current use of technology

Methods

The AEs of this domain were:

Assessment Element ID	Research question
A0001	A0001a: For which health condition is the technology proposed? A0001b: Which group of patients represents the target population for the technology? A0001c: For what purposes is the technology used?
A0002	What is the health condition in the scope of this assessment?
A0006	What are the statistics of incidence, prevalence, morbidity, and mortality of the health condition?
A0024	How is the health condition identified/diagnosed?
A0003	What are the known risk factors for the health condition?
A0004	What is the natural course of the health condition?
A0005	What are the symptoms for the patient at different stages of the health condition?
G0009	G0009a: Who decides which people are eligible for the technology? G0009b: On what basis is the eligibility for the technology decided?
A0017	What are the differences in the management for different stages of the health condition?
A0018	What are the alternatives to the current management of the health condition?
A0011	What is the diffusion of the technology across the Italian regions?
B0001b	What is the comparator?
B0003b	What is the phase of development of the comparator(s)?

All the AEs selected within the domain were developed. The health condition of interest was described using international and national literature. Specific searches were performed to identify the latest reviews and epidemiological studies. Data analysis and synthesis from the national hospital discharge records database (SDO database) were performed to present the burden of the condition and the level of use of sling operation and its comparators in Italy. The database's summary reports for the years 2010–2014 were accessed. The use of the sling insertion procedure was compared to Burch's procedure in women and AUS implantation in men. The Italian Official Statistical Service (ISTAT) average resident population data for the years 2010–2014 were used to calculate the intervention rates for women and men. Standardised rates for regions and geographical areas comprising various regions (North, Centre, and South) were calculated with the indirect method using the Italian population as reference population (see Appendix 3). The level of use of sling devices was described by presenting the data reported in the regional guidelines on the use of AUS, sling, and sacral neuromodulation systems published by Veneto region in June 2016[1]. Data were limited to the number of slings sold by the companies at national level since the

introduction on the Italian market of each device, and the mean price per kit (i.e., sling plus insertion needles) during 2015, together with its price range.

Results

Even if the optimal assessment of UI subtypes remains controversial, three main subtypes of UI can be described: stress UI (SUI), urgency UI (UUI), and mixed UI (MUI). SUI is defined as the complaint of involuntary loss of urine on effort or physical exertion or on sneezing or coughing **(A0002)**; UUI is defined as the complaint of involuntary loss of urine associated with urgency; MUI is defined as the complaint of involuntary loss of urine associated with urgency and also with effort or physical exertion or on sneezing or coughing[2].

Sling operation is proposed to women with uncomplicated SUI as the preferred surgical intervention, and to men with mild-to-moderate post-prostatectomy SUI (with terms "mild" and "moderate" remaining undefined)[3], with the aim to restore or enhance the patient's urethral support by the implantation of a tape of synthetic mesh material (known as sling) for preventing involuntary loss of urine[4 5] **(A0001)**.

Epidemiology of SUI

Women

Estimates of population prevalence of UI may be quite dissimilar as several factors may interfere with the measurement (e.g., cultural differences, willingness to report, methodological differences, definitions). However, the distribution of UI subtypes in women is consistent: isolated SUI accounts for the majority of cases (10–39% prevalence). MUI is found to be the next most common (7.5–25% prevalence) while isolated UUI is quite uncommon (1–7% prevalence) **(A0006)**. Prevalence rates from cross-sectional studies uniformly demonstrate an association with age. Several risk factors for UI in women have been identified: pregnancy, labour and vaginal delivery (vs Caesarean section), oral oestrogen, diabetes, dementia. Genetic components and correlations with body mass index (BMI) have been also found[2] **(A0003)**.

Men

In men, overall prevalence rates of UI ranges from 4.8% to 32.2%, with prevalence increasing with age. The predominant form of UI in men seems to be UUI (40–80%), followed by MUI (10–30%), while SUI only counts <10% of cases **(A0006)**. Even if risk factors are not always scientifically documented, several medical correlates have been reported: increasing age, presence of lower urinary tract symptoms (LUTS), urinary tract infections, functional and cognitive impairment, diabetes, neurological disorders, and prostatectomy[2] **(A0003)**.

Diagnosis of SUI in women and men

The main symptom of UI is a problem in controlling urination. For SUI, leaking of a small to moderate amount of urine is experienced by the patient, or observed by the carer or the physician during examination, when extra pressure is applied on the bladder. This may happen during coughing, sneezing, laughing, heavy lifting, and exercise **(A0005)**.

Substantial remission rates for UI have been documented in both female and male populations with ranges 11–13% in women and 27–32% in men[6]. More recently, remission of symptoms (defined as having UI at the first survey but not at the second one) has been observed in an 11-years longitudinal study on 14,000 women, with a rate of 34.1% in the whole period. Increasing age, increasing BMI and large weight gains (10 kg or more) were all associated with reduced remission of UI in the same study[7] **(A0004)**. Remission of symptoms have been also observed in men with post-prostatectomy UI up to 24 months after surgery in a study on 1,100 patients with a rate of 83%, 92.3% and 93.4%, depending on the definition of continence used (no or occasional pad use; 0–1 pads used daily but occasionally; 0–1 pads daily)[8] **(A0004)**.

The latest European Association of Urologists (EAU) guidelines do not suggest a pathway for the initial assessment of UI that is specific to women and men[3]. Taking a careful clinical history is widely considered the first step in the assessment of subjects with UI. Details on the type, timing and severity of UI, associated voiding and other urinary symptoms should be acquired to allow the categorisation of UI in one of the sub-types. Asking the patient about concomitant conditions and medications is relevant as these may impact on symptoms of UI. In addition, physical examination remains an essential part of assessment of subjects with UI. It should include abdominal, perineal, and examination of the prostate (by digital rectal examination) and/or vagina. In women, an assessment of oestrogen status and a careful assessment of any associated pelvic organ prolapse should be performed. Many additional diagnostic tools are available for a further assessment of UI: patients questionnaires, voiding diaries, urinalysis, ultrasound assessment of post-voiding residual (PVR) volume, pad testing, and urodynamic studies (UDS)[3] **(A0024)**.

Since incontinence severity has been shown being only a moderate predictor of specific QoL impairment, it is important to characterise both the severity of symptoms (e.g., frequency of leakage and/or quantity of loss) together with the perceived bother or impact on daily activities. Most questionnaires (e.g., ICIQ-SF, ICIQ-FLUTS, DAN-PSS) have been developed following this approach[2].

Management of SUI in woman and men

According to the latest EAU guidelines[3], the first-line approach to the management of UI should be non-surgical. Different solutions, such as adjustment of medication (even if there is very little evidence of benefit), containment (e.g., absorbent pads, urinary catheters, external collection devices), lifestyle modifications (e.g., reduction of obesity and smoking, increasing of physical activity), and behavioural and physical therapies (bladder training and pelvic floor muscle training) may be proposed alone or in combination. Pharmacological management may be an option for a subset of patients (e.g., elderly people with UUI or post-menopausal women with symptoms of vulvovaginal atrophy) but does not represent a cure for SUI **(A0018)**.

When first-line conservative or drug therapies have failed, surgical options should be presented to the patients and discussed. Physician (typically, urologist or urogynaecologist) and patient should discuss together all the available options, all the risks, benefits, and uncertainty areas linked to them **(G0009)**. Patient's preferences, related to the bother or impact of the condition on the activities of daily life, are crucial **(A0017)** and should be properly recorded.

Surgical options for women

For women with SUI (or stress-predominant MUI), the following surgical options are available[3] **(B0001b)**:

- Mid-urethral sling operation (including mini-sling);
- Burch colposuspension (open or laparoscopic);
- Autologous vaginal tape implantation;
- Bulking agents infiltration.

Mid-uretral sling operation is considered as the preferred surgical intervention (different risks and side effects depend on the surgical approach while long-term effectiveness of mini-slings is still uncertain) while colposuspension and autologous vaginal tape implantation should be considered only when sling operation is not feasible or available. Bulking agents are not suitable for women seeking for a permanent cure of UI[3] **(B0003b)**.

Surgical options for men

For men with SUI (or stress-predominant MUI), the following surgical options are available[3] **(B0001b)**:

- Artificial urinary sphincter (AUS);
- Sub-urethral sling operation;
- Adjustable continence therapy (ACT);
- Bulking agents' infiltration.

While the AUS remains the gold standard for the treatment of post-prostatectomy UI secondary to sphincter insufficiency in patients with severe incontinence or in those who received external beam radiation treatment, in men with mild to moderate degrees of SUI, or for patients demanding a less invasive procedure or a non-mechanical device, slings have established themselves as a viable alternative to AUS[2]. However, the latest EAU guidelines report that the terms "mild" and "moderate" remain undefined[3]. Evidence suggesting that ACT is effective for treatment of post-prostatectomy SUI is considered very limited by the latest guidelines[2 3]. Bulking agents are only suitable for men with mild post-prostatectomy UI who desire temporary symptoms relief[3] **(B0003b)**.

Current use of sling operation (A0011)

Women

The ICD-9-CM diagnosis code for SUI in women is 625.6 while the sling operation and the Burch procedure (retropubic urethral suspension) are coded with 59.4 and 59.5 codes, respectively (Table 1). Code 59.4 comprises both artificial and autologous sling procedures and therefore it is not possible to stratify by procedure. Diagnostic code 625.6 as principal or secondary diagnosis code and 59.4 or 59.5 procedure codes have been used to select the hospital discharges of interest. For the period of interest (2010–2014), 19,153 discharges with the procedure code 59.4 and 853 with the procedure 59.5 have been extracted. 37 discharges have been excluded because both procedures had been reported on the discharge record while 1 discharge was excluded because related to a male patient. Overall, 19,115 discharges for sling procedure and 816 with Burch procedure were reported during 2010-2014.

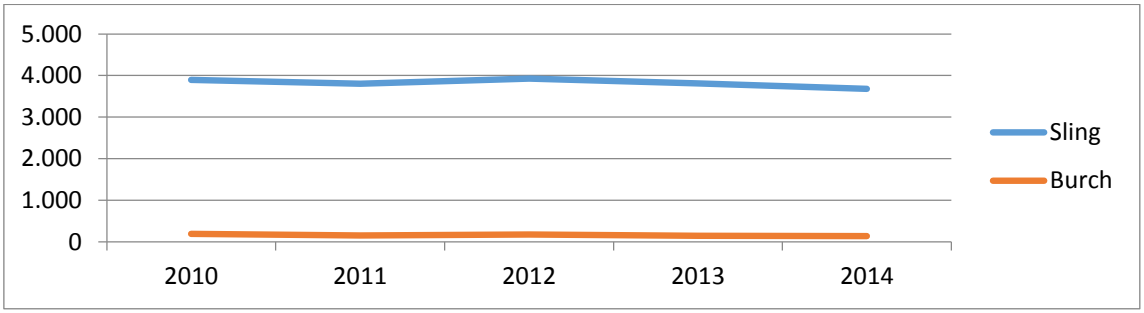
Figure 1 shows a slightly decreasing trend for both procedures in the period considered, even though the Burch procedure shows a more marked decreasing trend in respect to the sling procedure. It should be noticed however that the discharges with the Burch procedure correspond to less than 5% of total discharges identified.

Looking at trends for geographical areas the South shows a more marked decrease for the sling procedure while the Burch procedure appears to be stationary. Looking at the proportion of discharges with the sling procedure over total discharges, it appears that this proportion approaches 100% in the North, 90% in the South and an intermediate proportion of 95% in the Centre. The proportion of discharges relative to day hospital stay are 11.1% of the total of hospital discharges for the whole country with a wide variation by geographical area from 13.6% in the North to 7.4% in the Centre and 4.9% in the South.

Table 1: ICD-9-CM codes used for the analysis of the national hospital discharge records database – women.

ICD-9-CM codes	Description
Diagnosis	
625.6	Stress incontinence, female
Procedures	
59.4	Suprapubic sling operation *(including: Goebel-Frangenheim-Stoeckel urethrovesical suspension, Millin-Read urethrovesical suspension, Oxford operation for urinary incontinence, Urethrocystopexy by suprapubic suspension)*
59.5	Retropubic urethral suspension *(including Burch procedure, Marshall-Marchetti-Krantz operation, Suture of periurethral tissue to symphysis pubis, Urethral suspension NOS)*

Figure 1: Discharges for SUI with surgical intervention, NHS public hospitals and private profit and not for profit centres – women, 2010-2014. Source database SDO.



If we look at the type of hospital or clinical setting we can see that the sling procedure is carried out for the most part (60.7%) in public hospitals of the Unità Sanitarie Locali-ASL (Local Health Units), for 14.6% in contractor clinics to the NHS, 7.6 % in Ospedali Classificati (not for profit hospitals), for 6.3% in University Hospitals, for 5.3 % in Aziende Ospedaliere (public hospitals not belonging to ASLs) and for 4.0% in Research Hospitals. As far as the Burch procedure is concerned we see that at national level the procedure is carried out for the most part (53.3%) in ASL hospitals, 26.4% in contractor clinics to the NHS, 7.6 % in Aziende Ospedaliere, 7.4% in University Hospitals, 2.0 % in Ospedali Classificati and 0.7 % in Research Hospitals.

Health migration South to North consists of 331 South residents moving to North or Centre to undergo sling procedure in the whole period (9.2% of all discharges of South residents with this procedure) and 16 South residents moving to Centre or North to undergo Burch procedures (5.1%

of discharges of South residents with the procedure). Health migration in the opposite direction is much less frequent as 32 North residents moved to Centre or South to undergo the sling procedure (0.3% of discharges of North residents with the procedure) and 3 to undergo the Burch procedure (0.8% of discharges of North residents with the procedure). Finally, 131 Centre residents moved to the North or South to undergo the sling procedure (4.4% of discharges of Centre residents with the procedure) and 2 moved to the North to undergo the Burch procedure (1.4% of discharges of Centre residents with the procedure). Figure 2 and Figure 3 show the number of discharges for sling or Burch procedure respectively, by age-group and area of residence of the patient.

Figure 2: Age-specific discharges for SUI with surgical intervention (sling procedure), NHS public hospitals and private profit and not for profit centres – women, 2010-2014 (scale up to 6,000). ***Source:*** *SDO database.*

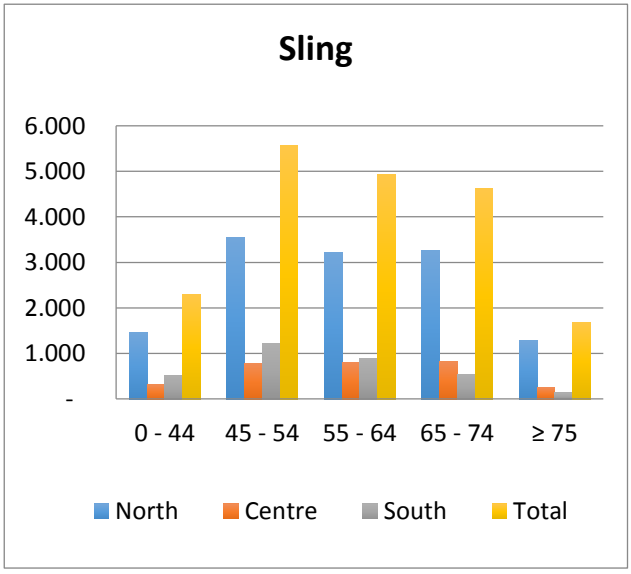


Figure 3: Age-specific discharges for SUI with surgical intervention (Burch procedure), NHS public hospitals and private profit and not for profit centres – women, 2010-2014 (scale up to 300). ***Source:*** *SDO database.*

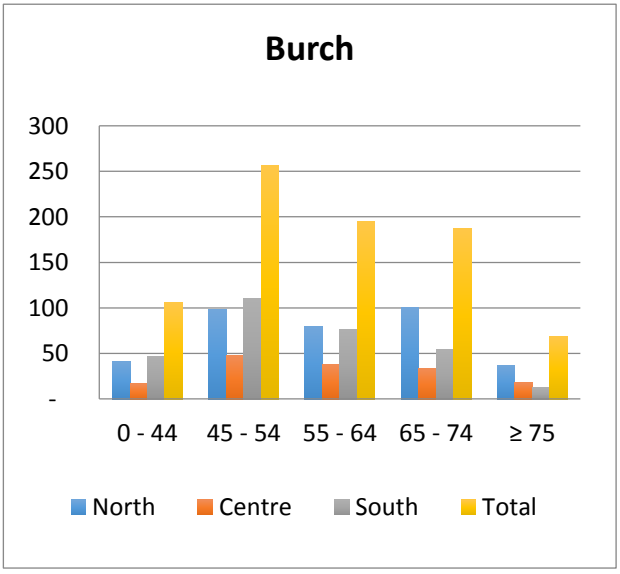


Table 2 reports the average annual rates per 1,000,000 population by age-group and geographical area for sling and Burch procedure. The average overall discharge rate for the sling procedure of 123.2 shows a slightly increasing trend with advancing age in the three central age-groups (from 243.0 in the 45-54 age-group to 275.6 in the 65-74 age-group per 1,000,000 population). Both crude and standardised discharge rates for this procedure show a marked decreasing trend North-to-South (standardised rates: 173.0 North, 96.1 Centre and 69.7 South). Age specific rates for the sling procedure in the North and Centre show a similar increasing trend even though the actual rates differ. Rates for North Italy are roughly two times higher than for the Centre (North: from 329.7 in the 45-54 age-group to 394.0 in the 65-74 age-group, Centre: from 171.2 in the 45-54

age-group to 237.2 in the 65-74 age-group per 1,000,000 population). The South shows an inverse trend, from 167.7 in the 45-54 age-group to 118.1 in the 65-74 age-group per 1,000,000 population. Standardised discharge rates for the Burch procedure are similar in the three geographical areas (4.9 North, 4.6 Centre and 6.1 South). Age specific discharge rates for this procedure are similar for North and Centre (North: from 9.2 in the 45-54 age-group to 12.3 in the 65-74 age-group, Centre: 9.4 in the 45-54 to 9.3 in the 65-74 age-group). In the South an age-specific discharge rate decreasing trend is observed in the three central age-groups (from 15.2 in the 45-54 age-group to 11.1 in the 65-74 age-group).

Table 2: Age-specific discharge rates per 1,000,000 residents for SUI with surgical intervention, NHS public hospitals and private profit and not for profit centres – women, 2010-2014. Source database SDO.

Age-group	North		Centre		South		Italy	
	Sling	Burch	Sling	Burch	Sling	Burch	Sling	Burch
0 – 44	42.1	1.2	22.9	1.1	19.0	1.7	30.0	1.4
45 – 54	329.7	9.2	171.2	9.4	167.7	15.2	243.0	11.3
55 – 64	352.5	9.1	207.1	9.5	150.8	11.8	255.0	10.1
65 – 74	394.0	12.3	237.2	9.3	118.1	11.1	275.6	11.3
75 and more	135.9	3.9	64.5	4.0	26.6	2.6	87.8	3.5
Crude rate	**176.4**	**5.0**	**97.8**	**4.7**	**67.2**	**5.9**	**123.2**	**5.3**
Age standardised rate	**173.0**	**4.9**	**96.1**	**4.6**	**69.7**	**6.1**		

The average hospital length of stay of inpatients for the sling procedure in Italy is 3.0 days (95% CI 2.97-3.03) being considerably less than the average hospital length of stay for the Burch procedure: 4.9 days (95% CI 4.70-5.16). The area-specific average lengths of stay for the sling procedure are: Northern Italy 2.7 (95% CI 2.69-2.76), Central Italy: 3.2 (95% CI 3.10-3.28), Southern Italy: 3.8 (95% CI 3.71-3.86). The average lengths of stay for the Burch procedure are: Northern Italy 5.1 days (95% CI 4.71-5.56), Central Italy: 4.0 days (95% CI 3.64-4.40), Southern Italy: 5.2 days (95% CI 4.90-5.49).

Men

The ICD-9-CM diagnosis code for SUI in men is 788.32, while the sling and AUS procedures are coded as 59.4 and 58.93, respectively (Table 3). Codes used are not able to distinguish cases of primary or secondary stress derived from procedures on the prostate. The diagnostic code 788.32 for principal or secondary diagnosis and 59.4 or 58.93 as procedure codes have been used to select the hospital discharges of interest. For the period 2010–2014, 922 discharges with the

procedure code 59.4 and 1,601 with the procedure 58.93 have been extracted. 17 discharges have been excluded because both procedures had been reported on the discharge record while 1 discharge with procedure code 59.4 was excluded because referred to a female patient. Overall, 904 discharges with the sling procedure and 1,584 with the AUS procedure were selected.

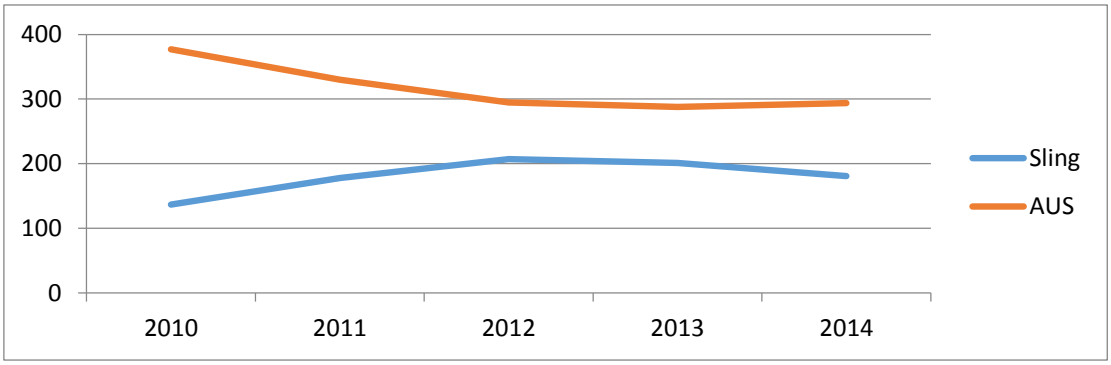
Table 3: ICD-9-CM codes used for the analysis of the national hospital discharge records database – men.

ICD-9-CM codes	Description
Diagnosis	
788.32	Stress incontinence, male
Procedures	
59.4	Suprapubic sling operation *(including: Goebel-Frangenheim-Stoeckel urethrovesical suspension, Millin-Read urethrovescical suspension, Oxford operation for urinary incontinence, Urethrocystopexy by suprapubic suspension)*
58.93	Implantation of artificial urinary sphincter [AUS] *(Placement of inflatable: bladder sphincter, urethral sphincter, Removal with replacement of sphincter device [AUS], With pump and/or reservoir)*

Figure 4 shows a slightly overall decreasing trend in the period considered. Looking at the two procedures separately, the AUS procedure shows a slightly decreasing trend (from 377 to 294), while the sling procedure shows an increasing trend until 2012 (from 137 to 207) to decrease thereafter to 181 in 2014. The overall proportion of sling procedures is 36.3% with a maximum of 41.2% in 2012. However discharges in Northern Italy correspond roughly to three fourths of total discharges with sling procedure (74.1 %) and four fifths of total discharges with the AUS procedure (79.7%). The proportion of discharges with the sling procedure increases in Central Italy from 40.3% in 2010 to 56.2% in 2014.

The analysis by type of hospital admission shows that the sling procedure in males in Italy is carried out mostly in ordinary hospital stay, while less than 1% is performed in day hospital. The procedure for AUS is performed in 6.8% of cases in day hospital.

Figure 4: Discharges for SUI with surgical intervention, NHS public hospitals and private profit and not for profit centres – men, 2010-2014. Source database SDO.



As for setting, the AUS procedure is carried out for the most part (46.5 %) in Local Health Unit (ASL) hospitals, 29.3% in University Hospitals and 11.6% in contractor clinics to the NHS, the remainder being equally distributed among not for profit hospitals Hospital Trusts and Research Hospitals.

Health migration in males is much more frequent than in females, irrespective of the procedure, even though much smaller numbers are involved. Migration from South to Centre and South to North for insertion represent 22.6% and 31.3% of all Southern Italy residents' discharges for the procedure. The figures for AUS procedures are 9.6% from South to Centre and 28.2% from South to North. Health migration of residents in Central Italy to Northern Italy is 28.2 % for the sling and 16.4 % for the AUS procedure. Finally, health migration from Northern Italy is limited to 2.3% to the Centre and 0.3% to the South for the sling procedure, while it is 0.7% and 0.1% respectively for the AUS procedure.

Figure 5 and Figure 6 show the number of discharges of males who underwent the sling or the AUS insertion procedure in the period 2010-2014 by age-group and area of residence.

In Table 4 the average rates per year per 1,000,000 population for age-group and area are reported for sling and AUS procedures, separately. The average overall discharge rate per year for sling procedure is 6.1 per million with a maximum of 36.6 in the age-group 65-74. Both crude and standardized discharge rates for this procedure show a marked decreasing North-to-South trend (standardized rates: 8.3 North, 6.6 Centre and 2.5 South). If we look at the 65-74 age group only, we can see that the rate is more than three times higher in the North compared to the South and 1.5 times higher in the North in respect to the Centre (North: 50.8, Centre: 35.1, South: 15.7).

The average overall discharge rate per year for the AUS procedure is 10.8 per million with a maximum of 63.7 in the age-group 65-74. Both crude and standardized discharge rates for this procedure show a marked decreasing North-to-South trend (standardized rates: 17.0 North, 7.4

Centre and 3.8 South). If we look at the 65-74 age group, we can see that the rate is more than four times higher in the North in respect to the South and more than 2 times higher in the North in respect to the Centre (North: 98.9, Centre: 41.9, South: 23.5).

Figure 5: Age-specific discharges for SUI with surgical intervention (sling), NHS public hospitals and private profit and not for profit centres – men, 2010-2014 (scale up to 600). ***Source:*** *SDO database.*

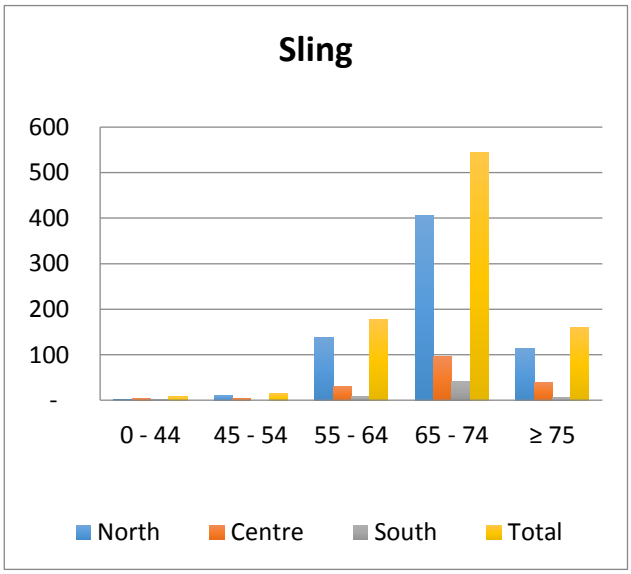


Figure 6: Age-specific discharges for SUI with surgical intervention (AUS), NHS public hospitals and private profit and not for profit centres – men 2010-2014 (scale up to 1,000). ***Source:*** *SDO database.*

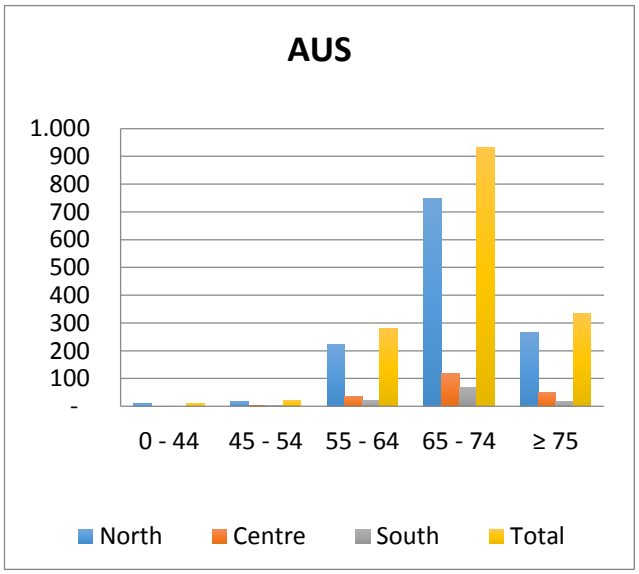


Table 4: Age-specific discharges rates per 1,000,000 residents for SUI with surgical intervention, NHS public hospitals and private profit and not for profit centres – men, 2010-2014. Source database SDO.

Age-group	North		Centre		South		Italy	
	Sling	AUS	Sling	AUS	Sling	AUS	Sling	AUS
0 - 44	0.1	0.2	0.3	0.0	0.0	0.1	0.1	0.1
45 - 54	0.9	1.6	1.1	0.5	0.0	0.5	0.7	1.0
55 - 64	13.0	24.6	10.7	11.3	4.2	5.4	9.6	15.5
65 - 74	50.8	98.9	35.1	41.9	15.7	23.5	36.6	63.7
75 and more	17.6	45.2	17.3	20.9	4.2	8.0	13.3	28.2
Crude rate	**8.7**	**17.7**	**6.9**	**7.7**	**2.3**	**3.5**	**6.1**	**10.8**
Age standardised rate	**8.3**	**17.0**	**6.6**	**7.4**	**2.5**	**3.8**		

The average hospital length of stay (in days) for the sling procedure for Italy is 3.6 (95% CI 3.51-3.77) similar to the hospital length of stay for AUS procedure: 3.7 (95% CI 3.55-3.79). The hospital lengths of stay are similar for the sling and AUS procedures in the North: 3.8 days (95% CI 3.63-3.94) versus 3.5 (95% CI 3.39-3.65) and South: 4.1 (95% CI 3.65-4.54) versus 4.7 (95% CI 4.15-5.21) with a marked difference in the Centre: 2.9 for the sling (95% CI 2.71-3.19) versus 4.0 for the AUS (95% CI 3.66-4.34).

Level of use of sling devices in Italy (A0011)

Data were collected by the Veneto region with a structured survey across the manufacturers and national distributors[1]. However, since not all the manufacturers and distributors returned the questionnaire, the figures may underestimate the real scenario in terms of units purchased.

Since their introduction in Italy, approximately 30,000 female slings have been sold (some models have been on the market for 15 years). In 2015 the mean price for a standard female sling kit was € 520 (€ 360 – € 730) while the mean price for a mini-sling was € 700 (€ 450 – € 920).

Since their introduction, approximately 3,000 male slings have been sold. Some models have been on the market for 12 years. In 2015 the mean price of a male sling kit was € 2,650 (€ 2,300 – € 3,300).

Conclusions

UI is a common condition among women and men, although population estimates may be dissimilar due to the interference of several factors such as, definitions and willingness to report. Among the three main subtypes of UI, SUI represents the most common among women (10–39% of cases) while, among men, SUI appears to be less common (less than 10% of cases) and mainly subsequent to radical prostatectomy. Remission rates have been documented in both populations, much higher and faster in men than in women in whom some variables affecting remission have been identified (increasing age, increasing BMI and large weight gains). First-level diagnosis starts from a careful clinical history and physical examination with ultrasound assessment of PVR volume, pad testing, and UDS for further assessments. However, severity of UI (e.g., frequency and quantity of leaking) needs to be always assessed together with the bother perceived by the patient and its impact on activities of daily life. Non-surgical first-line approaches are recommended from guidelines while surgical management is generally performed when conservative management strategies have failed. Risk-benefit assessment must be performed carefully by the physician, in accordance to patient's preferences and needs. In women, mid-urethral sling operation is considered as the preferred surgical intervention while the target population for a sling operation seems to be unclear in men.

Italian national data showed that the majority of surgical interventions for SUI are carried out in Northern Italy (13,518 discharges in women, 1,932 discharges in men, respectively 66% and 77.6% of the total). 95.5% of sling insertions was carried out in women, while only 36.3% of men undergo sling insertion.

Younger women, aged 45 to 54, are treated more frequently than older women in Southern Italy, in contrast to the rest of the country. Mean length of ordinary hospital stay for women is significantly shorter for sling insertion than Burch procedure (3 days vs 4.9 days), while in men length of stay is similar (3.6 days for sling insertion and 3.7 days for AUS insertion). Surgical correction of SUI is decreasing overall, but in men sling insertion is increasing (from 137 procedures in 2010 to 181 procedures in 2014).

Volume of units of medical devices purchased may underestimate the real scenario and final acquisition prices of the kits may differ from the figures, as prices are often negotiated by hospital tenders.

3. Description and technical characteristics of technology

Methods

The AEs of this domain were:

Assessment Element ID	Research question
B0001	What is this technology?
B0003	What is the phase of development of the technology?
B0004	How is the technology used?
B0005	In which setting and level of care is the technology used?
B0007	Does the technology require additional/special equipment/tools or accommodation?
B0009	What disposables and supplies are needed to use the technology?
F0001	F0001a: Is the technology new/innovative? F0001b: Is the technology an add-on, a replacement or a modification of the standard mode of care?

All the AEs selected within the domain were developed. The technology and its technical characteristics were presented by using information gathered by a structured questionnaire sent to the manufacturers (as described in Appendix 4) supplemented by *ad hoc* internet searches on manufacturers' websites, brochures, instructions for use (IFU) documents, and regulatory bodies' databases.

Results

Sling insertion is a surgical procedure performed in women and men with different approaches but with the same goal: to restore or enhance the patient's urethral support by the implantation of a tape of synthetic mesh material (known as sling) for preventing involuntary loss of urine[4 5] **(B0001)**. The procedure is generally performed under general or spinal anaesthesia, within the operating room, by urogynaecologists or urologists; patients may leave the hospital on the same day as surgery or stay for 1 or 2 days **(B0005)**. Equipment, tools, disposables, and supplies needed for a sling procedure are no different from those normally available within the operating room during any open perineal surgery. Slings are generally provided in kits, together with specific tools for sling introduction **(B0007) (B0009)**. Mesh material and structure are crucial features that have impact on outcomes. Typically, a synthetic mesh for sling procedure is made of monofilament, non-absorbable material (polypropylene but also polydimethylsiloxane or

polyvinylidene fluoride are used), and constructed as a 1-2 cm wide macroporous mesh (type I according to Amid classification, i.e., pour size >75 μm)[9].

Today sling procedures are proposed as a surgical option within the management pathway for those women and men with SUI (or stress-predominant MUI) that failed conservative or drug therapy[3] **(F0001)**. The surgical approaches are technically different for women and men: a brief description is reported in the following paragraphs) **(B0004)**.

Sling operation in women

The concept was introduced in 1993 by Ulmsten and Petros[10] and the first results from a multicentre study using the "tension-free vaginal tape" (TVT) were published in 1998[11]. A second-generation approach was proposed in 2001, the transobturator tape (TOT)[12] followed by a single-incision technique in 2008 (also known as mini-sling) that represents the latest version of the procedure[13]. The TVT is performed following the retropubic route (RPR) that involves the insertion of two needles passed through the retropubic space blindly from the vagina to the abdomen or from the abdomen to the vagina (i.e., bottom-to-top or top-to-bottom). The TOT follows the transobturator route (TOR) in which the tape is inserted in a horizontal plane underneath the middle of the urethra between the two obturator foramina (with out-in or in-out approach); the ends of the tape are tunnelled percutaneously with a curved needle[4]. The single-incision technique consists of a single incision into the vagina with no tape exit incisions. The tape, that is significantly shorter than those from previous generations (8–14 cm versus 22–50 cm), is advanced up to the obturator membrane or pelvic floor without penetrating the obturator fossa or the retropubic space[14] **(B0004)**.

Several manufacturers are proposing slings for urinary incontinence in women; the main features of the devices available on the Italian market are presented in Table 5 **(B0003)**.

Table 5: Slings for urinary incontinence in women registered within the Italian National Medical Devices Inventory and Database (Banca Dati e Repertorio Dispositivi Medici – BD/RDM). All the devices listed in the table are CE marked.

Manufacturer	Device name	BD/RDM registration number(s)	Sling type	Surgical approach
A.M.I.	A.M.I. TVA Sling and A.M.I. TOA Sling	15358	Traditional	RPR/TOR
	A.M.I. Multi Purpose Sling	73182	Traditional	RPR/TOR
Aspide Medical	SURGIMESH SLING	35953	Traditional and mini-sling	RPR/TOR/SI

BARD	Align (R, S, RS, and TO)	3820	Traditional	RPR/TOR
	Ajust	46890	Mini-sling	SI
	Ajust Helical	512933	Mini-sling	SI
Betatech Medikal	BETAMIX Vaginal Sling	1295302	Traditional	RPR/TOR
Boston Scientific	Obtryx and Obtryx II	7986270	Traditional	TOR
	Lynx	1323544	Traditional	RPR
	Advantage and Advantage Fit	14393, 208758	Traditional	RPR
	Solyx	208364	Mini-sling	SI
Caldera Medical	Desara	188362	Traditional	RPR/TOR
CL Medical	I-STOP	1273268, 443596, 315571, 371688	Traditional	RPR/TOR
Coloplast	Aris	109552, 109589	Traditional	TOR
	Supris	107263	Traditional	RPR
	Altis	479719	Mini-sling	SI
Desarrollo e Investigacion Medica Aragonesa (DIMA)	TRT Female System – Reemex	45602	Re-adjustable	RPR*
	Contasure Knotless Incontinence Mesh (KIM)	591294	Traditional	RPR/TOR
	Contasure Needleless System	33707	Mini-sling	SI
DIPRO Medical Devices	InGyne S	1033869, 1143622, 1130154, 536307, 536031, 535967, 536028, 536416, 535531, 535770, 535772	Traditional	RPR/TOR
	InGyne MIS	645155, 1143633	Traditional**	TOR
Ethicon	GYNECARE (TVT, TVT EXACT, and TVT O)	19981, 331308, 20014	Traditional	RPR/TOR
	GYNECARE TVT ABBREVO	346954	Traditional**	TOR
FEG Textiltechnik	DynaMesh-SIS and DynaMesh-SIS direct	44540, 594681, 44514, 45023,	Traditional	RPR/TOR
Gallini	Emerald and Emerald Plus	67140, 67196	Traditional	RPR
GTA	ECS Evolution	387401	Traditional	RPR

Herniamesh	T-Sling PP	9698, 26638	Traditional	RPR/TOR
	T-Sling Plus	346333	Mini-sling	SI
Promedon	Unitape (VS, T, and T Plus)	337920, 337919, 337918	Traditional	RPR/TOR
	Safyre (VS, T, and T Plus)	346778, 346776, 346774	Traditional	RPR/TOR
	Ophira	171302	Mini-sling	SI
Textile Hi-Tec (THT)	Swing-band	273837	Traditional	TOR
	Just-swing	273848	Mini-sling	SI

Key: *RPR, retropubic route; SI, single incision technique; TOR, transobturator route.*

Note: *American Medical Systems (AMS) slings for female urinary incontinence were not marketed anymore since April 2016 due to the company's women's health division closure. AMS devices were: Monarc, Sparc, Retroarc, MiniArc Precise, and Miniarc Pro.*

** A tension adjusting system needs to be implanted permanently in the abdominal rectus muscle fascia by a 4-cm abdominal transverse incision.*

*** Intermediate length slings (about 12 cm).*

Source: *Data from BD/RDM database (accessed on 10th May 2016) and Decreto Regione Veneto n.58 del 15 Giugno 2016[1]. Devices are listed in alphabetical order by manufacturer name.*

Sling operation in men

A male sling based on the needle suspension procedures used for incontinence in men was introduced in 1998[15]. Restoration of continence can be achieved by urethral compression or by repositioning the bulb of urethra. The different designs proposed can be grouped in two categories: slings in which tension is adjusted during surgery and cannot be re-adjusted postoperatively (traditional fixed slings) and slings allowing tension adjustability in postoperative setting (re-adjustable slings)[3] **(B0004)**. Like for women, sling implantation in men may follow the retropubic or the transobturator route, but require an additional incision in the perineum and at the abdominal level if a tension-adjusting unit has to be implanted.

Several companies are proposing slings for urinary incontinence in men; the main features of the devices available on the Italian market are presented in Table 6 **(B0003)**.

Table 6: Slings for urinary incontinence in men registered within the Italian National Medical Devices Inventory and Database (Banca Dati e Repertorio Dispositivi Medici – BD/RDM). All the devices listed in the table are CE marked.

Manufacturer	Device name	BD/RDM registration number(s)	Sling type	Surgical approach
A.M.I.	ATOMS	1243226	Re-adjustable*	TOR
American Medical Systems (AMS)	Advance XP	338355	Traditional	TOR
CL Medical	I-Stop TOMS	881894	Traditional	TOR
Coloplast	Virtue	442169	Traditional	TOR
Desarrollo e Investigacion Medica Aragonesa (DIMA)	MRS II Male System – Reemex	54488	Re-adjustable	RPR**
DIPRO Medical Devices	Andromesh MSI	538149, 538268	Traditional	RPR/TOR
FEG Textiltechnik	Dynamesh PRM	93124	Traditional	TOR
Herniamesh	Heracle	299791	Traditional	TOR
Promedon	Argus and Argus T	330113, 330114	Re-adjustable	RPR/TOR
	Phorbas	1031507	Re-adjustable	SI

Key: *RPR, retropubic route; SI, single incision technique; TOR, transobturator route.*

** The ATOMS implant consists of a urethral inflatable pad with a lateral mesh on either side, a titanium port for adjustments and a silicone connection for joining both elements.*

*** A tension-adjusting system needs to be implanted permanently in the abdominal rectus muscle fascia by a 4-cm abdominal transverse incision.*

Source: *Data from BD/RDM database (accessed on 10th May 2016) and Decreto Regione Veneto n.58 del 15 Giugno 2016[1]. Devices are listed in alphabetical order by manufacturer name.*

Conclusions

Sling operations for UI were introduced a few decades ago and consist in the implantation of a tape of synthetic mesh material (known as sling) to restore or enhance urethral support and prevent involuntary loss of urine. It's a surgical procedure proposed to women and men and performed under general, spinal or local anaesthesia by urogynaecologists or urologists.

The slings available on the market are typically sold in specific kits including implantation tools (specific needles for specific surgical approaches, RPR, TOR, and SI). Seventeen manufacturers of slings for women are present on the Italian market, offering a wide variety of sling solutions. Among these, various mini-slings (suitable for single-incision approach) are also present while only one re-adjustable sling system is available for women. The male sling market consists of nine

manufacturers, offering four re-adjustable sling systems and one sling suitable for the SI approach.

4. Regulatory aspects

Methods

The AEs of this domain were:

Assessment Element ID	Research question
A0020	What is the marketing authorisation status of the technology?
A0021	What is the reimbursement status of the technology across countries?
I0016	Does the technology need to be listed in a national/EU database?

All the AEs selected within the domain were developed. The regulatory status of the identified devices (CE marking and FDA approvals) was described by using information gathered by a structured questionnaire sent to the manufacturers (as described in Appendix 4) supplemented by *ad hoc* internet searches on regulatory bodies' websites and databases, and manufacturers' press releases.

Results

Approval

Slings are Risk Class IIb medical devices marketed in Europe since the late 90s. Some devices are also approved by the FDA (Table 7 and Table 8) **(A0020)**.

Like all the medical devices for sale to Italian public hospitals, slings for urinary incontinence need to be registered within the Italian National Medical Devices Inventory and Database (Banca Dati e Repertorio Dispositivi Medici – BD/RDM) **(I0016)**.

Table 7: Approval details of the slings for urinary incontinence in women available on the Italian market.

Manufacturer	Device name	Approvals
A.M.I.	A.M.I. TVA Sling and A.M.I. TOA Sling	CE
	A.M.I. Multi Purpose Sling	CE
Aspide Medical	SURGIMESH SLING	CE
BARD	Align (R, S, RS, and TO)	CE and FDA
	Ajust	CE and FDA
	Ajust Helical	CE and FDA
Betatech Medikal	BETAMIX Vaginal Sling	CE
Boston Scientific	Obtryx and Obtryx II	CE and FDA
	Lynx	CE and FDA
	Advantage and Advantage Fit	CE and FDA

	Solyx	CE and FDA
Caldera Medical	Desara	CE and FDA
CL Medical	I-STOP	CE and FDA
Coloplast	Aris	CE and FDA
	Supris	CE and FDA
	Altis	CE and FDA
Desarrollo e Investigacion Medica Aragonesa (DIMA)	TRT Female System – Reemex	CE and FDA
	Contasure Knotless Incontinence Mesh (KIM)	CE and FDA
	Contasure Needleless System	CE and FDA
DIPRO Medical Devices	InGyne S	CE
	InGyne MIS	CE
Ethicon	GYNECARE (TVT, TVT EXACT, and TVT O)	CE and FDA
	GYNECARE TVT ABBREVO	CE and FDA
FEG Textiltechnik	DynaMesh-SIS and DynaMesh-SIS direct	CE
Gallini	Emerald and Emerald Plus	CE
GTA	ECS Evolution	CE
Herniamesh	T-Sling PP	CE and FDA
	T-Sling Plus	CE and FDA
Promedon	Unitape (VS, T, and T Plus)	CE
	Safyre (VS, T, and T Plus)	CE and FDA
	Ophira	CE and FDA
Textile Hi-Tec (THT)	Swing-band	CE
	Just-swing	CE

Key: *CE = Conformité Européenne; FDA = US Food and Drugs Administration.*

Source: *Data from FDA 510(k) Premarket Notification Database (accessed on 28th June 2016) and Decreto Regione Veneto n.58 del 15 Giugno 2016[1]. Devices are listed in alphabetical order by manufacturer name.*

Table 8: Approval details of the slings for urinary incontinence in men available on the Italian market.

Manufacturer	Device name	Approvals
A.M.I.	ATOMS	CE
American Medical Systems (AMS)	Advance XP	CE and FDA
CL Medical	I-Stop TOMS	CE and FDA
Coloplast	Virtue	CE and FDA
Desarrollo e Investigacion Medica Aragonesa (DIMA)	MRS II Male System – Reemex	CE and FDA
DIPRO Medical Devices	Andromesh MSI	CE
FEG Textiltechnik	Dynamesh PRM	CE
Herniamesh	Heracle	CE
Promedon	Argus and Argus T	CE
	Phorbas	CE

Key: *CE = Conformité Européenne; FDA = US Food and Drugs Administration.*

Source: *Data from FDA 510(k) Premarket Notification Database (accessed on 28th June 2016) and Decreto Regione Veneto n.58 del 15 Giugno 2016[1]. Devices are listed in alphabetical order by manufacturer name.*

Reimbursement

In Italy, sling procedures may be reimbursed by using different DRG codes. No supplemental or extra-DRG reimbursement fees are in place for this procedure. The DRG codes typically used and the maximum national fees linked to them are the following[16] **(A0021)**:

- *308 - Minor bladder procedures with complications*: € 4,693;
- *309 - Minor bladder procedures without complications*: € 3,397;
- *356 - Female reproductive system reconstructive procedures*: € 2,901.

However, each Region can lay down its own reimbursement fees if necessary.

Conclusions

The slings for urinary incontinence available on the Italian market have been used for many years and many of them are also FDA-approved. In Italy, the procedure can be reimbursed under three different DRG codes: 308, 309, and 356 with a maximum national reimbursement fee of € 4,693, € 3,397, and € 2,901 respectively.

5. Clinical effectiveness and safety

Methods

The AEs of the "Clinical effectiveness" domain were:

Assessment Element ID	Research question
D0005	D0005a: How does the technology affect symptom frequency of the target condition? D0005b: How does the technology affect symptom severity of the target condition? D0005c: How does the technology affect symptom duration of the target condition?
D0006	D0006a: How does the technology affect the progression of the target condition? D0006b: How does the technology affect the recurrence of the target condition?
D0012	What is the effect of the technology on generic health-related quality of life?

The AEs of the "Safety" domain were:

Assessment Element ID	Research question
C0001	What harms are associated with the use of the technology?
C0060	How does the safety profile of the technology vary between different generations, approved versions or products?

All the AEs selected within the two domains were developed. Electronic searches were performed between 10th and 16th May 2016 on MEDLINE, Embase, and Cochrane Library, according to the specific search strategies designed for women and men. The two search strategies are presented in Appendix 5 and Appendix 6, respectively. The two sets of PICO framework and inclusion criteria defined for the present HTA report are presented in Table 9.

Data extraction and management

Two authors independently assessed titles and abstracts of all retrieved citations according to the defined inclusion criteria. Data extraction was performed using a standardised sheet developed by the authors.

Assessment of methodological quality of included studies

Methodological quality of included studies was assessed independently by two authors by using the AMSTAR checklist[17]. Scores were tabulated within the final evidence tables.

Table 9: PICO framework and inclusion criteria defined for the present HTA report "Sling operation for urinary incontinence in women and men".

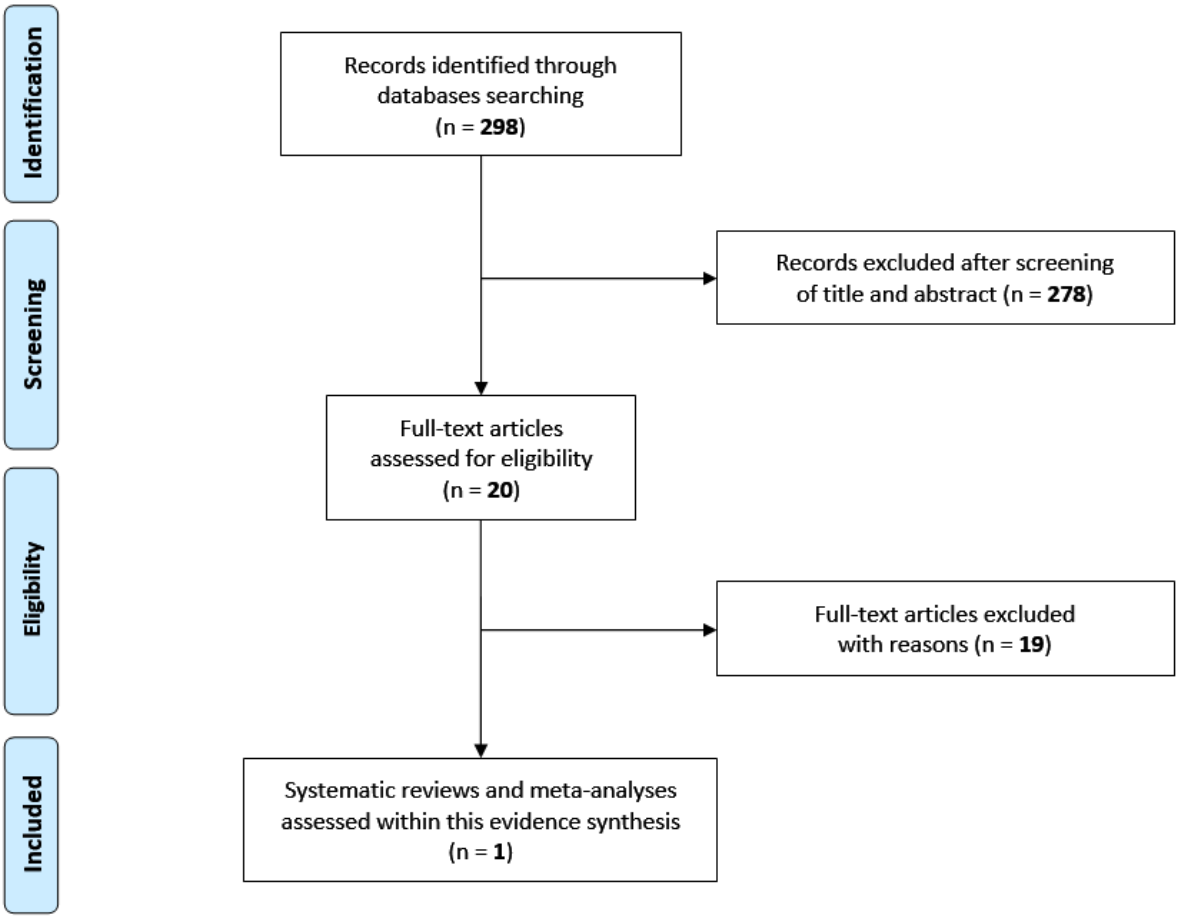
Women		Men	
Population	Women (aged 35 or more) with stress urinary incontinence (SUI)	**Population**	Men (aged 35 or more) with intrinsic sphincter deficiency (ISD) causing stress urinary incontinence (SUI).
Intervention	Mid-urethral sling operation (including single-incision sling, also called "mini-sling")	**Intervention**	Suburethral sling operation (also called "male sling")
Comparison(s)	Burch colposuspension (open or laparoscopic) or autologous vaginal tapes (open or laparoscopic) or conservative therapy with diapers	**Comparison(s)**	Artificial urinary sphincter (AUS) or adjustable continence therapy or conservative therapy with diapers
Outcome(s)	Effectiveness outcomes (primary): *Subjective (i.e., patient-reported stress incontinence) and objective (e.g., urine loss measured by stress test) measures of continence;* Surgical outcomes: *Duration of operation, length of inpatient stay, time to return to normal activity level, operative blood loss, type of anaesthetic technique required (local, regional or general).* Adverse events: *Major vascular or visceral injury, bladder, urethral or bowel perforation, nerve damage, perioperative surgical complications, voiding dysfunction or difficulty after three months or need for long-term catheterisation, infection related to use of synthetic mesh, tape erosion or extrusion, post operative pain, de novo urgency.*	**Outcome(s)**	Effectiveness outcomes (primary): *Subjective (i.e., patient-reported stress incontinence) and objective (e.g., urine loss measured by stress test) measures of continence;* Surgical outcomes: *Duration of operation, length of inpatient stay, time to return to normal activity level, operative blood loss, type of anaesthetics technique required (local, regional or general).* Adverse events: *Major vascular or visceral injury, bladder, urethral or bowel perforation, nerve damage, perioperative surgical complications, voiding dysfunction or difficulty after three months or need for long-term catheterisation, infection related to use of synthetic mesh, tape erosion or extrusion, post operative pain, de novo urgency*
Design of study HTA reports and systematic reviews of comparative studies and randomised controlled trials (RCTs) available since 2005.			

Results

Sling effectiveness and safety in women

Our searches identified 298 studies of possible interest to assess effectiveness of sling procedure in women. Of these, 278 studies were excluded on the basis of their title and/or abstract content. A further 19 studies were excluded because they had search dates preceding those of the latest synthesis research report, which was the Cochrane review by Lapitan et al.[18] (Figure 8). The summary data extraction is presented in Table 10.

Figure 8: Study screening process for effectiveness and safety of sling operation for urinary incontinence in women according to PRISMA. Adapted 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.



The review by Lapitan et al.[18] was aimed at assessing the effects of open retropubic colposuspension for the treatment of urinary incontinence in women. Randomised or quasi-randomised controlled trials in women with symptoms or urodynamic diagnoses of SUI or MUI that included open retropubic colposuspension surgery in at least one trial group were included. Several comparisons were reported by the review authors but only one was eligible for the purposes of the present HTA report: open retropubic colposuspension *versus* the sling procedure (including traditional sling procedures, self-fixing sling procedures, and single-incision sling procedures). The list of analyses presented by Lapitan et al.[18] and summarised in this HTA report is presented in Appendix 7. Readers interested in wider perspectives on the effect of surgical interventions for urinary incontinence in women should consult the source review[18].

The comparison of interest (open retropubic colposuspension *versus* sling procedure) was investigated by 22 trials. The total denominator was 2,343 randomised women with at least 1,089 undergoing colposuspension. The standard sling procedure was performed in 6 trials while 16 trials

reported on self-fixing sling procedures (12 trials on the tension-free vaginal tape – TVT; 3 trials on the transobturator tape procedure – TOT; 1 did not specify whether TVT or TOT procedure was the approach taken). No trials reporting on single-incision sling procedures were identified. For details of the trials, see the review by Lapitan et al[18].

Effectiveness outcomes

The review by Lapitan et al.[18] reported the outcomes by short-term, mid-term and long-term cure. In the short term (up to 1 year) there was no statistically significant difference between the two treatment groups in the risk for incontinence assessed subjectively (RR 0.90; 95% CI 0.69 to 1.18) **(D005)**. This group included self-fixing devices and a further subgroup analysis of those trials including traditional slings only showed no statistical difference between open colposuspension and traditional slings with wide confidence intervals (RR 1.92; 95% CI 0.57 to 6.50). The meta-analysis of 5 trials using the TVT procedure also showed no difference (RR 0.88; 95% CI 0.67 to 1.16) **(D0005)**.

For the medium term (one- to five-year follow-up), 6 trials combining traditional slings and self-fixing slings, showed a lower incontinence rate in women who had sling procedures (RR 1.18; 95% CI 1.01 to 1.39) **(D0006)**. Data from the TVT trials alone showed no difference in medium-term subjective incontinence rate) **(D0005a)** or improvement rate between open colposuspension and the TVT procedure) **(D0006)**.

For long term cure (five years or more), 3 trials showed no overall significant difference in effects (RR 1.11; 95% CI 0.97 to 1.27). However, traditional slings continued to be more effective than open colposuspension at long-term follow-up in 1 trial (RR 1.19; 95% CI 1.03 to 1.37) **(D0006a)**. Objective incontinence rates were not significantly different by any of the time periods **(D0006b)**.

Surgical outcomes

Operative time analysis between colposuspension and sling insertion from 4 trials showed conflicting results possibly due to the different types of sling operations performed. Length of stay in hospital (8 trials) also showed differences due to procedures. While 2 trials showed similar lengths of stay for both treatment groups, 1 trial reported that women stayed in hospital eight fewer days in the colposuspension group compared to the traditional sling group. The 6 trials that compared open colposuspension with TVT consistently showed shorter hospital stays with the self-fixing (TVT) group. Summary data of the TVT trials alone showed a shorter hospital stay of 4 days (mean days 3.99; 95% CI 3.71 to 4.28).

Adverse events

According to 8 trials, there were statistically significant fewer perioperative surgical complications in the open colposuspension group (complication rates RR 0.76; 95% CI 0.66 to 0.87) **(C0001)**, but there were no significant differences in the perioperative complications rates between colposuspension and self-fixing slings (RR 1.11; 95% CI 0.66 to 1.87) **(C0060)**. There was nearly 40% lesser risk of developing voiding difficulties after open colposuspension compared to sling procedures (RR 0.41; 95% CI 0.26 to 0.67) **(C0001)**. All these results were influenced by 1 large trial. Women undergoing open retropubic colposuspension had a nearly two-fold risk of developing new or recurrent prolapse compared to those undergoing sling procedures (33.9% versus 20.1%; RR 1.85; 95% CI 1.25 to 2.75) **(C0001)**. Nine trials reported data on bladder perforation but results from the one trial using the traditional sling differed from those trials using the TVT as it reported a five-fold higher risk of stitching sutures through the bladder during open colposuspension compared to the pubovaginal sling procedure (perforation rates: 3% versus 0.06%, RR 4.95; 95% CI 1.09 to 22.44) **(C0060)**. Data from the TVT trials consistently showed a trend towards lesser risk for bladder perforation than open colposuspension (perforation rate: 0.9% versus 6.3%; RR 0.20; 95% CI 0.08 to 0.49) and a significant vascular injury during TVT. None of these complications had serious consequences. The rate of TVT procedure tape complications was six women out of 170 at five-year follow-up according to a single trial **(C0001)**.

Quality of life

Quality of life was assessed in 2 trials. One trial reported no significant difference in Incontinence Impact Questionnaire (IIQ) and Urogenital Distress Inventory (UDI) scores between the colposuspension group and the sling group (but actual numbers were not reported in the study). Another trial used Short Form-36 (SF-36), EQ-5D, and Bristol Female Lower Urinary Tract Symptoms (B-FLUTS) scoring systems to compare quality of life after the open retropubic colposuspension and the TVT procedures. There was no difference in these measures apart from the SF-36 showing significantly less improvement in emotional and social functioning, vitality and mental health dimensions at 6 months and at 2 years in women in the colposuspension group. There was no difference between the groups in any of the health dimensions measured by the SF-36 at five years. There was also no significant difference in the quality-adjusted life years between the two groups) **(D0012)**.

Table 10: Evidence from research synthesis reports included in the present review.

Study ID	Date of searches	Objective	Design of included studies (n. of studies and patients)	Comparisons	Outcomes and Conclusions	AMSTAR score	Funding
Lapitan 2016[18]	5th May 2015	To determine the effects of open retropubic colposuspension for the treatment of urinary incontinence in women	RCTs (22 trials, 2,343 women)	Colposuspension vs Sling procedures*	No overall significant subjective difference in incontinence rates in all time periods evaluated colposuspension vs traditional slings or trans-vaginal tape or transobturator tape (RR 0.90; 95% CI 0.69 to 1.18) at 1 year of treatment (RR 1.18; 95%CI 1.01 to 1.39) at 1-5 years, (RR 1.11; 95% CI 0.97 to 1.27) at 5 or more years. The same was found for objective assessment at 1 year of treatment (RR 1.24; 95% CI 0.93 to 1.67), at 1-5 years (RR 1.12; 95% CI 0.82 to 1.54), and at more than 5 years (RR 0.70; 95% CI 0.30 to 1.64). Subgroup analysis comparing traditional slings and open colposuspension showed effectiveness of traditional slings in the medium and long term (RR 1.35; 95% CI 1.11 to 1.64 from 1 to 5 years follow up, RR 1.19; 95% CI 1.03 to 1.37). Newer minimal access sling procedures look promising in comparison with open colposuspension but their long-term performance is limited and closer monitoring of their adverse event profile must be carried out. Open colposuspension is associated with a higher risk of pelvic organ prolapse, but with a lower risk of voiding dysfunction compared to traditional sling surgery.	11/11	NIHR/HTA programme UK

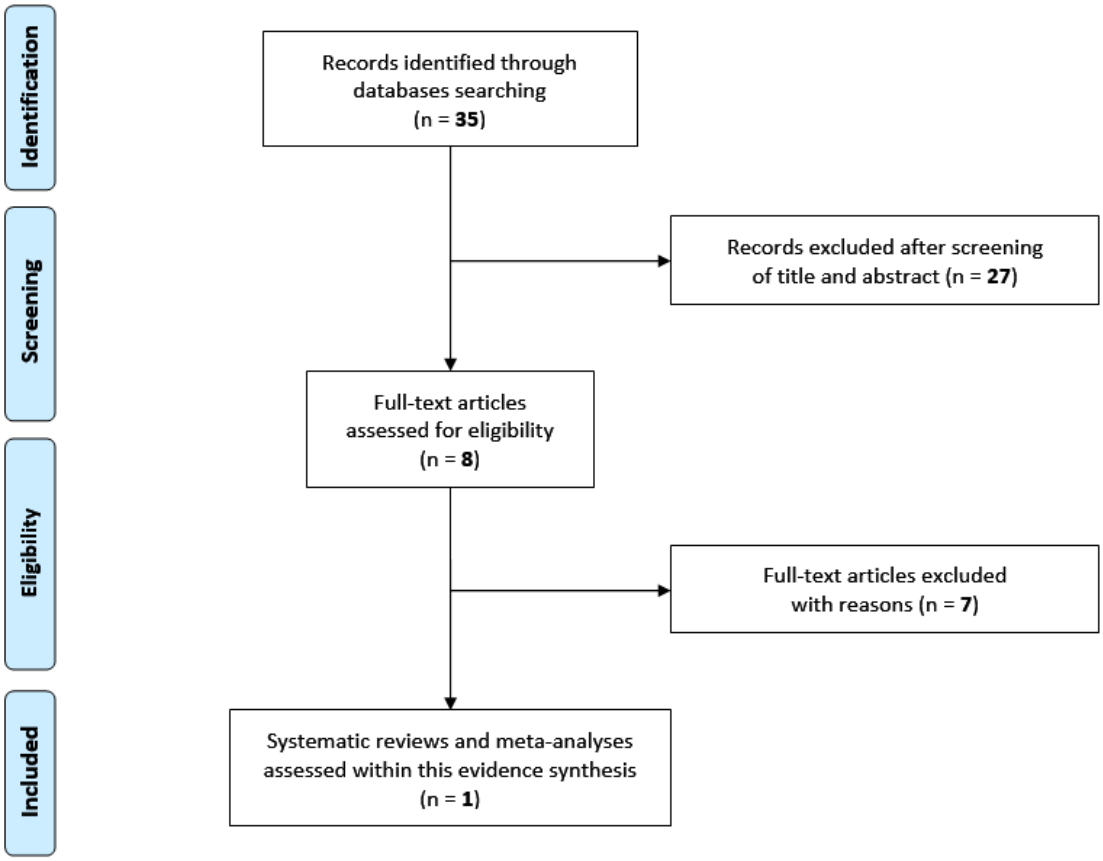
**Data from "Comparison 5" only reported from the review by Lapitan et al.*[18]

Key: *CI, confidence interval; RCT, randomised controlled trial; RR, risk ratio; vs, versus.*

Sling effectiveness and safety in men

Our searches identified 35 studies of possible interest to assess the effectiveness and safety of sling procedure in men. Of these, 27 were excluded on the basis of their title and/or abstract content. A further 7 studies in men were excluded because they had search dates preceding those of the latest synthesis research report: the Cochrane review by Silva et al.[19] (Figure 9).

Figure 9: Study screening process for effectiveness and safety of sling operation for urinary incontinence in men according to PRISMA. Adapted 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.



The review by Silva et al.[19] assessed the effects of surgical treatment for urinary incontinence related to presumed sphincter deficiency after prostate surgery in men. Randomised or quasi-randomised trials that include surgical treatments of urinary incontinence after prostate surgery were considered for inclusion. Despite the review authors extended the searches to a wide range of interventions, including those of interest within the present HTA report, i.e. AUS, ACT, and conservative therapy with diapers, their searches identified only 1 trial, comparing AUS to bulking agent injection (not fulfilling the inclusion criteria of the present HTA report). The review by Silva

et al.[19] was then used as a source for the identification of trials addressing the research questions of the present HTA report.

Three studies fulfilling the inclusion criteria of the present evidence review were cited by Silva et al.[19] and are here briefly described together with their status update.

- The study by Abrams et al.[20] (ISRCTN 49212975; MASTER) is a multicentre randomised controlled non-inferiority trial comparing the effectiveness of the synthetic sling (male sling) with AUS for 360 men with urodynamic stress incontinence (USI) after prostate surgery. The study was still ongoing at the time of writing and due to finish in August 2019. Further details (including the study protocol) are available by the following link: http://www.nets.nihr.ac.uk/projects/hta/1110601.
- The study by Haab et al.[21] (NCT01500603) is a prospective, randomised, multicentre trial to compare the efficacy of the Advance XP retrourethral male sling *versus* the periurethral Pro-ACT balloons for the management of SUI after radical prostatectomy at one year of follow-up. The study was terminated during October 2014 due to lack of inclusion.
- The study by Ockrim et al.[22] (ISRCTN55599282) was a single-site, two-arm randomised controlled study aimed to compare the effectiveness of the Advance male sling *versus* the AMS 800 AUS for mild to moderate post-prostatectomy incontinence. The study ended in February 2014 but no results are reported apart a conference abstract presenting early outcomes for the first 36 patients[23]: at 3 months of follow-up, 17/20 (85%) patients treated by sling insertion were cured or significantly improved; 3 sling patients were not improved (pad weight 143, 500, and 890 ml). 14/16 (87.5%) patients treated by AUS were cured or significantly improved; 2 AUS patients were not improved (bladder overactivity, pad weight 1,100 ml). Satisfaction rates between the two groups were similar.

No studies reporting on effectiveness and safety comparing sling insertion *versus* AUS, ACT, or conservative therapy with diapers in men with SUI were identified.

Conclusions

Comparative evidence of effectiveness and safety on the sling procedure for urinary incontinence in women is more plentiful than in men. While an updated systematic review reporting on 22 trials (2,343 women) was found on the sling procedure in women, no comparative studies were identified on the sling procedure in men.

Despite design and reporting limits, the evidence seems to support sling use in women (compared to colposuspension). Pelvic organ prolapse appear to be more common after colposuspension than

after sling procedures, while voiding dysfunctions seem to be more common after sling procedures than after colposuspension.

Only 2 studies focused on the impact of the interventions on quality of life after treatment and this represents a major limit as it is a key determinant for decision making.

It was not possible to link specific evidence to specific devices especially in older studies in which tested devices may have been not available on the market at the time of writing.

The general methodological quality of the comparative evidence base appear to be poor (Lapitan et al.[18] classified the quality of the evidence as "poor to moderate", partly due to poor reporting; the majority of the assessment items were marked as "unclear"), although this view derives from the analysis of synthesis studies. Lack of identification of each device, lack of clarity on study design and of reporting potential harms of the procedures appear to be the most common problems of available evidence.

6. Costs and economic evaluation

Methods

The AEs of this domain were:

Assessment Element ID	Research question
E0001	Can you identify what types of resources are used when delivering the assessed technology and its comparators (resource-use identification)?
E0002	Can you quantify what amounts of resources are used when delivering the assessed technology and its comparators (resource-use measurement)?
E0009	What were the measured and/or estimated unit costs of the resources used by the assessed technology and its comparator(s)?
E0005	What is(are) the measured and/or estimated health-related outcome(s) of the assessed technology and its comparator(s)?
E0006	What are the estimated differences in costs and outcomes between the technology and its comparator(s)?
E0010	What are the uncertainties surrounding the inputs and economic evaluation(s) of the technology and its comparator(s)?
E0012	To what extent can the model estimates of inputs, outcomes, or economic evaluation(s) be considered as providing valid descriptions of the technology and its comparator(s)?

All the AEs selected within the domain were developed. To answer the cost and economic AEs on sling insertion, we conducted two different systematic review (in women and men) of the Italian and international scientific literature to identify and describe the economic evaluation studies on sling devices.

Based on the inclusion criteria described in the effectiveness domain we included all types of economic evaluations: cost-effectiveness analysis (CEA), cost-utility analysis (CUA), cost-benefit analysis (CBA); cost-consequences analysis (CCA); cost-minimisation analysis (CMA) from 2005.

We searched all possible citations on Pubmed, Embase, Cochrane library (EED database - HTA database), CINAHL, EconLIT, HEED (search strategies are presented in Appendix 8 and Appendix 9). We screened title or abstract (if available) of studies identified in literature searches. We investigated the full texts of potential eligible studies to select studies to be included in the analysis, according to our inclusion criteria stated above. We used EndNote to manage retrieved studies. Data extraction from selected studies was carried out using a pre-defined extraction sheet. We analysed studies and synthesised using a tabulation built on the basis of the data extraction form and interpretation of the studies' results was in terms of size, quality and consistency.

The assessment of the methodological quality was carried out using the guidelines for authors and peer reviewers of economic submissions to the BMJ[24]. Using systematic review results, clinical experts and openly available information from manufacturers/distributors we estimated the cost of

single insertion (for both women and men). The estimate included all cost-related information (e.g. operating theatres, preoperative and postoperative examination, staff time, material cost, length of hospital stay, device cost).

Results

The electronic database searches yielded 66 items for female sling and 17 items for male sling. After reading the title and/or the abstract, the full-text of 19 female sling papers and 1 male sling paper were retrieved for further assessment. According to our predefined inclusion criteria, 2 studies on female sling were included in our systematic review; 1 cost-utility analysis and 1 cost analyses. No study on male sling was included. The PRISMA flow-charts describing the inclusion process of the economic studies for both search strategies are shown in Figure 10 and Figure 11, respectively. The included and excluded papers, along with the reason for exclusion, are reported in Appendix 10 and Appendix 11 for both female and male sling intervention.

Table 11 summarises the main information of the two included studies in the systematic review of economic studies. One study[25] was performed in USA and it was a cost utility analysis with outcome expressed as quality-adjusted life years (QALY); the second study[26] was performed in Sweden and it was a cost minimisation analysis. In both studies perspective was not reported and only one[25] analysed a ten-years time horizon. The study by Laudano et al.[25] evaluated the use of tension-free vaginal tape (TVT) compared to Burch colposuspension (BC) while the study by Ankardal et al.[26] evaluated and compared costs of four treatment options: TVT, BC, laparoscopic colposuspension with mesh and staples (LCM) and laparoscopic colposuspension with sutures (LCS). None on the studies considered conservative treatment as a comparator. The study by Laudano et al.[25] did not report funding sources and declared no conflict of interest, while Ankardal et al.[26] declared a grant sponsor by the Goteborg Medical Society Fund and reported no conflicts of interest.

Table 12 and Table 13 summarise the results of the resources used and costs and economic evaluation of the two included studies. We described the results of the economic evaluation for each of the studies.

Figure 10: Study screening process for economic studies on sling operation for urinary incontinence in women according to PRISMA. Adapted 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.

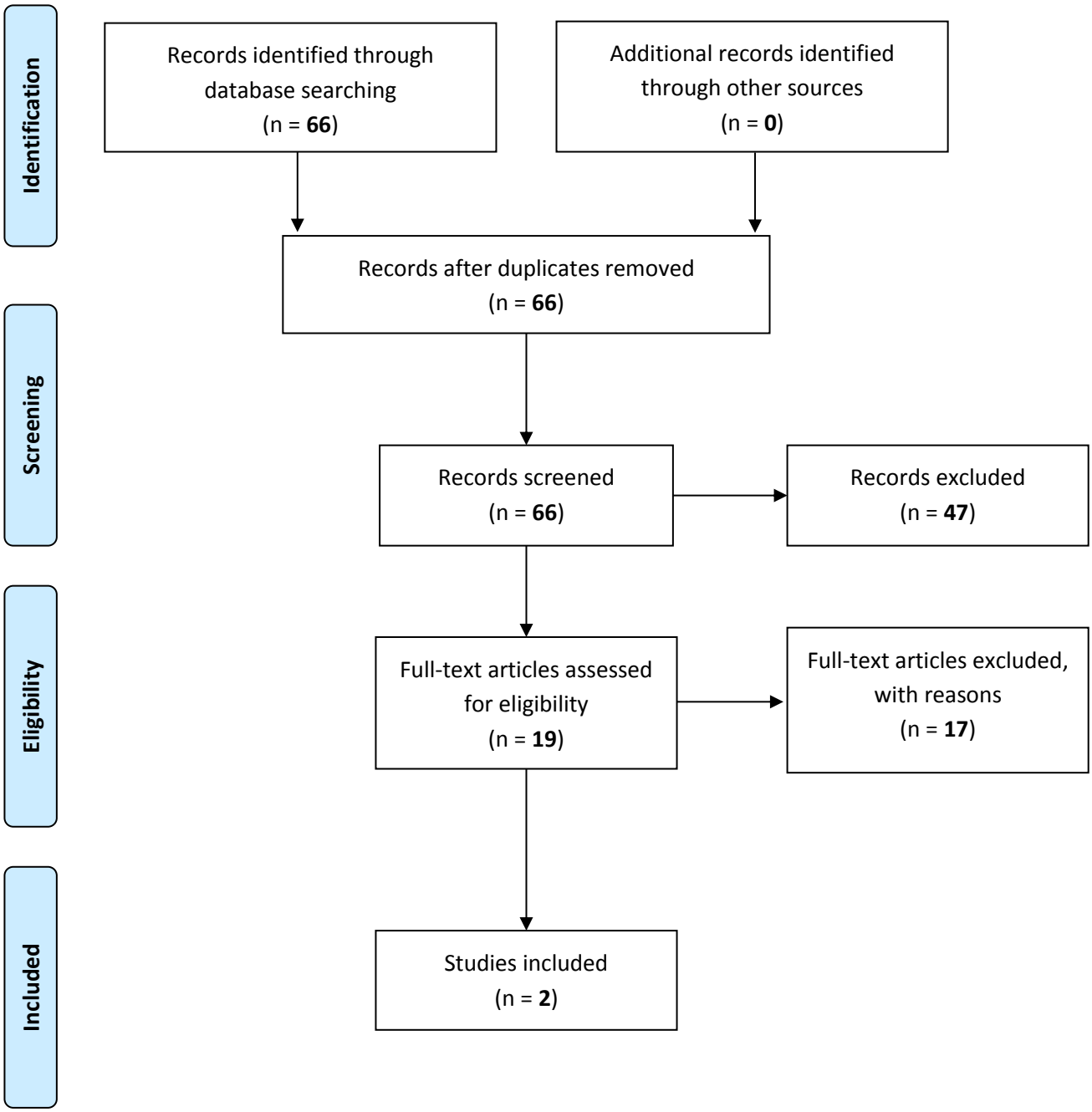
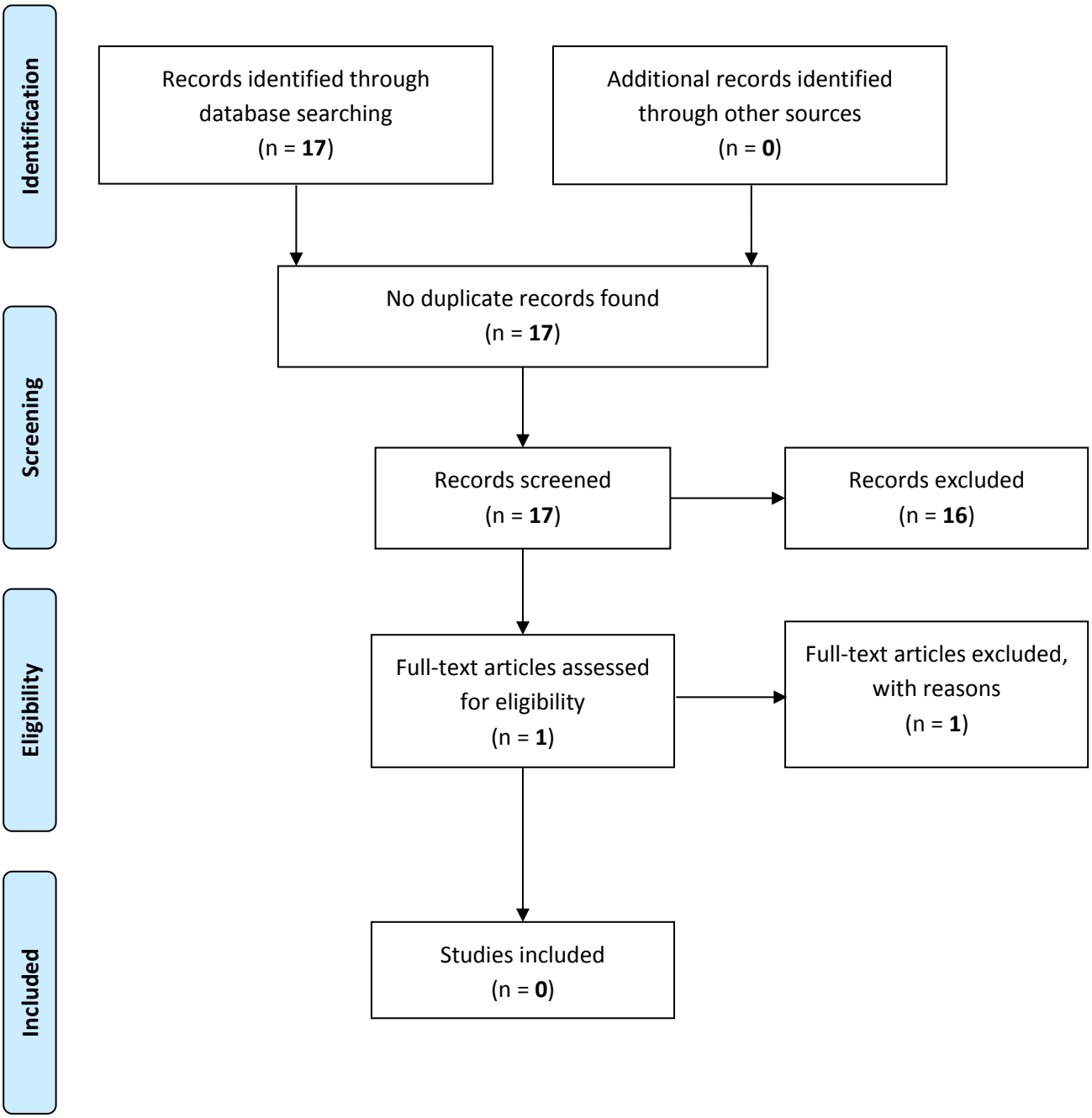


Figure 11: Study screening process for economic studies on sling operation for urinary incontinence in men according to PRISMA. Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097.



Description of included studies

The study by Laudano et al.[25] used Medicare Resource-Based Relative Value Scale to obtain cost data. QALYs were calculated on the basis of health-state utility scores, ranged from 0 (death) to 1 (perfect health). Future costs and outcomes were discounted at a rate of 4.54%, based on the 10-year AAA corporate bond yield. Cost's items considered were: cost of procedure; cost of device; cost of cystoscopy; cost of the operating room; cost of hospital stay, cost for level 5 visit; cost for level 3 visit; cost of treatment for urinary tract infections (UTI); and cost of mesh revision surgery **(E0001)**. Table 12 shows the resource-use valuation **(E0009)** of all the items identified for both intervention and comparator. No complete information about the amounts of resources used was reported **(E0002)**. The mean cost calculated for treatment with TVT was $ 8,651 and $ 10,545 with BC while the efficacy of TVT compared to BC was 5.79 QALY and 5.78 QALYs respectively **(E0005)**. The incremental cost-effectiveness ratio (ICER) was -$ 296,877 per QALY **(E0006)**, which represents the ratio of the difference in costs to the difference in QALYs. That means that treatment for SUI with TVT dominated treatment with BC. Sensitivity analysis **(E0010)** was performed in one way. The study found that TVT remained more cost-effective than BC as a treatment for SUI as long as the cost of the TVT device was <$ 3,220 and the efficacy was >42% (no variation in terms of the utility gain). Authors concluded that TVT was more cost-effective than BC as a treatment for female SUI, despite variations in complication rates, health utility and retreatment rates.

The study by Ankardal et al.[26] constructed a cost model in which were considered direct costs of the four interventions assessed. Cost data were obtained from a regional hospital while clinical data were obtained from different sources. Table 12 shows cost elements of the model for the four treatments considered **(E0001)** and their measurement **(E0009)**.

The study found that the mean total cost of TVT was lower (€ 1,366) than that of other three interventions (€ 2,431 for BC; € 2,118 for LCM, and € 2,310 for LCS) that were similar. The lower cost in favour of TVT was due to its less time consuming.

Table 11: Summary of findings of the included economic studies female sling - General information.

Study	Country	Objective	Economic analysis and Modelling	Perspective	Time horizon/currency /year	Intervention	Name of device	Comparator	Patients	Funding/ Conflict of interest (COI)
Laudano 2013[25]	USA	To compare the CE of TVT with that of BC for the treatment of female SUI	CUA/Markov model	NR	10 years $/year NR	TVT	NR	BC	NR	NR (COI) None declared
Ankardal 2007[26]	Sweden	Compare direct health care costs, of providing treatment for SUI in Sweden with four difference surgical procedures: OBC; LCS; LCM; TVT	CMA/Cost analysis	NR	NR €/2003	NA because there are four compared procedures; OBC; LCS; LCM)	NR	NA because there are four compared procedures; OBC; LCS; LCM)	Female with SUI OBC: (92 female mean age: 51.3) LCM: (101 female mean age: 51.2) LCS (42 female mean age: 55.1) TVT (479 female mean age: 59.9)	Grant sponsor: Goteborg Medical Society Fund (COI)No conflict of interest reported by the authors

Key: *BC, Burch colposuspension; CE, Cost-effectiveness; CMA, cost minimization analysis; LCM, laparoscopic colposuspension with mesh and staples; LCS, laparoscopic colposuspension with sutures; NR, Not reported; OCB, open Burch colposuspension; SUI, stress urinary incontinence; TVT, tension-free vaginal tape.*

Table 12: Summary of findings of included economic studies on female sling insertion – Resource use information (€).

Study	Resource use identification E0001	Resource-use measurement E0002	Type	Resource-use valuation [Source] E0009 intervention (±SD)				Resource-use valuation [Source] E0009 comparator (±SD)
Laudano 2013[25]	Cost: procedure; device; cystoscopy; operating room time; hospital stay, $/day; level 5 visit; level 3 visit; treatment for UTI; mesh revision surgery	Length of hospital stay: BC 3.2 days TVT 1.5 days Length of operating room time: BC 1.2 h TVT 10.7 h	procedure device cystoscopy operating room hospital stay level 5 visit level 3 visit treatment for UTI mesh revision surgery	**TVT** $2,324 $1,170 $419 $2,153 $1,074 $300 $60 $50 $1,836 [Medicare Resource -Based Relative Value Scale]				**BC** $2,362 - $459 $2,153 $1,074 $300 $60 $50 $1,836
Ankardal 2007[26]	Surgeon; Assistant surgeon; Anesthesiologist; Anesthesiologist-stand by; assisting personnel; operation facilities and capital cost; laparoscopic equipment; single use Stapler; TVT material; Antibiotics; Recovery; hospital day; urinary tract infection; wound infection; additional days with urinary retension	NR	Head Surgeon Assistant surgeon Anesthesiologist; assisting personnel; operation facilities capital laparoscopic equipment; single use Stapler; TVT material; Antibiotics; Recovery; hospital day; urinary tract infection; wound infection; urinary retension [costs data from one regional Swedish hospital]	**TVT** €105 0 €33 €191 €50 €43 0 0 €417 €15 €65 €418 €13 €1 €14	**OBC** €214 €71 €62 €330 €87 €74 0 0 0 €15 €109 €1,342 €37 €5 €86	**LCM** €260 €87 €69 €375 €99 €84 €74 €217 €0 €15 €51 €738 €15 €8 €27	**LCS** €282 €94 €72 €390 €103 €88 €80 0 0 €15 €57 €996 €34 €8 €92	

Table 13: Summary of finding of the included economic studies on female sling use. Effectiveness, cost and cost-effectiveness results.

Study	Costs results and Δ costs (€)	Efficacy results and Δ efficacy E0005 [source]	Discount rate	Δ in costs and efficacy [E0006]	Sensitivity analysis (SA)	Authors conclusions
Laudano 2013[25]	TVT $8,651 BC $10,545 Δ= $1,828	TVT 5.79 QALY BC 5.78 QALY Δ= -0.01 [efficacy from seven RCTs: Liapis 2002; Persson 2002; Paraiso2004; Valpas 2004; Ward 2004; Bai 2005; Foote 2006]	4.54% (ten year corporate bond yield)	TVT dominant vs BC ICER -$296,877	Probabilistic one way and two way SA	TVT was more cost-effective than BC as a treatment for female SUI, despite variations in complication rates, health utility and retreatment rates.
Ankardal 2007[26]	Total cost OBC: €2,431 LCM: €2,118 LCS: €2,310 TVT: €1,366	NA	NA	NA	NA	TVT procedures generate a lower direct cost than colposuspension, both with the open and laparoscopic approach.

Key: *NA, Not applicable.*

Quality assessment (E0012)

We evaluated the quality of the included studies using the checklist for economic evaluations of health programmes[24]. The checklist was divided in ten sections under three headings for a total of 35 items (questions):

1. study design (7 items),
2. data collection (14 items)
3. analysis and interpretation of results (14 items).

Each item had four answer options: yes, no, not clear, not appropriate. We evaluated the quality for only one of the two studies included in the systematic review as the other one[26] was not a full economic evaluation.

Although the study by Laudano et al.[25] had several limitations, mainly due to the quality of data available, it scored 24 out of 35 positive answers and was rated as of medium-high quality (Table 14).

Table 14: Summary of the quality assessment of the included studies.

Study ID	Overall	Study design	Data collection	Analysis and interpretation of results
Laudano, 2013[25]	Y: 24/35 N: 6/35 NC: 1/35 NA: 4/35	Y: 6/7; N:1/7 NC: 0/7; NA: 0/7	Y: 6/14; N:4/14 NC: 1/14;NA:3/14	Y: 12/14; N:1/14 NC: 0/14; NA: 1/14

Key: Y, Yes; N, No; NC, Not clear; NA, Not applicable.

Conclusions

There is a lack of economic data in literature. However on the basis of the findings of the systematic review of economic evaluation studies, TVT use accrues a mean cost saving. Although the cost of slings is high, sling insertion has shorter hospital stay and operating room time.

7. Discussion

SUI represents the most common type of UI among women. SUI is less common in men and mainly secondary to radical prostatectomy. Even if remission rates have been documented in both populations, the problems SUI causes and their impact on everyday life lead sufferers to seek solutions. Non-surgical approaches are recommended as first-line, while surgical management is generally performed when these strategies have failed.

The present HTA report focused on the impact of sling operation in women and men with SUI. Two different sets of comparators were necessary to develop the assessment: in women sling insertion was compared to Burch colposuspension or autologous vaginal tapes. In men, sling insertion was compared to AUS or adjustable continence therapy. Conservative therapy with diapers was considered a comparator for both populations.

As of today, 17 manufacturers of slings for women and 9 manufacturers of male slings are present on the Italian market, offering many different sling solutions. Sling operations represent 95.9% of all interventions for SUI in women and 36.3% in men (from 26.7% in 2010 to 38.1% in 2014) in 2010-2014. Intervention rates were 123.2/1,000,000 women and 6.1/1,000,000 men per year. In women this rate is roughly stationary in the age group 45 to 74 years and decreasing thereafter, while in men the interventions are centred in the age group 65-74. Mean length of hospital stay for women is significantly shorter for sling insertion than Burch procedure (3 days vs 4.9 days), while in men length of stay is similar (3.6 days for sling insertion and 3.7 days for AUS insertion).

The latest systematic review of sling insertion in women identified by our searches included 22 trials (2,343 women). The evidence supports sling compared to Burch procedure in women, but the studies were affected by methodological problems mainly related to poor reporting. Measures of QoL were reported in two studies only, despite being acknowledged as a major factor for decision-making. A recent NICE guidance, published during the editing of the present report, recommends that single-incision short sling mesh insertion for SUI in women should no longer be carried out because of uncertainty on long term effectiveness[27].

The latest systematic review aimed at assessing interventions for UI in men did not identify studies comparing sling insertion versus AUS or adjustable continence therapy. Of the three ongoing trials identified by the review, a status update showed that one study (sling versus ACT) was terminated for poor recruitment, one study was completed but no final results were available (sling versus AUS), and one study (sling versus AUS) is due to be completed in August 2019. In clinical practice, male slings are proposed to men with mild to moderate SUI, even if

the definitions of mild and moderate UI are not clear. According to the EAU, even acknowledging the lack of comparative evidence and long term results, fixed male slings should be offered to men with persistent (>6 months) post-prostatectomy incontinence who have not responded to conservative management[3]. Recommendations from NICE are more cautionary as they limit the use of male slings to manage SUI only as part of a randomised controlled trial[28].

The economic findings cannot be considered definitive as they are based only on one economic evaluation and one cost analysis study.

Other issues in assessing sling operation were related to the large variety of devices on the market and the difficulty to clearly link specific evidence to specific devices. An interesting analysis was performed by Hogewoning et al.[29] with the aim to review and evaluate the research conducted before the launch of a particular sling onto the market. By performing a literature search and by surveying 19 different manufacturers, the authors found that for only 10 out of 41 slings a study was available. Since the remaining 31 sling devices had no comparative pre-launch data, the authors concluded that slings have been often introduced without any scientifically proven basis or pre-launch research. In the same paper, the authors encouraged FDA and the European Union to introduce stricter rules for the registration of new slings, comparable to those suggested for meshes in vaginal prolapse surgery, as the two devices have essentially the same technical characteristics. Hogewoning et al.[29] suggested compulsory registration of the first 1,000 consecutive patients without any sponsorship from manufacturers. We agree with Hogewoning et al.[29]. We should also preferentially use and recommend those sling devices for which clinical data has been generated.

8. Recommendations

In women, only sling devices supported by robust clinical data should be used. Sling use in men with SUI is currently not supported by comparative clinical studies but European clinical guidelines recommend it on the basis of the results from uncontrolled studies and opinions from expert panels. We recommend the use of male slings only under evidence-generation frameworks. Procedures coding should be updated to represent current practice with a specific code for each procedure. For example the following procedures should have a specific code:

- Open retropubic colposuspension;
- Laparoscopic retropubic colposuspension;
- Pubo-vaginal sling;
- Synthetic female retropubic sling;
- Synthetic female transobturatory sling;
- Single-incision minisling;
- Artificial urinary sphincter (AUS);
- Adjustable continence therapy (ACT);
- Fixed synthetic male sling;
- Adjustable synthetic male sling.

All sling devices should be tested in prospective multicentre comparative studies before registration and current legislation should be changed accordingly. Such studies should include prospective economic evaluation with reproducible measures of QoL.

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List of acronyms and abbreviations

ACT: adjustable continence therapy

AE: assessment element

AUS: artificial urinary sphincter

BC: Burch colposuspension

BD/RDM: Italian National Medical Devices Inventory and Database

B-FLUTS: Bristol Female Lower Urinary Tract Symptoms

BMI: body mass index

BMJ: British Medical Journal

CBA: cost-benefit analysis

CCA: cost-consequences analysis

CCT: Comparative controlled trial

CE: Conformité Européene

CEA: cost-effectiveness analysis

CRD: Centre for Reviews and Dissemination

CI: confidence interval

CMA: cost-minimisation analysis

CUA: cost-utility analysis

DRG: diagnosis-related group

EAU: European Association of Urology

EU: European Union

FDA: United States Food and Drug Administration

HTA: Health technology assessment

ICD-9-CM: International Classification of Diseases, 9th revision, Clinical Modification

IFU: instructions for use

ICD: International Statistical Classification of Diseases and Related Health Problems

IIQ: Incontinence Impact Questionnaire

ISTAT: Italian Official Statistical Service

LCM: laparoscopic colposuspension with mesh and staples

LCS: laparoscopic colposuspension with sutures

LUTS: lower urinary tract symptoms

MeSH: Medical Subject Headings

MUI: mixed urinary incontinence

NHS: national health service

NICE: National Institute for Clinical Excellence

NR: Not reported

PICO framework: Population, Intervention, Comparison, Outcome

PVR volume: post-voiding residual volume

QALY: quality-adjusted life years

QoL: Quality of life

RCT: Randomised controlled trial

RPR: retropubic route

RR: risk ratio

SDO database: national hospital discharge records database

SF-36: Short Form-36

SI: single-incision technique

SUI: stress urinary incontinence

TOR: transobturator route

TOT: the transobturator tape

TVT: tension-free vaginal tape

UDI: Urogenital Distress Inventory

UDS: urodynamic studies

UI: Urinary Incontinence

USI: urodynamic stress incontinence

UTI: urinary tract infection

UUI: urgency urinary incontinence