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Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Urinary incontinence in neurological disease: management of lower urinary tract dysfunction in neurological disease

1.1 Short title

Lower urinary tract dysfunction in neurological disease

2 The remit

The Department of Health has asked NICE: 'To produce a clinical guideline on the management of incontinence in neurological disease in all ages'.

3 Clinical need for the guideline

3.1 Epidemiology

a) The function of the urinary bladder is to store and expel urine in a coordinated and controlled manner. The central and peripheral nervous systems regulate this activity. A wide range of neurological conditions can affect the function of the lower urinary tract. The impact of this subsequent urinary dysfunction is variable, with some people experiencing symptoms that relate to impaired bladder storage, while bladder emptying will be a problem for others. Storage and voiding problems may also arise in combination. Neurological lower urinary tract dysfunction can have further important consequences. For example, kidney function can be lost as a result of abnormally high pressures within the bladder, from the effects of urinary tract infection and as a result of urinary tract stone disease.

b) Urinary symptoms resulting from neurological disease can occur because of damage to the brain, the suprasacral spinal cord, the sacral spinal cord

(the conus medullaris) or the peripheral nervous system. Damage within each of these areas tends to produce characteristic patterns of bladder and sphincter dysfunction. The nature of the damage to the nervous system is also important. In children the neurological damage is often the result of congenital defects such as cerebral palsy, spina bifida (meningo-myelocoele) or sacral agenesis. It is important to distinguish between conditions that produce a fixed or stable injury to the nervous system (for example stroke, spinal cord injury and cauda equina compression) and those that produce progressive damage through inflammatory or degenerative processes. Progressive conditions include dementia, Parkinson's disease, multiple sclerosis and peripheral neuropathy.

c) One of the most distressing symptoms that arises from neurological lower urinary tract dysfunction is urinary incontinence. The prevalence of such incontinence in the population is not well understood and exact figures are difficult to obtain. The severity and nature of neurological incontinence is dependent on many factors, including the site, the extent and the development of the neurological lesion.

d) It is common for people to have multiple and varied symptoms. Storage symptoms include an increased frequency of urination (by day and/or night), urinary urgency and urinary incontinence. Problems with bladder emptying may lead to hesitancy, a slow urinary stream, the need to strain or urinary retention.

e) Urinary tract symptoms have a significant impact on quality of life; they can cause embarrassment, lead to social isolation and impair activities of daily living. They can also lead to impairments in renal function and reduce life expectancy. The secondary effects of neurological lower urinary tract dysfunction also have an impact on quality of life; for example, the morbidity associated with recurrent urinary tract infections can be severe. Medical interventions do not necessarily restore normal urinary function. Quality of life is affected by the medical regime used to treat the urinary tract dysfunction; many patients have to cope with the side effects of medication, the impact of catheterisation or the continuing use of pads or appliances.

f) The economic impact of neurogenic urinary tract dysfunction is substantial. Significant expenditure is associated with patient assessment and follow-up, and dealing with complications of treatment. Improving patient care would lead to a better use of public resources and enhance the cost-effectiveness of service delivery. There are also major costs associated with the provision and usage of catheters and pads. Other costs arise through the use of drug treatments and surgical interventions. There is also a huge financial impact as a result of patient requirements for carer, nursing and medical support.

3.2 Current practice

a) A diverse range of interventions is used in the management of urinary incontinence and there is considerable variation in clinical practice. The condition can be managed in a variety of different settings ranging from the community to specialist surgical services. Access to supplies of aids and to specialist advice and services lacks uniformity. The integration between community, primary care and secondary/tertiary hospital services is of great importance and the effectiveness of these links is variable. The transition from paediatric to adult services requires particularly careful management.

b) There are a number of national and international guidelines on neurological lower urinary tract dysfunction. Some relate to specific neurological conditions, others to the range of relevant neurological conditions. These guidelines are heavily reliant on consensus opinion rather than high-quality scientific evidence.

c) There are often several possible treatment strategies for neurological lower urinary tract dysfunction. A comprehensive review of benefits and risks of different management strategies in both the short and long term is needed to help patients and carers who are faced with a choice between different long-term treatment options.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Adults and children (from birth) with lower urinary tract dysfunction resulting from neurological disease and injury.

b) No subgroups of people have been identified as needing specific consideration.

4.1.2 Groups that will not be covered

a) No patient groups have been identified for exclusion.

4.2 Healthcare setting

a) All settings in which NHS care is received.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

a) Assessment of lower urinary tract function including:

- clinical history and examination
- simple functional tests (for example frequency and volume charts and pad testing)
- urodynamic studies (including cystometry, pressure/flow studies and video-urodynamics).

b) Identification of criteria that should trigger referral for specialist assessment.

c) Management of impaired voiding and storage of urine:

- Physical interventions to aid urinary storage, including behaviour and bladder training, pelvic floor muscle exercises and neuromuscular stimulation.
- Pharmacological therapies to aid urinary storage, for example: antimuscarinic agents and botulinum toxin.
- Surgical procedures to improving bladder storage capacity, for example augmentation cystoplasty and sacral nerve stimulation.
- Surgical procedures to treat incontinence resulting from sphincter weakness such as the use of urethral tapes, urethral slings, and the artificial urinary sphincter.
- Physical aids to bladder emptying for example:
  - intermittent catheterisation
  - indwelling urethral and suprapubic catheters
  - catheter valves.
- Drug therapy to improve bladder emptying, including alpha adrenergic antagonists.
- Urinary diversion procedures, including ileal conduit.
- Appliances and equipment to contain urinary incontinence.

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

d) Follow up protocols and management strategies to prevent and treat the complications of neurogenic lower urinary tract dysfunction and its management.

e) Managing the transition from child to adult services.

f) Information and support for patients and carers.

4.3.2 Clinical issues that will not be covered

a) General management of the underlying disorder.

b) Management of associated faecal incontinence, sexual dysfunction or psychological problems.

c) Management of comorbidities.

4.4 Main outcomes

There are many possible outcome measures that may be relevant to neurological lower urinary tract dysfunction. Among those we plan to consider are:

a) Frequency of voiding by day and night.

b) Number of incontinence episodes per week.

c) Severity of incontinence.

d) Urgency.

e) Symptoms relating to bladder emptying, for example poor urinary stream.

f) Quality of life.

g) Patients and carers' perception of symptoms.

h) Adverse events, including urinary tract infections, renal complications, bladder stones and unscheduled hospital admissions.

i) Treatment adherence.

j) Kidney function.

4.5 Economic aspects

Developers will take into account both clinical- and cost-effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year

(QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see ‘Further information’).

4.6 Status

4.6.1 Scope

This is the final scope.

4.6.2 Timing

The development of the guideline recommendations will begin in October2010.

5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

This guideline will update and replace part of the following NICE guidance (recommendations on bladder problems and urinary tract infections only):

- Multiple sclerosis. NICE clinical guideline 8 (2003). Available from www.nice.org.uk/guidance/CG8

5.1.2 Other related NICE guidance

- Constipation in children and young people. NICE clinical guideline 99 (2010). Available from www.nice.org.uk/guidance/CG99
- Male lower urinary tract symptoms. NICE clinical guideline 97 (2010). Available from www.nice.org.uk/guidance/CG97
- Lapararoscopic augmentation cystoplasty (including clam cystoplasty). NICE interventional procedure guidance 326 (2009). Available from www.nice.org.uk/guidance/IPG326
- Chronic kidney disease. NICE clinical guideline 73 (2008). Available from www.nice.org.uk/CG73
- Single-incision sub-urethral short tape insertion for stress urinary incontinence in women. NICE interventional procedure guidance 262 (2008). Available from www.nice.org.uk/guidance/IPG262

- Suburethral synthetic sling insertion for stress urinary incontinence in men. NICE interventional procedure guidance 256 (2008). Available from www.nice.org.uk/guidance/IPG256
- Insertion of extraurethral (non-circumferential) retropubic adjustable compression devices for stress urinary incontinence in men. NICE interventional procedure guidance 224 (2007). Available from www.nice.org.uk/guidance/IPG224
- Urinary tract infection in children. NICE clinical guideline 54 (2007). Available from www.nice.org.uk/guidance/CG54
- Faecal incontinence. NICE clinical guideline 49 (2007). Available from www.nice.org.uk/guidance/CG49
- Dementia. NICE clinical guideline 42 (2006). Available from www.nice.org.uk/guidance/CG42
- Parkinson's disease. NICE clinical guideline 35 (2006). Available from www.nice.org.uk/guidance/CG35
- Urinary incontinence. NICE clinical guideline 40 (2006). Available from www.nice.org.uk/guidance/CG40
- Insertion of biological slings for stress urinary incontinence. NICE interventional procedure guidance 174 (2006). Available from www.nice.org.uk/guidance/IPG154
- Intramural urethral bulking procedures for stress urinary incontinence. NICE interventional procedures guidance 138 (2005). Available from www.nice.org.uk/guidance/IPG138
- Insertion of extraurethral (non-circumferential) retropubic adjustable compression devices for stress urinary incontinence in women. NICE interventional procedure guidance 133 (2005). Available from www.nice.org.uk/guidance/IPG133
- Transobturator foramen procedures for stress urinary incontinence. NICE interventional procedure guidance 107 (2005). Available from www.nice.org/guidance/IPG107
- Sacral nerve stimulation for urge incontinence and urgency-frequency. NICE interventional procedure guidance 82 (2004). Available from www.nice.org.uk/guidance/IPG82
- Infection control, prevention of healthcare-associated infection in primary and community care. NICE clinical guideline 2 (2003). Available from www.nice.org.uk/guidance/CG2

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Nocturnal enuresis in children (bedwetting). NICE clinical guideline. Publication expected October 2010.
- Percutaneous posterior tibial nerve stimulation for overactive bladder syndrome. NICE interventional procedure guidance. Publication expected Autumn 2010.Infection control (update). NICE clinical guideline. Publication expected March 2012.
- Stroke rehabilitation. NICE clinical guideline. Publication expected April 2012.
- Spasticity in children. NICE clinical guideline. Publication expected June 2012.

6 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).

Appendix B: Declarations of Interest

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B.1 Declarations of interests of the GDG members

Introduction

All members of the GDG and all members of the NCGC staff were required to make formal declarations of interest at the outset of each meeting, and these were updated at every subsequent meeting throughout the development process. No interests were declared that required actions.

B.1.1 Anderson: Christine

GDG meeting	Date	Declaration of Interest
GDG Application		Personal pecuniary interest 10/01/2010 I wrote an article about Peristeen which was published in Charter Healthcare Magazine – honorarium paid by Coloplast. 02/03/2010 PromoCon symposium – Presentation to Nurses about my experiences and Peristeen – expenses and honorarium received and paid by Coloplast. 11/04/2010 preparation meeting in Copenhagen for ESPU conference – honorarium paid by Coloplast. 30/04/2010 ESPU conference in Turkey – demonstrating the use of educational tools developed by Coloplast for teaching catheterisation to children – expenses and honorarium received and paid by Coloplast. 05/05/2010 ASBAH Big Bowel and Bladder Day for parents sponsored by Coloplast at their Peterborough Office – expenses and honorarium received and paid by Coloplast. 23/06/2010 Peristeen Masterclass in Birmingham, for healthcare professionals – presentation of a parents perspective and our story with Peristeen. 01/03/2011 – PromoCon Symposium – I have been asked to present at the event next year – again based on Peristeen. To date all requests from Coloplast have been related to the Peristeen product and educational material. I have no involvement with bladder products and we do not use any of their bladder products todate. Personal family interest My son has received payment from Coloplast for photographic work for marketing material. 09/12/2009 Family trip to Coloplast Head Office Copenhagen – only expenses paid. Photographs and video filming for marketing material and educational tools.
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	Personal pecuniary interest £150 from Coloplast to deliver a presentation – Bowel and Bladder in Spina Bifida and Peristeen. Instigated funding from Coloplast for a family fund day in Liverpool. Coloplast sponsored the event.
GDG Meeting 7	20/05/2011	No change

GDG meeting	Date	Declaration of Interest
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

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B.1.2 Bardsley: Alison

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	Resigned
GDG Meeting 10	09/09/2011	n/a
GDG Meeting 11	14/10/2011	n/a
GDG Meeting 12	11/11/2011	n/a
GDG Meeting 13	09/12/2011	n/a
GDG Meeting 14	11/05/2011	No change

2

B.1.3 Barker: Noreen

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

2

B.1.4 Denny: Amelia

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	Non personal pecuniary interest Attended a workshop in Manchester hosted by Coloplast to discuss the eperisteen anal irrigation system. Travel and accommodation provided.
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	Non personal pecuniary interest Attended a meeting on 23rd November, 2011, sponsored by Covidien at which a new dressing suitable to help reduce granulomas around catheter sites, was presented. Refreshments were provided.
GDG Meeting 14	11/05/2011	No change

2

B.1.5 Fowler: Clare

GDG meeting	Date	Declaration of Interest
GDG Application		Non-personal pecuniary interest I have received unrestricted educational grants from Allergan, the manufacturer of Botox ®, to carry out laboratory investigations of the mechanism of action Botulinum toxin A when injected into the detrusor muscle as a treatment of detrusor over activity. The treatment is currently undergoing licensing trials, and my department is a trial centre. I have been an invited member of Allergan advisory boards and have spoken at teaching courses about the treatment. Personal non-pecuniary interest Publication of "a UK Consensus on the management of the bladder in multiple sclerosis" J Neurol Neurosurg Psychiatry (2009: 80:470-477) was the result of a working group of stakeholders convened by me. I have therefore expressed a public statement on the topic of the management of incontinence in MS, which is likely to be a topic covered by this new NICE initiative.
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	Personal non-pecuniary interest Educational grants from Allergran Inc. – Manufacturer of Botox ®. Speaker panel for Astellas (honoraria received)
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	Personal pecuniary interest Paid honorarium for attending Allergan advisory board meeting. Non-personal pecuniary interest
GDG Meeting 13	09/12/2011	Received money from TEVA for arranging a meeting on multiple system atrophy. Paid : attended an allergen advisory board. Attended advisory board of Biogen – payment to university. Royalties received from Allergan for speaking engagements.
GDG Meeting 14	11/05/2011	No change

2

B.1.6 Graham: Laura

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	Personal non-pecuniary interest Use of Botulinum toxin for spasticity in clinical practice (not for bladder function) sponsorship of teaching programme by IPSEN 1&2 providers of refreshment (ongoing) – not bladder related.
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	Personal non-pecuniary interest Use of Botulinum toxin for spasticity in clinical practice (not for bladder function) sponsorship of teaching programme by IPSEN 1&2 providers of refreshment (ongoing) – not bladder related.
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

2

B.1.7 Harrison: Simon

GDG meeting	Date	Declaration of Interest
GDG Application		Personal Pecuniary interest £500.00 lecture fee from Astellas Jaanuary 2010. No further lectures are planned. £200 lecture fee from Tonic Life Communications – Galen round table discussion June 2009. No further lectures are planned. Non-Personal pecuniary interest I lecture on a course twice each year on the Urological Care of the Patient with a Spinal Cord injury. I do not receive any payment or expenses in relation to the course and do not manage its finances (that role is undertaken by Mr. Paul Tophill, Consultant Urologist, Sheffield). However, I organise a one day segment of the course and this day has been sponsored by Coloplast in 2009. Sponsorship is by direct coverage of expenses with no additional payment beyond direct costs. Typically the total amount provided by Coloplast is £800 per course. This arrangement is currently in place for the two courses which are scheduled to take place in 2010.
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	Personal pecuniary interest £500 lecture fee from Astellas January 2010. No further lectures are planned. £200 lecture fee from Tonic Life Communications – Galen round table discussion June 2009. No further lectures are planned. Non-Personal pecuniary interest I lecture on a course twice each year on the Urological Care of the Patient with a Spinal Cord injury. I do not receive any payment or expenses in relation to the course and do not manage its finances (that role is undertaken by Mr. Paul Tophill, Consultant Urologist, Sheffield). However, I organise a one day segment of the course and this day has been sponsored by Coloplast in 2009. Sponsorship is by direct coverage of expenses with no additional payment beyond direct costs. Typically the total amount provided by Coloplast is £800 per course. The course in November 2010 was not sponsored by Coloplast but received support from Medtronic. I also attended sessions sponsored by Astellas, Glaxo Smith Kline and American Medical Systems during the course of the week.
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	Personal Non pecuniary interest Sponsorship of Spinal Injuries course – 9th – 13th May – Amdipharm, American medical systems GSK and Coloplast. Additional Urological Consultant's meetings – 4th May – sponsored by Pfizer.
GDG Meeting 8	24/06/2011	Attended evening symposium at Britisih Association of Urological Surgeons Annual Meeting – Sponsored by Pfizer
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change

GDG meeting	Date	Declaration of Interest
GDG Meeting 12	11/11/2011	Non-personal pecuniary interest Hosted a meeting on behalf of British Association of Urological Surgeons, Section of Female Neurological and Urodynamic Urology at Pinderfields Hospital on 26/10/2011. Catering sponsored by 'The Urology Company'.
GDG Meeting 13	09/12/2011	Non-personal pecuniary interest: Joint organiser of spinal injury course. Catering expenses covered by Coloplast, American Medical Systems, Pfizer, Karl Sotrz Endoscopy, Amdipharm and Astellas.
GDG Meeting 14	11/05/2012	Non-personal pecuniary interest: Medtronic paid my train fare to attend a meeting at the British Association of Urological Surgeon's offices. The meeting was an educational meeting relating to sacral nerve stimulation and also discussed the possibility of establishing an independent national database of neuromodulation procedures. I attended a meeting with a visiting urologist who was visiting Yorkshire in order to validate our use of Green Light Laser as part of a clinical trial that is comparing Laser prostatectomy with TURP. Dinner was provided by American Medical systems. The trial is sponsored by AMS and I am a local investigator.

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B.1.8 Jesky: Judith

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	Attended a workshop hosted by Coloplast to discuss the peristeen anal irrigation system. Travel and Accommodation were provided. This meeting was held in Manchester on 22nd and 23rd June, 2011.
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	Attended an evening meeting sponsored by Covidien at which they presented a new dressing suitable to help reduce granulomas around catheter sites. Refreshments were provided and this was held on 23rd November, 2011.
GDG Meeting 14	11/05/2011	No change

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B.1.9 Mc Clurg: Doreen

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	Personal non-pecuniary interest As part of my PhD I undertook two research studies relating to pelvic floor muscle training in people with multiple sclerosis. I am the author of two of the papers reviewed.
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

B.1.10 Mac Dermott: Keith

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

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B.1.11 Mangnall: Joanne (Cooptee)

GDG meeting	Date	Declaration of Interest
GDG Application		Personal pecuniary interest Speaker at Astellas educational event: speaker fees paid. Contributed to Pfizer educational resource: speaker fees paid. Speaker at MS Trust educational events: speaker fees paid.
GDG Meeting 1	29/09/2010	n/a
GDG Meeting 2	05/11/2010	n/a
GDG Meeting 3	15/12/2010	n/a
GDG Meeting 4	04/02/2011	n/a
GDG Meeting 5	11/03/2011	n/a
GDG Meeting 6	13/04/2011	n/a
GDG Meeting 7	20/05/2011	n/a
GDG Meeting 8	24/06/2011	n/a
GDG Meeting 9	29/07/2011	n/a
GDG Meeting 10	09/09/2011	n/a
GDG Meeting 11	14/10/2011	Personal pecuniary interest Delivered a workshop at an Astellas event on 26th September 2011 (received honorarium) The workshop title was 'Planning for improved service efficiencies and patient experience.' The workshop covered service redesign work I undertook with our Medicines Management team. Delivered continence training at MS Trust specialist Nurse course 25th March 2011 (speaker fee paid) Speaker at a Coloplast event 19th Jan 2010 Delivered continence training at MS Trust specialist Nurse course 8th October 2010 (speaker fee paid) Delivered workshop and was a speaker at a Rochester medical event 19th October 2010 (speaker fee paid) Delivered continence training at MS Trust specialist nurse course 19th March 2010 (speaker fee paid) I did one GP session sponsored by Pfizer in 2009 I was paid by Wyeth for my contribution in developing an educational resource in 2009 I was paid a consultancy fee by Pfizer for my contribution in developing an educational resource for nurses
GDG Meeting 12	11/11/2011	n/a
GDG Meeting 13	09/12/2011	n/a
GDG Meeting 14	11/05/2011	No change

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B.1.12 Orme: Susie

GDG meeting	Date	Declaration of Interest
GDG Application		Personal pecuniary interest I have given talks at sponsored symposiums on continence promotion for Astellas and Eli Lily. Personal family interest My sister Dr. Wendy Orme, PHD works as a financial director for Glaxo-Smith-Klein.
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	Personal non-pecuniary interest Bladder and Bowel foundation Trustee
GDG Meeting 11	14/10/2011	Personal pecuniary interest Spoken at symposium on continence care modelling (non promotional) at British Geriatric Society (UK) sponsored by Astellas.
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

B.1.13 Tophill: Paul

GDG meeting	Date	Declaration of Interest
GDG Application		Personal non-pecuniary interest I have clear views about the need for appropriate treatment of this group of patients which have been expressed in print and at professional meetings.
GDG Meeting 1	29/09/2010	Personal non-pecuniary interest Varms Drug Company – Provided lunches/meals at Educational Meetings.
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	Personal non-pecuniary interest 9.5.2011 sponsorship of a teaching course I manage by Amdipharm. 10/05/2011 sponsorship of a teaching course I manage by American Medical Systems. 10.05.2011 sponsorship of a teaching course I manage by GSK. 11.05.2011 sponsorship of a teaching course I manage by Coloplast.
GDG Meeting 8	24/06/2011	Personal non-pecuniary interest Evening meeting on 21st June, 2011 – sponsored by Pfizer. Accommodation on 20th and 21st June, 2011 – sponsored by Astellas.
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	Non personal non-pecuniary interest Manage a teaching course sponsored by Karl Storz Endoscopy, Pfizer, Amdipharm, American Medical Systems, Coloplast, Astellas Pharma.
GDG Meeting 14	11/12/2012	Non personal pecuniary interest Astellas sponsorship for attendance at European Association of Urology meeting in February. Also support received for Spinal injuries course in April.

2

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B.1.14 Vickerman: Julie

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	Non-personal pecuniary interest Attended RCN conference 1st to 3rd November 2010 – accommodation sponsored by Euron Limited.
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	Personal non-pecuniary interest Sponsorship of North West Association for Continence Advice (ACA) education meeting by Astellas. (I am chair of this group)
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

B.1.15 Williams: Alun

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	Personal non-pecuniary interest Attended meeting held by Pfizer on 30/06/2011.
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	Personal pecuniary interest Received an education grant of £1,000 from Oceana Theraputics (makers of Deflux) for attendance at the American Academy of Pediatrics, Congress in Boston.
GDG Meeting 14	11/05/2011	No change

2

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B.1.16 Woodward: Sue

GDG meeting	Date	Declaration of Interest
GDG Application		None
GDG Meeting 1	29/09/2010	No change
GDG Meeting 2	05/11/2010	No change
GDG Meeting 3	15/12/2010	No change
GDG Meeting 4	04/02/2011	No change
GDG Meeting 5	11/03/2011	No change
GDG Meeting 6	13/04/2011	No change
GDG Meeting 7	20/05/2011	No change
GDG Meeting 8	24/06/2011	No change
GDG Meeting 9	29/07/2011	No change
GDG Meeting 10	09/09/2011	No change
GDG Meeting 11	14/10/2011	No change
GDG Meeting 12	11/11/2011	No change
GDG Meeting 13	09/12/2011	No change
GDG Meeting 14	11/05/2011	No change

Appendix C: Literature search strategies

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Introduction

Search strategies used for the **Incontinence in Neurological Disease guideline** were run in accordance with the NICE Guidelines Manual 2009: http://www.nice.org.uk/media/5F2/44/The_guidelines_manual_2009_-_All_chapters.pdf

All searches were run up to 10/01/12. Any studies added to the databases after this date were not included unless specifically stated in the text.

Clinical searches

Searches for **clinical reviews** were run in Medline (OVID), Embase (OVID), the Cochrane Library (Wiley) and Cinahl (EBSCO). Typically, searches were constructed in the following way:

- A PICO format was used for intervention searches. **Population** (P) terms were combined with **Intervention** (I) and sometimes **Comparison** (C) terms (as indicated in the tables under each individual question in Section C.3). An intervention can be a drug, a procedure or a diagnostic test. **Outcomes** (O) are rarely used in search strategies for interventions. Study type filters were added where appropriate (see Section C.1).

Patient searches

In addition to the databases outlined above, the search for **patient information** (C.3.8.3) was run in PsycINFO (OVID).

Economic searches

Searches for **economic reviews** were run in Medline (Ovid), Embase (Ovid), the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database, and the Health Economic Evaluation Database (HEED). NHS EED and HTA were searched via the Centre for Reviews and Dissemination (CRD) interface. For Medline and Embase an economic filter (C.1.4) was added to the standard population terms (Section C.2). All other searches were conducted using only population terms.

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Section A.4	**Economic searches**

C.1 Study design search terms

C.1.1 Systematic review (SR) search terms

3 **Medline search terms**

1.	"Review"/ OR review.pt. OR review.ti.
2.	(systematic OR evidence* OR methodol* OR quantitative* OR analys* OR assessment*).ti,sh,ab.
3.	1 and 2
4.	meta-analysis.pt.
5.	exp Meta-analysis as topic/
6.	(meta-analy* OR metanaly* OR metaanaly* OR meta analy*).mp.
7.	((systematic* OR evidence* OR methodol* OR quantitative*) adj5 (review* OR survey* OR overview*)).ti,ab,sh.
8.	((pool* OR combined OR combining) adj (data OR trials OR studies OR results)).ti,ab.
9.	or/3-8

4 **Embase search terms**

1.	"Review"/ OR review.pt. OR review.ti.
2.	(systematic OR evidence* OR methodol* OR quantitative*).ti,ab.
3.	1 and 2
4.	Meta-analysis/
5.	"Systematic review"/
6.	(meta-analy* OR metanaly* OR metaanaly* OR meta analy*).ti,ab.

7.	((systematic* OR evidence* OR methodol* OR quantitative*) adj3 (review* OR survey* OR overview*)).ti,ab.
8.	((pool* OR combined OR combining) adj2 (data OR trials OR studies OR results)).ti,ab.
9.	or/3-8

C.1.2 Randomised controlled studies (RCTs) search terms

2 **Medline search terms**

1.	randomized controlled trial.pt.
2.	controlled clinical trial.pt.
3.	randomi#ed.ab.
4.	placebo.ab.
5.	randomly.ab.
6.	Clinical trials as topic.sh.
7.	trial*.ti.
8.	or/1-7

3 **Embase search terms**

1.	random*.ti,ab.
2.	factorial*.ti,ab.
3.	(crossover* OR cross over* OR cross-over*).ti,ab.
4.	((doubl* OR singl*) adj blind*).ti,ab.
5.	(assign* OR allocat* OR volunteer* OR placebo*).ti,ab.
6.	Crossover procedure/
7.	Single blind procedure/
8.	Randomized controlled trial/
9.	Double blind procedure/
10.	or/1-9

C.1.3 Observational studies search terms

5 **Medline search terms**

1.	Epidemiologic studies/
2.	exp Case control studies/
3.	exp Cohort studies/
4.	case control.tw.
5.	(cohort adj (study OR studies)).tw.
6.	cohort analy*.tw.
7.	(follow up adj (study OR studies)).tw.
8.	(observational adj (study OR studies)).tw.
9.	longitudinal.tw.
10.	retrospective.tw.
11.	cross sectional.tw.
12.	Cross-sectional studies/
13.	or/1-12

6 **Embase search terms**

1.	Clinical study/

2.	Case control study/
3.	Family study/
4.	Longitudinal study/
5.	Retrospective study/
6.	Prospective study/
7.	Randomized controlled trials/
8.	6 not 7
9.	Cohort analysis/
10.	(Cohort adj (study OR studies)).mp.
11.	(Case control adj (study OR studies)).tw.
12.	(follow up adj (study OR studies)).tw.
13.	(observational adj (study OR studies)).tw.
14.	(epidemiologic* adj (study OR studies)).tw.
15.	or/1-5,8-14

C.1.4 Health economic search terms

2 **Medline search terms**

1.	exp Economics/
2.	exp "Costs and cost analysis"/
3.	(economic* OR pharmacoeconomic*).ti,ab.
4.	(cost OR costs OR costed OR costly OR costing* OR price OR prices OR pricing).ti.
5.	(expenditure OR budget*).ti,ab.
6.	cost-effective*.ti,ab.
7.	(cost adj2 (effectiv* OR reduc* OR saving*)).ti,ab.
8.	(value adj2 money).ti,ab.
9.	Quality-adjusted life years/
10.	QALY*.ti,ab.
11.	or/1-10
12.	((metabolic OR energy OR oxygen) adj2 (expenditure OR cost*)).ti,ab.
13.	11 not 12

3 **Embase search terms**

1.	exp Economic aspect/
2.	(economic* OR pharmacoeconomic*).ti,ab.
3.	(cost OR costs OR costed OR costly OR costing* OR price OR prices OR pricing).ti.
4.	(expenditure OR budget*).ti,ab.
5.	(value adj1 money).tw.
6.	cost-effective*.ti,ab.
7.	(cost adj2 (effectiv* OR reduc* OR saving*)).ti,ab.
8.	(value adj2 money).ti,ab.
9.	exp Quality adjusted life years/
10.	QALY*.ti,ab.
11.	or/1-10
12.	((metabolic OR energy OR oxygen) adj2 (expenditure OR cost*)).ti,ab.
13.	11 not 12

C.2 Standard population search strategy

2 **Medline search terms**

1.	Urinary bladder, neurogenic/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor)).ti,ab.
3.	(overactiv* adj3 bladder).ti,ab.
4.	or/1-3
5.	Urinary bladder, overactive/ OR exp Enuresis/ OR exp Urinary incontinence/ OR Urinary retention/
6.	Nocturia/
7.	(lower urinary tract symptom* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
8.	((urin* OR bladder OR voiding OR micturation) adj3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.
9.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
10.	(bladder adj (obstruct* OR control OR management)).ti,ab.
11.	(urin* adj2 (retention OR retain*)).ti,ab.
12.	resid* urine.ti,ab.
13.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
14.	or/5-13
15.	exp Nervous system diseases/
16.	exp Nervous system neoplasms/
17.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
18.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
19.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
20.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
21.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
22.	(neurolog* adj4 spinal).ti,ab.
23.	(diabet* adj3 neuropath*).ti,ab.
24.	or/15-23
25.	14 and 24
26.	4 OR 25
27.	Limit 26 to english language
28.	Letter/
29.	Editorial/
30.	exp Historical article/
31.	Anecdotes as topic/
32.	Comment/
33.	Case report/
34.	Animal/ not (Animal/ and Human/)
35.	Animals, Laboratory/
36.	exp Animal experiment/
37.	exp Animal model/
38.	exp Rodentia/

39.	or/28-38
40.	27 not 39

1 **Embase search terms**

1.	Neurogenic bladder/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor OR vesical)).ti,ab.
3.	(overactive* adj3 bladder).ti,ab.
4.	or/1-3
5.	Overactive bladder/ OR exp Enuresis/ OR exp Urine incontinence/ OR Urine retention/
6.	Nocturia/
7.	((bladder OR detrusor) adj1 overactiv*).ti,ab.
8.	((bladder OR urin*) adj1 (incontinen* OR leakage OR wetting)).ti,ab.
9.	(lower urinary tract symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
10.	((urin* OR bladder OR voiding OR micturation) adj3 (disorders* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.
11.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
12.	(bladder adj (obstruct* OR control OR management)).ti,ab.
13.	(urin* adj2 (retent* OR retain*)).ti,ab.
14.	resid* urine.ti,ab.
15.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
16.	or/5-15
17.	exp Neurologic disease/
18.	exp Nervous system neoplasms/
19.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
20.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
21.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
22.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
23.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
24.	(neurolog* adj4 spinal).ti,ab.
25.	(diabet* adj3 neuropath*).ti,ab.
26.	or/17-25
27.	16 and 26
28.	4 OR 27
29.	Limit 28 to english language
30.	letter.pt.
31.	Letter/
32.	editorial.pt.
33.	note.pt.
34.	Case report/
35.	Case study/
36.	conference abstract.pt.
37.	Animal/ not (Animal/ and Human/)

38.	Nonhuman/
39.	exp Animal studies/
40.	Animals, Laboratory/
41.	exp Experimental animal/
42.	exp Animal experiment/
43.	exp Animal model/
44.	exp Rodent/
45.	or/30-44
46.	29 not 45

1 **Cinahl search terms**

S1	(MH "Bladder, Neurogenic")
S2	neurogenic* n3 bladder OR neurogenic* n3 urin* OR neurogenic* n3 incontinen* OR neurogenic* n3 detrusor
S3	neurologic* n3 bladder OR neurologic* n3 urin* OR neurologic* n3 incontinen* OR neurologic* n3 detrusor
S4	overactiv* n1 bladder
S5	S1 OR S2 OR S3 OR S4
S6	MH overactive bladder OR mh enuresis+ OR mh urinary incontinence+ OR MH urinary retension
S7	lower urinary tract symptom* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia
S8	urin* n3 disorder* OR urin* n3 symptom* OR urin* n3 urgency OR urin* n3 incontinen* OR urin* n3 dysfunction*
S9	bladder* n3 disorder* OR bladder* n3 symptom* OR bladder* n3 urgency OR bladder* n3 incontinen* OR bladder* n3 dysfunction*
S10	voiding* n3 disorder* OR voiding* n3 symptom* OR voiding* n3 urgency OR voiding* n3 incontinen* OR voiding* n3 dysfunction*
S11	incomplet* n2 bladder empt* OR impair* n2 bladder empt*
S12	bladder n1 obstruct* OR bladder n1 control OR bladder n1 management
S13	urin* n2 retent* OR urin* n2 retain*
S14	resid* urine
S15	(weak OR underactiv OR overactive*) and (detrusor OR lower urinary tract OR bladder)
S16	(hyper-reflex* OR hypereflex* OR hyperreflex*) and (detrusor OR lower urinary tract OR bladder)
S17	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	MH Nervous system diseases+ OR MH Nervous system neoplasms+
S19	neurological n2 impairment OR neurological n2 disease* OR neurological n2 disorder*
S20	spinal cord n2 injur* OR spinal cord n2 trauma OR spinal cord n2 disease*
S21	spinal n2 shock OR spinal n2 abnormalit*
S22	multiple sclerosis OR parkinson* OR stroke OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR hydronephro* OR dyssynergi* OR myelodysplas*
S23	brain n2 injur* OR brain n2 tumor* OR brain n2 tumour*
S24	neurolog* n4 spinal
S25	diabet* OR neuropath*
S26	S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25
S27	S17 and S26

S28	S5 OR S27
S29	exclude Medline records and limit to english language

Cochrane search terms

#1	MeSH descriptor Urinary Bladder, Neurogenic explode all trees
#2	(neurogenic* OR neurologic* OR spastic OR atonic OR overactiv*) NEAR/3 (bladder OR incontinen* OR detrusor OR urin*)
#3	(#1 OR #2)
#4	MeSH descriptor Nocturia explode all trees
#5	MeSH descriptor Urinary Bladder, Overactive explode all trees
#6	MeSH descriptor Enuresis explode all trees
#7	MeSH descriptor Urinary Incontinence explode all trees
#8	MeSH descriptor Urinary Retention explode all trees
#9	("lower urinary tract symptom*" OR "urinary symptom*" OR LUTS OR "irritable bladder" OR bedwetting OR enuresis OR nocturia):ti,ab
#10	((urin* OR bladder OR voiding OR micturation) NEAR/3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)):ti,ab
#11	((incomplete* OR impair*) NEXT "bladder emptying"):ti,ab
#12	(bladder NEXT (obstruct* OR control OR management OR compliance)):ti,ab
#13	("urinary retention" OR "residual urine"):ti,ab
#14	(Urin* NEAR/2 (retention OR retain* OR resid*)):ti,ab
#15	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) NEAR (detrusor OR "lower urinary tract" OR bladder)):ti,ab
#16	(#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)
#17	MeSH descriptor Nervous System Diseases explode all trees
#18	(neurological NEAR/2 (impair* OR disease* OR disorder*)):ti,ab
#19	(spinal cord NEAR/2 (injur* OR trauma* OR disease*)):ti,ab
#20	spinal NEAR/2 (shock* OR abnormalit*):ti,ab
#21	(brain NEAR/2 (injur* OR tumor* OR tumour* OR lesion*)):ti,ab
#22	myelopathy:ti,ab
#23	(neurolog* NEAR/4 spinal):ti,ab
#24	(diabet* NEAR/3 neuropath*):ti,ab
#25	(hydronephrosis OR dyssynergi* OR myelodysplas*):ti,ab
#26	("multiple sclerosis" OR parkinson* OR stroke* OR dementia OR alzheimer* OR "cerebral palsy" OR hydrocephalus OR "spina bifida"):ti,ab
#27	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26)
#28	(#3 OR (#16 AND #27))

C.3 Searches by specific questions

C.3.1 Clinical assessment

C.3.1.1 Clinical tools

Q. Does the use of the following, direct treatment: a) clinical assessment b) urine culture c) residual urine estimate d) bladder diary/frequency volume chart?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Clinical tools		RCTs OR SRs OR observational studies [Medline and Embase only]	All years – 10/01/12

1 **Medline search terms**

1.	exp Physical examination/
2.	exp Neurologic examination/
3.	exp Medical history taking/
4.	(clinical adj assess*).ti,ab.
5.	((decision OR diagnostic) adj (rule OR rules)).ti,ab.
6.	exp Decision trees/
7.	exp Decision support techniques/
8.	exp Urinalysis/
9.	(urin* adj culture*).ti,ab.
10.	resid* urine.ti,ab.
11.	Bladder/us
12.	(ultrasound OR (non adj invasive test)).ti,ab.
13.	(frequency volume chart* OR ((bladder OR volume OR void OR urine OR urinary OR incontinence) adj (diar* OR record*))).ti,ab.
14.	or/1-13

2 **Embase search terms**

1.	exp Physical examination/
2.	exp Neurologic examination/
3.	exp Anamnesis/
4.	patient history*.ti,ab.
5.	(clinical adj assess*).ti,ab.
6.	((decision OR diagnostic) adj (rule OR rules)).ti,ab.
7.	exp "Decision tree"/
8.	exp Decision support system/
9.	exp Urinalysis/
10.	(urin* adj culture*).ti,ab.
11.	resid* urine.ti,ab.
12.	exp Echography/
13.	(ultrasound OR (non adj invasive test)).ti,ab.
14.	(frequency volume chart* OR ((bladder OR volume OR void OR urine OR urinary OR incontinence) adj (diar* OR record*))).ti,ab.
15.	or/1-14

3 **Cinahl search terms**

S1	(MH "Neurologic Examination+")
S2	(MH "Physical Examination+")
S3	(MH "Patient History Taking+")
S4	patient history
S5	clinical n1 assess*
S6	decision n1 rule* OR diagnostic n1 rule*

S7	(MH "Decision Trees")
S8	(MH "Decision Support Systems, Clinical") OR (MH "Decision Support Techniques")
S9	urinalysis OR urin* n1 culture
S10	resid* urine
S11	(MH "Ultrasonography+")
S12	ultrasound OR non n1 invasive test
S13	frequency volume chart* OR bladder n1 diar* OR bladder n1 record* OR volume n1 diar* OR volume n1 record* OR void n1 diar* OR void n1 record* OR urine n1 record* OR urine n1 diar* OR urinary n1 record* OR urinary n1 diar*
S14	incontinence n1 diar* OR incontinence n1 record*
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14

Cochrane search terms

#1	MeSH descriptor Medical History Taking explode all trees
#2	MeSH descriptor Physical Examination explode all trees
#3	MeSH descriptor Neurologic Examination explode all trees
#4	patient and history:ti,ab
#5	(decision OR diagnostic) NEAR (rule OR rules):ti,ab
#6	clinical NEAR assess*:ti,ab
#7	MeSH descriptor Decision Support Techniques explode all trees
#8	decision tree*:ti,ab
#9	MeSH descriptor Urinalysis explode all trees
#10	urin* NEAR culture:ti,ab
#11	resid* urine:ti,ab
#12	MeSH descriptor Ultrasonography, Interventional explode all trees
#13	(ultrasound OR (non NEAR invasive test)):ti,ab
#14	(Frequency volume chart* OR ((bladder OR volume OR void OR urine OR urinary OR incontinence) NEAR (diar* OR record*))):ti,ab
#15	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14

C.3.122 Urodynamics

Q. Does use of the following direct treatment or stratify risk a) filling cystometry b) leak point pressure measurements c) pressure-flow studies of voiding d) video urodynamics?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Urodynamic techniques		RCTs OR SRs OR observational studies [Medline and Embase only]	All years – 10/01/12

Medline search terms

1.	exp Urodynamics/
2.	urodynamic*.ti,ab.
3.	(cystomet* OR videocysto* OR urethrocysto* OR cystoureth*).ti,ab.
4.	(videourodynamic* OR video urodynamic* OR video-urodynamic*).ti,ab.
5.	VCUG.ti,ab.
6.	(urinary flow rate* OR pressure flow stud* OR post void residual measurement*).ti,ab.
7.	(uroflowmet* OR profilemet*).ti,ab.

8.	leak point pressure*.ti,ab.
9.	or/1-8

Embase search terms

1.	exp Urodynamics/
2.	exp Cystometry/
3.	exp Urethrocystometry/
4.	exp Cystourethography/
5.	exp Uroflowmetry/
6.	(cystom* OR cystot* OR cmg OR urethrocysto* OR cystourethro*).ti,ab.
7.	(urodynamic* OR urine voiding dynamic*).ti,ab.
8.	(videocysto* OR videourodynamic* OR video urodynamic* OR video-urodynamic*).ti,ab.
9.	VCUG.ti,ab.
10.	((video* OR void*) adj3 cystoureth*).ti,ab.
11.	((urinary flow adj (rate* OR measurement*)) OR pressure flow stud* OR post void residual measurement*).ti,ab.
12.	(uroflowmet* OR profilemet* OR urine flowmet* OR urorheography).ti,ab.
13.	leak point pressure*.ti,ab.
14.	or/1-13

Cinahl search terms

S1	(MM "Urodynamics")
S2	urodynamic* OR cystomet* OR videocysto* OR urethrocysto* OR cystoureth*
S3	videourodynamic* OR video urodynamic* OR video-urodynamic* OR vcug*
S4	urinary flow rate* OR pressure flow stud* OR post void residual measurement*
S5	uroflowmet* OR profilemet*
S6	leak point pressure*
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6

Cochrane search terms

#1	MeSH descriptor Urodynamics explode all trees
#2	(urodynamic* OR cystomet* OR videocysto* OR urethrocysto* OR cystoureth*):ti,ab
#3	(videourodynamic* OR video urodynamic* OR video-urodynamic* OR vcug*):ti,ab
#4	(urinary flow rate* OR pressure flow stud* OR post void residual measurement*):ti,ab
#5	(uroflowmet* OR profilemet*):ti,ab
#6	leak point pressure*:ti,ab.
#7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)

C.3.2 Treatment – improving bladder storage

C.3.2.1 Behavioural management programmes

Q. Do behavioural management programmes compared with a) each other b) usual care, improve outcomes?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND	Behavioural management programmes		None	All years – 10/01/12

Population	Intervention	Comparison	Study filter used	Date parameters
incontinence				

1 **Medline search terms**

1.	exp Behavior therapy/
2.	exp "Conditioning (Psychology)"/
3.	Feedback, Psychological/
4.	Toilet training/
5.	urotherap*.ti,ab.
6.	(bladder adj3 (train* OR retrain*)).ti,ab.
7.	((prompt* OR timed OR program* OR request* OR schedul*) adj3 void*).ti,ab.
8.	(habit* adj2 (train* OR retrain*)).ti,ab.
9.	((behavio* OR cognitive) adj3 (train* OR management OR intervention* OR modif* OR program* OR therap*)).ti,ab.
10.	(cognitive adj behavio*).ti,ab.
11.	biofeedback.ti,ab.
12.	(toileting adj3 (assist* OR plan* OR schedule* OR program* OR train*)).ti,ab.
13.	(conservative adj (management OR treatment* OR intervention*)).ti,ab.
14.	or/1-13

2 **Embase search terms**

1.	Behavior therapy/
2.	Cognitive therapy/
3.	Adaptive behavior/
4.	Behavior modification/
5.	Behavior change/
6.	Behavior control/
7.	Behavioral medicine/
8.	Conditioning/
9.	Conditioned reflex/
10.	urotherap*.ti,ab.
11.	(bladder adj3 (train* OR retrain*)).ti,ab.
12.	((prompt* OR timed OR program* OR request* OR schedul*) adj3 voiding).ti,ab.
13.	(habit adj2 (train* OR retrain*)).ti,ab.
14.	((behavio* OR cognitive) adj3 (train* OR management OR intervention* OR modif* OR program* OR therap*)).ti,ab.
15.	(cognitive adj behavio*).ti,ab.
16.	biofeedback.ti,ab.
17.	(toileting adj3 (assist* OR plan* OR schedule* OR program* OR train*)).ti,ab.
18.	(conservative adj (management OR treatment* OR intervention*)).ti,ab.
19.	or/1-18

3 **Cinahl search terms**

S1	(MH "Behavior Therapy+")
S2	(MH "Conditioning (Psychology)")
S3	(MH "Biofeedback")
S4	(MH "Toileting")

S5	urotherap*
S6	bladder AND (train* OR retrain*)
S7	(prompt* OR timed OR request*) AND voiding
S8	habit train* OR habit retrain*
S9	behavio* train* OR behavio* management OR behavio* modif* OR behavio* therap* OR behavio* intervention*
S10	cognitive behavio* OR cognitive modif* OR cognitive therap*
S11	biofeedback
S12	toileting AND (assist* OR plan* OR schedule* OR program* OR train*)
S13	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12

1 **Cochrane search terms**

#1	MeSH descriptor Behavior Therapy explode all trees
#2	MeSH descriptor Conditioning (Psychology) explode all trees
#3	MeSH descriptor Feedback, Psychological, this term only
#4	MeSH descriptor Toilet Training, this term only
#5	urotherap*:ti,ab
#6	(bladder NEAR/3 (train* OR retrain*)):ti,ab
#7	((prompt* OR timed OR program* OR request* OR schedul*) NEAR/3 voiding):ti,ab
#8	(habit NEAR/2 (train* OR retrain*)):ti,ab
#9	((behavio* OR cognitive) NEAR/3 (train* OR management OR intervention* OR modif* OR program* OR therap*)):ti,ab
#10	(cognitive NEXT behavio*):ti,ab
#11	biofeedback:ti,ab
#12	(toileting NEAR/3 (assist* OR plan* OR schedule* OR program* OR train*)):ti,ab
#13	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)

C.3.222 Antimuscarinics

3 **Q. What is the safety and efficacy of antimuscarinics compared with a) placebo or treatment**
4 **as usual or b) other antimuscarinics?**

5 Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Antimuscarinics		RCTs OR SRs [Medline and Embase only]	All years – 10/01/12

6 **Medline search terms**

1.	Muscarinic antagonists/ OR Cholinergic antagonists/
2.	(darifenacin OR duloxetine OR flavoxate hydrochloride OR oxybutynin hydrochloride OR propantheline bromide OR propiverine hydrochloride OR solifenacin succinate OR tolterodine tartrate OR tropsium chloride OR fesoterodine fumarate).ti,ab.
3.	(emselex OR yentreve OR cymbalta OR toviaz OR urispas 200 OR oxybutynin hydrochloride OR cystrin OR ditropan OR lyrinal OR kentera OR vesicare OR ((detrunorm OR detrusitol OR regurin) adj XL)).ti,ab.
4.	or/1-3

7 **Embase search terms**

1.	exp Darifenacin/ OR exp Duloxetine/ OR Flavoxate/ OR Oxybutynin/ OR exp Propantheline Bromide/ OR exp Propiverine/ OR exp Solifenacin/ OR exp Tolerodine/ OR exp Fesoterodine/

2.	(emselex OR yentreve OR cymbalta OR toviaz OR urispas 200 OR oxybutynin hydrochloride OR cystrin OR ditropan OR lyrinal OR kentera OR vesicare OR ((detrunorm OR detrusitol OR regurin) adj XL)).ti,ab.
3.	antimuscarinics.ti,ab.
4.	or/1-3

Cinahl search terms

S1	(MH "Muscarinic Antagonists+")
S2	(MH "Cholinergic Antagonists+")
S3	darifenacin OR duloxetine OR flavoxate hydrochloride OR oxybutynin hydrochloride OR propantheline bromide OR propiverine hydrochloride OR solifenacin succinate OR tolterodine tartrate OR tropsium chloride OR fesoterodine fumarate
S4	emselex OR yentreve OR cymbalta OR toviaz OR urispas 200 OR oxybutynin hydrochloride OR cystrin OR ditropan OR lyrinal OR kentera OR vesicare
S5	detrunorm OR detrusitol OR regurin
S6	S1 OR S2 OR S3 OR S4 OR S5

Cochrane search terms

#1	MeSH descriptor Muscarinic Agonists explode all trees
#2	MeSH descriptor Cholinergic Antagonists explode all trees
#3	(darifenacin OR duloxetine OR flavoxate hydrochloride OR oxybutynin hydrochloride OR propantheline bromide OR propiverine hydrochloride OR solifenacin succinate OR tolterodine tartrate OR tropsium chloride OR fesoterodine fumarate):ti,ab
#4	(emselex OR yentreve OR cymbalta OR toviaz OR urispas 200 OR oxybutynin hydrochloride OR cystrin OR ditropan OR lyrinal OR kentera OR vesicare OR ((detrunorm OR detrusitol OR regurin) adj XL)):ti,ab
#5	(#1 OR #2 OR #3 OR #4)

C.3.233 Botulinum toxin

Q. What is the safety and efficacy of intravesical botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in neurological disease?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Botulinum toxin		RCTs OR SRs OR observational studies [Medline and Embase only]	All years – 10/01/12

Medline search terms

1.	exp Botulinum toxins/
2.	(botulinum* or onabotulinum* or rimabotulinum* or abobotulinum*).ti,ab.
3.	(dysport OR botox OR btx OR oculinum OR xeomin OR reloxin OR prosigne OR purtox OR nt201 OR mybloc OR neurobloc).ti,ab.
4.	or/1-3

Embase search terms

1.	exp Botulinum toxin/
2.	exp Botulinum toxin A/
3.	exp Botulinum toxin B/
4.	(botulinum* or onabotulinum* or rimabotulinum* or abobotulinum*).ti,ab.

5.	(dysport OR botox OR btx OR oculinum OR xeomin OR reloxin OR prosigne OR purtox OR nt201 OR mybloc OR neurobloc).ti,ab.
6.	or/1-5

Cinahl search terms

S1	(MH "botulinum toxins")
S2	(botulinum* OR onabotulinum* OR rimabotulinum* OR abobotulinum* OR dysport OR btx OR oculinum OR xeomin OR reloxin OR prosigne OR purtox OR nt201 OR mybloc OR neurobloc)
S3	S1 OR S2

Cochrane search terms

#1	MeSH descriptor Botulinum Toxins explode all trees
#2	(botulinum* or onabotulinum* or rimabotulinum* or abobotulinum*):ti,ab
#3	(dysport OR botox OR btx OR oculinum OR xeomin OR reloxin OR prosigne OR purtox OR nt201 OR mybloc OR neurobloc):ti,ab
#4	(#1 OR #2 OR #3)

C.3.234 Augmentation cystoplasty

Q. What is the safety and efficacy of augmentation cystoplasty compared with usual care in neurological disease?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Augmentation cystoplasty		None	All years – 10/01/12

Medline search terms

1.	(cystoplast* OR ileocecocystoplast* OR ileocystoplast* OR intestinocystoplast* OR enterocystoplast* OR gastrocystoplast* OR colocystoplast* OR ureterocystoplast* OR sigmoidocystoplast*).ti,ab.
2.	(bladder adj4 augment*).ti,ab.
3.	1 OR 2

Embase search terms

1.	(cystoplast* OR ileocecocystoplast* OR ileocystoplast* OR intestinocystoplast* OR enterocystoplast* OR gastrocystoplast* OR colocystoplast* OR ureterocystoplast* OR sigmoidocystoplast*).ti,ab.
2.	(bladder adj4 augment*).ti,ab.
3.	1 OR 2

Cinahl search terms*

S1	(cystoplast* OR ileocecocystoplast* OR ileocystoplast* OR intestinocystoplast* OR enterocystoplast* OR gastrocystoplast* OR colocystoplast* OR ureterocystoplast* OR sigmoidocystoplast*)
S2	bladder n4 augment*
S3	S1 OR S2

*Only intervention terms used for this search (i.e. no population) due to very small retrieval set.

Cochrane search terms

#1	(cystoplast* OR ileocecocystoplast* OR ileocystoplast* OR intestinocystoplast* OR enterocystoplast* OR gastrocystoplast* OR colocystoplast* OR ureterocystoplast* OR

	sigmoidocystoplast*):ti,ab
#2	(bladder NEAR/4 augment*):ti,ab
#3	(#1 OR #2)

C.3.3 Treatment – stress incontinence

C.3.3.1 Pelvic floor muscle training

Q. Does pelvic floor muscle training, with or without electrical stimulation or biofeedback, compared with treatment as usual, improve outcomes?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Pelvic floor muscle training		RCTs OR SRs OR observational studies [Medline and Embase only]	All years – 10/01/12

Medline search terms

1.	Pelvic floor/
2.	Exercise therapy/
3.	Biofeedback, Psychology/
4.	Muscle contraction/ph [Physiology]
5.	((pelvi* floor OR pelvi* muscle*) adj4 (train* OR retrain* OR exercis* OR rehabilit* OR strength OR stimulat* OR function OR endurance OR physical therapy OR physiotherap* OR biofeedback OR educat* OR reeducat*)).ti,ab.
6.	(palpation adj3 (digital OR vagina* OR intravaginal OR tactile)).ti,ab.
7.	PFM*.ti,ab.
8.	or/1-7

Embase search terms

1.	Pelvis floor/
2.	Kinesiotherapy/ OR Muscle training/
3.	Muscle contraction/
4.	((pelvic floor OR pelvic muscle*) adj4 (train* OR retrain* OR exercis* OR rehabilit* OR strength OR stimulat* OR function OR endurance OR physical therapy OR physiotherap* OR biofeedback OR reeducat* OR educat*)).ti,ab.
5.	(palpation adj3 (digital OR vagina* OR intravaginal OR tactile)).ti,ab.
6.	PFM*.ti,ab.
7.	or/1-6

Cinahl search terms

S1	(MH "Pelvic Floor Muscles")
S2	(MH "Muscle Strengthening+")
S3	(MH "Muscle Contraction+/PH")
S4	pelvi* floor AND (train* OR retrain* OR exercis* OR rehabilit* OR strength OR stimulat* OR function OR endurance OR physical therapy OR physiotherap* OR biofeedback OR reeducat* OR educat*)
S5	PFM*
S6	palpation AND (digital OR vagina* OR intravaginal OR tactile)
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6

1 Cochrane search terms

#1	MeSH descriptor Pelvic Floor, this term only
#2	MeSH descriptor Exercise Therapy, this term only
#3	MeSH descriptor Biofeedback, Psychology, this term only
#4	MeSH descriptor Muscle Contraction, this term only
#5	((pelvi* floor OR pelvi* muscle*) NEAR/4 (train* OR retrain* OR exercis* OR rehabilit* OR strength OR stimulat* OR function OR endurance OR physical therapy OR physiotherap* OR biofeedback OR reeducat* OR educat*)):ti,ab
#6	(palpation NEAR/3 (digital OR vagina* OR intravaginal OR tactile)):ti,ab
#7	PFM*:ti,ab
#8	(#1 OR #2OR #3 OR #4 OR #5 OR #6 OR #7)

C.3.322 Urethral tape and sling surgery

3 Q. What is the safety and efficacy of urethral tape and sling surgery compared with usual care 4 in neurological disease?

5 Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Urethral tape and sling surgery		None	All years – 10/01/12

6 Medline search terms

1.	Suburethral slings/
2.	exp Polytetrafluoroethylene/tu
3.	((tension* OR vagina* OR pubovagina* OR intravagina* OR transvagina* OR suburethra* OR urethra* OR midurethra* OR retropubic* OR transobturat* OR obturat* OR TOT OR rectus OR fascia*) adj5 (tape* OR sling* OR mesh*)).ti,ab.
4.	(sling adj2 (procedure* OR system* OR placement*)).ti,ab.
5.	TVT*.ti,ab.
6.	colposuspension*.ti,ab.
7.	Rectus abdominis/tr
8.	Urologic surgical procedures/mt
9.	bladder neck.ti,ab.
10.	8 and 9
11.	or/1-7, 10

7 Embase search terms

1.	exp Suburethral slings/
2.	Pubovaginal sling/
3.	Politef/
4.	((tension* OR vagina* OR pubovagina* OR intravagina* OR transvagina* OR suburethra* OR urethra* OR midurethra* OR retropubic* OR transobturat* OR obturat* OR TOT OR rectus OR fascia*) adj5 (tape* OR sling* OR mesh*)).ti,ab.
5.	(sling adj2 (procedure* OR system* OR placement*)).ti,ab.
6.	TVT*.ti,ab.
7.	colposuspension*.ti,ab.
8.	Bladder surgery/
9.	Urethra surgery/

10.	or/1-9

1 **Cinahl search terms**

S1	(MH "Suburethral Slings")
S2	(MH "Polytetrafluoroethylene/TU")
S3	(tension* OR vagina* or pubovagina* OR intravagina* OR transvagina* OR suburethra* OR urethra* OR midurethra* OR retropubic* OR transobturat* OR obturat* OR TOT OR rectus OR fascia*) AND (tape* OR sling* OR mesh*)
S4	(sling n2 procedure*) OR (sling n2 system*) OR (sling n2 placement*)
S5	TVT* OR colposuspension*
S6	bladder neck
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6

2 **Cochrane search terms**

#1	MeSH descriptor Suburethral Slings, this term only
#2	MeSH descriptor Polytetrafluoroethylene explode all trees with qualifier: TU
#3	((tension* OR vagina* OR pubovagina* OR intravagina* OR transvagina* OR suburethra* OR urethra* OR midurethra* OR retropubic* OR transobturat* OR obturat* OR TOT OR rectus OR fascia*) NEAR/5 (tape* OR sling* OR mesh*)):ti,ab
#4	(sling NEAR/2 (procedure* OR system* OR placement*)):ti,ab
#5	TVT*:ti,ab
#6	colposuspension*:ti,ab
#7	MeSH descriptor Rectus Abdominis, this term only with qualifier: TR
#8	MeSH descriptor Urologic Surgical Procedures, this term only with qualifier: MT
#9	“bladder neck”:ti,ab
#10	(#8 AND #9)
#11	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #10)

C.3.333 Artificial urinary sphincter

4 **Q. What is the safety and efficacy of artificial urinary sphincter compared with usual care in**
5 **neurological disease?**

6 Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Artificial urinary sphincter		None	All years – 10/01/12

7 **Medline search terms**

1.	Urinary sphincter, artificial/
2.	((artificial* OR prosthe*) and sphincter*).ti,ab.
3.	(bladder and cuff).ti,ab.
4.	or/1-3

8 **Embase search terms**

1.	Bladder sphincter prosthesis/
2.	((artificial* OR prosthe*) and sphincter*).ti,ab.
3.	(bladder and cuff).ti,ab.
4.	or/1-3

Cinahl search terms

S1	(MH "Urinary Sphincter, Artificial")
S2	(artificial* OR prosthe*) and sphincter*
S3	bladder and cuff
S4	S1 OR S2 OR S3

Cochrane search terms

#1	MeSH descriptor Urinary Sphincter, Artificial, this term only
#2	((artificial* OR prosthe*) and sphincter*):ti,ab
#3	(bladder and cuff):ti,ab
#4	(#1 OR #2 OR #3)

C.3.4 Treatment – improving bladder emptying

C.3.4.1 Alpha andrenergic antagonists

Q. What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care in neurological disease?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Alpha antagonists		RCTs OR SRs OR observational studies [Medline and Embase only]	All years – 10/01/12

Medline search terms

1.	exp Adrenergic alpha-antagonists/
2.	((adrenergic OR adrenoceptor OR adrenolytic OR antiadrenergic) adj2 alpha adj2 (block* OR receptor* OR antagonist*)).ti,ab.
3.	(alfuzosin OR alfuzosin hydrochloride OR doxazosin OR indoramin OR prazosin OR tamsulosin OR tamsulosin hydrochloride OR terazosin OR silodosin).ti,ab.
4.	(xatral OR besavar OR vasran OR cardura* OR doralese OR baratol OR minipress OR vasoflex OR pressin OR hypovase OR flomax* OR urimax OR combodart OR hytrin).ti,ab.
5.	(dibenzylchlorethamine OR dihydroergotoxine OR ergoloid mesylates idazoxan OR labetalol OR mianserin OR moxisylyte OR nicergoline OR phenxybenzamine OR phentolamine OR piperoxan OR quinidine OR tolazoline OR yohimbine).ti,ab.
6.	or/1-5

Embase search terms

1.	exp Alpha adrenergic receptor blocking agent/
2.	((adrenergic OR adrenoceptor OR adrenolytic OR antiadrenergic) adj2 alpha adj2 (block* OR receptor* OR antagonist*)).ti,ab.
3.	(alfuzosin OR alfuzosin hydrochloride OR doxazosin OR indoramin OR prazosin OR tamsulosin OR tamsulosin hydrochloride OR terazosin OR silodosin).ti,ab.
4.	(xatral OR besavar OR vasran OR cardura* OR doralese OR baratol OR minipress OR vasoflex OR pressin OR hypovase OR flomax* OR urimax OR combodart OR hytrin).ti,ab.
5.	(dibenzylchlorethamine OR dihydroergotoxine OR ergoloid mesylates idazoxan OR labetalol OR mianserin OR moxisylyte OR nicergoline OR phenxybenzamine OR phentolamine OR piperoxan OR quinidine OR tolazoline OR yohimbine).ti,ab.
6.	or/1-5

Cinahl search terms

S1	(MH "Adrenergic Alpha-Antagonists+")
S2	alfuzosin OR alfuzosin hydrochloride OR doxazosin OR indoramin OR prazosin OR tamsulosin OR tamsulosin hydrochloride OR terazosin OR silodosin
S3	xatral OR besavar OR vasran OR cardura* OR doralese OR baratol OR minipress OR vasoflex OR pressin OR hypovase OR flomax* OR urimax OR combodart OR hytrin
S4	dibenzylchlorethamine OR dihydroergotoxine OR ergoloid mesylates idazoxan OR labetalol OR mianserin OR moxisylyte OR nicergoline OR phenxybenzamine OR phentolamine OR piperoxan OR quinidine OR tolazoline OR yohimbine
S5	adrenergic OR adrenoceptor OR adrenolytic OR antiadrenergic
S6	S1 OR S2 OR S3 OR S4 OR S5

Cochrane search terms

#1	MeSH descriptor Adrenergic alpha-Antagonists explode all trees
#2	((adrenergic OR adrenoceptor OR adrenolytic OR antiadrenergic) NEAR/2 alpha NEAR/2 (block* OR receptor* OR antagonist*)):ti,ab
#3	(alfuzosin OR alfuzosin hydrochloride OR doxazosin OR indoramin OR prazosin OR tamsulosin OR tamsulosin hydrochloride OR terazosin OR silodosin):ti,ab
#4	(xatral OR besavar OR vasran OR cardura* OR doralese OR baratol OR minipress OR vasoflex OR pressin OR hypovase OR flomax* OR urimax OR combodart OR hytrin):ti,ab
#5	(dibenzylchlorethamine OR dihydroergotoxine OR ergoloid mesylates idazoxan OR labetalol OR mianserin OR moxisylyte OR nicergoline OR phenxybenzamine OR phentolamine OR piperoxan OR quinidine OR tolazoline OR yohimbine):ti,ab
#6	(#1 OR #2 OR #3 OR #4 OR #5)

C.3.5 Treatment – reducing urinary tract infections

C.3.5.1 Antibiotic prophylaxis

Q. Do prophylactic antibiotics compared with a) no treatment b) other antibiotic reduce the risk of symptomatic urinary tract infections?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological AND (incontinence OR UTI)*	Prophylactic antibiotics		RCTs OR SRs [Medline and Embase only]	All years – 10/01/12

*Population differs from standard population search strategy outlined in Section C.2, with additional terms included for urinary tract infection. As a consequence both population and intervention terms have been included below for each database.

Medline search terms

1.	Urinary bladder, neurogenic/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor)).ti,ab.
3.	(overactiv* adj3 bladder).ti,ab.
4.	or/1-3
5.	Urinary bladder, overactive/ OR exp Enuresis/ OR exp Urinary incontinence/ OR Urinary retention/
6.	Nocturia/
7.	(lower urinary tract symptom* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
8.	((urin* OR bladder OR voiding OR micturation) adj3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.

9.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
10.	(bladder adj (obstruct* OR control OR management)).ti,ab.
11.	(urin* adj2 (retention OR retain*)).ti,ab.
12.	resid* urine.ti,ab.
13.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
14.	Urinary tract infections/
15.	Bacteriuria/
16.	Pyuria/
17.	Pyelonephritis/
18.	exp Cystitis/
19.	Urethritis/
20.	Prostatitis/
21.	(urinary tract infection* OR UTI* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*).ti,ab.
22.	or/5-21
23.	exp Nervous system diseases/
24.	exp Nervous system neoplasms/
25.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
26.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
27.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
28.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
29.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
30.	(neurolog* adj4 spinal).ti,ab.
31.	(diabet* adj3 neuropath*).ti,ab.
32.	or/23-31
33.	22 and 32
34.	4 OR 33
35.	limit 34 to english language
36.	Letter/
37.	Editorial/
38.	exp Historical article/
39.	Anecdotes as Topic/
40.	Comment/
41.	Case report/
42.	Animal/ not (animal/ and human/)
43.	Animals, Laboratory/
44.	exp Animal experiment/
45.	exp Animal model/
46.	exp Rodentia/
47.	or/36-46
48.	35 not 47
49.	Antibiotic prophylaxis/
50.	Anti-infective agents, urinary/

51.	((antibiotic* OR antimicrobial* OR anti-infective*) and (prevent* OR prophyla*)).ti,ab.
52.	exp Amdinocillin/
53.	exp Amoxicillin/
54.	exp Cephalosporins/
55.	exp Quinolones/
56.	Amoxicillin-potassium clavulanate combination/
57.	Carfecillin/
58.	Cycloserine/
59.	Carbapenems/
60.	exp Nitrofurans/
61.	exp Gentamicins/
62.	exp Mandelic acids/
63.	Methenamine/
64.	Pipemidic acid/
65.	Piromidic acid/
66.	exp Sulfonamides/
67.	exp Trimethoprim/
68.	(amdinocillin OR amifloxacin OR amoxicillin OR amoxiclav OR cinoxacin OR cephalosporin* OR cefalexin OR enoxacin OR levofloxacin OR nifurtoinol OR lomefloxacin OR cefotaxime OR cefuroxime OR difloxacin OR quinolone* OR flouroquinolone* OR ciproflax* OR cotrimoxazole OR carfecillin OR cycloserine OR carbapenem* OR doripenem* OR nitrofurans OR furaltadone OR flumequine OR fleroxacin OR furagin OR fosfomycin* OR furazolidone OR isepamicin OR nitrofurantoin OR gentamicin* OR mandelic acid* OR nitroxoline OR methenamine* OR nalidixic acid* OR norfloxacin OR ofloxacin OR oxolinic acid OR pipemidic acid OR pefloxacin OR piromidic acid OR pivmecillinam OR sulphanilamide* OR sulfacetamide OR sulfachlorpyridazine OR sulfadoxin OR sulfalene OR sulfamet* OR sul?onamide* OR trimethoprim* OR TMP-SMX).ti,ab.
69.	or/49-68
70.	48 and 69

1 **Embase search terms**

1.	Neurogenic bladder/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor OR vesical)).ti,ab.
3.	(overactive* adj3 bladder).ti,ab.
4.	or/1-3
5.	Overactive bladder/ OR exp Enuresis/ OR exp Urine incontinence/ OR Urine retention/
6.	Nocturia/
7.	((bladder OR detrusor) adj1 overactiv*).ti,ab.
8.	((bladder OR urin*) adj1 (incontinen* OR leakage OR wetting)).ti,ab.
9.	(lower urinary tract symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
10.	((urin* OR bladder OR voiding OR micturation) adj3 (disorders* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.
11.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
12.	(bladder adj (obstruct* OR control OR management)).ti,ab.
13.	(urin* adj2 (retent* OR retain*)).ti,ab.
14.	resid* urine.ti,ab.

15.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
16.	exp Urinary tract infection/
17.	exp Urogenital tract inflammation/
18.	exp Urinary tract inflammation/
19.	Bacteriuria/
20.	Asymptomatic bacteriuria/
21.	Pyuria/
22.	exp Prostatitis/
23.	(urinary tract infection* OR UTI* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*).ti,ab.
24.	or/5-23
25.	exp Neurologic disease/
26.	exp Nervous system neoplasms/
27.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
28.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
29.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
30.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
31.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
32.	(neurolog* adj4 spinal).ti,ab.
33.	(diabet* adj3 neuropath*).ti,ab.
34.	or/25-33
35.	24 and 34
36.	4 OR 35
37.	limit 28 to english language
38.	letter.pt.
39.	Letter/
40.	editorial.pt.
41.	note.pt.
42.	Case report/
43.	Case study/
44.	conference abstract.pt.
45.	Animal/ not (Animal/ and Human/)
46.	Nonhuman/
47.	exp Animal studies/
48.	Animals, Laboratory/
49.	exp Experimental animal/
50.	exp Animal experiment/
51.	exp Animal model/
52.	exp Rodent/
53.	or/38-52
54.	37 not 53
55.	Antibiotic prophylaxis/
56.	exp Urinary tract antiinfective agent/

57.	((antibiotic* OR antimicrobial* OR anti-infective*) and (prevent* OR prophyla*)).ti,ab.
58.	Mecillinam/
59.	Amoxicillin/
60.	exp Cephalosporin derivative/
61.	exp Quinolone derivative/
62.	exp Quinoline derived antiinfective agent/
63.	Carfecillin/
64.	Cycloserine/
65.	Carbapenem/
66.	exp Carbapenem derivative/
67.	exp Nitrofuran derivative/
68.	Gentamicin/
69.	Mandelic acid derivative/
70.	exp Sulfonamide/
71.	Trimethoprim/
72.	Trimethoprim derivative/
73.	(amdinocillin OR amifloxacin OR amoxicillin OR amoxiclav OR cinoxacin OR cephalosporin* OR cefalexin OR enoxacin OR levofloxacin OR nifurtoinol OR lomefloxacin OR cefotaxime OR cefuroxime OR difloxacin OR quinolone* OR flouroquinolone* OR ciproflax* OR cotrimoxazole OR carfecillin OR cycloserine OR carbapenem* OR doripenem* OR nitrofurans OR furaltadone OR flumequine OR fleroxacin OR furagin OR fosfomycin* OR furazolidone OR isepamicin OR nitrofurantoin OR gentamicin* OR mandelic acid* OR nitroxoline OR methenamine* OR nalidixic acid* OR norfloxacin OR ofloxacin OR oxolinic acid OR pipemidic acid OR pefloxacin OR piromidic acid OR pivmecillinam OR sulphanilamide* OR sulfacetamide OR sulfachlorpyridazine OR sulfadoxin OR sulfalene OR sulfamet* OR sul?onamide* OR trimethoprim* OR TMP-SMX).ti,ab.
74.	or/55-73
75.	54 and 74

1 **Cinahl search terms**

S1	(MH "Bladder, Neurogenic")
S2	neurogenic* n3 bladder OR neurogenic* n3 urin* OR neurogenic* n3 incontinen* OR neurogenic* n3 detrusor
S3	neurologic* n3 bladder OR neurologic* n3 urin* OR neurologic* n3 incontinen* OR neurologic* n3 detrusor
S4	overactiv* n1 bladder
S5	S1 OR S2 OR S3 OR S4
S6	MH overactive bladder OR mh enuresis+ OR mh urinary incontinence+ OR MH urinary retension
S7	lower urinary tract symptom* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia
S8	urin* n3 disorder* OR urin* n3 symptom* OR urin* n3 urgency OR urin* n3 incontinen* OR urin* n3 dysfunction*
S9	bladder* n3 disorder* OR bladder* n3 symptom* OR bladder* n3 urgency OR bladder* n3 incontinen* OR bladder* n3 dysfunction*
S10	voiding* n3 disorder* OR voiding* n3 symptom* OR voiding* n3 urgency OR voiding* n3 incontinen* OR voiding* n3 dysfunction*
S11	incomplet* n2 bladder empt* OR impair* n2 bladder empt*
S12	bladder n1 obstruct* OR bladder n1 control OR bladder n1 management

S13	urin* n2 retent* OR urin* n2 retain*
S14	resid* urine
S15	(weak OR underactiv OR overactive*) and (detrusor OR lower urinary tract OR bladder)
S16	(hyper-reflex* OR hypereflex* OR hyperreflex*) and (detrusor OR lower urinary tract OR bladder)
S17	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	MH nervous system diseases+ OR MH nervous system neoplasms+
S19	neurological n2 impairment OR neurological n2 disease* OR neurological n2 disorder*
S20	spinal cord n2 injur* OR spinal cord n2 trauma OR spinal cord n2 disease*
S21	spinal n2 shock OR spinal n2 abnormalit*
S22	multiple sclerosis OR parkinson* OR stroke OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR hydronephro* OR dyssynergi* OR myelodysplas*
S23	brain n2 injur* OR brain n2 tumor* OR brain n2 tumour*
S24	neurolog* n4 spinal
S25	diabet* OR neuropath*
S26	S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25
S27	(MH "Urinary Tract Infections+")
S28	(MH "Pyelonephritis")
S29	(MH "Cystitis+")
S30	(MH "Urethritis")
S31	(MH "Prostatitis")
S32	urinary tract infection* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*
S33	S27 OR S28 OR S29 OR S30 OR S31 OR S32
S34	(S17 OR S33) and S26
S35	S5 OR S34
S36	(MH "Antibiotic Prophylaxis")
S37	(antibiotic* OR antimicrobial* OR anti-infective*) and (prevent* OR prophyla*)
S38	(MH "Antiinfective Agents, Urinary+")
S39	amdinocillin OR amifloxacin OR amoxicillin OR amoxiclav OR cinoxacin OR cephalosporin* OR cefalexin OR enoxacin OR levofloxacin OR nifurtoinol OR lomefloxacin OR cefotaxime OR cefuroxime OR difloxacin OR quinolone* OR flouroquinolone* OR ciproflax* OR cotrimoxazole OR carfecillin OR cycloserine OR carbapenem* OR doripenem* OR nitrofurans OR furaltadone OR flumequine OR fleroxacin OR furagin OR fosfomycin* OR furazolidone OR isepamicin OR nitrofurantoin OR gentamicin* OR mandelic acid* OR nitroxoline OR methenamine* OR nalidixic acid* OR norfloxacin OR ofloxacin OR oxolinic acid OR pipemidic acid OR pefloxacin OR piromidic acid OR pivmecillinam OR sulphanilamide* OR sulfacetamide OR sulfachlorpyridazine OR sulfadoxin OR sulfalene OR sulfamet* OR sul?onamide* OR trimethoprim* OR TMP-SMX
S40	S36 OR S37 OR S38 OR S39
S41	S35 and S40
S42	English Language; Exclude MEDLINE
S43	S41 and S42

1 **Cochrane search terms**

#1	MeSH descriptor Urinary Bladder, Neurogenic explode all trees
#2	(neurogenic* OR neurologic* OR spastic OR atonic OR overactiv*) NEAR/3 (bladder OR incontinen* OR detrusor OR urin*)

#3	(#1 OR #2)
#4	MeSH descriptor Nocturia explode all trees
#5	MeSH descriptor Urinary Bladder, Overactive explode all trees
#6	MeSH descriptor Enuresis explode all trees
#7	MeSH descriptor Urinary Incontinence explode all trees
#8	MeSH descriptor Urinary Retention explode all trees
#9	("lower urinary tract symptom*" OR "urinary symptom*" OR LUTS OR "irritable bladder" OR bedwetting OR enuresis OR nocturia):ti,ab
#10	((urin* OR bladder OR voiding OR micturation) NEAR/3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)):ti,ab
#11	((incomplete* OR impair*) NEXT "bladder emptying"):ti,ab
#12	(bladder NEXT (obstruct* OR control OR management OR compliance)):ti,ab
#13	("urinary retention" OR "residual urine"):ti,ab
#14	(urin* NEAR/2 (retention OR retain* OR resid*)):ti,ab
#15	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) NEAR (detrusor OR "lower urinary tract" OR bladder)):ti,ab
#16	(#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)
#17	MeSH descriptor Nervous System Diseases explode all trees
#18	(neurological NEAR/2 (impair* OR disease* OR disorder*)):ti,ab
#19	(spinal cord NEAR/2 (injur* OR trauma* OR disease*)):ti,ab
#20	spinal NEAR/2 (shock* OR abnormalit*):ti,ab
#21	(brain NEAR/2 (injur* OR tumor* OR tumour* OR lesion*)):ti,ab
#22	myelopathy:ti,ab
#23	(neurolog* NEAR/4 spinal):ti,ab
#24	(diabet* NEAR/3 neuropath*):ti,ab
#25	(hydronephrosis OR dyssynergi* OR myelodysplas*):ti,ab
#26	("multiple sclerosis" OR parkinson* OR stroke* OR dementia OR alzheimer* OR "cerebral palsy" OR hydrocephalus OR "spina bifida"):ti,ab
#27	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26)
#28	MeSH descriptor Urinary Tract Infections, this term only
#29	MeSH descriptor Bacteriuria, this term only
#30	MeSH descriptor Pyuria, this term only
#31	MeSH descriptor Pyelonephritis, this term only
#32	MeSH descriptor Cystitis explode all trees
#33	MeSH descriptor Urethritis, this term only
#34	MeSH descriptor Prostatitis, this term only
#35	(urinary tract infection* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*):ti,ab
#36	(#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35)
#37	(#16 OR #36)
#38	(#3 OR (#27 AND #37))
#39	MeSH descriptor Antibiotic Prophylaxis, this term only
#40	MeSH descriptor Anti-Infective Agents, Urinary, this term only
#41	((antibiotic* OR antimicrobial* OR anti-infective*) and (prevent* OR prophyla*)):ti,ab
#42	MeSH descriptor Amdinocillin explode all trees
#43	MeSH descriptor Amoxicillin explode all trees

#44	MeSH descriptor Cephalosporins explode all trees
#45	MeSH descriptor Quinolones explode all trees
#46	MeSH descriptor Amoxicillin-Potassium Clavulanate Combination, this term only
#47	MeSH descriptor Carfecillin, this term only
#48	MeSH descriptor Cycloserine, this term only
#49	MeSH descriptor Carbapenems, this term only
#50	MeSH descriptor Nitrofurans explode all trees
#51	MeSH descriptor Gentamicins explode all trees
#52	MeSH descriptor Mandelic Acids explode all trees
#53	MeSH descriptor Methenamine, this term only
#54	MeSH descriptor Pipemidic Acid, this term only
#55	MeSH descriptor Piromidic Acid, this term only
#56	MeSH descriptor Sulfonamides explode all trees
#57	MeSH descriptor Trimethoprim explode all trees
#58	(amdinocillin OR amifloxacin OR amoxicillin OR amoxiclav OR cinoxacin OR cephalosporin* OR cefalexin OR enoxacin OR levofloxacin OR nifurtoinol OR lomefloxacin OR cefotaxime OR cefuroxime OR difloxacin OR quinolone* OR flouroquinolone* OR ciproflax* OR cotrimoxazole OR carfecillin OR cycloserine OR carbapenem* OR doripenem* OR nitrofurans OR furaltadone OR flumequine OR fleroxacin OR furagin OR fosfomycin* OR furazolidone OR isepamicin OR nitrofurantoin OR gentamicin* OR mandelic acid* OR nitroxoline OR methenamine* OR nalidixic acid* OR norfloxacin OR ofloxacin OR oxolinic acid OR pipemidic acid OR pefloxacin OR piromidic acid OR pivmecillinam OR sulphanilamide* OR sulfacetamide OR sulfachlorpyridazine OR sulfadoxin OR sulfalene OR sulfamet* OR sul?onamide* OR trimethoprim* OR TMP-SMX):ti,ab
#59	(#39 OR #40 OR #41 OR #42 #OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58)
#60	(#38 AND #59)

C.3.6 Safety and efficacy of alternative management approaches

C.3.6.1 Catheter and catheter valve

Searches for the following two questions were run as one search:

Q1. What are the long term risks associated with the long term use of intermittent catheterisation, indwelling catheters and penile sheath collection/pads. What is the quality of life associated with the above?

Q2. What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease?

Searches constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological AND (incontinence OR UTI)*	Catheter OR catheter valve OR penile sheath		RCTs OR SRs OR observational studies [Medline and Embase only]	All years – 10/01/12

*Population differs from standard population search strategy outlined in Section C.2, with additional terms included for urinary tract infection. As a consequence both population and intervention terms have been included below for each database.

Medline search terms

1.	Urinary bladder, Neurogenic/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor)).ti,ab.
3.	(overactiv* adj3 bladder).ti,ab.
4.	or/1-3
5.	Urinary bladder, overactive/ OR exp Enuresis/ OR exp Urinary incontinence/ OR Urinary retention/
6.	Nocturia/
7.	(lower urinary tract symptom* urinary tract infection* OR UTI* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
8.	((urin* OR bladder OR voiding OR micturation) adj3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.
9.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
10.	(bladder adj (obstruct* OR control OR management)).ti,ab.
11.	(urin* adj2 (retention OR retain*)).ti,ab.
12.	resid* urine.ti,ab.
13.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
14.	or/5-13
15.	exp Nervous system diseases/
16.	exp Nervous system neoplasms/
17.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
18.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
19.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
20.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
21.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
22.	(neurolog* adj4 spinal).ti,ab.
23.	(diabet* adj3 neuropath*).ti,ab.
24.	or/15-23
25.	14 and 24
26.	4 OR 25
27.	Limit 26 to english language
28.	Letter/
29.	Editorial/
30.	exp Historical article/
31.	Anecdotes as Topic/
32.	Comment/
33.	Case report/
34.	Animal/ not (Animal/ and Human/)
35.	Animals, Laboratory/
36.	exp Animal experiment/
37.	exp Animal model/
38.	exp Rodentia/
39.	or/28-38
40.	27 not 39

41.	Catheterization/
42.	Urinary catheterization/
43.	Catheters, indwelling/
44.	Catheter-related infections/
45.	((urin* OR ureter* OR urethra* OR suprapubic OR indwelling) adj catheter*).ti,ab.
46.	(intermittent adj2 catheter*).ti,ab.
47.	(catheter adj valve*).ti,ab.
48.	(sheath* OR condom*).ti,ab.
49.	or/41-48
50.	40 and 49

1 **Embase search terms**

1.	Neurogenic bladder/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor OR vesical)).ti,ab.
3.	(overactive* adj3 bladder).ti,ab.
4.	or/1-3
5.	Overactive bladder/ OR exp Enuresis/ OR exp Urine incontinence/ OR Urine retention/
6.	Nocturia/
7.	((bladder OR detrusor) adj1 overactiv*).ti,ab.
8.	((bladder OR urin*) adj1 (incontinen* OR leakage OR wetting)).ti,ab.
9.	(lower urinary tract symptom* OR urinary tract infection* OR UTI* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
10.	((urin* OR bladder OR voiding OR micturation) adj3 (disorders* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.
11.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
12.	(bladder adj (obstruct* OR control OR management)).ti,ab.
13.	(urin* adj2 (retent* OR retain*)).ti,ab.
14.	resid* urine.ti,ab.
15.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
16.	or/5-15
17.	exp Neurologic disease/
18.	exp Nervous system neoplasms/
19.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
20.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
21.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
22.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
23.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
24.	(neurolog* adj4 spinal).ti,ab.
25.	(diabet* adj3 neuropath*).ti,ab.
26.	or/17-25
27.	16 and 26
28.	4 OR 27
29.	limit 28 to english language

30.	letter.pt.
31.	Letter/
32.	editorial.pt.
33.	note.pt.
34.	Case report/
35.	Case study/
36.	conference abstract.pt.
37.	Animal/ not (Animal/ and Human/)
38.	Nonhuman/
39.	exp Animal studies/
40.	Animals, Laboratory/
41.	exp Experimental animal/
42.	exp Animal experiment/
43.	exp Animal model/
44.	exp Rodent/
45.	or/30-44
46.	29 not 45
47.	Catheter/
48.	exp Urinary catheter/
49.	Ureter catheter/
50.	Indwelling catheter/
51.	exp Catheter complication/
52.	Catheterization/
53.	Ureter catheterization/
54.	exp Bladder catheterization/
55.	((urin* OR ureter* OR urethra* OR suprapubic OR indwelling) adj catheter*).ti,ab.
56.	(intermittent adj2 catheter*).ti,ab.
57.	(catheter adj valve*).ti,ab.
58.	sheath* OR condom*.ti,ab.
59.	or/47-58
60.	46 and 59

1 **Cinahl search terms**

S1	(MH "Bladder, Neurogenic")
S2	neurogenic* n3 bladder OR neurogenic* n3 urin* OR neurogenic* n3 incontinen* OR neurogenic* n3 detrusor
S3	neurologic* n3 bladder OR neurologic* n3 urin* OR neurologic* n3 incontinen* OR neurologic* n3 detrusor
S4	overactiv* n1 bladder
S5	S1 OR S2 OR S3 OR S4
S6	MH overactive bladder OR mh enuresis+ OR mh urinary incontinence+ OR MH urinary retension
S7	lower urinary tract symptom* OR urinary tract infection* OR UTI* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia
S8	urin* n3 disorder* OR urin* n3 symptom* OR urin* n3 urgency OR urin* n3 incontinen* OR urin* n3 dysfunction*
S9	bladder* n3 disorder* OR bladder* n3 symptom* OR bladder* n3 urgency OR bladder* n3

	incontinen* OR bladder* n3 dysfunction*
S10	voiding* n3 disorder* OR voiding* n3 symptom* OR voiding* n3 urgency OR voiding* n3 incontinen* OR voiding* n3 dysfunction*
S11	incomplet* n2 bladder empt* OR impair* n2 bladder empt*
S12	bladder n1 obstruct* OR bladder n1 control OR bladder n1 management
S13	urin* n2 retent* OR urin* n2 retain*
S14	resid* urine
S15	(weak OR underactiv OR overactive*) and (detrusor OR lower urinary tract OR bladder)
S16	(hyper-reflex* OR hypereflex* OR hyperreflex*) and (detrusor OR lower urinary tract OR bladder)
S17	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	MH nervous system diseases+ OR MH nervous system neoplasms+
S19	neurological n2 impairment OR neurological n2 disease* OR neurological n2 disorder*
S20	spinal cord n2 injur* OR spinal cord n2 trauma OR spinal cord n2 disease*
S21	spinal n2 shock OR spinal n2 abnormalit*
S22	multiple sclerosis OR parkinson* OR stroke OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR hydronephro* OR dyssynergi* OR myelodysplas*
S23	brain n2 injur* OR brain n2 tumor* OR brain n2 tumour*
S24	neurolog* n4 spinal
S25	diabet* OR neuropath*
S26	S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25
S27	S17 and S26
S28	S5 OR S27
S29	(MH "Catheterization")
S30	(MH "Urinary Catheterization+")
S31	(MH "Catheters, Urinary+")
S32	(MH "Catheter-Related Infections")
S33	(urin* OR ureter* OR urethra* OR suprapubic OR indwelling OR valve OR intermittent) and catheter*
S34	(sheath* and pen*) OR condom*
S35	S29 OR S30 OR S31 OR S32 OR S33 OR S34
S36	S28 and S35

1 **Cochrane search terms**

#1	MeSH descriptor Urinary Bladder, Neurogenic explode all trees
#2	(neurogenic* OR neurologic* OR spastic OR atonic OR overactiv*) NEAR/3 (bladder OR incontinen* OR detrusor OR urin*)
#3	(#1 OR #2)
#4	MeSH descriptor Nocturia explode all trees
#5	MeSH descriptor Urinary Bladder, Overactive explode all trees
#6	MeSH descriptor Enuresis explode all trees
#7	MeSH descriptor Urinary Incontinence explode all trees
#8	MeSH descriptor Urinary Retention explode all trees
#9	("lower urinary tract symptom*" OR "urinary tract infection*" OR "urinary symptom*" OR LUTS OR "irritable bladder" OR bedwetting OR enuresis OR nocturia):ti,ab
#10	((urin* OR bladder OR voiding OR micturation) NEAR/3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)):ti,ab

#11	((incomplete* OR impair*) NEXT "bladder emptying"):ti,ab
#12	(bladder NEXT (obstruct* OR control OR management OR compliance)):ti,ab
#13	("urinary retention" OR "residual urine"):ti,ab
#14	(urin* NEAR/2 (retention OR retain* OR resid*)):ti,ab
#15	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) NEAR (detrusor OR "lower urinary tract" OR bladder)):ti,ab
#16	(#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)
#17	MeSH descriptor Nervous System Diseases explode all trees
#18	(neurological NEAR/2 (impair* OR disease* OR disorder*)):ti,ab
#19	(spinal cord NEAR/2 (injur* OR trauma* OR disease*)):ti,ab
#20	spinal NEAR/2 (shock* OR abnormalit*):ti,ab
#21	(brain NEAR/2 (injur* OR tumor* OR tumour* OR lesion*)):ti,ab
#22	myelopathy:ti,ab
#23	(neurolog* NEAR/4 spinal):ti,ab
#24	(diabet* NEAR/3 neuropath*):ti,ab
#25	(hydronephrosis OR dyssynergi* OR myelodysplas*):ti,ab
#26	("multiple sclerosis" OR parkinson* OR stroke* OR dementia OR alzheimer* OR "cerebral palsy" OR hydrocephalus OR "spina bifida"):ti,ab
#27	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26)
#28	(#3 OR (#16 AND #27))
#29	MeSH descriptor Catheterization, this term only
#30	MeSH descriptor Urinary Catheterization, this term only
#31	MeSH descriptor Catheters, Indwelling, this term only
#32	MeSH descriptor Catheter-Related Infections, this term only
#33	((urin* OR ureter* OR urethra* OR suprapubic OR indwelling) NEXT catheter*):ti,ab
#34	(intermittent NEAR/2 catheter*):ti,ab
#35	(catheter NEXT valve*):ti,ab
#36	sheath* OR condom*:ti,ab
#37	(#29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36)
#38	(#28 AND #37)

C.3.612 Ileal conduit diversion

Q. What is the safety and efficacy of ileal conduit diversion compared with usual care in neurological disease?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Ileal conduit diversion		RCTs OR SRs OR observational studies [Medline and Embase only]	All years – 10/01/12

Medline search terms

1.	Urinary diversion/
2.	Cystostomy/
3.	Ureterostomy/
4.	Cystectomy/
5.	Ileostomy/

6.	Urinary reservoirs, continent/
7.	*Ileum/su [Surgery]
8.	(conduit* adj5 (ile* OR urin* OR diversion* OR continen* OR Bricker)).ti,ab.
9.	(diversion* adj5 (urin* OR continen* OR ile*)).ti,ab.
10.	(reservoir* adj5 (ile* OR urin* OR continen* OR sigmoid* OR uret*)).ti,ab.
11.	(bladder adj2 (reconstruct* OR replac* OR substitut*)).ti,ab.
12.	(neobladder* OR urostom* OR cystectom* OR ureterostom*OR ileostom* OR cystostom* OR vesicostom*).ti,ab.
13.	(anastomo* adj5 ureter*).ti,ab.
14.	Colonic pouches/
15.	(pouch* OR ostom*).ti,ab.
16.	or/1-15

1 **Embase search terms**

1.	exp Urinary diversion/
2.	Cystectomy/
3.	Cystostomy/
4.	Ureterostomy/
5.	Ileostomy/
6.	Ileum pouch/
7.	exp Intestine anastomosis/
8.	*Ileum/su [Surgery]
9.	(conduit* adj5 (ile* OR urin* OR diversion* OR continen* OR Bricker)).ti,ab.
10.	(diversion* adj5 (urin* OR continen* OR ile*)).ti,ab.
11.	(reservoir* adj5 (ile* OR urin* OR continen* OR sigmoid* OR uret*)).ti,ab.
12.	(bladder adj2 (reconstruct* OR replac* OR substitut*)).ti,ab.
13.	(neobladder* OR urostom* OR cystectom* OR ureterostom*OR ileostom* OR cystostom* OR vesicostom*).ti,ab.
14.	(anastomo* adj5 ureter*).ti,ab.
15.	(pouch* OR ostom*).ti,ab.
16.	or/1-15

2 **Cinahl search terms**

S1	(MH "Urinary Diversion+")
S2	(MH "Cystectomy")
S3	(MH "Cystostomy")
S4	(MH "Ureterostomy")
S5	(MH "Ileostomy")
S6	(MH "Ileoanal Reservoir")
S7	(MH "Ileum+/SU")
S8	conduit* AND (ile* OR urin* OR diversion* OR continen* OR Bricker)
S9	diversion* AND (urin* OR continen* OR ile*)
S10	reservoir* AND (ile* OR urin* OR continen* OR sigmoid* OR uret*)
S11	neobladder* OR urostom* OR cystectom* OR ureterostom* OR ileostom* OR cystostom* OR vesicostom*
S12	anastomo* AND ureter*
S13	pouch*

S14	bladder AND (reconstruct* OR replac* OR substitut*)
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14

Cochrane search terms

#1	MeSH descriptor Urinary Diversion, this term only
#2	MeSH descriptor Cystectomy, this term only
#3	MeSH descriptor Cystostomy, this term only
#4	MeSH descriptor Ureterostomy, this term only
#5	MeSH descriptor Ileostomy, this term only
#6	MeSH descriptor Urinary Reservoirs, Continent, this term only
#7	MeSH descriptor Colonic Pouches, this term only
#8	MeSH descriptor Ileum, this term only with qualifier: SU
#9	(conduit* NEAR/5 (ile* OR urin* OR diversion* OR continen* OR Bricker)):ti,ab
#10	(diversion* NEAR/5 (urin* OR continen* OR ile*)):ti,ab
#11	(reservoir* NEAR/5 (ile* OR urin* OR continen* OR sigmoid* OR uret*)):ti,ab
#12	(bladder NEAR/2 (reconstruct* OR replac* OR substitut*)):ti,ab
#13	(neobladder* OR urostom* OR cystectom* OR ureterostom*OR ileostom* OR cystostom* OR vesicostom*):ti,ab
#14	(anastomo* NEAR/5 ureter*):ti,ab
#15	(pouch* OR ostom*):ti,ab
#16	(#1OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)

C.3.7 Monitoring and surveillance

Q. Does monitoring, or do surveillance protocols, improve patient outcomes?

Two searches were run for this question. Both searches used the same intervention terms (as outlined in C.3.7.1), but the population was adjusted for the second search (C.3.7.2).

C.3.7.1 Search using STANDARD population

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence	Clinical monitoring and surveillance techniques		None	All years – 10/01/12

Medline search terms

1.	exp Kidney function tests/
2.	exp Ultrasonography/ and (renal OR kidney* OR bladder).ti,ab.
3.	Urodynamics/
4.	Urography/
5.	Urinalysis/
6.	Diagnostic techniques, Urological/
7.	Radiography, Abdominal/
8.	Reagent strips/
9.	(cystometr* OR CMG* OR cystoscop*).ti,ab.
10.	(renogra* OR DMSA OR renal scan* OR kidney scan*).ti,ab.

11.	(blood adj (test* OR pressure* OR chemistry)).ti,ab.
12.	((ultrason* OR ultrasound) adj3 (renal OR kidney* OR bladder)).ti,ab.
13.	(intravenous adj (urogram* OR pylogram*)).ti,ab.
14.	(videourodynamic* OR VUDS).ti,ab.
15.	(uroflowmetr* OR flowmetr*).ti,ab.
16.	(urodynamic* adj2 (stud* OR evaluat* OR test* OR monitor*)).ti,ab.
17.	((abdominal OR abdomen OR urinary tract OR LUT) adj3 (x ray* OR imag* OR radiograph*)).ti,ab.
18.	(glomerul* adj filtrat*).ti,ab.
19.	((reagent* OR test*) adj2 (strip* OR tape*)).ti,ab.
20.	(dipstick* OR dip stick* OR urine culture* OR urinalys*).ti,ab.
21.	(creatinin* adj (ratio* OR clearance*)).ti,ab.
22.	or/1-21
23.	Monitoring, Physiologic/
24.	(self monitor* OR monitor* OR track* OR surveillance OR screen* OR diari* OR diary* OR history tak*).ti,ab.
25.	((medical OR care OR follow up) adj4 (plan* OR protocol* OR review* OR management OR polic* OR program*)).ti,ab.
26.	((regular OR routine* OR periodic* OR specialist* OR consultant* OR outpatient* OR out patient*) adj3 (review* OR visit* OR examin* OR attend* OR check up* OR recall* OR follow up* OR investigation* OR test*)).ti,ab.
27.	(visit* adj5 clinic*).ti,ab.
28.	or/23-27
29.	22 and 28

1 **Embase search terms**

1.	Kidney function test/
2.	Echography/ and (renal OR kidney* OR bladder).ti,ab.
3.	exp Glomerulus filtration/
4.	Urodynamics/
5.	Uroflowmetry/
6.	exp Urinalysis/
7.	exp Urography/
8.	exp Bladder examination/
9.	Abdominal radiography/
10.	Test strip/
11.	(cystometr* OR CMG* OR cystoscop*).ti,ab.
12.	(renogra* OR DMSA OR renal scan* OR kidney scan*).ti,ab.
13.	(blood adj (test* OR pressure* OR chemistry)).ti,ab.
14.	((ultrason* OR ultrasound) adj3 (renal OR kidney* OR bladder)).ti,ab.
15.	(intravenous adj (urogra* OR pylogra*)).ti,ab.
16.	(videourodynamic* OR VUDS).ti,ab.
17.	(uroflowmetr* OR flowmetr*).ti,ab.
18.	(urodynamic* adj2 (stud* OR evaluat* OR test* OR monitor*)).ti,ab.
19.	((abdominal OR abdomen OR urinary tract OR LUT) adj3 (x ray* OR imag* OR radiograph*)).ti,ab.
20.	(glomerul* adj filtrat*).ti,ab.

21.	((reagent* OR test*) adj2 (strip* OR tape*)).ti,ab.
22.	(dipstick* OR dip stick* OR urine culture* OR urinalys*).ti,ab.
23.	(creatinin* adj (ratio* OR clearance*)).ti,ab.
24.	or/1-23
25.	exp Monitoring/
26.	(self monitor* OR monitor* OR track* OR surveillance OR screen* OR diari* OR diary* OR history tak*).ti,ab.
27.	((medical OR care OR follow up) adj4 (plan* OR protocol* OR review* OR management OR polic* OR program*)).ti,ab.
28.	((regular OR routine* OR periodic* OR specialist* OR consultant* OR outpatient* OR out patient*) adj3 (review* OR visit* OR examin* OR attend* OR check up* OR recall* OR follow up* OR investigation* OR test*)).ti,ab.
29.	(visit* adj5 clinic*).ti,ab.
30.	or/25-29
31.	24 and 30

1 **Cinahl search terms**

S1	(MH "Kidney Function Tests+")
S2	(MH Ultrasonography+) and (renal OR kidney* OR bladder)
S3	(MH "Urodynamics")
S4	(MH "Urography")
S5	(MH "Urinalysis")
S6	(MH "Diagnosis, Urologic+")
S7	(MH "Radiography, Abdominal")
S8	(MH "Reagent Strips")
S9	(cystometr* OR CMG* OR cystoscop*)
S10	(renogra* OR DMSA OR renal scan* OR kidney scan*)
S11	("blood test" OR "blood pressure" OR "blood chemistry")
S12	(ultrason* OR ultrasound) and (renal OR kidney* OR bladder)
S13	(intravenous and (urogra* OR pylogra*))
S14	(videourodynamic* OR VUDS)
S15	(uroflowmetr* OR flowmetr*)
S16	(urodynamic* and (stud* OR evaluat* OR test* OR monitor*))
S17	((abdominal OR abdomen OR urinary tract OR LUT) and (x ray* OR imag* OR radiograph*))
S18	(“glomerul* filtrat*”)
S19	(reagent strip* OR reagent tape* OR test strip* OR test tape*)
S20	(dipstick* OR dip stick* OR urine culture* OR urinalys*)
S21	(creatinin* ratio* OR creatinin* clearance*)
S22	(S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21)
S23	(MH "Monitoring, Physiologic+")
S24	(self monitor* OR monitor* OR track* OR surveillance OR screen* OR diari* OR diary* OR history tak*)
S25	((medical OR care OR follow up) AND (plan* OR protocol* OR review* OR management OR polic* OR program*))
S26	((regular OR routine* OR periodic* OR specialist* OR consultant* OR outpatient* OR out patient*) AND (review* OR visit* OR examin* OR attend* OR check up* OR recall* OR follow

	up* OR investigation* OR test*))
S27	(visit* n5 clinic*)
S28	(S23 OR S24 OR S25 OR S26 OR S27)
S29	S22 AND S28

1 **Cochrane search terms**

#1	MeSH descriptor Ultrasonography explode all trees
#2	(renal OR kidney* OR bladder):ti,ab
#3	(#1 AND #2)
#4	MeSH descriptor Kidney Function Tests explode all trees
#5	MeSH descriptor Urodynamics, this term only
#6	MeSH descriptor Urography, this term only
#7	MeSH descriptor Urinalysis, this term only
#8	MeSH descriptor Diagnostic Techniques, Urological, this term only
#9	MeSH descriptor Radiography, Abdominal, this term only
#10	MeSH descriptor Reagent Strips, this term only
#11	(cystometr* OR CMG* OR cystoscop*):ti,ab
#12	(renogra* OR DMSA OR renal scan* OR kidney scan*):ti,ab
#13	(blood NEXT (test* OR pressure* OR chemistry)):ti,ab
#14	((ultrason* OR ultrasound) NEAR/3 (renal OR kidney* OR bladder)):ti,ab
#15	(intravenous NEXT (urogram* OR pylogram*)):ti,ab
#16	(videourodynamic* OR VUDS):ti,ab
#17	(uroflowmetr* OR flowmetr*):ti,ab
#18	(urodynamic* NEAR/2 (stud* OR evaluat* OR test* OR monitor*)):ti,ab
#19	((abdominal OR abdomen OR urinary tract OR LUT) NEAR/3 (x ray* OR imag* OR radiograph*)):ti,ab
#20	(glomerul* NEXT filtrat*):ti,ab
#21	((reagent* OR test*) NEAR/2 (strip* OR tape*)):ti,ab
#22	(dipstick* OR dip stick* OR urine culture* OR urinalys*):ti,ab
#23	(creatinin* NEXT (ratio* OR clearance*)):ti,ab
#24	(#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25	MeSH descriptor Monitoring, Physiologic, this term only
#26	(self monitor* OR monitor* OR track* OR surveillance OR screen* OR diari* OR diary* OR history tak*):ti,ab
#27	((medical OR care OR follow up) NEAR/4 (plan* OR protocol* OR review* OR management OR polic* OR program*)):ti,ab
#28	((regular OR routine* OR periodic* OR specialist* OR consultant* OR outpatient* OR out patient*) NEAR/3 (review* OR visit* OR examin* OR attend* OR check up* OR recall* OR follow up* OR investigation* OR test*)):ti,ab
#29	(visit* NEAR/5 clinic*):ti,ab
#30	(#25 OR #26 OR #27 OR #28 OR #29)
#31	#24 OR #30

C.3.722 Search using ADJUSTED population

3 Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters

Population	Intervention	Comparison	Study filter used	Date parameters
Multiple sclerosis OR spinal cord injury OR spina bifida	Clinical monitoring and surveillance techniques		None	All years – 10/01/12

For this additional search the interventions outlined in C.3.7.1 were run with the following adjusted populations:

Medline search terms

1.	exp Multiple sclerosis/
2.	exp Spinal dysraphism/
3.	exp Spinal cord injuries/
4.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
5.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
6.	(multiple sclerosis OR spina bifida).ti,ab.
7.	(neurolog* adj4 spinal).ti,ab.
8.	or/1-7

Embase search terms

1.	Spinal cord injury/
2.	exp Spina bifida/
3.	exp Multiple sclerosis/
4.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
5.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
6.	(multiple sclerosis OR spina bifida).ti,ab.
7.	(neurolog* adj4 spinal).ti,ab.
8.	or/1-7

Cinahl search terms

S1	(MH "Multiple Sclerosis")
S2	(MH "Spina Bifida")
S3	(MH "Spinal Cord Injuries+")
S4	S1 OR S2 OR S3

Cochrane search terms

#1	MeSH descriptor Multiple Sclerosis explode all trees
#2	MeSH descriptor Spinal Dysraphism explode all trees
#3	MeSH descriptor Spinal Cord Injuries explode all trees
#4	(spinal cord NEAR/2 (injur* OR trauma* OR disease*)):ti,ab
#5	spinal NEAR/2 (shock* OR abnormalit*):ti,ab
#6	(neurolog* NEAR/4 spinal):ti,ab
#7	("multiple sclerosis" OR "spina bifida"):ti,ab
#8	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)

C.3.8 Services and information

C.3.8.1 Transition to adult services

Q. What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease*	Transition services		None	All years – 10/01/12

*Population differs from standard population search strategy outlined in Section C.2, with terms focused on a neurologically impaired (rather than neurologically incontinent) population. As a consequence both population and intervention terms have been included below for each database.

Medline search terms

1.	Urinary bladder, neurogenic/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinent* OR detrusor)).ti,ab.
3.	(overactiv* adj3 bladder).ti,ab.
4.	exp Nervous System Diseases/
5.	exp Nervous System Neoplasms/
6.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
7.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
8.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
9.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
10.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
11.	(neurolog* adj4 spinal).ti,ab.
12.	(diabet* adj3 neuropath*).ti,ab.
13.	or/1-12
14.	limit 13 to english
15.	Letter/
16.	Editorial/
17.	exp Historical article/
18.	Anecdotes as topic/
19.	Comment/
20.	Case report/
21.	Animal/ not (Animal/ and Human/)
22.	Animals, Laboratory/
23.	exp Animal experiment/
24.	exp Animal model/
25.	exp Rodentia/
26.	or/15-25
27.	14 not 26
28.	Adolescent health services/og, st [Organization & Administration, Standards]
29.	((p?ediatric OR adolescen* OR child* OR teenager* OR young people OR young person OR young adult*) adj5 (transition* OR transfer* OR handover* OR hand over* OR handoff* OR

	continuity OR interface*)).ti,ab.
30.	((transition* OR transfer* OR pathway* OR continuity OR interface*) and (adult OR care OR service*)).ti.
31.	or/28-30
32.	Adolescent/
33.	Young adult/
34.	(adolescen* OR teenager* OR young people OR young person OR young adult*).ti.
35.	OR/32-34
36.	"Continuity of patient care"/
37.	*Health services accessibility/
38.	Interinstitutional relations/
39.	Models, Organizational/
40.	Interdisciplinary communication/
41.	Long-term care/og, st [Organization & Administration, Standards]
42.	Patient-centered care/og, st [Organization & Administration, Standards]
43.	Patient transfer/mt, og, st [Methods, Organization & Administration, Standards]
44.	or/36-43
45.	31 OR (35 and 44)
46.	27 and 45

1 **Embase search terms**

1.	Neurogenic bladder/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor OR vesical)).ti,ab.
3.	((spinal OR spastic) adj1 bladder).ti,ab.
4.	exp Neurologic disease/
5.	exp Nervous system neoplasms/
6.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
7.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
8.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
9.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
10.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
11.	(neurolog* adj4 spinal).ti,ab.
12.	(diabet* adj3 neuropath*).ti,ab.
13.	or/1-12
14.	letter.pt.
15.	Letter/
16.	editorial.pt.
17.	note.pt.
18.	Case report/
19.	Case study/
20.	conference abstract.pt.
21.	Animal/ not (Animal/ and Human/)
22.	Nonhuman/
23.	exp Animal studies/

24.	Animals, Laboratory/
25.	exp Experimental animal/
26.	exp Animal experiment/
27.	exp Animal model/
28.	exp Rodent/
29.	or/14-28
30.	13 not 29
31.	limit 30 to english
32.	((p?ediatric OR adolescen* OR child* OR teenager* OR young people OR young person OR young adult*) adj5 (transition* OR transfer* OR handover* OR hand over* OR handoff* OR continuity OR interface*)).ti,ab.
33.	((transition* OR transfer* OR pathway* OR continuity OR interface*) and (adult OR care OR service*)).ti.
34.	32 OR 33
35.	Adolescence/
36.	Adolescent/
37.	Adolescent health/
38.	Child health care/
39.	or/35-38
40.	Patient care planning/
41.	Health care planning/
42.	Health care access/
43.	Clinical pathway/
44.	Interdisciplinary communication/
45.	Integrated health care system/
46.	*Patient care/
47.	or/40-46
48.	39 and 47
49.	34 OR 48
50.	31 and 49

1 **Cinahl search terms**

S1	(MH "Bladder, Neurogenic")
S2	neurogenic* n3 bladder OR neurogenic* n3 urin* OR neurogenic* n3 incontinen* OR neurogenic* n3 detrusor
S3	neurologic* n3 bladder OR neurologic* n3 urin* OR neurologic* n3 incontinen* OR neurologic* n3 detrusor
S4	neurological n2 impairment OR neurological n2 disease* OR neurological n2 disorder*
S5	spinal cord n2 injur* OR spinal cord n2 trauma OR spinal cord n2 disease*
S6	spinal n2 shock OR spinal n2 abnormalit*
S7	multiple sclerosis OR parkinson* OR stroke OR cerebral palsy OR hydrocephalus OR spina bifida
S8	brain n2 injur* OR brain n2 tumor* OR brain n2 tumour*
S9	neurolog* n4 spinal
S10	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9
S11	(MH "Adolescent Health Services/OG/ST")
S12	(pediatric OR paediatric OR adolescen* OR child* OR teenager* OR young people OR young

	person OR young adult*) and (transition* OR handover* OR hand over* OR handoff* OR continuity OR interface*)
S13	transition* and (adult* OR care OR service*)
S14	S10 OR S11 OR S12
S15	S10 and S14

Cochrane search terms

#1	(neurogenic* OR neurologic* OR spastic OR atonic OR unihibited OR overactiv*) NEAR/3 (bladder OR incontinen* OR detrusor OR urin*)
#2	MeSH descriptor Nervous System Diseases explode all trees
#3	(neurological NEAR/2 (impair* OR disease* OR disorder*)):ti,ab
#4	(spinal cord NEAR/2 (injur* OR trauma* OR disease*)):ti,ab
#5	spinal NEAR/2 (shock* OR abnormalit*):ti,ab
#6	(brain NEAR/2 (injur* OR tumor* OR tumour* OR lesion*)):ti,ab
#7	myelopathy:ti,ab
#8	(neurolog* NEAR/4 spinal):ti,ab
#9	(diabet* NEAR/3 neuropath*):ti,ab
#10	(hydronephrosis OR dyssynergi* OR myelodysplas*):ti,ab
#11	("multiple sclerosis" OR parkinson* OR stroke* OR dementia OR alzheimer* OR "cerebral palsy" OR hydrocephalus OR "spina bifida"):ti,ab
#12	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)
#13	MeSH descriptor Adolescent Health Services, this term only with qualifier: OG
#14	MeSH descriptor Adolescent Health Services, this term only with qualifier: ST
#15	((p?ediatric OR adolescen* OR child* OR teenager* OR young people OR young person OR young adult*) NEAR/5 (transition* OR handover* OR hand over* OR handoff* OR continuity OR interface*)):ti,ab
#16	((transition* OR pathway* OR continuity OR interface*) and (adult OR care OR service*)):ti
#17	(#14 OR #15 OR #16)
#18	MeSH descriptor Adolescent, this term only
#19	(adolescen* OR teenager* OR young people OR young person OR young adult*):ti
#20	MeSH descriptor Continuity of Patient Care, this term only
#21	MeSH descriptor Patient-Centered Care, this term only
#22	MeSH descriptor Health Services Accessibility, this term only
#23	MeSH descriptor Interinstitutional Relations, this term only
#24	MeSH descriptor Models, Organizational, this term only
#25	MeSH descriptor Interdisciplinary Communication, this term only
#26	MeSH descriptor Patient Transfer, this term only with qualifier: OG
#27	MeSH descriptor Long-Term Care, this term only with qualifier: OG
#28	(#18 OR #19)
#29	(#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27)
#30	(#17 OR (#28 AND #29))
#31	(#12 AND #30)

C.3.822 Patient/carer access to services

Q. For patients with lower urinary tract dysfunction associated with neurological disorders, and their carers, what are the experiences of access to, and interaction with, services that address these issues?

1 Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease OR incontinence*	Patient experience AND access to services		None	All years – 10/01/12

2 *Population differs from standard population search strategy outlined in Section C.2. A more limited
3 neurological component has been combined (OR) with incontinence terms. As a consequence both population
4 and intervention terms have been included below for each database.

5 **Medline search terms**

1.	Urinary bladder, neurogenic/
2.	((neurogenic* or neurologic*) adj3 (bladder or urin* or incontinent* or detrusor)).ti,ab.
3.	(overactiv* adj3 bladder).ti,ab.
4.	Urinary bladder, overactive/ or exp Enuresis/ or exp Urinary incontinence/ or Urinary retention/
5.	Nocturia/
6.	(lower urinary tract symptom* or urinary symptom* or LUTS or irritable bladder or bedwetting or enuresis or nocturia).ti,ab.
7.	((urin* or bladder or voiding or micturation) adj3 (disorder* or symptom* or urgency or incontinence or dysfunction)).ti,ab.
8.	((incomplet* or impair*) adj2 bladder empt*).ti,ab.
9.	(bladder adj (obstruct* or control or management)).ti,ab.
10.	(urin* adj2 (retention or retain*)).ti,ab.
11.	resid$ urine.ti,ab.
12.	((overactiv* or weak or underactiv* or hyperreflex* or hyper-reflex*) adj3 (detrusor or lower urinary tract or bladder)).ti,ab.
13.	(multiple sclerosis or parkinson* or stroke* or dementia or alzheimer* or cerebral palsy or hydrocephalus or spina bifida or myelopath* or hydronephro* or dyssynergi* or myelodysplas*).ti,ab.
14.	or/1-13
15.	((client* or patient* or user* or carer* or consumer* or customer*) adj2 (attitude* or priorit* or perception* or preferen* or belief* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or concern* or feeling* or advoca*)).ti,ab,hw.
16.	((patient* or satisfaction*) adj2 (questionnaire* or survey*)).ti,ab.
17.	Patient acceptance of health care/
18.	Health care surveys/
19.	*Questionnaires/
20.	Quality of health care/
21.	or/15-20
22.	Health services accessibility/
23.	"Continuity of patient care"/
24.	Patient-centered care/
25.	access*.ti.
26.	(patient* adj3 (access* or pathway* or continuity)).ti,ab.
27.	or/22-26
28.	14 and 21 and 27
29.	letter/
30.	editorial/

31.	news/
32.	exp Historical article/
33.	Anecdotes as topic/
34.	Comment/
35.	Case report/
36.	(letter or comment* or abstracts).ti.
37.	or/29-36
38.	37 not (Randomized controlled trial/ or random*.ti,ab.)
39.	Animals/ not Humans/
40.	exp Animals, Laboratory/
41.	exp Animal experimentation/
42.	exp Models, Animal/
43.	exp Rodentia/
44.	(rat or rats or mouse or mice).ti.
45.	or/38-44
46.	28 not 45

1 **Embase search terms**

1.	Neurogenic bladder/
2.	((neurogenic* or neurologic*) adj3 (bladder or urin* or incontinen* or detrusor or vesical)).ti,ab.
3.	((spinal or spastic) adj1 bladder).ti,ab.
4.	Overactive bladder/ or exp Enuresis/ or exp Urine incontinence/ or Urine retention/
5.	Nocturia/
6.	((bladder or detrusor) adj1 overactiv*).ti,ab.
7.	((bladder or urin*) adj1 (incontinen* or leakage or wetting)).ti,ab.
8.	(lower urinary tract symptom* or LUTS or irritable bladder or bedwetting or enuresis or nocturia or nycturia).ti,ab.
9.	((urin* or bladder or voiding or micturation) adj3 (disorders* or symptom* or urgency or incontinence or dysfunction)).ti,ab.
10.	((incomplet* or impair*) adj2 bladder empt*).ti,ab.
11.	(bladder adj (obstruct* or control or management)).ti,ab.
12.	(urin* adj2 (retent* or retain*)).ti,ab.
13.	resid* urine.ti,ab.
14.	((overactiv* or weak or underactiv* or hyperreflex* or hyper-reflex*) adj3 (detrusor or lower urinary tract or bladder)).ti,ab.
15.	(multiple sclerosis or parkinson* or stroke* or dementia or alzheimer* or cerebral palsy or hydrocephalus or spina bifida or myelopath* or hydronephro* or dyssynergi* or myelodysplas*).ti,ab.
16.	or/1-15
17.	((client* or patient* or user* or carer* or consumer* or customer*) adj2 (attitude* or priorit* or perception* or preferen* or belief* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or concern* or feeling* or advoca*)).ti,ab,hw.
18.	((patient* or satisfaction*) adj2 (questionnaire* or survey*)).ti,ab.
19.	Health care survey/
20.	exp Attitude to health/
21.	exp *Questionnaire/

22.	*Health care quality/
23.	or/17-22
24.	Health care access/
25.	Health care availability/
26.	*Health care delivery/
27.	access*.ti.
28.	(patient* adj3 (access* or pathway* or continuity)).ti,ab.
29.	or/24-28
30.	Conference abstract.pt.
31.	letter.pt. or Letter/
32.	note.pt.
33.	editorial.pt.
34.	Case report/ or Case study/
35.	(letter or comment* or abstracts).ti.
36.	or/30-35
37.	36 not (Randomized controlled trial/ or random*.ti,ab.)
38.	Animal/ not Human/
39.	Nonhuman/
40.	exp Animal experiment/
41.	exp Experimental animal/
42.	Animal model/
43.	exp Rodent/
44.	(rat or rats or mouse or mice).ti.
45.	or/37-44
46.	16 and 23 and 29
47.	46 not 45
48.	limit 47 to english language

1 **Cochrane search terms**

#1	MeSH descriptor Urinary Bladder, Neurogenic explode all trees
#2	(neurogenic* or neurologic* or spastic or atonic or unihibited or overactiv*) NEAR/3 (bladder or incontinen* or detrusor or urin*):ti,ab
#3	MeSH descriptor Nocturia explode all trees
#4	MeSH descriptor Urinary Bladder, Overactive explode all trees
#5	MeSH descriptor Enuresis explode all trees
#6	MeSH descriptor Urinary Incontinence explode all trees
#7	MeSH descriptor Urinary Retention explode all trees
#8	("lower urinary tract symptom*" or "urinary symptom*" or LUTS or "irritable bladder" or bedwetting or enuresis or nocturia):ti,ab
#9	((urin* or bladder or voiding or micturation) NEAR/3 (disorder* or symptom* or urgency or incontinence or dysfunction)):ti,ab
#10	((incomplete* or impair*) NEXT "bladder emptying"):ti,ab
#11	(bladder NEXT (obstruct* or control or management or compliance)):ti,ab
#12	("urinary retention" or "residual urine"):ti,ab
#13	(Urin* near/2 (retention or retain* or resid*)):ti,ab
#14	((overactiv* or weak or underactiv* or hyperreflex* or hyper-reflex*) NEAR (detrusor or

	"lower urinary tract" or bladder)):ti,ab
#15	("multiple sclerosis" or parkinson* or stroke* or dementia or alzheimer* or "cerebral palsy" or hydrocephalus or "spina bifida"):ti,ab
#16	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
#17	((client* or patient* or user* or carer* or consumer* or customer*) NEAR/2 (attitude* or priorit* or perception* or preferen* or belief* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or concern* or feeling* or advoca*)):ti,ab,hw
#18	((patient* or satisfaction*) NEAR/2 (questionnaire* or survey*)):ti,ab
#19	MeSH descriptor Patient Acceptance of Health Care, this term only
#20	MeSH descriptor Health Care Surveys, this term only
#21	MeSH descriptor Quality of Health Care, this term only
#22	#17 OR #18 OR #19 OR #20 OR #21
#23	MeSH descriptor Health Services Accessibility, this term only
#24	MeSH descriptor Continuity of Patient Care, this term only
#25	MeSH descriptor Patient-Centered Care, this term only
#26	access*:ti
#27	(patient* NEAR/3 (access* or pathway* or continuity)):ti,ab
#28	#23 OR #24 OR #25 OR #26 OR #27
#29	#16 AND #22 AND #28

C.3.813 Patient information

Q. Does provision of information about the management of neurological lower urinary tract dysfunction improve patient outcomes?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological AND (incontinence OR outcomes)*	Patient information		RCTs, Systematic reviews and observational studies [Medline and Embase only]	All years – 10/01/12

*Population differs from standard population search strategy outlined in Section C.2. The neurological component of the population has been combined (AND) with incontinence terms OR outcome terms (morbidity, quality of life, adherence to care, patient satisfaction). As a consequence both population and intervention terms have been included below for each database.

Medline search terms

1.	Urinary bladder, neurogenic/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor)).ti,ab.
3.	(overactiv* adj3 bladder).ti,ab.
4.	or/1-3
5.	Urinary bladder, overactive/ OR exp Enuresis/ OR exp Urinary incontinence/ OR Urinary retention/
6.	Nocturia/
7.	(lower urinary tract symptom* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
8.	((urin* OR bladder OR voiding OR micturation) adj3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.

9.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
10.	(bladder adj (obstruct* OR control OR management)).ti,ab.
11.	(urin* adj2 (retention OR retain*)).ti,ab.
12.	resid* urine.ti,ab.
13.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
14.	Urinary tract infections/
15.	Bacteriuria/
16.	Pyuria/
17.	Pyelonephritis/
18.	exp Cystitis/
19.	Urethritis/
20.	Prostatitis/
21.	(urinary tract infection* OR UTI* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*).ti,ab.
22.	Renal insufficiency/
23.	exp Renal insufficiency, chronic/
24.	((renal OR kidney*) adj2 (insufficien* OR impair* OR failure*)).ti,ab.
25.	glomerul* filtration.ti,ab,hw.
26.	exp Patient compliance/
27.	Health care surveys/
28.	Patient satisfaction/
29.	Quality of life/
30.	"Continuity of patient care"/
31.	Self care/
32.	or/5-31
33.	exp Nervous system diseases/
34.	exp Nervous system neoplasms/
35.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
36.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
37.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
38.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
39.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
40.	(neurolog* adj4 spinal).ti,ab.
41.	(diabet* adj3 neuropath*).ti,ab.
42.	or/33-41
43.	32 and 42
44.	4 OR 43
45.	limit 44 to english language
46.	Letter/
47.	Editorial/
48.	exp Historical article/
49.	Anecdotes as topic/
50.	Comment/

51.	Case report/
52.	Animal/ not (Animal/ and Human/)
53.	Animals, Laboratory/
54.	exp Animal experiment/
55.	exp Animal model/
56.	exp Rodentia/
57.	or/46-56
58.	45 not 57
59.	((client* OR patient* OR user* OR carer* OR consumer* OR customer* OR health) adj2 (information* OR educat* OR knowledge)).ti,ab,hw.
60.	(information* adj (need* OR requirement* OR support* OR seek* OR access* OR disseminat*)).ti,ab,hw.
61.	(patient* adj3 (literature OR leaflet* OR booklet* OR pamphlet* OR questionnaire* OR survey* OR handout* OR internet OR website*)).ti,ab.
62.	Telemedicine/
63.	patient education handout.pt.
64.	Access to information/
65.	Telephone/
66.	Publications/
67.	Pamphlets/
68.	or/59-67
69.	58 and 68

1 **Embase search terms**

1.	Neurogenic bladder/
2.	((neurogenic* OR neurologic*) adj3 (bladder OR urin* OR incontinen* OR detrusor OR vesical)).ti,ab.
3.	(overactive* adj3 bladder).ti,ab.
4.	or/1-3
5.	Overactive bladder/ OR exp Enuresis/ OR exp Urine incontinence/ OR Urine retention/
6.	Nocturia/
7.	((bladder OR detrusor) adj1 overactiv*).ti,ab.
8.	((bladder OR urin*) adj1 (incontinen* OR leakage OR wetting)).ti,ab.
9.	(lower urinary tract symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia).ti,ab.
10.	((urin* OR bladder OR voiding OR micturation) adj3 (disorders* OR symptom* OR urgency OR incontinence OR dysfunction)).ti,ab.
11.	((incomplet* OR impair*) adj2 bladder empt*).ti,ab.
12.	(bladder adj (obstruct* OR control OR management)).ti,ab.
13.	(urin* adj2 (retent* OR retain*)).ti,ab.
14.	resid* urine.ti,ab.
15.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab.
16.	exp Urinary tract infection/
17.	exp Urogenital tract inflammation/
18.	exp Urinary tract inflammation/
19.	Bacteriuria/

20.	Asymptomatic bacteriuria/
21.	Pyuria/
22.	exp Prostatitis/
23.	(urinary tract infection* OR UTI* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*).ti,ab.
24.	exp Kidney failure/
25.	((renal OR kidney*) adj2 (insufficien* OR impair* OR failure*)).ti,ab.
26.	glomerul* filtration*.ti,ab,hw.
27.	Health care survey/
28.	exp Self care/
29.	Patient compliance/
30.	Patient satisfaction/
31.	"Quality of life"/
32.	or/5-31
33.	exp Neurologic disease/
34.	exp Nervous system neoplasms/
35.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab.
36.	(spinal cord adj2 (injur* OR trauma OR disease*)).ti,ab.
37.	(spinal adj2 (shock OR abnormalit*)).ti,ab.
38.	(multiple sclerosis OR parkinson* OR stroke* OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab.
39.	(brain adj2 (injur* OR tumo?r*)).ti,ab.
40.	(neurolog* adj4 spinal).ti,ab.
41.	(diabet* adj3 neuropath*).ti,ab.
42.	or/33-41
43.	32 and 42
44.	4 OR 43
45.	Limit 44 to english language
46.	letter.pt.
47.	Letter/
48.	editorial.pt.
49.	note.pt.
50.	Case report/
51.	Case study/
52.	conference abstract.pt.
53.	Animal/ not (Animal/ and Human/)
54.	Nonhuman/
55.	exp Animal studies/
56.	Animals, Laboratory/
57.	exp Experimental animal/
58.	exp Animal experiment/
59.	exp Animal model/
60.	exp Rodent/
61.	or/46-60
62.	45 not 61

63.	((client* OR patient* OR user* OR carer* OR consumer* OR customer* OR health) adj2 (information* OR educat* OR knowledge)).ti,ab,hw.
64.	(information* adj (need* OR requirement* OR support* OR seek* OR access* OR disseminat* OR service*)).ti,ab,hw.
65.	(patient* adj3 (literature OR leaflet* OR booklet* OR pamphlet* OR interview* OR questionnaire* OR survey* OR handout* OR internet OR website* OR web based)).ti,ab.
66.	exp Telehealth/
67.	Telephone/
68.	Access to information/
69.	or/63-68
70.	62 and 69

1 **Cinahl search terms**

S1	(MH "Bladder, Neurogenic")
S2	neurogenic* n3 bladder OR neurogenic* n3 urin* OR neurogenic* n3 incontinen* OR neurogenic* n3 detrusor
S3	neurologic* n3 bladder OR neurologic* n3 urin* OR neurologic* n3 incontinen* OR neurologic* n3 detrusor
S4	overactiv* n1 bladder
S5	S1 OR S2 OR S3 OR S4
S6	MH overactive bladder OR mh enuresis+ OR mh urinary incontinence+ OR MH urinary retension
S7	lower urinary tract symptom* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia
S8	urin* n3 disorder* OR urin* n3 symptom* OR urin* n3 urgency OR urin* n3 incontinen* OR urin* n3 dysfunction*
S9	bladder* n3 disorder* OR bladder* n3 symptom* OR bladder* n3 urgency OR bladder* n3 incontinen* OR bladder* n3 dysfunction*
S10	voiding* n3 disorder* OR voiding* n3 symptom* OR voiding* n3 urgency OR voiding* n3 incontinen* OR voiding* n3 dysfunction*
S11	incomplet* n2 bladder empt* OR impair* n2 bladder empt*
S12	bladder n1 obstruct* OR bladder n1 control OR bladder n1 management
S13	urin* n2 retent* OR urin* n2 retain*
S14	resid* urine
S15	(weak OR underactiv OR overactive*) and (detrusor OR lower urinary tract OR bladder)
S16	(hyper-reflex* OR hypereflex* OR hyperreflex*) and (detrusor OR lower urinary tract OR bladder)
S17	(MH "Urinary Tract Infections+")
S18	(MH "Pyelonephritis")
S19	(MH "Cystitis+")
S20	(MH "Urethritis")
S21	(MH "Prostatitis")
S22	urinary tract infection* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*
S23	renal n2 insufficien* OR renal n2 impair* OR renal n2 failure*
S24	kidney n2 insufficien* OR kidney n2 impair* OR kidney n2 failure*
S25	glomerul* filtration*
S26	(MH "Patient Compliance+")

S27	(MH "Patient Satisfaction")
S28	(MH "Quality of Life")
S29	(MH "Continuity of Patient Care")
S30	(MH "Self Care")
S31	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30
S32	MH nervous system diseases+ OR MH nervous system neoplasms+
S33	neurological n2 impairment OR neurological n2 disease* OR neurological n2 disorder*
S34	spinal cord n2 injur* OR spinal cord n2 trauma OR spinal cord n2 disease*
S35	spinal n2 shock OR spinal n2 abnormalit*
S36	multiple sclerosis OR parkinson* OR stroke OR dementia OR alzheimer* OR cerebral palsy OR hydrocephalus OR spina bifida OR hydronephro* OR dyssynergi* OR myelodysplas*
S37	brain n2 injur* OR brain n2 tumor* OR brain n2 tumour*
S38	neurolog* n4 spinal
S39	diabet* OR neuropath*
S40	S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S41	S31 and S40
S42	S5 OR S41
S43	information* n2 need* OR information* n2 requirement* OR information* n2 support* OR information* n2 seek* OR information* n2 access* OR information* n2 disseminat*
S44	patient* n3 information* OR patient* n3 knowledge OR patient* n3 educat*
S45	carer* n3 information* OR carer* n3 knowledge OR carer* n3 educat* OR health* n3 information* OR health* n3 educat*
S46	patient* n3 literature OR patient* n3 leaflet* OR patient* n3 booklet* OR patient* n3 pamphlet* OR patient* n3 questionnaire* OR patient* n3 survey* OR patient* n3 handout* OR patient* n3 internet OR patient* n3 website*
S47	(MH "Access to Information+")
S48	(MH "Pamphlets")
S49	(MH "Telemedicine") OR (MH "Telehealth+")
S50	S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49
S51	S42 and S50
S52	English language and exclude Medline
S53	S51 and S52

1 **Cochrane search terms**

#1	MeSH descriptor Urinary Bladder, Neurogenic explode all trees
#2	(neurogenic* OR neurologic* OR spastic OR atonic OR overactiv*) NEAR/3 (bladder OR incontinen* OR detrusor OR urin*)
#3	(#1 OR #2)
#4	MeSH descriptor Nocturia explode all trees
#5	MeSH descriptor Urinary Bladder, Overactive explode all trees
#6	MeSH descriptor Enuresis explode all trees
#7	MeSH descriptor Urinary Incontinence explode all trees
#8	MeSH descriptor Urinary Retention explode all trees
#9	("lower urinary tract symptom*" OR "urinary symptom*" OR LUTS OR "irritable bladder" OR bedwetting OR enuresis OR nocturia):ti,ab

#10	((urin* OR bladder OR voiding OR micturation) NEAR/3 (disorder* OR symptom* OR urgency OR incontinence OR dysfunction)):ti,ab
#11	((incomplete* OR impair*) NEXT "bladder emptying"):ti,ab
#12	(bladder NEXT (obstruct* OR control OR management OR compliance)):ti,ab
#13	("urinary retention" OR "residual urine"):ti,ab
#14	(urin* NEAR/2 (retention OR retain* OR resid*)):ti,ab
#15	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) NEAR (detrusor OR "lower urinary tract" OR bladder)):ti,ab
#16	MeSH descriptor Urinary Tract Infections, this term only
#17	MeSH descriptor Bacteriuria, this term only
#18	MeSH descriptor Pyuria, this term only
#19	MeSH descriptor Pyelonephritis, this term only
#20	MeSH descriptor Cystitis explode all trees
#21	MeSH descriptor Urethritis, this term only
#22	MeSH descriptor Prostatitis, this term only
#23	(urinary tract infection* OR bacteriuria* OR pyuria* OR pyelonephriti* OR cystiti* OR urethriti* OR prostatiti*):ti,ab
#24	MeSH descriptor Renal Insufficiency explode all trees
#25	((renal OR kidney*) NEAR/2 (insufficien* OR impair* OR failure*)):ti,ab
#26	(glomerul* NEXT filtration):ti,ab,hw
#27	MeSH descriptor Health Care Surveys, this term only
#28	MeSH descriptor Patient Compliance explode all trees
#29	MeSH descriptor Patient Satisfaction, this term only
#30	MeSH descriptor Quality of Life, this term only
#31	MeSH descriptor Continuity of Patient Care, this term only
#32	MeSH descriptor Self Care, this term only
#33	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32
#34	MeSH descriptor Nervous System Diseases explode all trees
#35	(neurological NEAR/2 (impair* OR disease* OR disorder*)):ti,ab
#36	(spinal cord NEAR/2 (injur* OR trauma* OR disease*)):ti,ab
	spinal NEAR/2 (shock* OR abnormalit*):ti,ab
#37	(brain NEAR/2 (injur* OR tumor* OR tumour* OR lesion*)):ti,ab
#38	myelopathy:ti,ab
#39	(neurolog* NEAR/4 spinal):ti,ab
#40	(diabet* NEAR/3 neuropath*):ti,ab
#41	(hydronephrosis OR dyssynergi* OR myelodysplas*):ti,ab
#42	("multiple sclerosis" OR parkinson* OR stroke* OR dementia OR alzheimer* OR "cerebral palsy" OR hydrocephalus OR "spina bifida"):ti,ab
#43	(#34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42)
#44	(#3 OR (#33 AND #43))
#45	MeSH descriptor Telemedicine, this term only
#46	MeSH descriptor Telephone explode all trees
#47	MeSH descriptor Access to Information, this term only
#48	MeSH descriptor Self-Help Groups, this term only

#49	MeSH descriptor Publications, this term only
#50	MeSH descriptor Pamphlets, this term only
#51	patient education handout:pt
#52	(information* NEXT (need* OR requirement* OR support* OR seek* OR access* OR disseminat*)):ti,ab,hw
#53	((client* OR patient* OR user* OR carer* OR consumer* OR customer* OR health) NEAR/2 (information* OR educat* OR knowledge)):ti,ab,hw
#54	(patient* NEAR/3 (literature OR leaflet* OR booklet* OR pamphlet* OR questionnaire* OR survey* OR handout* OR internet OR website*)):ti,ab
#55	(#45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54)
#56	(#44 AND #55)

1 **PsycINFO search terms**

1.	((neurogenic* OR neurologic*) AND (bladder OR urin* OR incontinent* OR detrusor)).ti,ab
2.	(overactiv* adj3 bladder).ti,ab
3.	exp Urinary incontinence/
4.	((lower urinary tract symptom* OR urinary symptom* OR LUTS OR irritable bladder OR bedwetting OR enuresis OR nocturia)).ti,ab
5.	(((incomplet* OR impair*) adj2 bladder AND empt*)).ti,ab
6.	((bladder adj2 (obstruct* OR control OR management))).ti,ab
7.	((urin* adj2 (retention OR retain*))).ti,ab
8.	"resid* urine".ti,ab
9.	((overactiv* OR weak OR underactiv* OR hyperreflex* OR hyper-reflex*) adj3 (detrusor OR lower urinary tract OR bladder)).ti,ab
10.	((renal OR kidney*) adj2 (insufficien* OR impair* OR failure*)).ti,ab
11.	"urinary tract infection*".ti,ab
12.	exp Treatment compliance/
13.	Client satisfaction/
14.	Self care skills/
15.	"Continuum of care"/
16.	"Quality of life"/
17.	2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18.	(nervous AND system AND diseases).ti,ab
19.	exp Nervous system disorders/
20.	Nervous system neoplasms/
21.	(neurological adj2 (impairment OR disease* OR disorder*)).ti,ab
22.	("spinal cord" adj2 (injur* OR trauma OR disease*)).ti,ab
23.	(spinal adj2 (shock OR abnormalit*)).ti,ab
24.	("multiple sclerosis" OR parkinson* OR stroke* OR dementia OR alzheimer* OR "cerebral palsy" OR hydrocephalus OR spina AND bifida OR myelopath* OR hydronephro* OR dyssynergi* OR myelodysplas*).ti,ab
25.	(brain adj2 (injur* OR tumor* OR tumour)).ti,ab
26.	(neurolog* adj4 spinal).ti,ab
27.	(diabet* adj3 neuropath*).ti,ab
28.	18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27
29.	17 AND 28
30.	1 OR 29

31.	(patient* adj3 (literature OR leaflet* OR booklet* OR pamphlet* OR questionnaire* OR survey* OR handout* OR internet OR website*)).ti,ab
32.	((client* OR patient* OR user* OR carer* OR consumer* OR customer* OR health) adj3 (information* OR educat* OR knowledge)).ti,ab
33.	Client education/ OR Health knowledge/ OR Health literacy/ OR Information seeking/
34.	31 OR 32 OR 33
35.	30 AND 34 [Limit to: English Language]

C.4 Economic searches

Economic searches were run in Medline and Embase by combining the standard population with the economic filter and limiting by date range. Economic searches were executed in the NHS EED and HTA (CRD) databases by simply running the standard population without a date limitation. Search terms for the CRD and HEED databases are given below.

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Neurological disease AND incontinence			Economic [only Embase and Medline]	2009 – 10/01/12 (Medline and Embase) All years – 10/01/12 (CRD and HEED)

HEED search terms

1.	AX=neurogenic* OR neurologic*
2.	AX=bladder OR urin* OR incontinent* OR detrusor
3.	CS=1 AND 2

CRD search terms

1.	MeSH Urinary Bladder, Neurogenic EXPLODE
2.	(neurogenic* OR neurologic*) AND (bladder OR urin* OR incontinen* OR detrusor)
3.	(overact* OR obstruct* OR control OR manage* OR complian*) AND bladder
4.	#1 OR #2 OR #3

Appendix D: Review Protocols

D.1 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care for the treatment of incontinence due to neurological disease? 88

D.2 Do prophylactic antibiotics compared with a)no treatment b) other antibiotic reduce the risk of symptomatic urinary tract infections? 89

D.3 What is the safety and efficacy of antimuscarinics compared with a) placebo or treatment as usual b) other antimuscarinics for the treatment of incontinence due to neurological disease/ overactive bladder due to neurological disease? 90

D.4 Do behavioural management programmes (timed voiding, voiding on request, prompted voiding, bladder retraining, habit retraining, urotherapy) compared with a) each other b) usual care, improve outcomes? 91

D.5 What is the safety and efficacy of detrusor injections of botulinum toxin compared with a) usual care b) antimuscarinics in neurological disease 92

D.6 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? And, what is the quality of life associated with the above. 93

D.7 Does the use of the following direct treatment: Clinical assessment, Urine culture, Residual urine estimate, Bladder diary/frequency volume chart? 94

D.8 What is the efficacy of the ileal conduit diversion compared with usual care in neurological disease? 95

D.9 What is the safety and efficacy of augmentation cystoplasty compared with a) botulinum toxin b) usual care in neurological disease? 96

D.10 For people with incontinence due to neurological disorders, what are their experiences of access to services, and of assessment and treatment? 97

D.11 Does the provision of information and support regarding the different management systems improve patient outcomes? 98

D.12 Does monitoring or do surveillance protocols improve patient outcomes? 99

D.13 Does pelvic floor muscle training with or without electrical stimulation or biofeedback compared with treatment as usual, improve outcomes? 100

D.14 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the short and long-term use of intermittent catheterisation, indwelling catheters and penile sheath collection/pads? 101

D.15 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services? 102

D.16 What criteria or signs/symptoms should be used to refer patients for specialist assessment? 103

D.17 What is the safety and efficacy of artificial urinary sphincter compared with other treatments in neurological disease? 104

D.18 What is the safety and efficacy of urethral tape and sling surgery compared with usual care in neurological disease? 105

D.19 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services? 106

D.20 Does the use of the following direct treatment or stratify risk (of renal complications such as hydronephrosis): Filling cystometry, Leak point pressure measurements, Pressure-flow studies of voiding, Video urodynamics? 107

D.21 What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease? 108

D.22 Health economic review protocol 109

D.1 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care for the treatment of incontinence due to neurological disease?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	Alpha adrenergic antagonists: Alfuzosin hydrochloride, Doxazosin, Indoramin, Prazosin, Tamsulosin hydrochloride, Terazosin
Comparison	Other alpha adrenergic antagonists Placebo/Usual care
Outcomes	Frequency of voiding by day and night Adverse events, including postural hypotension and other unscheduled hospital admissions. Urgency Quality of life Symptoms relating to bladder emptying, for example poor urinary stream Treatment adherence Q-max (maximum flow rate) Residual urine volume
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	As above.
The review strategy	RCTs for adults Observational studies for children. All study types for adverse events
Key Paper	
Analysis	

D.2 Do prophylactic antibiotics compared with a)no treatment b) other antibiotic reduce the risk of symptomatic urinary tract infections?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	Symptomatic urine infections Adverse events
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Key papers	
The review strategy	RCTs
Analysis	

D.3 What is the safety and efficacy of antimuscarinics compared with a) placebo or treatment as usual b) other antimuscarinics for the treatment of incontinence due to neurological disease/ overactive bladder due to neurological disease?

Review Protocol - IND	
Component	Description
Population	Neurological disease Patients with neurogenic detrusor over activity Patients with reduced bladder compliance
Intervention	Antimuscarinics
Comparison	Placebo or treatment as usual Other antimuscarinics
Outcomes	Frequency of voiding by day and night. Number of incontinence episodes per week. Quality of life. Patients and carers' perception of symptoms. Adverse events, including urinary tract infections, renal complications and unscheduled hospital admissions. Treatment adherence Kidney function (hydronephrosis) Maximum cystometric capacity Bladder compliance Residual urine
Exclusion	Incontinence due to non-neurological cause (abstracts selected only if entire population specified as neurological) N < 20
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years Studies will be restricted to English language only
Search terms	Anticholinergics: Darifenacin, flavoxate hydrochloride, oxybutynin hydrochloride, propantheline bromide, propiverine hydrochloride, solifenacin succinate, tolterodine tartrate, tropsium chloride, atropine Antimuscarinics are also known as anticholinergics
The review strategy	RCTs and for adults and Kidney function and adverse events observational studies for adults. RCTs and observational studies for children
Analysis	Subgroups By condition Adults analysed separately to children

D.4 Do behavioural management programmes (timed voiding, voiding on request, prompted voiding, bladder retraining, habit retraining, urotherapy) compared with a) each other b) usual care, improve outcomes?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	Frequency of voiding by day and night No. of incontinence episodes per week Patient and carer perception of symptoms Quality of life Treatment adherence Adverse events
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	RCTs
Analysis	

D.5 What is the safety and efficacy of detrusor injections of botulinum toxin compared with a) usual care b) antimuscarinics in neurological disease

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	Botulinum toxin A and B
Comparison	Usual care antimuscarinics
Outcomes	Increased bladder capacity Residual urine Frequency of voiding by day and night. Number of incontinence episodes per week.. Urgency. Quality of life. Adverse events, including urinary tract infections, unscheduled hospital admissions, generalised muscle weakness Treatment continuance. Kidney function.
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	RCT's
Analysis	

D.6 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? And, what is the quality of life associated with the above.

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	Long term risks as specified in question Include kidney, bladder and renal stones Calculi is another term for stones Include Cystolithiasis Other terms for stone formation include urolithiasis, renal lithiasis and nephrolithiasis Include Pyelonephritis
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	
Analysis	

D.17 Does the use of the following direct treatment: Clinical assessment, Urine culture, Residual urine estimate, Bladder diary/frequency volume chart?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	As above
Comparison	None
Outcomes	Change in management of the patient's condition.
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	Observational studies.
The review strategy	
Analysis	

D.8 What is the efficacy of the ileal conduit diversion compared with usual care in neurological disease?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	Ileal conduit diversion
Comparison	Usual care
Outcomes	Quality of life. Patients and carers' perception of symptoms. Adverse events, including urinary tract infections, renal complications, pyocystis, complications with the stoma (eg parastomal hernia) and unscheduled hospital admissions.
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Kay papers	
The review strategy	Observational studies
Analysis	

D.9 What is the safety and efficacy of augmentation cystoplasty compared with a) botulinum toxin b) usual care in neurological disease?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	Augmentation cystoplasty
Comparison	Usual care
Outcomes	Frequency of voiding by day and night. Number of incontinence episodes per week. Severity of incontinence. Symptoms relating to bladder emptying, for example poor urinary stream. Quality of life. Patients and carers' perception of symptoms. Adverse events, including urinary tract infections, renal complications, bladder stones, metabolic complications, cancer and unscheduled hospital admissions. Kidney function.
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Key papers	
The review strategy	Observational studies
Analysis	

D.10 For people with incontinence due to neurological disorders, what are their experiences of access to services, and of assessment and treatment?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Key papers	
The review strategy	
Analysis	

D.11 Does the provision of information and support regarding the different management systems improve patient outcomes?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	Frequency of voiding by day and night No. of incontinence episodes per week Symptoms related to bladder emptying eg poor urinary stream Patient and carer perception of symptoms Quality of life Kidney function (hydronephrosis) Maximum cystometric capacity Bladder compliance Residual urine Treatment adherence Adverse events
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Key papers	
The review strategy	
Analysis	

D.12 Does monitoring or do surveillance protocols improve patient outcomes?

Review Protocol - IND	
Component	Description
Population	Spina bifida,spinal cord injury and multiple sclerosis, anorectal malformations
Intervention	Ultrasound, renography, intravenous urograms, abdominal x-rays, urodynamics, blood tests, blood pressure
Comparison	
Outcomes	Quality of life. Kidney function. renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer unplanned hospital admissions
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	
Analysis	

D.13 Does pelvic floor muscle training with or without electrical stimulation or biofeedback compared with treatment as usual, improve outcomes?

Review Protocol - IND	
Component	Description
Population	MS and stroke
Intervention	
Comparison	
Outcomes	Frequency of voiding by day and night No. of incontinence episodes per week Quality of life Maximum cystometric capacity Residual urine Treatment adherence
Exclusion	children
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	
Analysis	

D.14 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the short and long-term use of intermittent catheterisation, indwelling catheters and penile sheath collection/pads?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	short and long-term use of intermittent catheterisation, indwelling catheters and penile sheath collection/pads?
Comparison	
Outcomes	renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer)
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	
Analysis	

D.15 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	Frequency of voiding by day and night No. of incontinence episodes per week Symptoms related to bladder emptying eg poor urinary stream Patient and carer perception of symptoms Quality of life Kidney function (hydronephrosis) Maximum cystometric capacity Bladder compliance Residual urine Treatment adherence Adverse events
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Key papers	
The review strategy	
Analysis	

D.16 What criteria or signs/symptoms should be used to refer patients for specialist assessment?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	
Analysis	

D.17 What is the safety and efficacy of artificial urinary sphincter compared with other treatments in neurological disease?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	Artificial urinary sphincter
Comparison	Other treatments
Outcomes	Frequency of voiding by day and night. Number of incontinence episodes per week. Severity of incontinence. Symptoms relating to bladder emptying, for example poor urinary stream. Quality of life. Patients and carers' perception of symptoms. Adverse events, including urinary tract infections, renal complications, bladder stones, infection of prosthesis, device failure and unscheduled hospital admissions.
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Key papers	
The review strategy	Observational studies
Analysis	

D.18 What is the safety and efficacy of urethral tape and sling surgery compared with usual care in neurological disease?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	Urethral tape and sling surgery
Comparison	Usual care
Outcomes	Frequency of voiding by day and night. Number of incontinence episodes per week. Severity of incontinence. Symptoms relating to bladder emptying, for example poor urinary stream. Quality of life. Patients and carers' perception of symptoms. Adverse events, including urinary tract infections, renal complications, bladder stones and unscheduled hospital admissions.
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
Key papers	
The review strategy	Observational studies
Analysis	

D.19 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services?

Review Protocol - IND	
Component	Description
Population	Neurological disease Patients <19 yrs
Intervention	Specialist Adolescent Care Services (transition management)
Comparison	Usual Care
Outcomes	Patient Experience Quality of Life Morbidity (renal impairment, incontinence, urinary tract infections) Continuity of Care Readmission to hospital
Exclusion	None
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	Transition management, transition pathways, transition clinics Adolescent
Key papers	Transition services for young people (Baron) Good practice in Transition services for young people Department of Health
The review strategy	Neurological population Other NICE guidance for Recs made in other areas
Analysis	

D.20 Does the use of the following direct treatment or stratify risk (of renal complications such as hydronephrosis): Filling cystometry, Leak point pressure measurements, Pressure-flow studies of voiding, Video urodynamics?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	None
Comparison	None
Outcomes	Change in management of the patient's condition.
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	Observational studies
The review strategy	
Analysis	

D.21 What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease?

Review Protocol - IND	
Component	Description
Population	Neurological disease
Intervention	
Comparison	
Outcomes	No. of incontinence episodes per week Patient and carer perception of symptoms Quality of life Kidney function (hydronephrosis) Treatment adherence Adverse events (UTI, catheter blockage) Successful trial without a catheter
Exclusion	
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL All years. Studies will be restricted to English language only
Search terms	
The review strategy	
Analysis	Include observational

D.22 Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify economic studies relevant to the review questions set out above.
Criteria	Populations, interventions and comparators as specified in the individual review protocols above. Must be a relevant economic study design (cost-utility analysis, cost-benefit analysis, cost-effectiveness analysis, cost-consequence analysis, comparative cost analysis).
Search strategy	An economic study search was undertaken using population specific terms and an economic study filter – see Appendix C.
Review strategy	Each study is assessed using the NICE economic evaluation checklist – NICE (2009) Guidelines Manual, Appendix H. **Inclusion/exclusion criteria** • If a study is rated as both 'Directly applicable' and 'Minor limitations' (using the NICE economic evaluation checklist) then it should be included in the guideline. An evidence table should be completed and it should be included in the economic profile. • If a study is rated as either 'Not applicable' or 'Very serious limitations' then it should be excluded from the guideline. It should not be included in the economic profile and there is no need to include an evidence table. • If a study is rated as 'Partially applicable' and/or 'Potentially serious limitations' then there is discretion over whether it should be included. The health economist should make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim being to include studies that are helpful for decision making in the context of the guideline and current NHS setting. Where exclusions occur on this basis, this should be noted in the relevant section of the guideline with references. Also exclude: • unpublished reports unless submitted as part of a call for evidence • abstract-only studies • letters • editorials • reviews of economic evaluations(a) • foreign language articles **Where there is discretion** The health economist should be guided by the following hierarchies. *Setting:* • UK NHS • OECD countries with predominantly public health insurance systems (e.g. France, Germany, Sweden) • OECD countries with predominantly private health insurance systems (e.g. USA, Switzerland) • Non-OECD settings (always 'Not applicable') *Economic study type:* • Cost-utility analysis • Other type of full economic evaluation (cost-benefit analysis, cost-effectiveness analysis, cost-consequence analysis) • Comparative cost analysis • Non-comparative cost analyses including cost of illness studies (always 'Not applicable') *Year of analysis:* • The more recent the study, the more applicable it is *Quality and relevance of effectiveness data used in the economic analysis:* • The more closely the effectiveness data used in the economic analysis matches with the studies included for the clinical review the more useful the analysis will be to decision making for the guideline.

(a) Recent reviews will not be reviewed but will be ordered to provide additional information and the bibliographies will be checked for relevant studies. Any additional studies found through this method will be ordered.

Appendix E: Flow charts of selected studies

E.1 What is the safety and efficacy of antimuscarincs compared with a) placebo/usual care b) other antimuscarinics? 112

E.2 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care in neurological disease? 113

E.3 Does the use of the following direct treatment : clinical assessment, urine culture, residual urine estimate, bladder diary/frequency volume chart. 114

E.4 Does the use of the following direct treatment or stratify risk (of renal complications such as hydronephrosis): Filling cystometry, leak point pressure measurements, pressure-flow studies of voiding, video urodynamics. 115

E.5 What criteria or signs/symptoms should be used to refer patients for specialist assessment? 115

E.6 What is the safety and efficacy of intravesical botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in neurological disease 116

E.7 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? What is the quality of life associated with the above? 117

E.8 Does monitoring or do surveillance protocols improve patient outcomes? 118

E.9 What is the safety and efficacy of augmentation cystoplasty compared with usual care in neurological disease? 119

E.10 Do behavioural management programmes (timed voiding, voiding on request, bladder retraining, habit retraining,) compared with a) each other b) usual care, improve outcomes? 120

E.11 Does pelvic floor muscle training with or without electrical stimulation or biofeedback compared with treatment as usual, improve outcomes? 121

E.12 What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease? Same search as for 'What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? What is the quality of life associated with the above?' 122

E.13 What is the safety and efficacy of urethral tape and sling surgery compared with usual care in neurological disease? 123

E.14 What is the safety and efficacy of artificial urinary sphincter compared with other treatments in neurological disease? 124

E.15 What is the efficacy of the ileal conduit diversion compared with usual care in neurological disease? 125

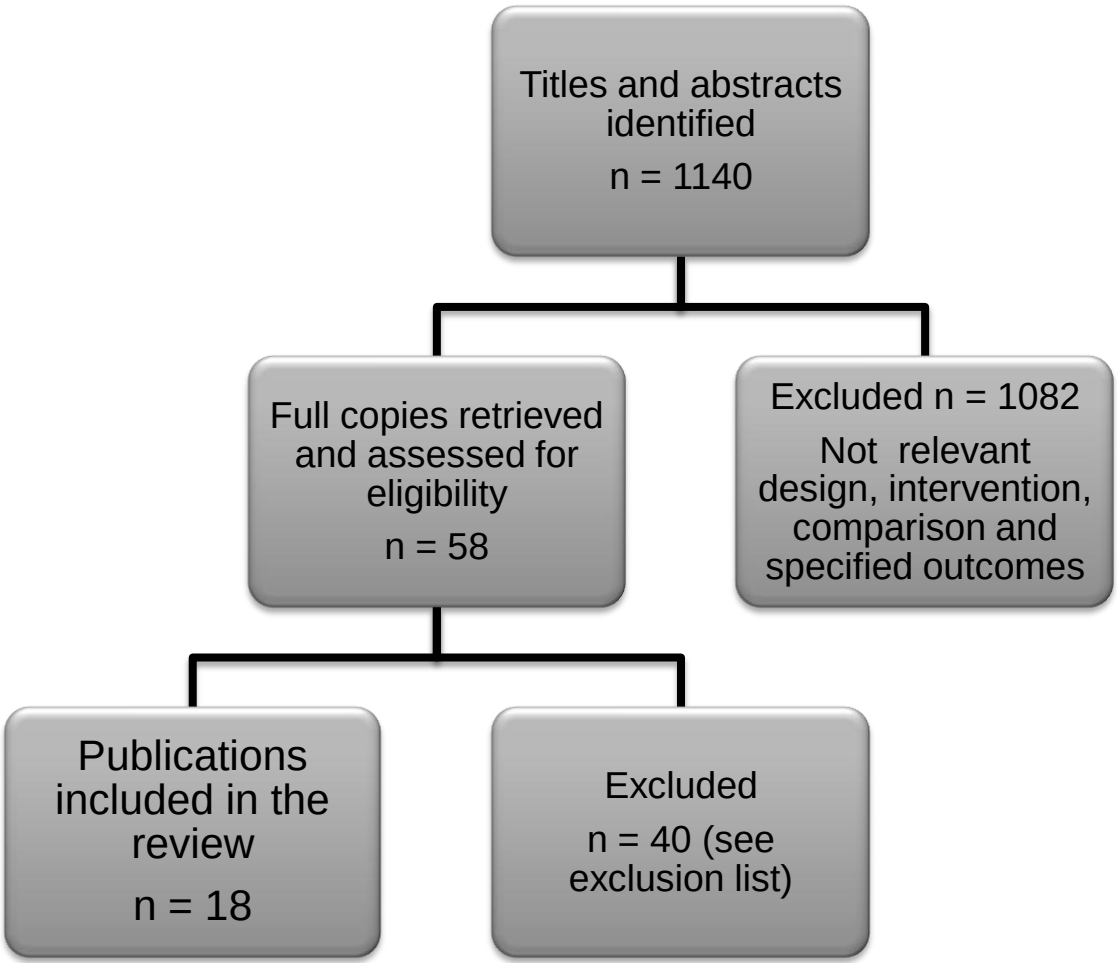
E.17 Do prophylactic antibiotics reduce the risk of symptomatic urinary tract infections? 126

E.19 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services? 127

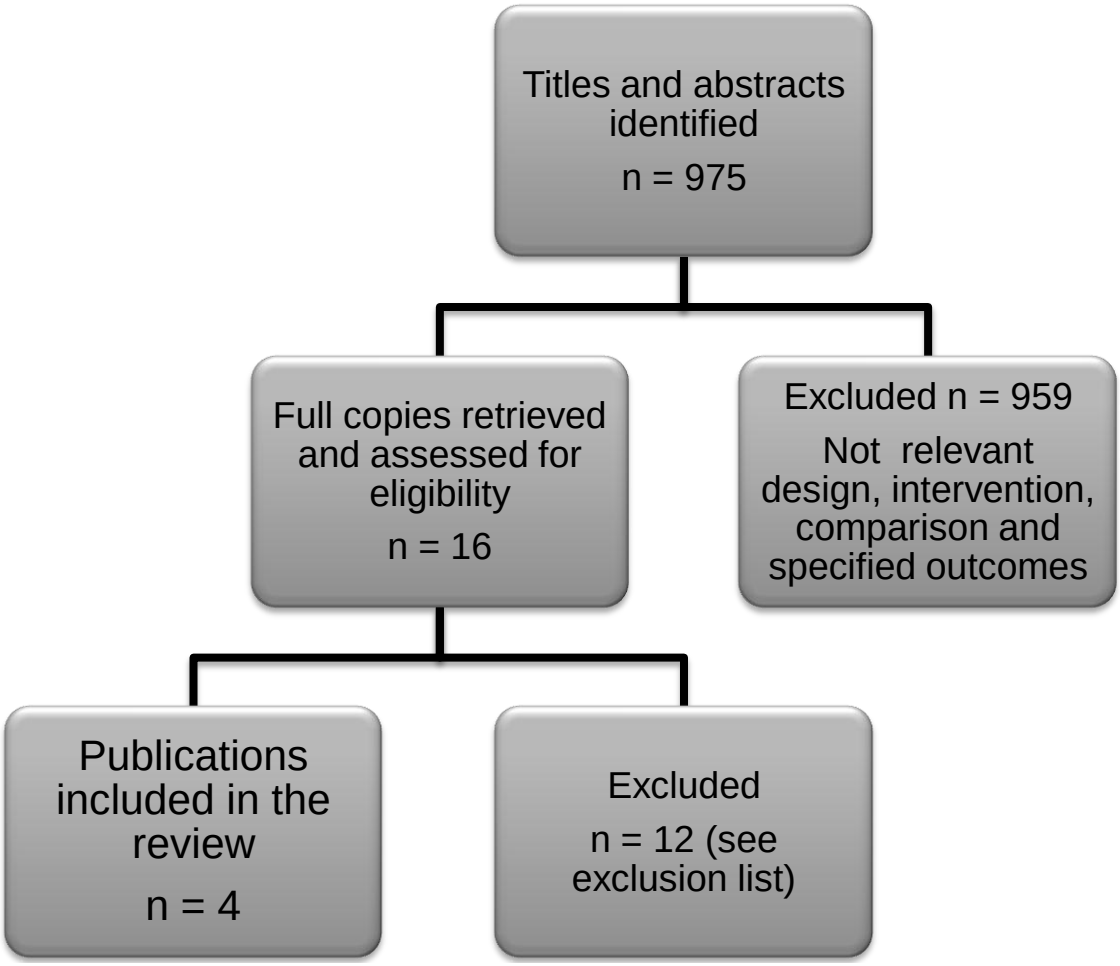
E.20 Does provision of information about the management of neurological lower urinary tract dysfunction improve patient outcomes?.....128

E.22 For patients and their carers with lower urinary tract dysfunction associated with neurological disorders, what are the experiences of access to and interaction with services, that address these issues?.....129

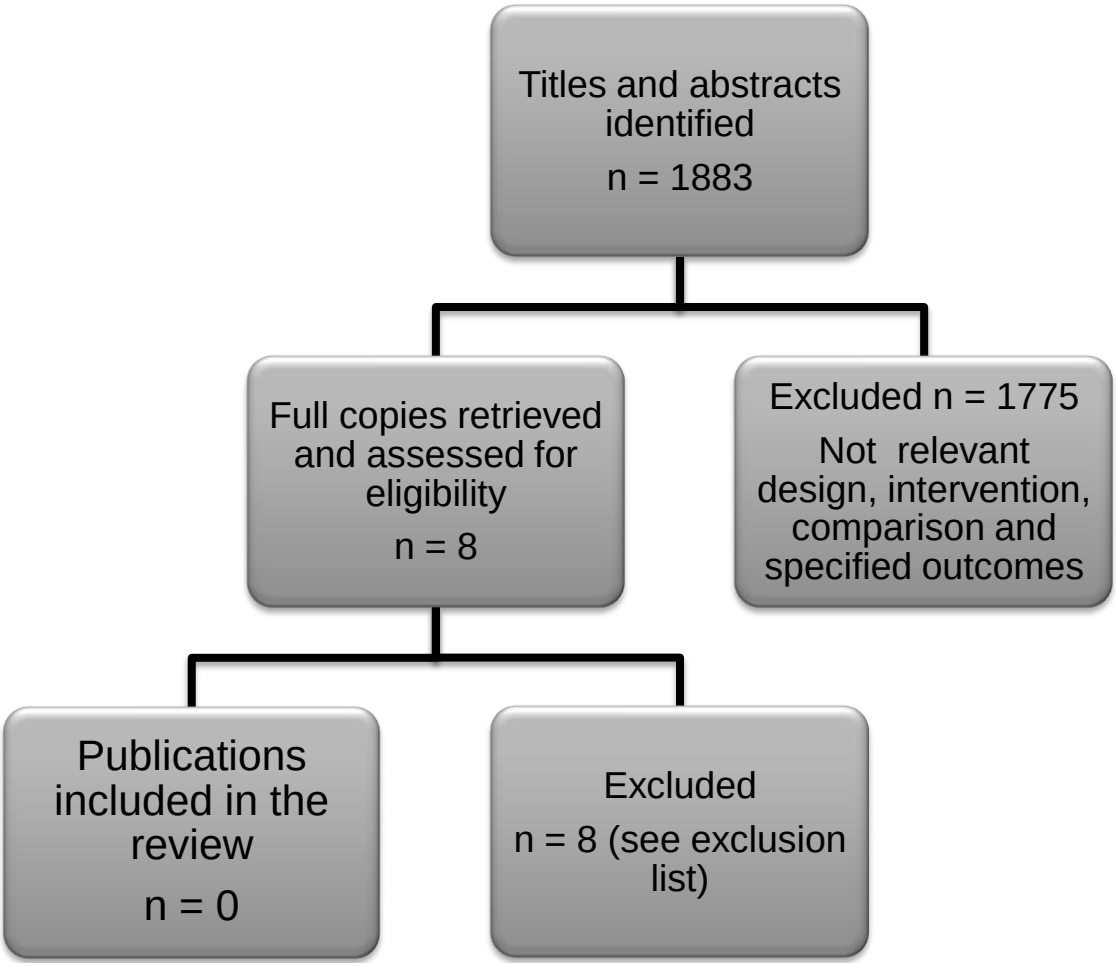
E.1 What is the safety and efficacy of antimuscarincs compared with a) placebo/usual care b) other antimuscarinics?



E.2 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care in neurological disease?



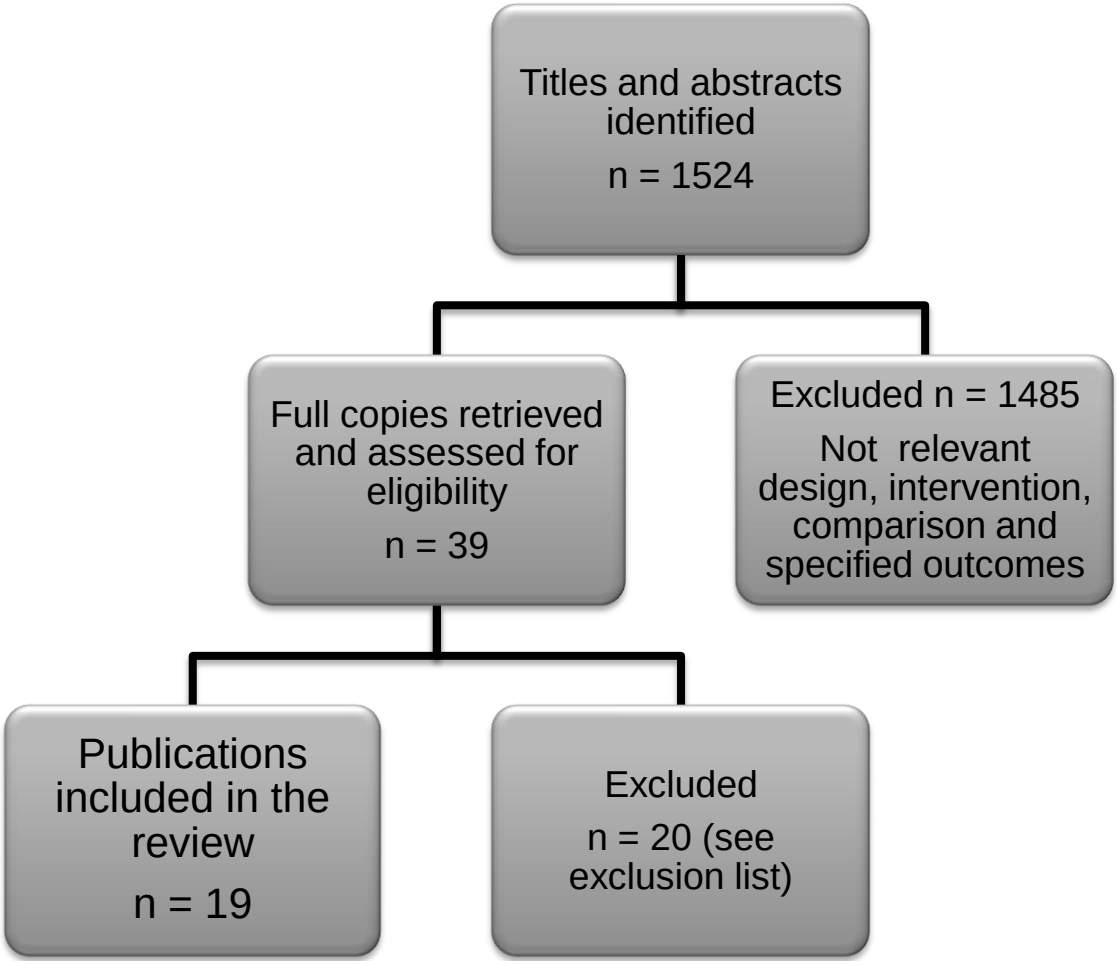
E.3 Does the use of the following direct treatment : clinical assessment, urine culture, residual urine estimate, bladder diary/frequency volume chart.



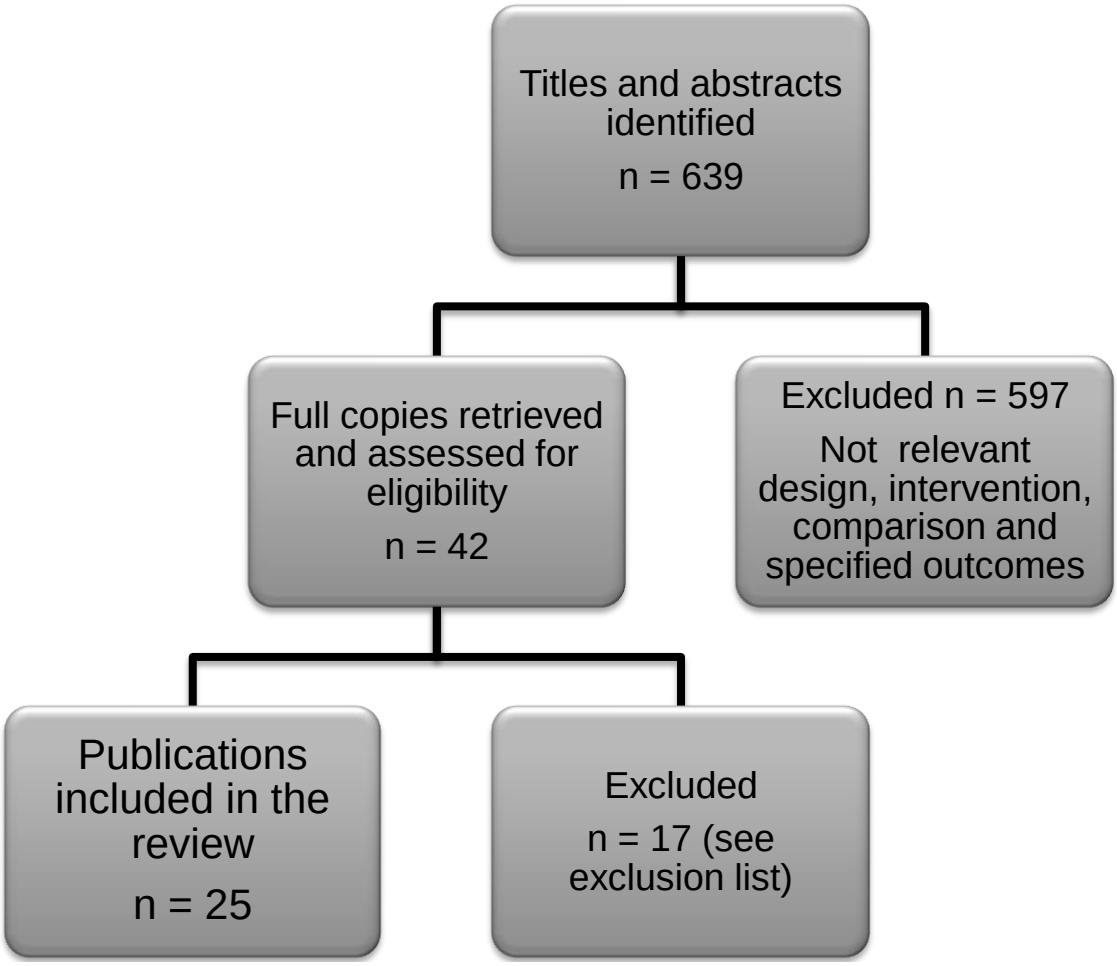
E.4 Does the use of the following direct treatment or stratify risk (of renal complications such as hydronephrosis): Filling cystometry, leak point pressure measurements, pressure-flow studies of voiding, video urodynamics.

E.5 What criteria or signs/symptoms should be used to refer patients for specialist assessment?

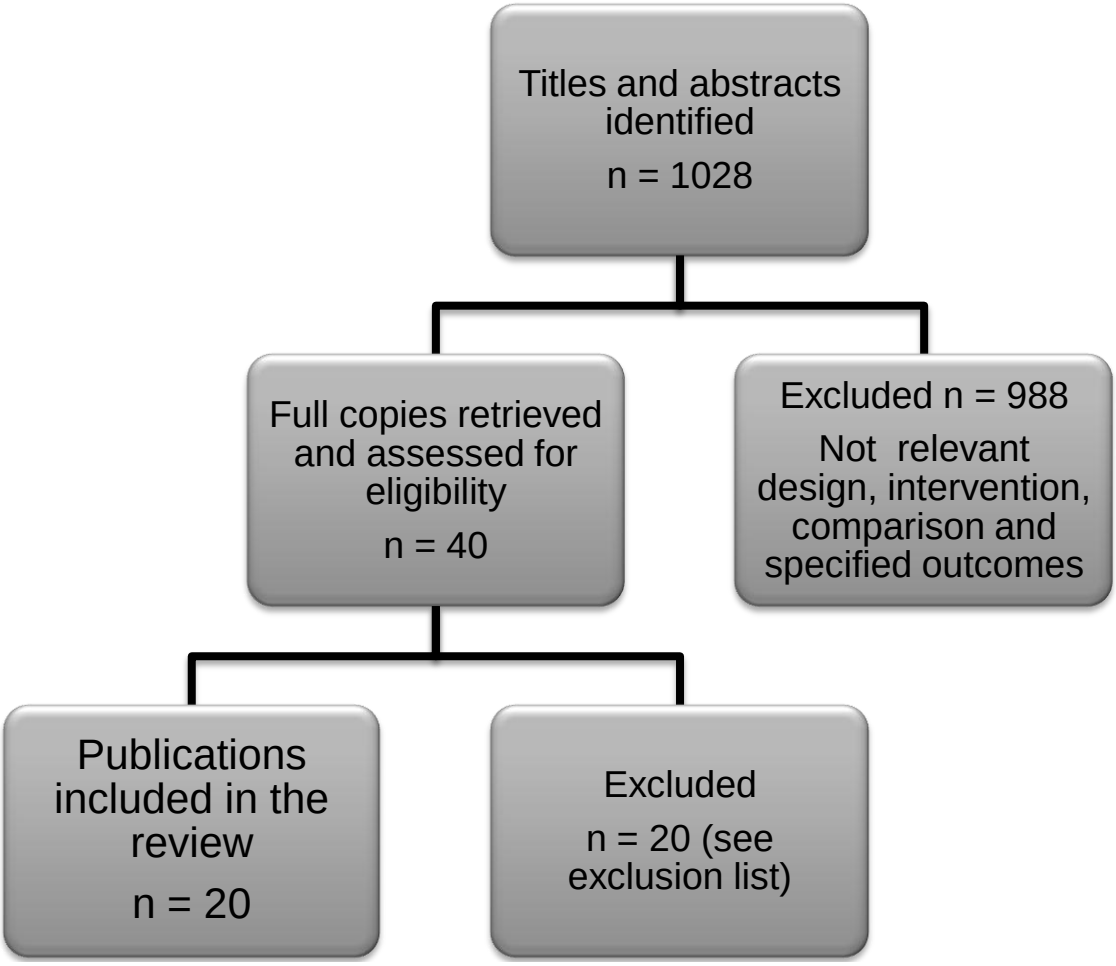
No search conducted



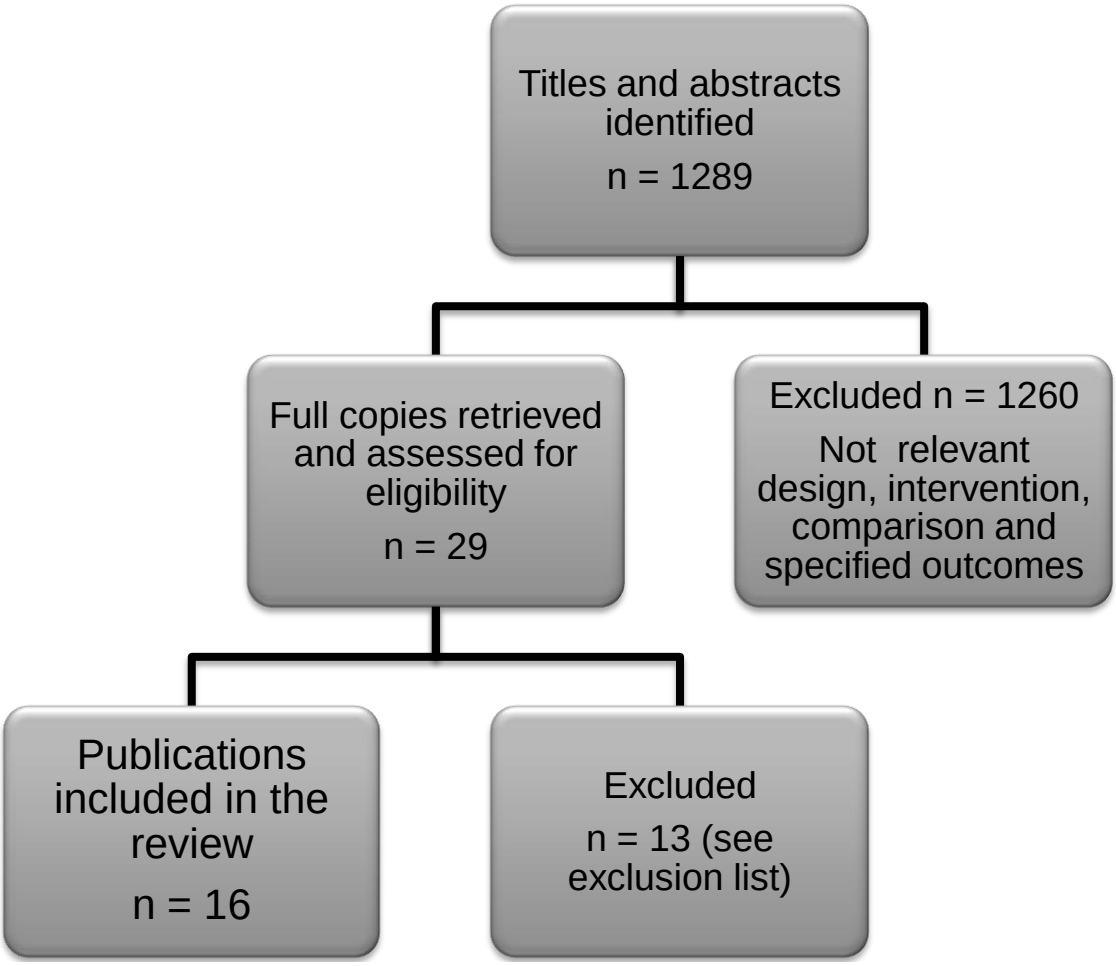
E.6 What is the safety and efficacy of intravesical botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in neurological disease



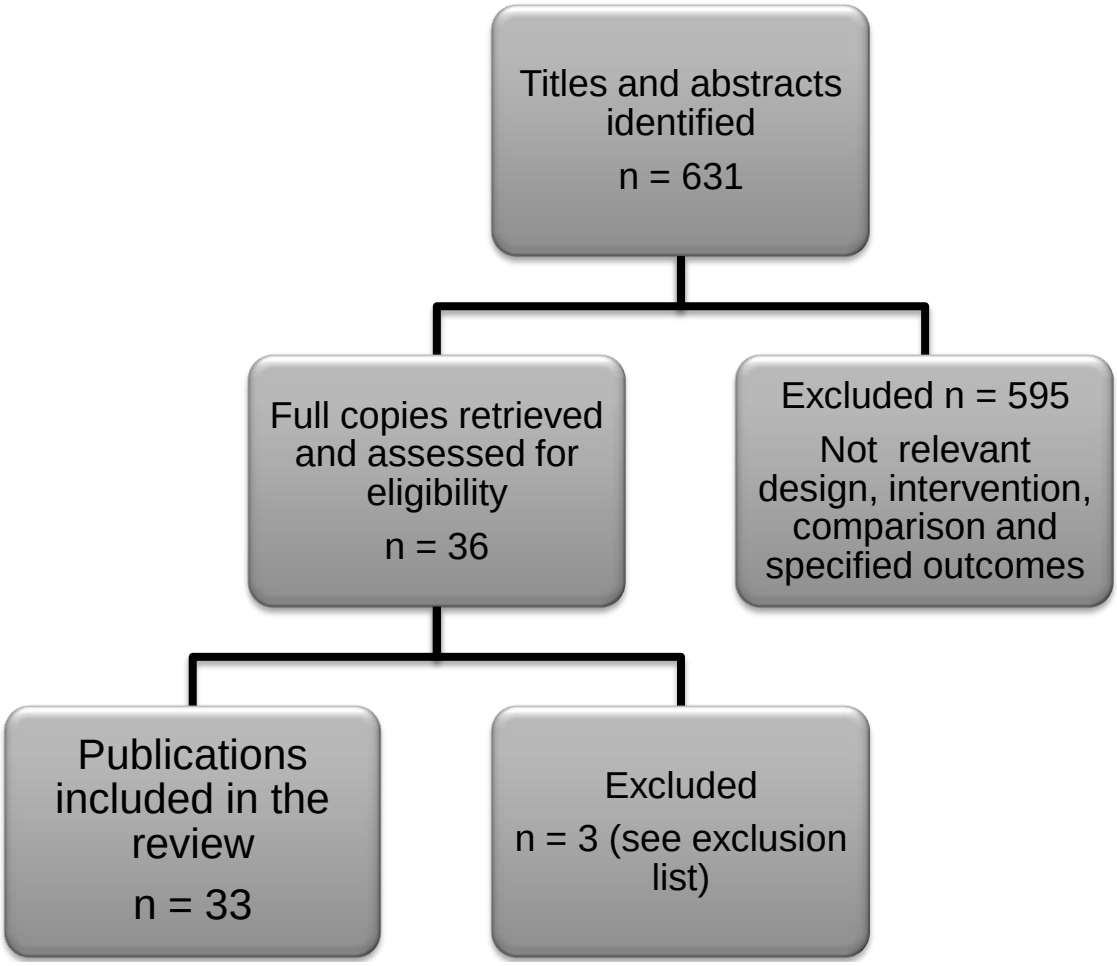
E.7 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? What is the quality of life associated with the above?



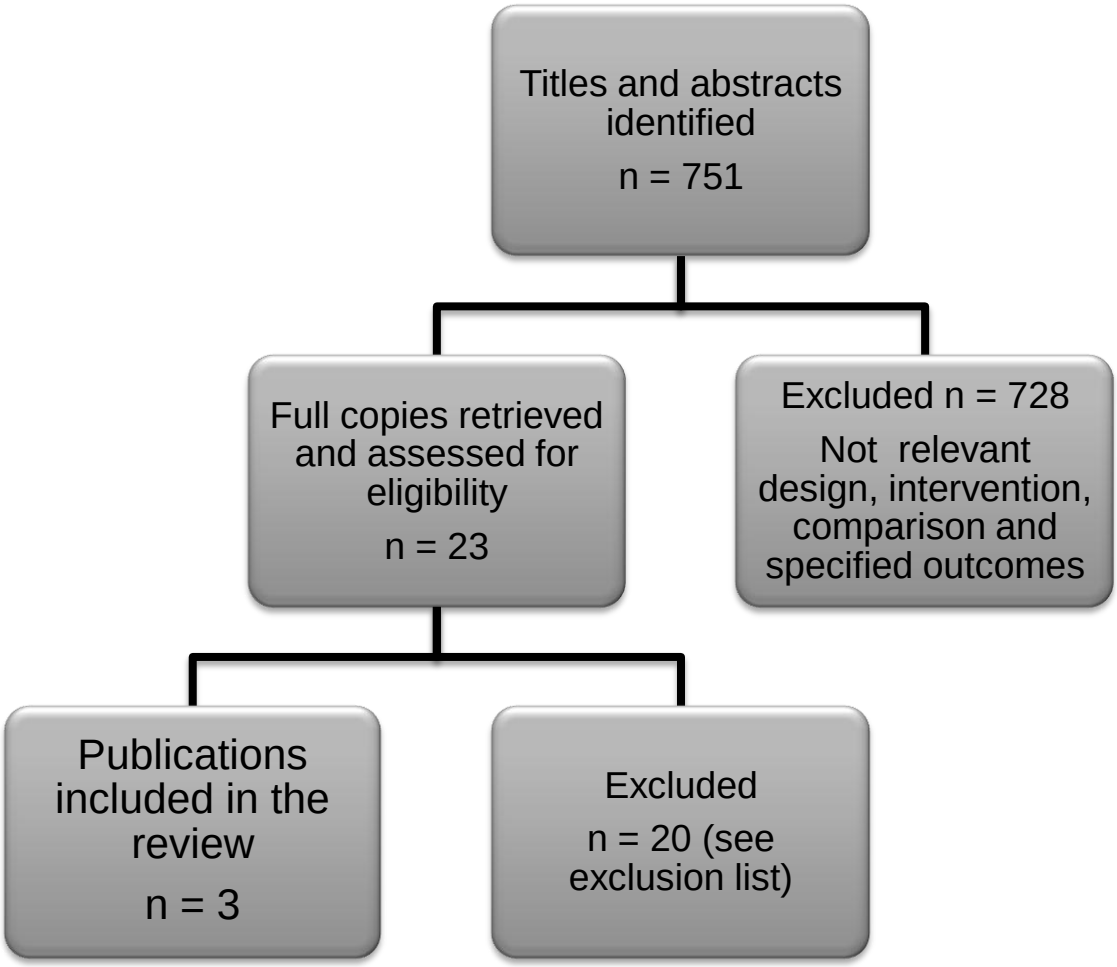
E.8 Does monitoring or do surveillance protocols improve patient outcomes?



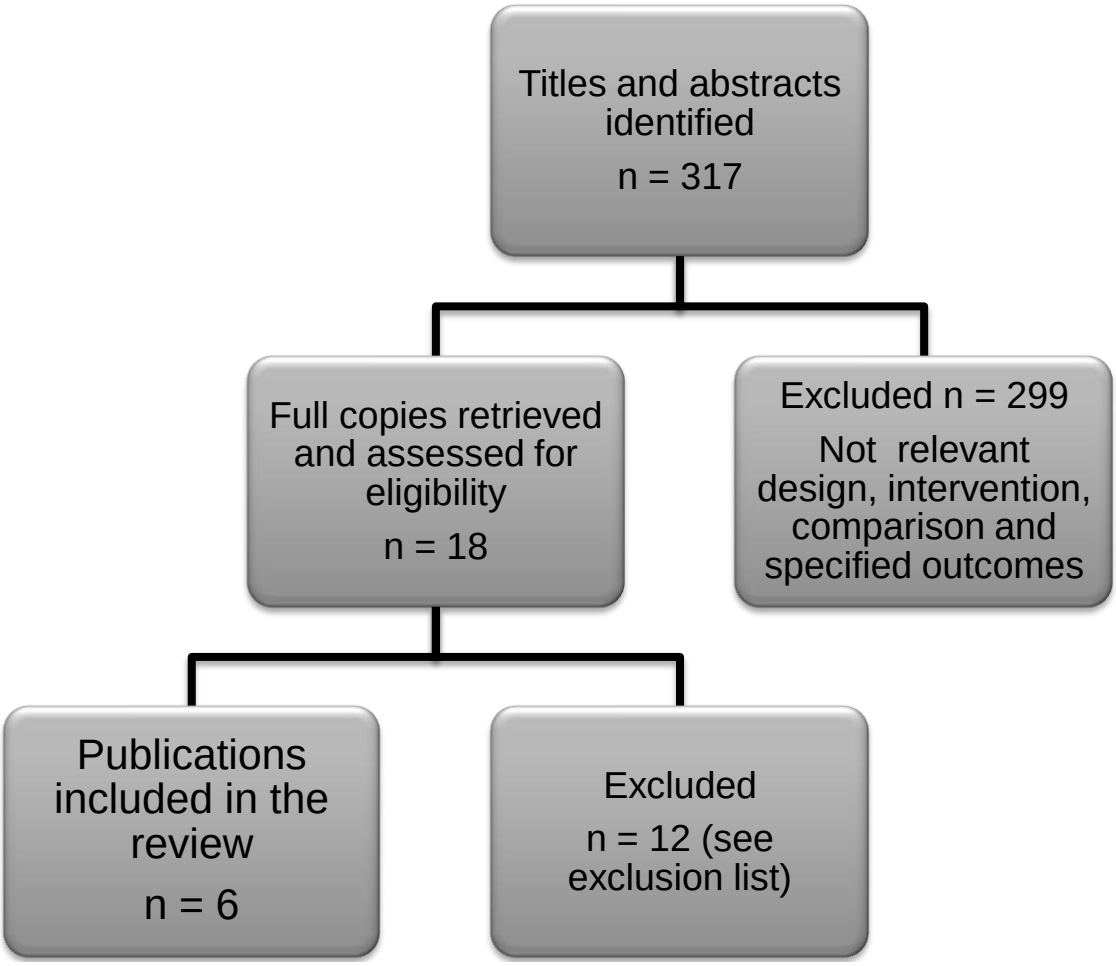
E.9 What is the safety and efficacy of augmentation cystoplasty compared with usual care in neurological disease?



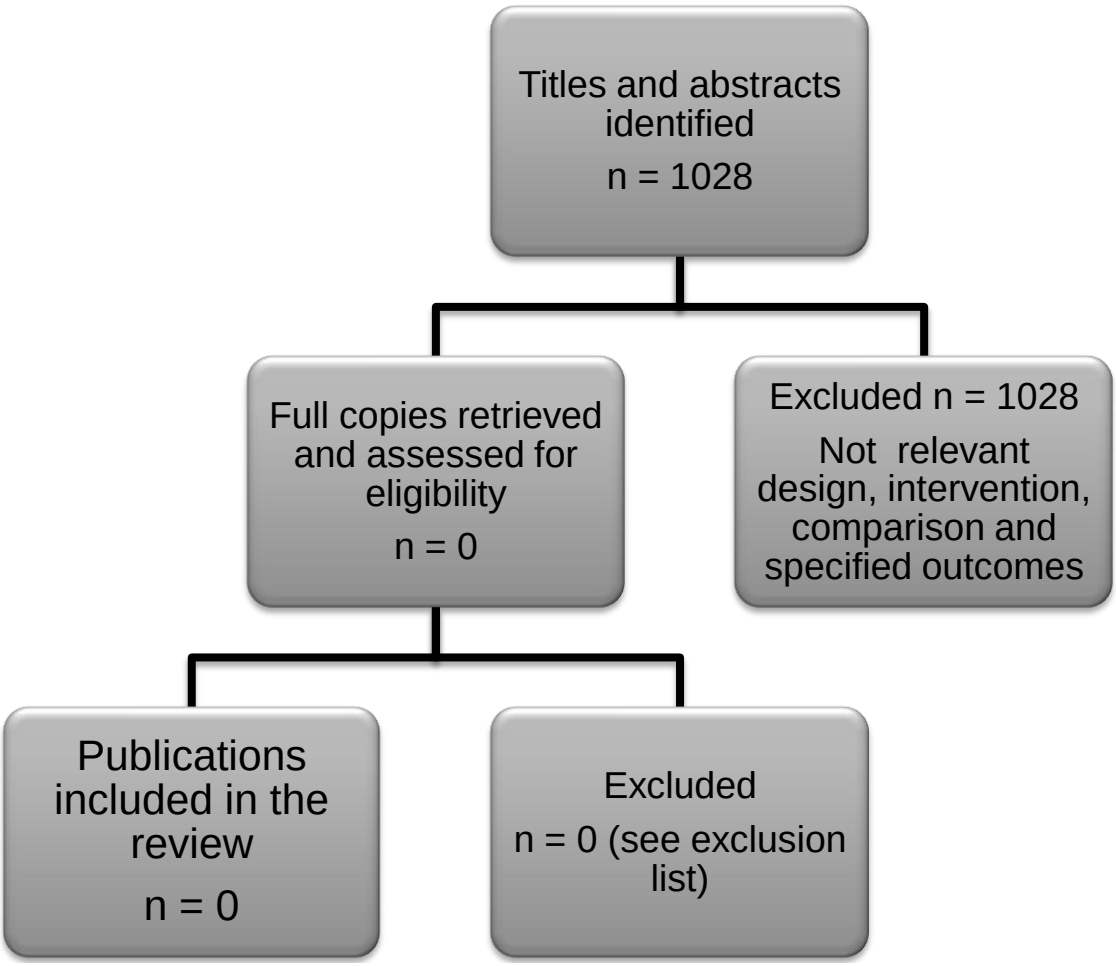
E.10 Do behavioural management programmes (timed voiding, voiding on request, bladder retraining, habit retraining,) compared with a) each other b) usual care, improve outcomes?



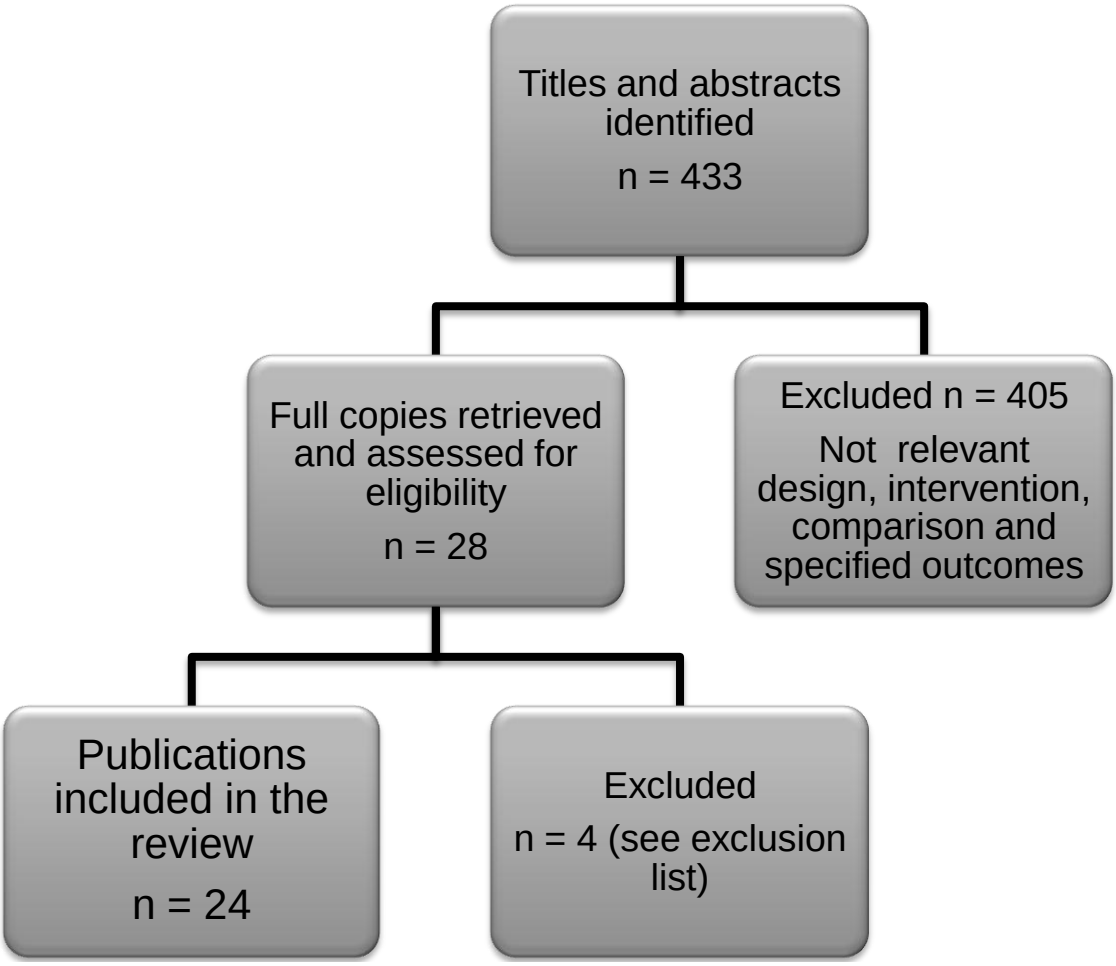
E.11 Does pelvic floor muscle training with or without electrical stimulation or biofeedback compared with treatment as usual, improve outcomes?



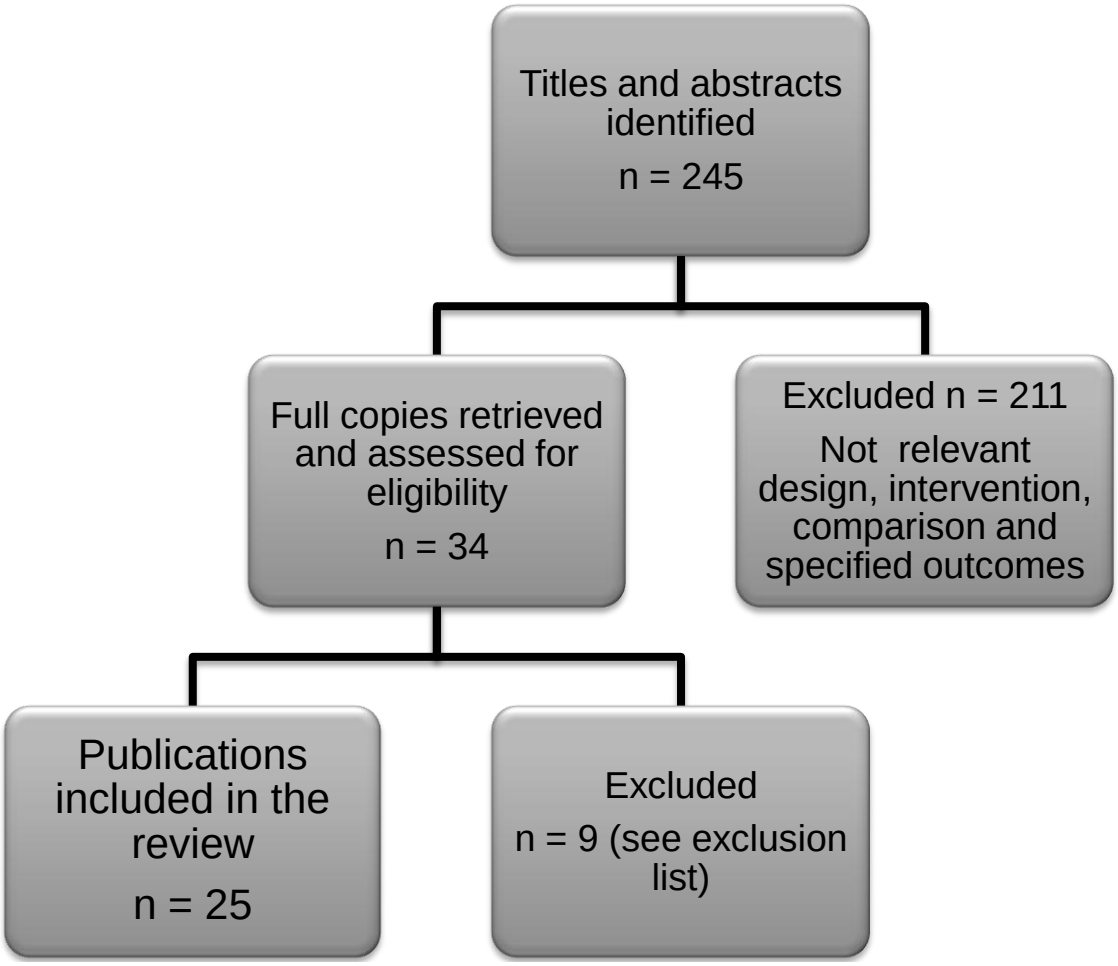
E.12 What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease? Same search as for 'What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? What is the quality of life associated with the above?'



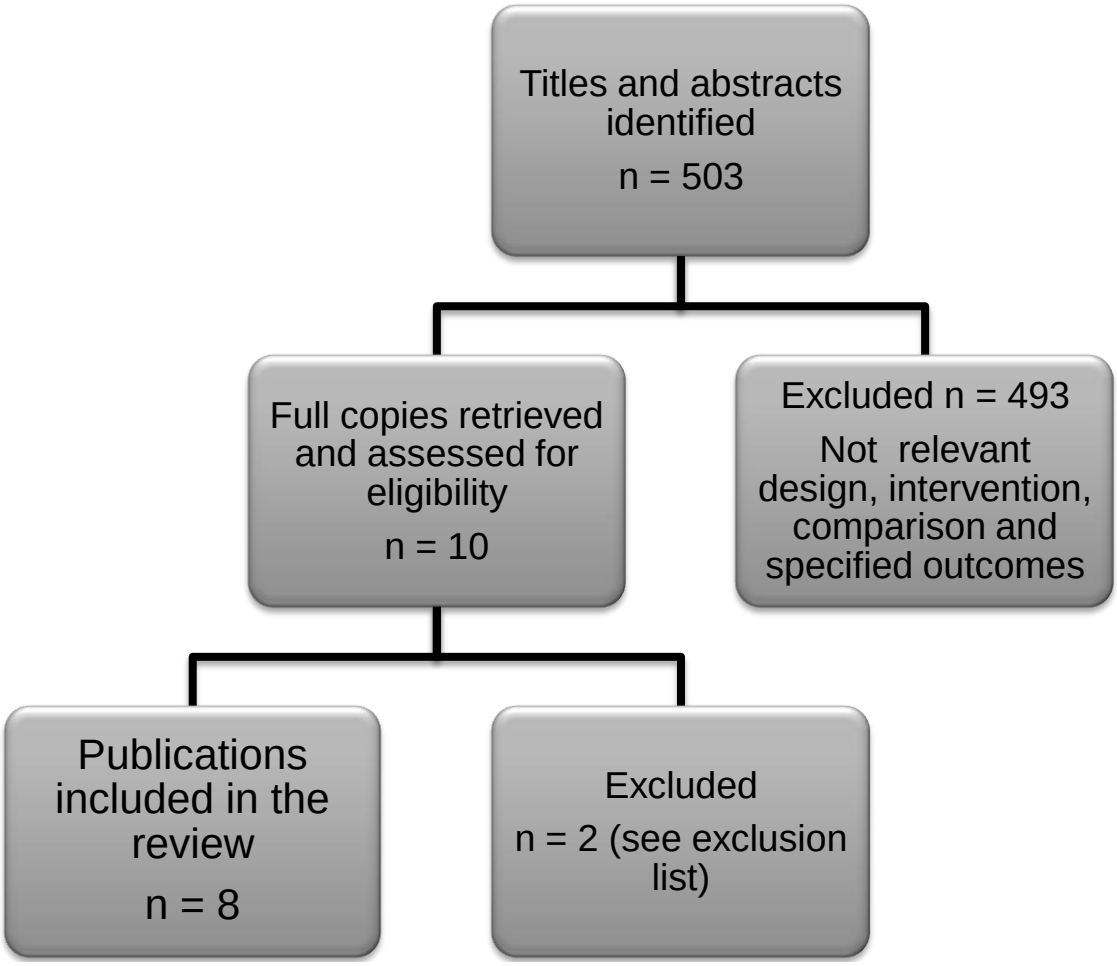
E.13 What is the safety and efficacy of urethral tape and sling surgery compared with usual care in neurological disease?



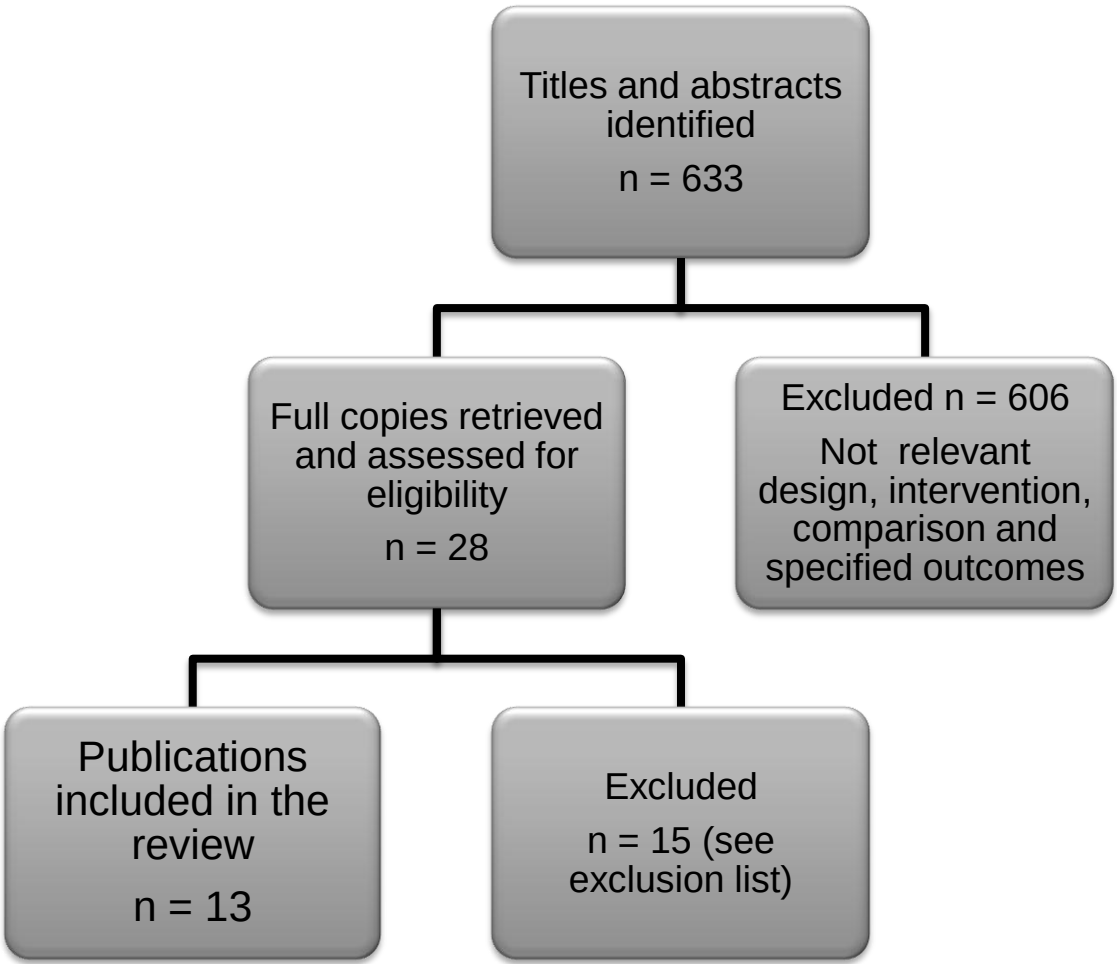
E.14 What is the safety and efficacy of artificial urinary sphincter compared with other treatments in neurological disease?



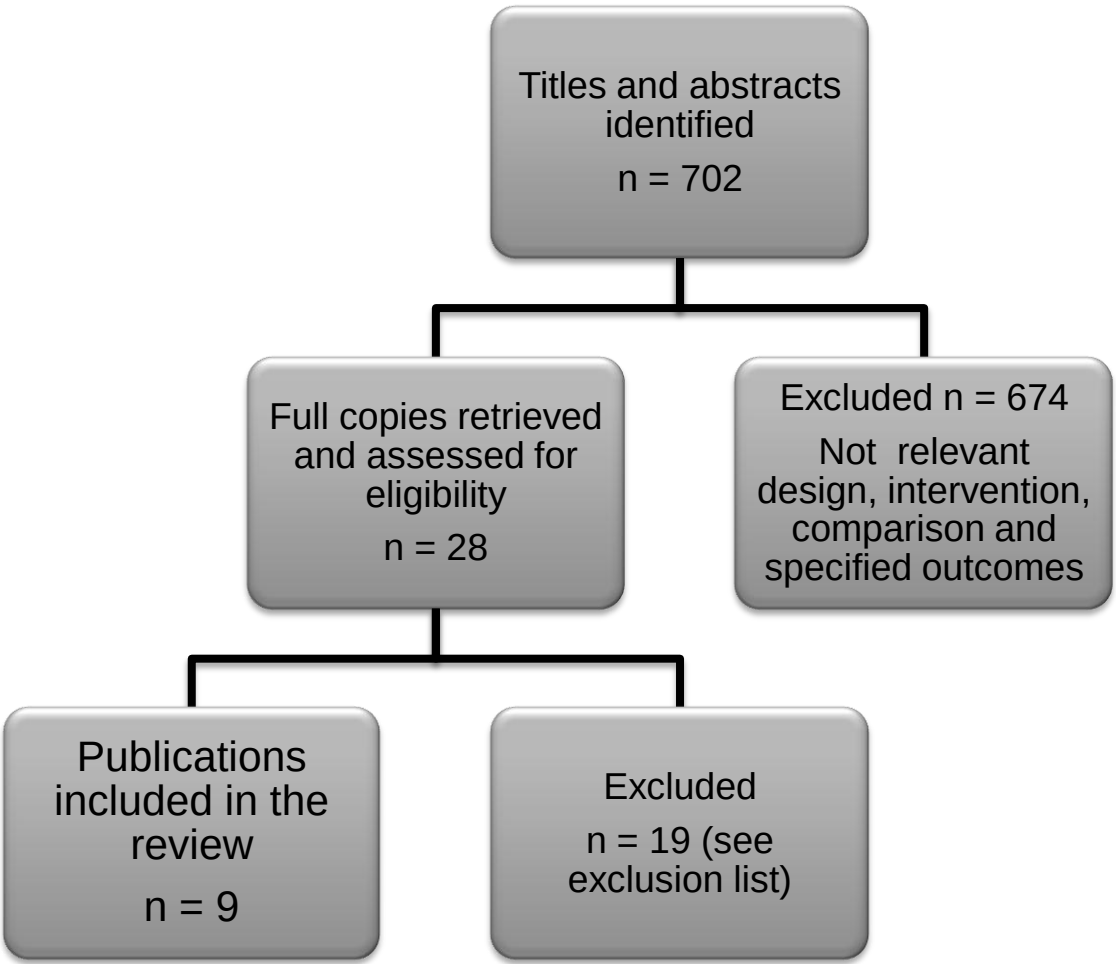
E.15 What is the efficacy of the ileal conduit diversion compared with usual care in neurological disease?



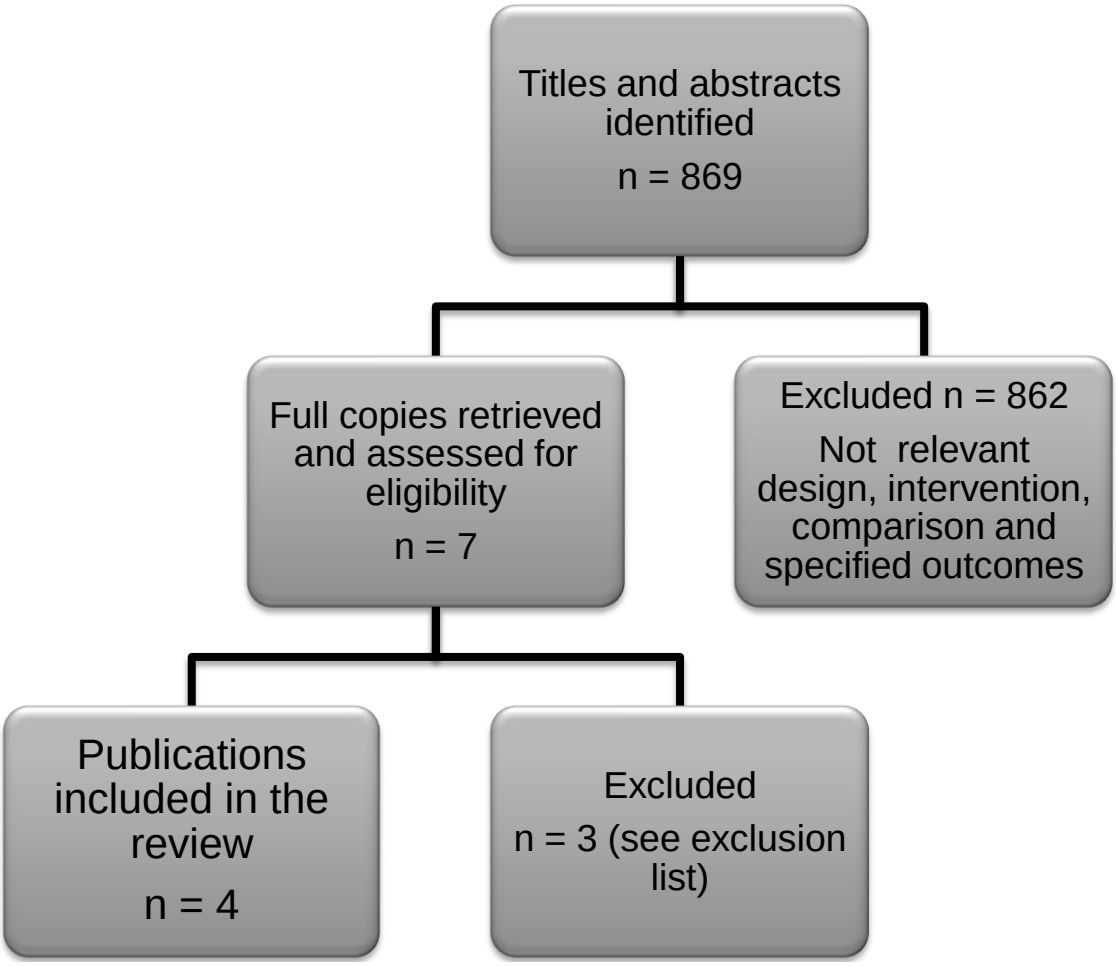
E.17 Do prophylactic antibiotics reduce the risk of symptomatic urinary tract infections?



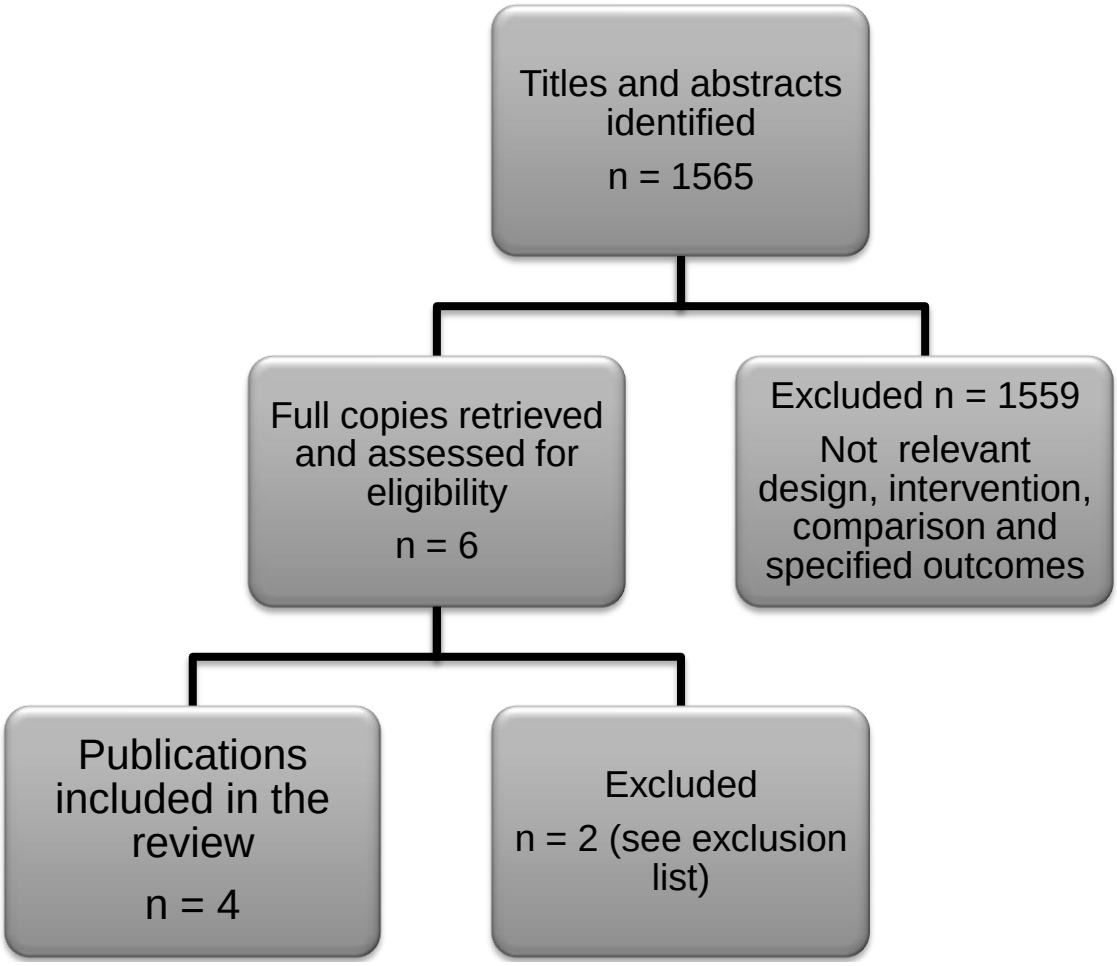
E.19 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services?



E.20 Does provision of information about the management of neurological lower urinary tract dysfunction improve patient outcomes?



E.22 For patients and their carers with lower urinary tract dysfunction associated with neurological disorders, what are the experiences of access to and interaction with services, that address these issues?



Appendix F: Evidence tables – clinical studies

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F.1 What is the safety and efficacy of antimuscarincs compared with a) placebo/usual care b) other antimuscarinics

F.1.1 Adults

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
M. Fader, S. Glickman, V. Haggar, R. Barton, R. Brooks, and J. Malone-Lee. Intravesical atropine compared to oral oxybutynin for neurogenic detrusor overactivity: a double-blind, randomized crossover trial. J.Urol. 177 (1):208-213, 2007.	Randomised crossover trial Randomisation: computer generated block sequence Allocation concealment: pharmacy staff labeled medications with the order of testing Double blind	N=79 recruited N=57 completers (analysed)	Adults with multiple sclerosis who (i) had previously benefited from or were using oral antimuscarinic treatment for overactive bladder (ii) were performing intermittent catheterisation at least twice daily Exclusions criteria included: symptomatic urinary tract infection Patient population IC intermittent catheterisation Mean age yrs: 52 (31-72) % yrs since MS diagnosis (No. pts) 1-5: 11 (6) 6-10: 23 (13) 11-20: 39 (22) > 21: 28 (16) % IC history (No. pts) 3-12 mths	Atropine or placebo 6.67 mg in 20 ml 0.9% saline to provide 6 mg in 18 ml x 4 times daily	Oxybutynin or placebo Dose was the equivalent to what the patient was on before the study began Mode dose in 26 patients was 5 mg oxybutynin IR twice daily (range 2.5 mg twice to 5 mg 4 times daily)	2 weeks	No. of incontinence episodes Bladder capacity ml Quality of life Adverse events	Catheters provided by Astra-Tech

			1-5 yrs 6-10 yrs > 11 yrs	6 (10) 44 (25) 23 (13) 16 (9)				
			% IC freq. (no. pts) 2 3 4 5	 36 (20) 21 (12) 14 (8) 30 (17)				
			Median Barthel index (range)	18 (6-20)				
Effect Bladder capacity ml Mean (SD) vs Mean (SD) change Baseline vs oxybutynin 221.9 (106.9) vs 55.5 (67.2) Baseline vs Atropine 221.9 (106.9) vs 79.6 (89.6) Oxybutynin vs atropine p=0.053 No. incontinence events Mean (SD) vs Mean (SD) change Baseline vs oxybutynin 1.7 (2.1) vs -0.9 (1.6) Baseline vs atropine 1.7 (2.1) vs -0.9 (1.7) Adverse events (dry mouth) Odds of a worse score on treatment compared with baseline 9 (95%CI 4 to 22); p<0.0001.								
Gajewski JB,	Prospective	N=34	Patients with multiple sclerosis with	Oral	Oral	6 to 8	Clinical	None

<table>
<tr>
<td>Awad SA. Oxybutynin versus propantheline in patients with multiple sclerosis and detrusor hyperreflexia. Journal of Urology. 1986; 135(5):966-968.</td>
<td>randomised trial

Randomisation: no details
Allocation concealment: no details
Blinding: no details</td>
<td></td>
<td>urinary symptoms

Proportion of patients using catheters not stated

<table>
<tr><td></td><td>Oxybuty nin</td><td>Propantheline</td></tr>
<tr><td>Male
Female</td><td>15
4</td><td>11
4</td></tr>
<tr><td>Mean disability score (0-3) (SD)</td><td>2 (0.8)</td><td>2.3 (0.8)</td></tr>
<tr><td>Grade of symptoms
(0-3)
Freq

Nocturia

Urgency

Urge incontinence</td><td>

1.9 (1.0)
1.6 (0.9)
2.0 (0.8)
1.9 (0.8)</td><td>

1.6 (1.0)

1.3 (1.1)

1.6 (0.8)

1.5 (0.8)</td></tr>
<tr><td>MMC mLmean (SD)</td><td>133.4 (62)</td><td>171 (86)</td></tr>
</table>
MMC – maximum cystometric capacity</td>
<td>oxybutynin 5 mg three times daily

N=19</td>
<td>propantheline 15 mg three times daily

N=15</td>
<td>weeks (duration of treatment)</td>
<td>response (good-all symptoms improved; fair – 1 or more symptoms improved; poor – no change in any symptoms),
Change in Maximum Cystometic capacity (MMC) ml</td>
<td>reported</td>
</tr>
</table>

Effect
Oxbutynin vs propantheline
Side effects
13/19 (68%) vs 8/15 (53%)
Side effects leading to discontinuation
4/19 (22%) vs 4/15 (27%)

	Oxybutynin	Propantheline
Urinary symptoms	N=19	N=15
Frequency N (%)	15 (79)	11 (73)
Nocturia	16 (84)	9 (60)
Urgency	17 (89)	12 (80)
Urge incontinence	17 (88)	13 (87)
Clinical response N (%)	N=15	N=11
Good	10 (67)	4 (36)
Fair	2 (13)	1 (9)
Poor	3 (20)	6 (55)
Decrease in grades of symptoms, mean (SD)	*	**
Frequency	1.3 (0.8)	0.6 (0.7)
Nocturia	1.0 (0.8)	0.6 (0.8)
Urgency	0.8 (0.6)	0.5 (0.7)
Urge incontinence	1.0 (0.8)	(0.8)

* p <0.05 ** p>0.05

Maximum cystometric capacity ml
Before vs after mean (SD)
Oxbutynin (n=12)
138.3 (64) vs 282.5 (117.9) p<0.05
propantheline (n=6)
163.3 (77.6) vs 198.3 (129) ns

Madersbacher H, Stohrer M,	RCT, multicentre	N=95	Patients with detrusor hyper-reflexia with spinal cord injury aged 18 yrs or	Tropsium chloride 20	Oxybutynin 5 mg three	3 weeks (one week	Maximum bladder	None reported

<table>
<tr>
<td>Richter R et al. Trospium chloride versus oxybutynin: A randomized, doubleblind, multicentre trial in the treatment of detrusor hyper-reflexia. British Journal of Urology. 1995; 75(4):452-456.</td>
<td>Randomisation and allocation concealment – no details

Double blind</td>
<td></td>
<td>older.

Proportion of patients using catheters not stated
<table>
<tr><th></th><th>Tropsiu , m=53</th><th>Oxybutynin N=43</th></tr>
<tr><td>Sex %
Male
Female</td><td>
54
46</td><td>
44
55</td></tr>
<tr><td>Age yrs Mean (range)</td><td>32.8 (16-56)</td><td>31.3 (18-54)</td></tr>
<tr><td>Maximum cystometric bladder capacity mL mean (range)</td><td>215.5 (20-650)</td><td>185.1 (20-450)</td></tr>
<tr><td>Compliance mL/cmH20</td><td>74.6 (2-480)</td><td>59.5 (3-375)</td></tr>
</table>
</td>
<td>mg twice daily (plus one placebo dummy)
N=52</td>
<td>times daily
N=43</td>
<td>without treatment and two weeks on treatment)</td>
<td>capacity, residual urine, bladder compliance, adverse events</td>
<td></td>
</tr>
</table>

Effect

There was no statistical difference between the two groups

	Tropsium N=53	Oxybutynin N=43
Maximum bladder capacity, mean (SD) mL Pre Post P value	 215.2 (132) 311.9 (139) <0.001	 187.8 (110) 350.9 (154) <0.001
Bladder compliance mean ml/cm Pre	 74.62	 59.49

Post P value	92.75 <0.001	78.24 Not reported
Residual urine mean (SD) mL Pre Post P value	 49.22 (92) 128.32 (168) P<0.001	 48.14 (83) 154.36 (210) <0.001

Adverse events
Antiparasympathetic side-effects
Tropsium vs oxybutynin
26/53 (54%) vs 22/43 (56%)
However, the severity grading showed marked differences. Dryness of mouth deteriorated to 'severe' in 4% tropsium patients but 23% on oxybutynine.

Withdrawal from trial
Tropsium vs oxybutynine
7/53 (16%) vs 3/43 (6%)

Stohrer M, Madersbacher H, Richter R et al. Efficacy and safety of propiverine in SCI-patients suffering from detrusor hyperreflexia - A double-blind, placebo-controlled clinical trial. Spinal Cord. 1999; 37(3):196-200.	RCT, multicentre, Europe (?) No details of randomisation or allocation concealment Double blind	N=113	In-patients over the age of 18 yrs with detrusor hyperreflexia and suprasacral spinal cord injury. Clean intermittent catheterisation of all patients implied Exclusion criteria included cardiac, hepatic or renal dysfunction, intestinal and urogenital obstructions Population: Propiverine male:female 37:23, mean age 30.3 (SD11.7) yrs Placebo male:female 32:21, mean age 29.3 (SD 10.9)	Oral propiverine 15 mg tid N=60	Placebo N=53	14 days (length of treatment)	Maximum cystometric bladder capacity, residual urine, compliance (detrusor coeffient) patient symptoms (3-point scale: improved, unchanged or worsened), physician assessment of efficacy (3-point scale:	None reported

							very good or good, satisfactory or insufficient)	
Effect Maximal cystometric bladder capacity Baseline vs follow-up mean (SD) ml Propiverine 262 (132) vs 366 (143) (p<0.0001) Placebo 296 (151) vs 289 (163) The difference between propiverine and placebo was not significant Residual urine Baseline vs follow-up mean (SD) ml Propiverine 49.7 (109.4) vs 86.5 (109.3) Placebo 58.9 (90.2) vs 60.8 (71.9) The increase was significant with propiverine compared with placebo p=0.01 Compliance (detrusor coefficient) Baseline vs follow-up mean (SD) ml/cmH20 Propiverine 16.6 (12.9) vs 21.8 (15.8) Placebo 15.2 (10.9) vs 17.2 (11.9) Clinical symptoms Patient assessment 63.3% were improved under propiverine compared with 22.6% under placebo Physician assessment								

<table>
<tr><td colspan="8">53% were ‘very good’ or ‘good’ under propiverine compared with 11% under placebo
Safety
Dryness of mouth
Propiverine 22/60 (37%) vs placebo 4/53 (8%)
Drop-outs due to adverse events
Propiverine 5/60 vs placebo 1/53</td></tr>
<tr>
<td>Stohrer M, Murtz G, Kramer G et al. Propiverine compared to oxybutynin in neurogenic detrusor overactivity--results of a randomized, double-blind, multicenter clinical study. European Urology. 2007; 51(1):235-242.</td>
<td>RCT
Multicentre, multinational trial

Randomisation: computer generated list prepared by trial independent statistician allocation concealment: Medication pre-package according to list and assigned to subject consequtively
Double blind</td>
<td>N=131 (safety population)

N=107 Included in ITT population

N=91 per protocol population

N=16 propiverine and n=9 oxybutynin premature treatment termimations</td>
<td>Patients 18 yrs or over with known neurological disorder and demonstrable detrusor activity at urodynamic assessment. Maximum cystometric capacity was restricted to 300 ml. Exclusions included: other genitourinary tract anomalies, a post void residuao >15% of bladder capacity, acute infections of the genitourinary tract or clinically relevant disease of the kidneys
“Most patients practising intermittent catheterisation”
Aetiology: 122/131 spinal cord injury
<table>
<tr><th></th><th>Propiverine N=70</th><th>Oxbutynin N=61</th></tr>
<tr><td>Gender
Male %
Female %</td><td>
77.1
22.9</td><td>
73.8
26.2</td></tr>
<tr><td>Age yrs, mean (SD)</td><td>38.8 (13.9)</td><td>37.7 (15.1)</td></tr>
<tr><td>Height cm, mean (SD)</td><td>175.8 (9.2)</td><td>173.9 (9.8)</td></tr>
<tr><td>Weight kg, mean</td><td>74.5 (13.6)</td><td>72.1 (11.2)</td></tr>
</table>
</td>
<td>Oral propiverine 15 mg tid

N=70

One week run-in period</td>
<td>Oral oxybutynin 5mg tid (immediate release)

N=61

One week run-in period</td>
<td>21 days (length of treatment)</td>
<td>Maximum cystometric capacity, detrusor compliance assessed during filling cystometry, residual urine,
24 hr micturation frequency, 24 hr incontinence episodes</td>
<td>APOGEPHA, Arzneimittel GmbH, Dresden Germany</td>
</tr>
</table>

			(SD)							

Effects
Premature treatment terminations due to adverse events
Propiverine vs Oxybutynin
11/70 vs 4/61 (ns)

Maximum cystometric capacity
Before vs after
Mean (SD)
Propiverine (n=46)
198 (110) vs 309 (166) ml
Oxybutynin (n=45)
164 (64) vs 298 (125) ml
There was no significant difference between the two groups

Detrusor compliance
Before vs after
Mean (SD)
Propiverine
10.8 (13.8) vs 22.7 (24.3) ml/cm H20
Oxybutynin
12.7 (12.1) vs 37.8 (48.3) ml/cm H20
The inter-group difference was not significant

Residual urine
Before vs after
Mean (SD)
Propiverine
72.6 (115) vs 140.9 (167) ml
Oxybutynin
65.3 (78) vs149 (133) ml
There was no significant difference between the two groups

Per-protocol population. No significant differences reported between propiverine and oxybutynin

	Propiverine	Oxybutynin
24-h micturition frequency, mean (SD)		
Pre	10.9 (6.9)	12.0 (12.7)
Post	7.9 (5.7)	9.5 (10.4)
Difference	-2.9 (2.9)	-2.5 (3.3)
p-value	P<0.05	P<0.05
24-h incontinence episodes, mean (SD)		
Pre	3.9 (4.5)	3.3 (3.4)
Post	2.3 (4.6)	2.0 (3.2)
Difference	-1.6 (2.3)	-1.3 (2.0)
p-value	P <0.05)	P<0.05

Adverse events – safety population
Propiverine vs oxybutynin
48/70(68.6%) vs 48/61 (78.7%) (ns)

E.1.2 CHILDREN AND YOUNG PEOPLE

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Amark P et al. Follow-up of long-time treatment with intravesical oxybutinin for neurogenic bladder in children. Eur Urol 1998; 34: 148-153.	Non-comparative case series	N=39	Patients with myelodysplasia, neurogenic bladder disturbance with detrusor hyperreflexia (detrusor contractions >10cm water over a period of >10s) and/or high bladder pressure (>40cm water) during bladder filling All using clean intermittent catheterisation	Oxybutynin 0.1mg/kg twice daily intravesical Plus clean intermittent catheterisation	No comparator	0.66 to 5 years (mean 2.25 years)	Occurrence of urinary tract infections 1 year prior to treatment and during follow up (for 1 year	Folke Bernadotte Foundation

	Oxybutynin
Male Female	23 16
Age	0.5-18 years (mean 7.9 years)
Upper level of spinal lesion	5 T12 or above 21 L1 to L5 13 S1 or below

Weight not stated

after starting treatment in 26 patients and 8-12 months for 7 patients); 5 patients data not available.

Continence evaluated according to Nergardh et al.

Effect
Before vs. after use of oxybutinin

Urinary tract infection (data available for 33 patients)

	Asymptomatic bacteriuria	Lower UTI	Upper UTI	Use of prophylactic antibiotics
Before	10	11	9	15
After	14	21	8	15

Degree of continence (data available for 37 patients)

	A (regularly dry for 3-hour	B (daily dry periods between 1-3	C (occasional dry periods between 1-3	D (always wet between

	periods)	hours)	hours)	micturitions)
Before	1 (urge incontinence)	5	13	18
After	18	14	2	3

Adverse reaction
Anticholinergic side effects were reported by 2 patients; in 1 of them, dose reduction by half maintained a good effect but abolished side effects.

Discontinuation of therapy
7 patients discontinued after 0.5-8 months; 5 had no effect on incontinence; 1 had upper UTI and 1 stopped after surgery for intestinal volvulus.

1

<table>
<tr><th>Reference</th><th>Study type Evidence level</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr><td>Baskin LS et al. Treatment of infants with neurogenic bladder dysfunction using anticholinergic drugs and intermittent catheterisation. Br J Urol 1990; 66: 532-534.</td><td>Case series</td><td>N=48</td><td>Patients with myelomeningocoele and neurogenic bladder dysfunction

Patients using clean intermittent catheterisation
<table>
<tr><td></td><td>Treatment group (spastic or hypertonic bladder and significant sphincter dyssynergia)</td><td>Observation group (extremely lax external sphincter)</td></tr>
<tr><td>Male
Female</td><td>11
24</td><td>8
5</td></tr>
<tr><td>Age</td><td colspan="2">1-30 days</td></tr>
<tr><td>Level of defect</td><td></td><td></td></tr>
</table></td><td>Oxybutynin 0.1mg/kg three times daily

n=35

In combination with clean intermittent catheterisation</td><td>Observation group

n=13</td><td>Treatment group: 6-72 months (mean 39 [18] months)
Observation group: 20 to 60 months (mean 44 [16] months)</td><td>Occurrence of urinary tract infections

Side effects</td><td>not stated</td></tr>
</table>

Thoracic	1	0
Thoracic/ lumbar	2	0
Lumbar	17	7
Lumbar/ sacral	13	5
Sacral	2	1
Vesico-ureteric reflux		
Bilateral	3	1
Left	6	2
Right	3	1
None	23	9

Weight not stated

Effect

After use of oxybutinin (treatment group; main focus of paper) or during observation (observation group)

Urinary tract infection (treatment group)

	Asymptomatic bacteriuria	UTI	No UTI	Withdrew
Treatment group	21	2	10	2

Observation group had no UTI or upper tract deterioration.

Degree of continence (treatment group)

	Virtually dry between catheterisations	Significant wetting
Treatment group	25	8

Adverse reaction

Constipation common; managed by diet or bowel programme. 1 stopped due to sedation; 1 stopped temporarily as disliked taste. Facial flushing common in summer

heat; dosage adjusted (smaller daytime & larger evening dose).

Discontinuation of therapy
2 patients withdrew; 1 urethral trauma and 1 progressive hydronephrosis due to failure to take or respond to oxybutinin.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Connor JP et al. Early cystometrograms can predict the response to intravesical instillation of oxybutinin chloride in myelomeningocele patients. J Urol 1994; 151: 1045-1047.	Non-comparative Case series	N=28	Patients with myelodysplasia and severe neurogenic bladder dysfunction; incontinent; could not tolerate, or had an inadequate response to, oral oxybutinin Male 9 Female 4 Age 1-19 years (mean 8.7 years; median 8 years) Weight not stated	Intravesical oxybutynin 5mg twice daily for minimum of 3 months	No comparator	4-9 months	Bladder capacity Intravesical pressure Bladder compliance Continence Side effects	not stated
Effect After use of oxybutinin Bladder capacity (data available for 13 patients i.e. completers) 10 increased capacity (mean increase 41% (range -24% to +95%). Compliance 12 patients had improved compliance on follow up urodynamic studies.								

Continence
5 achieved continence apart from rare leaks; 3 reported significant improvement (reduction in number of pads required); 5 had no improvement (3 had bladder neck incompetence and 2 required bladder augmentation).

Discontinuation of therapy
Withdrawal due to inconvenience of crushing and administering the medication in 14 cases; 1 reduced oxygen saturation.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Ferrara P, D'Aleo CM, Tarquini E et al. Side-effects of oral or intravesical oxybutynin chloride in children with spina bifida. BJU International. 2001; 87(7):674-677.	Non-comparative case study	N=225 records evaluated N=101 included	Children who had undergone surgical repair for meningomyelocele (MMC) within 24-48 h after birth and a neurogenic bladder 34/101 clean intermittent catheterisation All patients underwent a urodynamic assessment, renal ultrasonography and voiding cysto-urethrography. Those at high risk of upper urinary tract deterioration were then identified, if they had one of the following urodynamic findings: a low bladder capacity for their age, detrusor hyper-reflexia, low bladder compliance, a leak-point pressure of ≥ 40 cmH2O, or detrusor-external sphincter	Oxybutynin orally or intravesically mean dose 0.1 to 0.2 mg/kg two to three times daily Oral N=67 Intravesical N=34 plus clean intermittent catheterisation	Before therapy	3 yrs	Bladder capacity Bladder compliance	None reported

			dysynergia					

Effect

Mean (SD)	Oral		Intravesical	
	Before	After	Before	After
Bladder capacity mL	128 (107)	214 (110)	132 (103)	226 (118)
Bladder compliance mL/cmH2O	8.1 (6.3)	14.8 (11.6)	8.5 (6.1)	16.0 (11.0)

Adverse events

Oral vs intravesical

Of the 11/67 (16%) vs 6/34 (18%) patients on oxybutynin discontinued because of side effects

Incidence of urinary tract infections

70/101 (69%) decrease in the incidence of urinary tract infections

Mean frequency of clean intermittent self-catheterisation

Mean frequency of clean intermittent self-catheterisation decreased from 5 to 3 times daily

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Franco I, Horowitz M, Grady R et al. Efficacy and safety of oxybutynin in children with detrusor hyperreflexia secondary to neurogenic bladder dysfunction. Journal of Urology. 2005; 173(1):221-	Prospective open label trial, multicentre USA and The Netherlands	N=116 recruited N=111 completers	Children aged 6 to 15 yrs with documented diagnosis of detrusor hyperreflexia due to neurogenic conditions, and were using a total daily dose of 10 or 15 mg oral oxybutynin chloride with clean intermittent catheterisation	Oxybutynin Extended release tablets 5-20 mg per day Tablets 7.5 to 15 mg 2 to 4 times daily Syrup 5 to 30	Before treatment / baseline	24 weeks	Maximum cystometric capacity, % catheterisations without an intermittent leaking accident	None reported

225.				mg per day Total daily dose ranged from 0.20 to 0.40 mg/kg (46% patients) 0.40 to less than 0.60 mg/kg (35%) in the majority of patients				
Effects Baseline vs 24 weeks Maximum cystometric capacity mean ml (SEM) Baseline 196.9 (11.61), week 24 260.5 (11.97), change from baseline 75.4 (9.75) (p<0.001) % catheterisations without an intermittent leaking accident Increased 21.5% from baseline to week 24 (p<0.001)								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Goessl C, Knispel HH, Fiedler U et al. Urodynamic effects of oral oxybutynin chloride in children with myelomeningocele and detrusor	Non-comparative case study	N=41	Consecutive children with myelomeningocele (MMC) identified with previously untreated detrusor hyperreflexia. Detrusor hyperreflexia was defined as maximal detrusor pressures exceeding 40 cm H2O	Oxybutynin 0.2 to 0.3 mg/kg/day oral combined with clean intermittent catheterisation four times	No comparator	Urodynamic invesitgation repeated at 3 mths, 2 yr clinical follow-up	Maximal bladder capacity Continence Adverse events	None reported

hyperreflexia. Urology. 1998; 51(1):94-98.			Population: Mean age 4.9 yrs (range 2 months to 15 yrs)	daily				
Effect Before vs after Maximal bladder capacity ml Mean (SD) 141 (96) to197 (99) (+40%, p<0.01) Detrusor compliance mL/H2O Mean (SD) 6.5 (5.6) vs 16.8 (13.7 (+158%;p<0.01) Continence 6/41 were continent at initial urodynamic investigation and remained so on oxybutynin No. incontinent Before vs after 35/41vs 11/41 gained complete continence and 20/41 'exhibited marked improvement' Adverse effects 13/41 experienced side effects Follow-up 37/41 conservative treatment with oxybutynin and concomitant clean intermittent catheterisation was found to be effective and was maintained during follow-up for at least 2 yrs.								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hehir M, Fitzpatrick JM. Oxybutinin and teh prevention of urinary incontinence in spina bifida. Eur Urol 1985; 11: 254-256.	Crossover study with randomisation of first treatment as active drug or placebo (2 weeks washout)	N= 24	Patients with spina bifida (lumbosacral meningomyelocoele) with neuropathic bladder; incontinent. All using clean intermittent catheterisation	Intravesical oxybutynin 5mg three times daily for 4 weeks	Placebo	4 weeks on each treatment plus washout period	Bladder capacity Maximum bladder pressure Continence	not stated

			Male Female	12 12				
			Age	10-22 years (mean 14 years)				
			Completely ambulant Partial paraplegia Total paraplegia	12 8 4				
			Normal upper urinary tract Hydronephrosis with pyelonephrotic scarring	17 7				

Effect

Oxybutinin or placebo vs. baseline

Bladder capacity (n=23)

Baseline	197 (24) mL	
Oxybutinin	299 (32) mL	p=0.001
Placebo	218 (29) mL	NS

Bladder maximum filling pressure (n=23)

Baseline	47 (4) cm water	
Oxybutinin	37 (4) cm water	p=0.02
Placebo	45 (4) cm water	NS

Symptoms on oxybutinin

Dry	4 (16.6%)
Improved	12 (50.0%)
Wet	8 (33.3%) (including 3 girls with stress incontinence)

Adverse effects

Dry mouth: 3 on oxybutinin, 1 on placebo; no discontinuations as a result.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kaplinsky R, Greenfield S, Wan J et al. Expanded followup of intravesical oxybutynin chloride use in children with neurogenic bladder. Journal of Urology. 1996; 156(2:Pt 2):753-756.	Crossover study with randomisation of first treatment as active drug or placebo (2 weeks washout)	N= 28	Children with neurogenic bladder refractory to, or who could not tolerate oral therapy; incontinence and/or elevated bladder pressures refractory to intermittent catheterisation and oral anticholinergic medication Male 15 Female 13 Age 3-18 years (mean 14 years) Myelomeningocoele 27 Imperforate anus 1	Intravesical oxybutynin 5mg twice daily for 4 weeks	Placebo	21 continuing treatment followed for mean of 35 months (range 3 to 67 months)	Bladder capacity Continence Side effects	not stated
Effect After treatment Continence								

Dry day and night	daytime continence between catheterisations	Clinically unchanged
12 (57%)	5 (24%)	4 (19%) of whom 2 had sphincteric incompetence

Bladder capacity

Increased in 17/21 patients; mean increase 237% from pre-treatment values, p<0.0001

Side effects

7 patients could not tolerate anticholinergic side effects (dry mouth, dizziness, constipation, hyperactivity and seizures.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Madersbacher H, Murtz G, Alloussi S et al. Propiverine vs oxybutynin for treating neurogenic detrusor overactivity in children and adolescents: results of a multicentre observational cohort study. BJU International. 2009; 103(6):776-781.	Retrospective cohort study, multicentre Germany	N=265 records identified N=255 records included 10 patients with non myelomeningocele (MMC) or spinal cord injury were subsequently excluded	Children and adolescents Inclusion criteria: i) confirmed neurogenic detrusor overactivity due to MMC or spinal cord injury confirmed by the history of the patients and a urodynamic assessment (ii) aged 1 to 18 rs (iii) treatment periods ≥ 12 months (v) urodynamic assessment either at ≥ 12 months of treatment or al last follow-up Population: 199 MMC, 46 spinal cord injury, 10 other diagnosis Intermittent catheterisation 80.4% propiverine 90.2% oxybutynin MCC maximum cystometric bladder capacity Propiverine N=127 / Oxybutynin N=128 Median age yrs: 7.18 / 7.98	Propiverine 5 mg, or of higher body weight, 15 mg Immediate release N=127	Oral oxybutynin Immediate release N=128	Urodynamic assessment either at ≥ 12 months of treatment or al last follow-up	maximum cystometric bladder capacity,	APOGEPHA Arzneimittel, Dresden, Germany

			Median body weight kg: 29.2 / 31.6 Male:female %: 53:47 / 54:46 Incontinence %: 92.3 / 79.2 MCC, mL Before: 145.9 / 221.8					

Effect
Propiverine vs oxybutynin
MCC maximum cystometric bladder capacity mL
Before 145.9, after 242.3 (difference +96.4) vs 221.8, 310.0 (+88.2) (p=0.001 but doesn't reported if for between or within differences)

Continence %
Before 7.7, after 31.6 (difference + 23.9) vs 20.8, 50.4 (+29.6)

No. of patients reporting adverse events
11/127 (9.4%) vs 22/128 (17.2%) RR 0.50 (0.26 to 1.00)

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Painter KA et al. Long-term intravesical oxybutinin chloride therapy in children with	Retrospective case series N=63 recommended for oxybutinin therapy; 21 declined; 12	N=30	Children with myelodysplasia and neurogenic bladder who could not tolerate, or had no response to, oral anticholinergics, or had high pressures on initial urodynamic studies and intravesical oxybutinin was first line therapy. Male: 18	Intravesical oxybutynin 5mg twice daily	No comparator	2-26 months (mean 13months, median 12 months)	Bladder capacity Continence Side effects	not stated

myelodysplasia. J Urol 1996; 156: 1459-1462.	withdrew before follow up cysto-metrography (3 recurrent UTIs; 9 inconvenience of crushing tablets)		Female: 12 Age: 1-17 years					
Effect After treatment Bladder capacity Mean total bladder capacity increased from 209 (103) to 282 (148) mL, p<0.01 (mean 65% increase) Safe bladder capacity increased from 157 (105) to 234 (147) mL, p<0.01 (mean 161% increase) Mean end filling pressure decreased from 63 (24) to 56 (31) cm water, NS (mean 2.5% decrease) Continence Of the 29 incontinent, 3 (10%) achieved continence and 19 (65%) reported decreased use of pads; 1 continent and remained dry. Side effects No patient had systemic side effects.								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Palmer LS. Complications of intravesical oxybutinin	Non-comparative Case series	N= 23	Children with myelodysplasia and neurogenic bladder dysfunction with inadequate response to, or intolerable side effects of, oral	Intravesical oxybutynin 1.25mg three times daily,	No comparator	5 years	Side effects Discontinuations	not stated

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
chloride therapy in the pediatric myelomeningocele population. J Urol 1997; 157: 638-640.			therapy Male not stated Female Age 5-11 years	increased as necessary for satisfactory response				
Effect After treatment: Discontinuations 15/23 discontinued over 5 years; due to side effects in 6 patients (included agoraphobia, hyperactivity, dizziness, flushing, dry mouth, insomnia, rash, nausea, headache, and bladder pain ; ineffectiveness in 5 patients; and inconvenience in 4 patients.								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Reddy PP et al. Long-term efficacy and safety of tolterodine in children with neurogenic detrusor overactivity. J Pediatr Urol 2008; 4: 428-433.	Non-comparative Case series	N=30	Subjects who successfully completed one of three 12-week open-label dose-escalation studies of oral tolterodine; stable neurological disease (meningomyleocoele, sacral agenesis, spinal dysraphism, cerebral palsy, traumatic spinal cord injury) and neurogenic detrusor overactivity; between 5th and 95th percentile for weight or BMI. Key exclusion criteria: urinary tract abnormalities (except vesicoureteric reflux grade III or less) Male 15 Female 15 Age mean 6.5 (4.6) yrs 6 month-4 yrs 14	Oral tolterodine (4 months-4 years 0.2-2mg twice daily; 5-10 years 0.5-4mg twice daily; 11-16 years 2, 4 or 6mg once daily (starting dose according to response in original studydose	No comparator	12 months	Bladder capacity Continence Withdrawals Treatment satisfaction	Pfizer

			5-10 years: 9 11-16 years: 7 Race White: 24 Black: 4 Not reported: 2	adjustments within these ranges for efficacy or safety reasons).				

Effect
After treatment

Bladder capacity
Functional bladder capacity increased in first month of treatment in infants and children aged 6 months-4 years and 5-10 years (maintained at 12 months) but not aged 11-16 years.

Continence
Mean number of incontinence episodes per 24 hours decreased in all age groups (by around 45%, shown graphically)

Withdrawals
1 withdrew due to incontinence

Adverse events
29/30 had adverse event (most mild or moderate); most infections, gastrointestinal disorders, respiratory, thoracic and mediastinal disorders; none treatment-related.
7 treatment-related: 3 constipation; 1 moderate faecal incontinence, 1 dry mouth, 1 mild headache, 1 mild weight gain.

Treatment satisfaction
Parents of 24/26 completers willing to continue the treatment; 100% would recommend the treatment.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schulte-Baukloh H et al. Urodynamic	Non-comparative Case series	N=20	Children with neurogenic detrusor overactivity due to an upper motor neurone lesion; inclusion criteria 3 months to 18 years	Propiverine hydrochloride 0.4mg/kg body	No comparator	3-6 months	Reflex volume	not stated

<table>
<tr>
<td>effects of propiverine hydrochloride in children with neurogenic detrusor overactivity: a prospective analysis. BJU Int 2006; 97: 355-358.</td>
<td></td>
<td></td>
<td>18/20 using clean intermittent catheterisation
<table>
<tr><td>Age

6 month-4 yrs
5-10 years
11-16 years</td><td>mean 8.9 yrs; median 5.6 yrs

14
9
7</td></tr>
<tr><td>meningomyelocoele
hypoxic brain damage at birth
spinal cord injury</td><td>17
2

1</td></tr>
</table>
</td>
<td>weight twice daily; increased as appropriate (anticholinergic and calcium channel modulator; fewer side effects of dry mouth and cognitive impairment than oxybutinin)</td>
<td></td>
<td></td>
<td>Maximum cystometric bladder capacity

Bladder compliance

Incontinence score

Adverse events</td>
<td></td>
</tr>
<tr>
<td colspan="8">Effect
After treatment
Maximum cystometric bladder capacity
Mean (standard error)
Increased from 166 (28.8) to 231.9 (34.8) mL, p<0.005

Bladder compliance
Mean (standard error)
Improved from 11.2 (2.8) to 30.6 (9.7) mL/cm water, p<0.01

Incontinence
Incontinence score (0=continent; 1=wet only once daily, usually during the night; 2=incontinence episodes less frequent than 50% between catheterisations; 3= incontinence episodes less frequent than 50% between catheterisations) improved from 2.4 (0.2) to 1.6 (0.3), p<0.05 (i.e. improved 33%)

Adverse events
Incidence 10% (although 3 children had higher doses than recommended); 2 mothers reported difficulties with child’s concentration in school.</td>
</tr>
</table>

1

2

F.2 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care in neurological disease?

Reference	Study type Evidence level	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Abrams P, Amarenco G, Bakke A et al. Tamsulosin: efficacy and safety in patients with neurogenic lower urinary tract dysfunction due to suprasacral spinal cord injury. Journal of Urology. 2003; 170(4 Pt 1):1242-1251. Ref ID: ABRAMS2003	RCT, multicentre, several countries in Europe Randomisation and allocation concealment unclear, double-blind	263	Inclusion/exclusion: 18 years old or older, neurogenic lower urinary tract dysfunction (NLUTD) due to suprasacral spinal cord injury; out of spinal shock and in stable phase; neurogenic detrusor overactivity (phasic wave 15cm H2O or greater) or a voiding contraction; could have other neurogenic voiding dysfunctions; maximum urethral pressure (MUP) during urethral pressure profilometry (UPP) 60cm H2O or greater; one or more urodynamic findings during filling cystometry (detrusor pressure 80cm H2O or greater, bladder compliance 15mL/cm H2O or less at filling rate 20mL/min) or voiding cystometry (maximum detrusor pressure during voiding 60cm H2O or greater, residual volume greater than 30% maximum cystometric capacity or greater than 100mL). Drugs influencing pharmacodynamics of tamsulosin not allowed 1 month before to end of study; medical treatment for NLUTDonly if stable dose 1 month before to end of study; antihypertensives had to remain unchanged during study.	Tamsulosin 0.4 mg (n=88) or 0.8mg (n=83)	Placebo (n=92)	4 weeks double-blind RCT (plus open label follow up of 76% of the patients to 1 year)	Primary: urethral pressure profilometry: maximal urethral pressure (not reported) Secondary: cystometry variables; urinary frequency, urgency, pads used, catheterisations, Urinary Symptoms Questionnaire; International Prostate Symptom Score; adverse events	Yamanouchi Europe BV.

Baseline characteristics:

	Plac	Tam 0.4	Tam 0.8
Lesion duration (mo)	97.9	103.9	85.0
Cervical (%)	31.5	30.7	42.2
Thoracic (%)	52.2	54.6	47.0
Lumbar (%)	15.2	13.6	10.8
Complete (%)	51.1	64.8	59.0
Incomplete (%)	48.9	34.1	41.0
Paraparesis (%)	21.7	20.5	10.8
Paraplegia (%)	45.7	51.1	45.8
Tetraparesis (%)	9.8	8.0	16.9
Tetraplegia (%)	21.7	19.3	26.5
Intermittent catheterisaton (%)	48.9	40.9	44.6
Intermittent self-catheterisaton (%)	30.8	35.2	34.9

Results:

	Placebo	Tamsulosin 0.4mg	Tamsulosin 0.8mg
Residual urine vol (mL):			
No. pts with baseline + endpoint data	46	41	41
Baseline mean (SD)	178.4 (147.1)	159.1 (136.8)	171.0 (155.7)
Change at end point mean (SE), p vs. baseline	-23.7 (13.7), NS vs. baseline	-5.6 (19.5), NS vs. baseline	-7.3 (19.7), NS vs. baseline
p value vs. placebo	-	0.443	0.491
Mean frequency of incontinence/24 hours:			
No. pts with baseline + endpoint data	60	62	55
Baseline mean (SD)	1.0 (1.4)	1.0 (1.6)	1.0 (1.7)
Change at end point mean (SE), p vs. baseline	-0.2 (0.1), NS vs. baseline	-0.3 (0.1), p<0.01	-0.0 (0.1), NS vs. baseline
p value vs. placebo	-	0.412	0.915
Mean frequency of pads changed/24 hours:			
No. pts with baseline + endpoint data	61	63	55
Baseline mean (SD)	2.0 (2.2)	3.2 (2.8)	2.4 (2.1)
Change at end point mean (SE), p vs. baseline	0.1 (0.1), NS vs. baseline	-0.3 (0.2), p<0.05	0.2 (0.1), NS vs. baseline
p value vs. placebo	-	0.009	0.823
Mean frequency of urgency episodes/24 hours:			
No. pts with baseline + endpoint data	65	69	62
Baseline mean (SD)	2.0 (3.0)	1.5 (2.6)	1.5 (2.5)
Change at end point mean (SE), p vs. baseline	-0.1 (0.2), NS vs. baseline	-0.2 (0.1), NS vs. baseline	-0.3 (0.2), p<0.001
p value vs. placebo	-	0.688	0.230
Urinary Symptoms Questionnaire total (frequency and severity urinary leakage; range 0-48):			
No. pts with baseline + endpoint data	82	82	76
Baseline mean (SD)	16.6 (9.2)	17.1 (9.1)	17.6 (8.9)
Change at end point mean (SE), p vs. baseline	-0.8 (0.7), NS vs. baseline	-0.3 (0.5), NS vs. baseline	-0.6 (0.5), NS vs. baseline
Adverse events n (%):	n=90	n=86	n=81
Any adverse events	38 (42.2%)	31 (36.0%)	26 (32.1%)
Drug-related (possibly or probably)	13 (14.4%)	14 (16.3%)	12 (14.8%)

Discontinued due to any adverse events	4 (4.4%)	2 (2.3%)	2 (2.5%)
Most commonly reported adverse events:			
Dizziness	5 (5.6%)	1 (1.2%)	6 (7.4%)
Abnormal ejaculation	0 (0%)	3 (3.5%)	2 (2.5%)
Asthenia	1 (1.1%)	2 (2.3%)	1 (1.2%)

The authors concluded that most of the outcomes were not significantly different between tamsulosin and placebo after 4 weeks. They reported benefits in the 1 year open label phase of the study (outside the scope of our clinical question) and concluded that placebo controlled trials may need to last for at least 6 to 12 months to demonstrate superiority of active treatment over placebo.

O'Riordan JI, Doherty C, Javed M et al. Do alpha-blockers have a role in lower urinary tract dysfunction in multiple sclerosis? Journal of Urology. 1995; 153(4):1114-1116. Ref ID: ORIORDAN1995	RCT, Ireland Randomisation and allocation concealment unclear; single blind	18	Inclusion: Men younger than 50 years with multiple sclerosis attending a neurology service; symptoms of urinary tract dysfunction and residual volume greater than 50mL. Exclusion: History of spinal injury, significant cardiovascular, renal or hepatic disease, taking beta-blockers or other antihypertensives, clinical relapse during trial period. Baseline characteristics not stated except that mean flow rate was significantly better in the placebo group than the intervention group at baseline ($p<0.05$). Proportion using catheters no stated	Indoramin 20mg twice daily (n=9)	Placebo (n=9)	4 weeks	Residual volume; self-administered symptom score: irritative symptoms of frequency, urgency and nocturia, and obstructive symptoms of hesitancy, quality of stream, sensation of incomplete emptying and terminal dribbling (each symptom graded 0-3)	not stated

Results:

	Placebo	Indoramin	p value for difference
Peak flow rate	Worsened by 7.4%	Improved by 41%	$p<0.05$
Mean residual volume (mL)			

Baseline After treatment Change	162 124 24%	223 166 26%	
Meant total symptoms score Baseline After treatment Change	 8.75 7.75 12%	 9.40 7.80 18%	NS

Adverse effects on indoramin: 1 patient suffered a generalised macular rash; 2 patients had retrograde ejaculation.
Adverse effects on placebo: 1 patient suffered nausea.

No patients withdrew due to side effects.

Authors concluded that improvements in urinary flow rates and symptoms were only mild and there were side effects suggesting that indoramin is unlikely to be of general clinical value.

Petersen T, Husted SE, Sidenius P. Prazosin treatment of neurological patients with detrusor hyperreflexia and bladder emptying disability. Scandinavian Journal of Urology & Nephrology. 1989; 23(3):189-194. Ref ID: PETERSEN1989	RCT, Denmark Randomisation and allocation unclear; double-blind crossover design with 6 weeks each active treatment + 2 weeks washout in between treatments. However, dose increased by half a tablet per day until maximum	19	Inclusion: Difficulty in voiding, residual urine above 20% of the actual bladder capacity and detrusor hyperreflexia. Exclusion: Age above 70 years, mental reduction, renal and liver insufficiency and prostatic hypertrophy. Baseline characteristics (not shown by treatment group): Mean age 51 years (range 27 to 68 years), 4 men and 15 women. Diagnoses: multiple sclerosis 14, spastic paraparesis familiaris 4, arachnoiditis 1. Proportion using catheters not reported	Prazosin increased by 0.5mg daily to 3mg three times a day N=19	Placebo N=19	6 weeks each active treatment + 2 weeks washout in between treatments.	Maximal flow Residual urine	Danish Multiple Sclerosis Society

	dose reached or side effects; could unblind patients and/or investigators.							

Results:

Subjective preference: In one patient, voiding difficulty disappeared and micturition became normal after prazosin treatment. In the remaining patients, the sensation of incomplete bladder emptying and difficulty in voiding were reported unchanged. Concerning frequency of voiding and incontinence episodes, 5 patients preferred the active treatment, 1 preferred placebo and 12 did not prefer either treatment to the run-in periods. Mean number of voluntary micturitions per day: 7.0 (2.9) on placebo and 7.0 (2.6) on prazosin. Incontinence episodes (registered in 9 patients during both treatment periods) fell insignificantly from 2.6 daily with placebo to 2.1with prazosin.

	N	Placebo	Prazosin	Paired difference
Maximal flow (mL/s)	18	7 (3.8)	8 (6.8)	1 (4.8)
Residual urine (mL)	18	248 (168)	250 (219)	2 (171)

Side effects:

An increase in incontinence episodes was reported by 4 patients during placebo and 2 during active treatment.

Dizziness was reported by 3 patients during placebo and 7 during active treatment.

Oedema in the legs was reported by 1 patients during placebo and 4 during active treatment.

The authors concluded that only in very few patients did prazosin ameliorate the bladder emptying disability.

Schulte-Baukloh HM. Alfuzosin in the treatment of high leak-point pressure in children with neurogenic bladder. BJU International. 2002; 90(7):716-720. Ref ID:	Observational study	N=17	Children with upper motor neurone lesions with urodynamically confirned detrusor hyper-reflexia. Patient population: females:male 6:11, mean age 6.3 yrs (range 0.25 to 16). Aetiology: 12 myelomeningocele, 1 tethered cord syndrome, one intraspinal tumour, 2 spinal cord injury and 1	Alfuzosin 2.5 mg in children > 2 yrs one times daily increased to three times daily	None	3 weeks	Continence Side effects	None reported

SCHULTEBAUKLOH2002			perinatal cerebral palsy. N=4 on anticholinergics for at least 6 months. N=5 clean intermittent catheterisation was used but this therapy alone was insufficient to keep the bladder pressure at < 40 cmH2O	In the younger children medication was started at 0.625 mg two or three times daily				
Effect Continence "There was no measurable change in continence" Side effects 3/17 "side effects were rare and not severe"								

F.3 Does the use of the following direct treatment

- Clinical assessment
- Urine culture
- Residual urine estimate
- Bladder diary/frequency volume chart

No papers were identified for this question

F.4 Does the use of the following direct treatment or stratify risk (of renal complications such as hydronephrosis):

- Filling cystometry
- Leak point pressure measurements.

- Pressure-flow studies of voiding
- Video urodynamics

Higher risk group – children with myelodysplasia

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bauer SB, Hallett M, Khoshbin S et al. Predictive value of urodynamic evaluation in newborns with myelodysplasia. JAMA. 1984; 252(5):650-652. Ref ID: BAUER1984	Observational study (prospective)	N=36	Consecutive newborns with myelodysplasia. In each child the myelomeningocele was repaired with 24 hrs of birth, and, when indicated, the CSF diverted.	As soon as possible after the neurosurgical operations or when the child's condition allowed, serum creatinine level, urine cultures, neurologic examination, excretory urogram and urodynamic studies were performed. If the excretory urogram was abnormal or if the urodynamic study disclosed incoordination of the detrusor external urethral sphincter, a voiding cystourethrogram was obtained	-	Follow-up urodynamic studies were done semiannually in all children with dyssynergic sphincter activity, as increasing postvoiding volume of urine, or an abnormal urogram. In the remainder, urodynamic assessment was performed yearly. Follow-up ranged from 18 to 48 months	Urodynamic findings	None reported

Effect

The urodynamic studies showed that 18 (50%) of the 36 children had incoordination of the detrusor-external urethral sphincter. Three of these had hydronephrosis on the initial excretory urogram. Severe hydroureteronephrosis, massive reflux, or an enlarged bladder with a large post voiding volume or urine developed within six months of birth in seven, before 2 yrs of age in two, after two years of age in one. Thirteen (72%) of 18 children with dyssynergia were found to have these abnormalities. The five infants with incoordination of the detrusor-external urethral sphincter who urinary tracts did not deteriorate had milder forms of dyssynergia.

Nine newborns had synergic activity of the external uretheral sphincter. In two (22%), dyssynergia and subsequent decompensation of the urinary tract developed. Of the nine neonates with absent electromyographic activity in the external urethral sphincter, only one experienced deterioration of the urinary tract, and this child had elevated urethral resistance.

The incidence of urinary tract decompensation was significant different (χ^2=19.6, 2 df, p<0.001) among the three groups of newborns differentiated by the nature of electromyographic activity at the time of initial urodynamic study. No correlation could be made between the level of the neurological lesion and the type of activity of the external sphincter or the development of deterioration of the urinary tract.

16/36 (44%) of infants required treatment for deterioration of the urinary tract.

Authors conclusion

Infants with dyssynergia of the detrusor-external sphincter are at high risk of deterioration of the urinary tract; they should be followed up closely and intermittent catheterisation should be started early.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
McGuire EJ, Woodside JR, Borden TA et al. Prognostic value of urodynamic testing in myelodysplastic patients. Journal of Urology. 1981; 126(2):205-209. Ref ID: MCGUIRE1981	Retrospective observational	N=42	Patients with myelodsplasia	Serial radiographic studies that included excretory urography (IVP) and voiding cystourethrography, all had undergone urodynamic evaluation (urethral pressure profilometry, cystometrogram)	-	Mean 7.1 yrs (range 3 to 15 yrs)	Detrusor response to filling Urodynamic findings in relation to IVP and voiding cystourethrography	None reported

Effect

Detrusor response to filling

Of the 42 patients 7 (17%) showed reflex detrusor activity in response to bladder filling. In 3 of these 7 patients intravesical pressure at the time of urethral leakage (urethral opening pressure) was higher than maximal resting urethral closing pressure values as determined by the profile technique, while in 4 it was lower. In the

former 3 patients discoordinate activity between the detrusuor and external sphincter was present, while in the latter 4 patients coordinate detrusor and sphincter activity occurred. 35/42 (83%) patients showed areflexic detrusor dysfunction. Detrusor pressure response to volume increments varied: 5 patients showed no significant intravescial pressure response to volume increments and demonstrated a large bladder capacity without urethral leakage, while 30 showed a progressive increase in pressure without increasing volume culminating in urethral leakage when intravesical and intraurethral pressures were equal.

Urodynamic findings in relation to excretory urography (IVP) and voiding cystourethrography

A total of 20 patients showed intravesical pressures ≤ 40 cm. water at the time of urethral leakage, while 22 showed pressures greater than this value. No patients in the low pressure group suffered vesicoureteral reflux and only 2 showed evidence of urethral dilation on an IVP. Urethral dilation resulted in resolution of upper urinary tract changes in these 2 patients. In contrast, the patients who demonstrated higher peak urethral closing pressures and, consequently, higher intravesical pressures at the time of urethral leakage had significantly more clinical problems. 15 (68%) had vesicoureteral reflux, 18 (81%) showed uretral dilation on an IVP, 8 underwent an operative procedure to decrease urethral resistance and 7 underwent urinary diversion. One patient ultimately required a renal transplant into an ileal loop diversion. In all, 17 operative procedures were performed, including 2 ureteral reimplantations.

Relationship of urethral opening pressure to ureteral complications

	Urethral opening pressure	
	< 40 cm water No. (%)	> 40 cm water No. (%)
Vesicoureteral reflux	0	15 (68)
Ureteral dilation	2 (10%)	18 (81)

The major clinical problems were incontinence in patients with low urethral closing pressures and the degree of urinary retention, upper urinary tract deterioration and the development of vesicoureteral reflux in those with higher urethral closing pressures

Authors conclusion

There is a striking relationship between urethral closure pressure and intravesical pressure at the time of urethral leakage and the clinical course in this group of myelodysplastic patients is demonstrated. Every patient with a normally closed vesical outlet was continent on intermittent catheterisation and an anticholinergic agent, while nly 60% of patients with open bladder outlets similarly treated achieved good urinary control and none was dry. Treatment options for patients with high urethral closed pressures include intermittent catheterisation and anticholinergic medications or a sphincter ablative procedure to decrease the outlet resistance combined with anticholinergic therapy and implantation of an artificial sphincter. However, only longer follow,up will determine if these therapeutic regimens will prevent upper urinary tract deterioration

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Seki NA. An analysis of risk factors for upper urinary tract deterioration in patients with myelodysplasia. BJU International. 1999; 84(6):679-682. Ref ID: SEKI1999	Observational study (cross-sectional)	N=39 N=63 reviewed	Patients with myelodysplasia. Inclusion criteria included: not to have been managed by either intermittent or indwelling catheterisation before being referred to the hospital. The basic evaluations for inclusion in the study were an excretory urogram, a voiding cysto-urethrogram and a baseline urodynamic study which had been performed within 30 days after the first visit. None of the patients were managed using anticholinergic agents during the study.	Basic evaluations for inclusion in the study were excretory urogram, a voiding cysto-urethrogram and a baseline urodynamic study which had been performed within 30 days after the first visit	-	NA	Predictors of vesico-utereric reflux (VUR) and hydronephrosis	None reported

Of the 39 patients, 15 (39%) showed some degree of vesico-ureteric reflux (VUR) and hydronephrosis was identified in five patients (13%) at evaluation. The results of the stepwise logistic regression analysis showed that a high level of MUCP and the presence of DSD were selected as having the most effective combination of factors for the incidence of VUR. A high level of MUCP was also selected as a significant factor that correlated with the incidence of hydronephrosis. The OR of the selected factors were all > 1, indicating that the presence of DSD and a high level of MUCP increased with risk of upper urinary tract deterioration.

Authors conclusion

The results clinically confirm a significant correlation in myelodysplastic patients between the degree of upper urinary tract deterioration and abnormal lower urinary tract function, especially for the disordered function of the urethral control mechanism.

Variables	Coefficient	SEM	OR	P
VUR				
MUCP	0.10	0.04	1.10	0.013
DSD	2.93	1.04	18.76	0.005
Hydronephrosis				
MUCP	0.07	0.03	1.08	0.034

DSD	ns	ns	ns	0.074

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sidi AA, Dykstra DD, Gonzalez R. The value of urodynamic testing in the management of neonates with myelodysplasia: a prospective study. Journal of Urology. 1986; 135(1):90-93. Ref ID: SIDI1986A	Prospective observational study	N=30	Neonates with myelodysplasia. Patient population: 18 female and 12 male newborns	Voiding cystourethrography with fluoroscopic monitoring, normal excretory urogram (IVP) and urodynamics (including filling cystometry, electromyography)	-	Testing including urodynamic performed 7 to 10 days after birth and after surgical repair	Detrusor characteristics, electromyography findings, radiographic findings	None reported

Effect

Detrusor characteristics

Of the new borns 12 (40%) showed reflex detrusor contraction in response to filling, including 9 (30%) with a coordinated detrusor and sphincter, and 3 (10%) with detrusor-sphincter dyssynergia. Of the 18 newborns in whom a detrusor contraction was absent 3 (10%) had atonic large bladders without an increase in intravesical pressure and 15 (50%) showed decreased-compliance bladders, including 6 (20%) with high pressures and 9 (30%) with low pressures.

When classified into groups 9 newborns were classified as group 1 (detrusor-sphincter dyssynergia and high pressure, decreased-compliance) and 21 as group 2 (atonic, nondyssynergic and low pressure, decreased compliance)

Electromyography findings

Detrusor characteristics	Lower motor neuron lesions No. (%)	Normal bioelectrical activity	Total No. examined
Detrusor-sphincter dyssynergia	2 (67)	1	3
Normal	1 (11)	8	9
Atonic	2 (100)	-	2
Decreased compliance Low pressure High pressure	 8 (100) 2 (50)	 - 2	 8 4

Radiographic findings, treatment and follow-up

The initial studies showed that 5 (55.5%) newborns in group 1 had abnormal radiographic findings, 4 of whom were treated with suppressive antibiotics, clean intermittent catheterisation and anticholinergic medication. The remaining patient underwent vesicostomy that was closed when he was 12 months old, and anticholinergics and clean intermittent catheterisation were instituted. Follow up has shown that in 2 children radiographic changes reversed to normal after 5 and 14 months, in 2 the changes remained stable for a follow up periof of 12 and 14 months, and in 1 deterioration occurred after a follow-up period of 36 months.

Four neonates in group 1 with normal radiographic findings were treated expectantly. On follow up examinations they all had radiographic changes (at ages of 6, 7, 19, and 22 months) and, subsequentky, were placed on anticholinergics and clean intermittent catheterisation.

The intitial studies revealed abnormal radiographic findings in only 6 newborns from group 2 (28.5%). A suppressive antibiotic was instituted for those patients and follow up has shown that radiographic changes reversed to normal in 4. One child remained stable after a follow up period of 12 months and 1 progrssed from grade I to grade IV vesicoureteral reflux within 6 months. Repeat urodynamic testing in this child has shown that the previously atonic bladder changed to a high pressure, decreased-compliance bladder. Subsequently, he underwent ureteral reimplantation and was placed on clean intermittent catherisation with anticholinergics. None of the children from group 2 with normal intial radiographic studies has shown changes on follow up.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Galloway NT, Mekras JA, Helms M et al. An objective score to predict upper tract deterioration in myelodysplasia. Journal of Urology. 1991; 145(3):535-537. Ref ID: GALLOWAY1991	Prospective and retrospective observational study	N=171	Patients with myelodysplasia Patient population: Mean patient age at the time of urodynamics 4.8 yrs (range newborn to 36 yrs)	Urodynamics: fluid filled cystometry and sphincter electromyography	-	Mean 2.3 yrs	Development of upper tract changes	None reported

Effect

AIM: To develop and objective score to describe urodynamic findings in myelodysplasia

Scores (hostility scores) were calculated for each patient (total score 0 to 10). A score of 10 would mean the bladder is of low compliance and has high pressurr hyperreflexic detrsor contractions, sphincter dyssynergia, high leak pressure and significant vasicoureteral reflux.

Reference scale

		Score	
	0	1	2
Reflux (rt and lt)	Absent	Grade I-II	Grade III+
Hyperreflexia	Absent	15-50	>50 cm water
Compliance	>20	10-20	<10
Leak Pressure	<25	25-50	>50 cm water
Sphincter	Relaxing	Nonrelaxing	Dyssynergic

Mean score for the total group was 5.02 (range 0 to 10)

Relation of hostility score to the fate of the upper tracts

To investigate the predictive value of the hostility score only patients who had normal upper tracts at the time of urodynamic study we included. For those patients who were managed expectantly the urodynamic study was considered to reflect truly the lower urinary tract status during follow up. For patients in whom a treatment change was made, the result of a further study while on treatment was used so that the study would reflect more truly the lower tract status during followup.

Of 73 patients with normal upper tracts at the time of urodynamics the hostility scores ranged from 1 to 7. Hydronephrosis later developed in 14 of these patients. The mean duration of follow-up was 2.2 yrs and for those in whom it did not develop was 2.3 yrs. No patient who initially presented with normal upper tracts had a hostility score of less than 5 later had upper tract changes. There was a highly significant difference between the groups (p=0.0005). Four of the individual components of the score had predictive value. Outlet resistance (leak pressure) (p=0.001), compliance (p=0.004), sphincter behaviour (p=0.015) and reflux (p-0.017). The score for detrusor contractility did not demonstrate a significant trend.

Authors conclusion

In 171 myelodysplastic patients a significant correlation was demonstrated between the score and upper tract studies at the time of urodynamics and the score and the management decision.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of fundin g
McLorie GA, Perez-Marero R, Csima A et al. Determinants of hydronephrosis and renal injury in patients with myelomeningocele.	Prospective observationa l study	N=213	Patients with myelodysplasia and neurogenic bladder impairment. Patients were included in the study when they were advised to start a program of clean intermittent catheterisation (CIC). The	Continence, urinary tract infections, radiographic evaluations (excretory urograms (IVPs) and voiding cystourethrograms,		2 yrs of data collection	Urodyanmics including cystometry and urethral pressure profilometry	None reporte d

Journal of Urology. 1988; 140(5 Pt 2):1289-1292. Ref ID: MCLORIE1988			indications for CIC included incomplete bladder emptying, upper urinary tract decompensation, vesicoureteral reflux and combination of these conditions. Patient population: The majority were infants and young children, and the study included both sexes. Children with all spinal levels involved were treated	single urodynamics Sought to determine those factors present at the initial visit that would correlate with the hydronephrosis grading on the IVPs at that or any of the visits. All parameters including patient age, sex, site of neurological lesion, reflux, bladder shape, bladder volume, uninhibited contractions, maximum urethral pressure and dyssynergia, as measured in the initial visit were contrasted against the hydronephrosis grade at any visit				
Effect In the regression analysis we identified a constellation of urodynamic and radiographic parameters that influenced the grade of hydronephrosis. The regression coefficient was 0.49. These factors included an elevated urethral pressure profile, bladder volume smaller than the mean volume for age, presence of urethrovesical dyssynergia, and presence and grade of vesicoureteral reflux. Each of these was treated as independent variables in the analysis and reached a significant level of less than 0.05. Urodynamic variables Elevated urethral pressure profile (p=0.008), bladder volume at or less than the mean for age (p=0.01) and presence of vesicourethral dyssynergia (p0.02) contributed to elevated hydronephrosis grade. Conclusion We described a statistical analysis confirming that radiographic and urodynamic criteria can correlate with deterioration of the upper urinary tract.								

1

<table>
<tr><th>Reference</th><th>Study type
Evidence level</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr><td>Wang QW, Wen JG, Song DK et al. Is it possible to use urodynamic variables to predict upper urinary tract dilatation in children with neurogenic bladder-sphincter dysfunction? BJU International. 2006; 98(6):1295-1300. Ref ID: WANG2006.</td><td>Retrospective study, China</td><td>200</td><td>Inclusion: Children with neurogenic bladder sphincter dysfunction
Exclusion: Hydronephrosis due to renal calculi and PUJ obstruction

Baseline characteristics:

<table><tr><th></th><th>upper urinary tract dilatation (UUTD: bilateral hydronephrosis and VUR)</th><th>no UUTD</th></tr><tr><td>n</td><td>103</td><td>97</td></tr><tr><td>boys</td><td>71</td><td>68</td></tr><tr><td>girls</td><td>32</td><td>29</td></tr><tr><td>Mean (SD) age, range</td><td>10 yr, range 1-18 yr</td><td>11, 0.25-18 yr</td></tr><tr><td>Occult spina bifida</td><td>24</td><td>28</td></tr><tr><td>Cystica spina bifida</td><td>33</td><td>33</td></tr><tr><td>Cystica spina bifida repaired</td><td>25</td><td>24</td></tr><tr><td>Primary tethered cord syndrome</td><td>15</td><td>7</td></tr><tr><td>Spinal cord</td><td>6 (mean time</td><td>5</td></tr></table></td><td>Routine urological, neurological and urodynamic examinations; ultrasound, IVU, cystography, spinal MRI.

Urodynamic risk score (URS): bladder compliance (BC) <9mL/cm H2O = 1 point, detrusor leak point pressure (DLPP) >40cm H2O = 1 point, and acontractile detrusor (ACD) = 1 point; summed to give a score</td><td>-</td><td>Unclear</td><td>Predicting upper urinary tract dilatation (UUTD) from urodynamic risk score based on bladder compliance (BC) <9mL/cm H2O, detrusor leak point pressure (DLPP) >40cm H2O and acontractile detrusor (ACD)</td><td>Innovation and Talent Research Foundation of Henan Province, China, Henan Innovation Project ofr University Prominent Research Talents (HAIPURT) and National Natural Science Foundation of China</td></tr>
</table>

			injury	after trauma 14 mo, range 6-21 mo)	(13mo, 6-20 mo)	range 0-3.			
			Grade 1 hydronephrosis + pelvic dilatation <1cm Grade 2-3 hydronephrosis + pelvic dilatation 1-1.5cm + mild dilatation of renal calyces Grade 4-5 hydronephrosis + pelvic dilatation >1.5cm + mid-range dilatation of renal calyces + thinning renal parenchyma	34 34 35	NA				
			Voluntary contractile bladder	31 (30%)	67 (65%)				

Results:

	Control (no UUTD)	UUTD group 1 (Grade 1 hydronephrosis + pelvic dilatation <1cm)	UUTD group 2 (Grade 2-3 hydronephrosis + pelvic dilatation 1-1.5cm + mild dilatation of renal calyces)	UUTD group 3 (Grade 4-5 hydronephrosis + pelvic dilatation >1.5cm + mid-range dilatation of renal calyces + thinning renal parenchyma)	p value
Mean (SD) urodynamic variables:					
Maximum free flow rate mL/s	8.7 (3.3)	7.9 (4.4)	7.5 (3.6)	7.4 (3.6)	0.147
Post-void residual volume mL	47 (35)	108 (92)	132 (97)	183 (122)	<0.001
Bladder compliance mL/cm H2O	25.6 (17.5)	15.1 (12.2)	6.4 (4.5)	5.9 (3.0)	<0.001
Detrusor leak point pressure cm H2O	19 (12)	34 (16)	54 (21)	68 (27)	<0.001
Static urethral functional length mm	28 (11)	24 (9)	27 (11)	28 (9)	0.176
Maximum urethral closure pressure cm H2O	85 (27)	74 (28)	74 (24)	78 (24)	0.108
Neurogenic detrusor overactivity (yes)	45 (46%)	16 (47%)	14 (41%)	10 (29%)	0.297
Acontractile detrusor (yes)	30 (31%)	21 (62%)	24 (71%)	27 (77%)	<0.001
Detrusor leak point pressure >40cm H2O (yes)	10 (10%)	13 (38%)	27 (79%)	31 (89%)	<0.001
Detrusor-sphincter dyssynergia (yes)	50 (52%)	21 (62%)	21 (62%)	20 (57%)	0.633

Group 1- grade 1 hydronephrosis and pelvic dilatation of < 1 cm; group 2 – grade 2-3 hydronephrosis and pelvic dilatation of > 1 cm but < 1.5 cm, and mild dilatation of the renal calyces; and group 3 – grade 4-5
hydronephrosis with pelvic dilatation of > 1.5 cm, mid-range dilatation of the renal calyces and thinning of renal parenchyma. Control group – children with NSBD but no upper urinary tract dilatation and vesicoureteral reflux

Urodynamic risk score and upper urinary tract changes

		Upper urinary tract dilation group (n=103)			
Risk score	Control	1	2	3	Total
0	52 (54)	4	5	1	10 (10)
1	30 (31)	17	3	3	23 (22)
2	11 (11)	7	6	11	24 (23)
3	4 (4)	6	20	20	46 (45)

Using a urodynamic risk score ≥2, sensitivity to predict upper urinary tract dilatation in children with neurogenic bladder sphincter dysfunction was 68% (70/103) and specificity was 82% (70/85).

Authors concluded that a low bladder compliance, increased detrusor leak point pressure and acontractile detrusor arte good urodynamic factors to predict upper urinary tract dilatation in children with neurogenic bladder sphincter dysfunction, and these factors increase the occurrence and grade of upper urinary tract dilatation. A urodynamic risk score ≥2 is the criterion for an accurate diagnosis of upper urinary tract dilatation, with a sensitivity of 68% and a specificity of 82%. Even for children with normal urodynamic findings, close follow up is important for early diagnosis and timely treatment, as well as preventing progressive upper urinary tract dilatation.

1 **Higher risk groups – spinal cord injury**

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Khanna R, Sandhu AS, Doddamani D. Urodynamic management of neurogenic bladder in spinal cord injury. Medical Journal Armed Forces India. 2009; 65(4):300-304. Ref ID: KHANNA2009	Prospective observational study	N=100	Males with spinal cord injury aged 21-56 yrs	Urodynamics	Na	Urodynamics performed every 3 to 6 mths. 82% patients underwent 3 or four studies	Urodynamic findings	None reported

Effect

At baseline, no urodynamic findings were normal. Findings included detrusor hyperreflexia with detrusor external sphincter dyssynergia (DESD) in 85% of patients with thoracic lesions; detrusor hyperreflexia without DESD in 35% of patients with cervical and lumbar lesions; and detrusor areflexia in 40% of patients with lumbar lesions. The use of clean intermittent catheterisation and anticholinergic medication was instituted in all patients. The table below describes the complications found in this study. The authors conclude that repeated urodynamic studies are an essential aid in managing the evolving nature of the bladder dysfunction in spinal cord injury.

Complication	Number of cases (%)
Upper tract changes (Backpressure)	15 (15)
Autonomic dysreflexia	12 (12)
Chronic renal failure	6 (6)
Stricture urethra	6 (6)
Bladder calculi	4 (4)
Refractory hypotension	1 (1)

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kim YH, Kattan MW, Boone TB. Bladder leak point pressure: the measure for sphincterotomy success in spinal cord injured patients with external detrusor-sphincter dyssynergia. [Review] [23 refs]. Journal of Urology. 1998; 159(2):493-496. Ref ID: KIM1998	Retrospective observational study	N=55	Patients with spinal cord injury who had undergone transurethral resection of the external bladder for bladder management Patient population: mean age 50 yrs range 34 to 7). Levels of spinal cord injury included 37 cervical (67.3%), 17 thoracic (30.9%) and 1 lumbar (1.8%). Each patient underwent a mean of 1.3 resections (range 1 to 3). The interval since the last resection ranged from 1 to 27 yrs (mean 11.9 yrs). Mean duration of injury was 21 yrs (range 6 to 47 yrs)	Urodynamics	-	Performed every 1 to 3 yrs, most recent reviewed for this study	Leak point pressure, bladder compliance, persisting external detrusor sphincter dyssynergia	None reported

Effect

AIM: Examination of elevated bladder leak point pressure after transurethral resection of the external sphincter as an indicator of failure

36/55 (65%) patients had bladder leak point pressure greater than 40 cm water and 19/55 (35%) had pressure less than 40 cm water. There was no significant correlation between elevated bladder leak point pressure and the presence of reflux, stones, bacteriuria or autonomic dysreflexia. There was a significant correlation between elevated bladder leak point pressure and renal damage (p=0.021) and persistent external detrusor-sphinecter dyssynergia (p=0.00008). There was no significant correlation between bladder leak point pressure greater than 40 cm water and the presence of an indwelling catheter.

Authors conclusion

Bladder leak point pressure greater than 40 cm. of water is a valid indicator of failure of transurethral resection of the external sphincter since there is a significantly higher incidence of upper tract damage and persisting external detrusor-sphincter dyssynergia in these patients.

1 **Higher risk groups - Parkisonson's disease and transurethral prostatectomy**

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Staskin DS, Vardi Y, Siroky MB. Post-prostatectomy continence in the parkinsonian patient: the significance of poor voluntary sphincter control. Journal of Urology. 1988; 140(1):117-118. Ref ID: STASKIN1988	Retrospective observational study	N=50	Patients with Parkinson's disease undergoing transurethral prostatectomy for benign prostatic hypertrophy Patient population: Mean age 67 yrs (range 50 to 82 yrs)	Urodynamics including cystometry, voluntary sphincter control and presence of detrusor hyperreflexia	-	mean postoperative duration 9.2 mths (range 1 to 28 mths),	Continence, Urodynamics	None reported

Effect

Of the patients 36 required transurethral prostatectomy, while 14 were unobstructed and did not undergo an operation.

Continence status

Of 50 patients 39 (78%) were continent, while 11 (22%) were not (nine had urge and two overflow incontinence), The continence rate in the operative group was 83%

and it was not statistically different from that in the nonoperative group which was 63%.

Change in continence status

Postoperatively, 26 of the 36 patients (72%) were continent and 10 had urge incontinence, Of 30 patients continent before transurethral prostatectomy 24 remained continent postoperatively, while six had urge incontinence. Thus, the incidence of de novo incontinence was 6 of 30 patient (20%), Of six patients continent before the operation, four continued to have urge incontinence and two patient became continent.

Of 50 patients 46 (92%) had detrusor hyperreflexis while four had noncontractile bladder. In the operative group two patients had a noncontractile bladder regained detrusor contractility postoperatively, Since hyperreflexia was extremely common preoperatively and postoperatively, no relationship to the development of incontinence could be discerned,

Voluntary sphincter control

Of the 50 patients 33 (66%) demonstrated normal sphincter control and 17 did not. In the operative group normal voluntary sphincter control was found in 26 patients (72%), while in the nonoperative group it was present in only 50% but this was not statistically significant,

In the entire group of 50 patients, continence was highly associated with the presence of normal voluntary sphincter control. Of the 33 patients with normal voluntary sphincter control 31 were continent compared to only 8 of 17 with poor voluntary sphincter control ($p<0.01$). The association between continence and normal voluntary sphincter control was present within the operative and nonoperative subgroups as well.

The presence or absence of voluntary sphincter control did not change postoperatively. Postoperatively, 25 of 26 patients with normal voluntary sphincter control were continent, compared with only one of ten with abnormal voluntary sphincter control ($p<0.002$). Of the patients who were continent preoperatively five of six with abnormal voluntary sphincter control became incontinent postoperatively compared to only one of 24 with normal voluntary sphincter control. Surprisingly, both patients who were incontinent preoperatively but who had normal voluntary sphincter control became continent postoperatively and none of the four with abnormal voluntary sphincter control became continent.

1 ## Higher risk patients – men with multiple sclerosis

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Blaivas JG, Barbalias GA. Detrusor-external sphincter dyssynergia in men with multiple sclerosis: an ominous urologic condition. Journal of Urology. 1984; 131(1):91-94. Ref ID: BLAIVAS1984	Observational study (prospective)	N=27	Consecutive patients with multiple sclerosis underwent synchronous video/pressure/flow electromyography studies as part of a prospective evaluation of voiding disturbances in these patients. Each patient underwent detailed neurological and urological evaluation, excretory urography (IVP) and	On the basis of the clinical history and urodynamic findings patients were managed according to a rationale dictated by the underlying pathophysiological conditions. All patients initially were managed	-	Not reported	Development of serious complications	None reported

			routine blood and urine studies. Study reports on 27 males. Patient population: male:female 27:59. Males were aged between 22 and 64 yrs, mean 41 yrs. In the 27 men the duration of multiple sclerosis averaged 11 yrs (1 to 21 yrs). Average grade of multiple sclerosis 2 (Grade of multiple sclerosis: grade 1 – minimal neurological disease, and patients were ambulatory, self sufficient and led normal active lives, grade 2 – moderate neurological abnormalities with obvious neurologic findings that interfered with daily-life style yet patients remained ambulatory and self-sufficient and grade 3 – overt neurological findings and patients were confined to bed or wheelchair)	conservatively, with minimally invasive or pharmacologic treatment. For patients with detrusor-external sphincter dyssynergia treatment with propantheline bromide and intermittent self-catheterisation was recommended. Patients who could not tolerate propantheline or in whom it was ineffective, or those who could not master intermittent self-catheterisation were treated with a condom catheter. Patients who could not tolerate a condom catheter were treated with an indwelling vesical catheter.				
Effect 18 men had detrusor-external sphincter dyssynergia. Only 7 of the 18 men with dyssynergia agreed to be treated with propantheline and intermittent self catheterisation: 2 suffered urinary sepsis during the 1 yr of treatment (1 underwent external sphincterotomy), 2 had persistent incontinence despite treatment (1 underwent elective supravesical urinary diversion and 1 was treated with condom catheter drainage), 1 had vesicoureteral reflux without sepsis and 2 had no further complications. Of the remaining patients 5 were treated with condom catheter drainage alone (2 underwent transurethral external sphincterotomy at 2 and 3 years, respectively, for urinary sepsis and 3 had no urinary complications), 5 were treated with an indwelling vesical catheter and 1 refused any treatment at all. Episodes of life-threatening sepsis recurred after 1 to 4 yrs in 4 of the 5 patients treated with indwelling catheters (2 ultimately underwent transurethral supravesical urinary diversion and 2 underwent transurethral external								

sphincterotomy), while in the remaining patient remission of the multiple sclerosis was associated with the disappearance of detrusor-external sphincter dyssynergia.

An excretory urography (IVP) revealed normal upper tracts in 21 patients, while 5 with detrusor-external sphincter dyssynergia has bilateral hydronephrosis (grades 3 to 4 in 3 patients with type 3 dyssynergia, and grades 1 to 2 in type 1 and 1 with type 3 dyssynergia). One patients with type 1 dyssynergia had a small caliceal stone.

Of the 9 men without detrusor-external sphincter dyssynergia 3 underwent transurethral prostatectomy because of benign prostatic hypertrophy, 1 had elective supravesical urinary diversion because of persistent urinary incontinence despite multiple trials of conservative treatment, 1 was treated with a condom catheter alone and the remaining 4 did not undergo specific treatment. None of these patients suffered any serious complication.

Relationship among urologic complications, grade of multiple sclerosis and type of detrusor-external sphincter dyssynergia

Complications	Grade of multiple sclerosis			Type of detrusor-external sphincter dyssynergia*	
	1	2	3	1	3
None	3	8	6	4	2
Sepsis	0	1	6	3	3 (2)
Reflux	1	1	- (1)	1	1 (1)
Stones	0	0	1 (2)	1	1 (1)
Hydronephrosis	0	- (1)	1 (4)	1	- (4)
Totals	4	10	14	10	7**

Numbers in parenthesis refer to patients with > 1 complication * Excludes 1 patients in whom the grade of dyssynergia was not recorded ** 1 patient had sepsis, vesicoureteral reflux and hydronephrosis; 1 had stone and hydronephrosis, and 1 had sepsis without other complications

Authors conclusions

Urological complications were correlated highly to the presence of detrusor-external sphincter dyssynergia and the severity of the multiple sclerosis but not the duration of multiple sclerosis, age of the patient or type of dyssynergia. Although no treatment was without complications it appears that either anticholingerics plus intermittent self-catheterisation or condom catheter drainage is superior to an indwelling catheter for initial conservative treatment. External sphincterotomy or urinary diversion may be necessary if conservative treatment fails.

1 ## Higher risk patients – children with anorectal anomalies

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
De Filippo RE, Shaul DB, Harrison EA et al. Neurogenic	Prospective observational study	N=26	Infants born with anorectal malformations. Patient population: 20 with	Urodynamics Patients entered the study along a continuum from	-	Urodynamic data was collected at different	Leak point pressure	None reported

bladder in infants born with anorectal malformations: comparison with spinal and urologic status. Journal of Pediatric Surgery. 1999; 34(5):825-827. Ref ID: DEFILIPPO1999			isolated imperforate anus (IA) and six with persistent cloaca. All patients with IA underwent a diverting colostomy and subsequent posterior sagittal anorectoplasty (PSARP). Mean age 25.6 mths (range 3 to 106 mths), A subset of eight patients underwent urodynamic studies both before and after PSARP, The ages of these patients were 11.8 mths (range 3 to 31 mths),	birth, surgery or postoperatively. Urodynamic data was collected at different time points Ultrasound or MRI and radiological imaging of the genitourinary tract with both a renal ultrasound scan and voiding cystourethrogram (VCUG)		time points		

Effect

Summary of patient data

Total patients in study	26
No. of patients with normal leak point pressures	5
No. of patients with elevated leak point pressures	21
Patients with normal uroradiography	9
Patients with abnormal uroradiography	12
Abnormal spinal cords	6
Normal spinal cords	6

21/26 had elevated leak point pressures (LPPs). 15/21 children had normal spinal imaging findings, where as six demonstrated spinal abnormalities. 10 of these 21 had bony abnormalities of the spine or sacrum. By comparison, two of the five with normal LPPs had spinal cord abnormalities, and four had bony abnormalities. The spinal evaluation does not predict the urodynamic result.

1

2

1 Lower risk – women with multiple sclerosis

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lemack GE, Frohman E, Ramnarayan P. Women with voiding dysfunction secondary to bladder outlet dyssynergia in the setting of multiple sclerosis do not demonstrate significantly elevated intravesical pressures. Urology. 2007; 69(5):893-897. Ref ID: LEMACK2007	Prospective observational study	N=143 referrals N=127 women N=108 completed urodynamic testing	The data from all patients with multiple sclerosis (MS) referred for the evaluation of lower urinary tract symptoms from 2002 to 2006 were prospectively entered into a database consisting of urodynamic and demographic findings. Patient population:52% were referred for evaluation of urgency, frequency, and/or urgency incontinence. The remaining patients were referred for voiding difficulties (21%), presumed recurrent urinary tract infection (13%), or other complaints (14%). Time since diagnosis 14.4 yrs	All patients with MS presenting for an initial evaluation were asked to undergo a complete examination, including multichannel urodynamic testing with fluoroscopy, if available (after 2004), and renal ultrasonography after an initial consultation.	-	NA	Urodynamics, upper tract changes	None reported
Effect Of the 108 women, 62 (57%) had detrusor overactivity during testing. This study compared with urodynamic characteristics of patients of the patients who had detrusor overactivity with coexisting bladder neck or external sphincter dyssynergia (n=30) and the patients who had detrusor overactivity only (n=32) Urodynamic parameters. Nonsignificant minor elevations in virtually all parameters of intravesical pressure were noted among the patients with bladder outlet dyssyneriga (BOD)								

Variable	Patients with DO + DSD (n=30)	Patients with DO, no DSD (n=32)	P value
Amplitude at initial DO (cm H2O)	21.93 ± 20.712	21.33 ± 12.863	0.530
Volume at DO (mL)	202.27 ± 146.704	173 ± 150.87	0.788
Pdetmax (cm H2O)	49.77 ± 20.88	41.03 ± 22.590	0.428
Cystometric capacity	301.52 ± 175.418	272.58 ± 192.582	0.517
Qmax (mL/s)	11.26 ± 5.833	12.96 ± 7.203	0.690
PdetQmax (cm H2O)	35.77 ± 14.429	30.00 ± 14.431	0.566
Voided volume (mL)	208.74 ± 123.729	182.38 ± 129.96	0.800
PVR (mL) Median Range	 50 0-500	 37 0-500	

Pdetmax – maximal detrusor pressure; Qmax – maximal flow rate; PdetQmax – detrusor pressure at Qmax; PVR – postvoid residual urine volume; DO – detrusor overactivity; DSD – detrusor sphincter dyssynergia

With regard to upper tract findings, all patients underwent ultrasonography, and no patients in either group had hydronephrosis. Two of the patients with bladder outlet dyssynergia and three with detrusor activity alone had focal caliectasis

Authors conclusion

No significant elevations were found in the intravesical pressures of female patients with MS, detrusor overactivity and bladder outlet dyssynergia compared with those with detrusor activity. These findings, along with the very low incidence of upper tract abnormalities at the initial presentation in patients with multiple sclerosis, suggest that consideration of clean intermittent catheterisation should not necessarily be dictated by a concern for upper tract damage secondary to increases in intravesical pressure, even among women with dyssynergia. Rather starting clean intermittent catheterisation in women with MS should be discussed if the lower urinary tract symptoms (resulting from a reduced functional bladder capacity) and/or the risk of recurrent infections warrant such therapy.

1 ## Lower risk – bladder augmentation

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lopez PP, Moreno Valle JA, Espinosa L et al. Are urodynamic studies really needed during bladder	Retrospective observational study	N=32	Patients with neurogenic bladder who underwent bladder augmentation before or at puberty, and who also had a minimum follow-up of 10 yrs after	Bladder augementation A total of 22 augmentations were performed with ileum, seven with sigmoid colon	Urodynamic evaluations	"All urodynamic evaluations were routinely performed preoperatively,	Urodynamic findings	None reported

augmentation follow-up? Journal of Pediatric Urology. 2009; 5(1):30-33. Ref ID: LOPEZ2009			surgery. Patient population: Aetiology: myelomeningocele in 30 patients, sacral agenesis in one patient and sacrococcygeal teratoma in one patient.	and three with ureter associated with a transureteroureterostomy. In ten patients with noncompliant bladder and urinary incontinence, testing revealed low sphincteric resistance in four. An artificial sphincter was placed in combination with bladder augmentation in these four patients		during and at the end of follow-up" Cystoscopy at end of follow-up Mean follow up 12 yrs (range 10 to 14.5 yrs)		

Effect

Before augmenting the bladder only eight patients had normal upper urinary tract. Seventeen had vesicouretral reflux (VUR) and four had moderate-to-severe hydronephrosis. Three patients (9.3%) had VUR in one kidney and hydronephrosis in the contralateral kidney. Of the 28 refluxing units, 23 (82%) had high grade reflux. DMSA scintigraphy showed renal scars in 25 patients and in three kidneys the differential renal function was between 18% and 20%. The DMSA scintigraphy was normal in one seven patients.

Based on age-adjusted serum creatinine levels, all patients except one had normal renal function at the time of bladder augmentation.

The urodynamic evaluation before bladder augmentation showed a poorly compliant bladder in all patients which was associated with detrusor overactivity in eight. Despite clean intermittent catheterisation and anticholinergic therapy, VUP, hydronephrosis and bladder compliance did not improve satisfactorily in any patient. 16 patients had recurrent urinary tract infections and 10 had urinary incontinence.

After surgery

One year after augmenting the bladder, urodynamic studies showed a significant improvement in bladder capacity and a significant decrease in detrusor pressure during filling in all patients. Bladder capacity improvement was more marked at the end of follow up than at one year after bladder augmentation; however, the filling detrusor pressure did not change with time. Therefore, bladder capacity improved over time in these patients.

Urodynamic results (32 patients): preoperative, 1 year after augmenting the bladder and at end of follow up

	Preoperative	1 year	P	End	P
MBC	106±52	396±125	<0.0001	507.8±165*	<0.002*
MEFDP	50±32	7±4	<0.0001	10±4	NS*

MBC – mean bladder capacity (ml); MEFDP – mean end-filling detrusor pressure (cm of water); ns – not significant. * statistical significance between the urodynamic results at 1 yr after bladder augmentation and at the end of follow up.

After bladder augmentation, hydronephrosis disappeared in all patients and VUR in 16/20 (80%) patients. Of the four patients with persistent VUR, it improved from bilateral high grade to bilateral low grade in one but VUR grade did not change in the other three patients.

DMSA scintigraphy has shown no new scarring during the course of this long-term follow up. Three patients have presented with bladder stones that required surgical

intervention, one patients had a symptomatic urinary tract infection due to temporary non compliance with clean intermittent catheterisation,one patients had an intestinal obstruction in the immediate postoperative period and another patients with an artificial urinary sphincter required a continent catheterisable channel made from ileum because of problems with clean intermittent catheterisation through the urethra.

Authors conclusions

..We believe that urodynamic studies are not essential after augmenting the bladder. They are only necessary in those cases where upper urinary tract dilation or continence does not improve…

1 **Lower risk – head injury**

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Singhania PA. Urodynamic evaluation of urinary disturbances following traumatic brain injury. Urologia Internationalis. 2010; 84(1):89-93. Ref ID: SINGHANIA2010	Prospective small case series, India	N=11	Inclusion: patients with head injury and positive CT findings Exclusion: none stated Baseline characteristics: 10 males; 1 female. Mean age 40 years (range 17-77 years). All had detrusor hyperreflexia	Urodynamic studies when patients could cooperate (mean 9.2 days post-injury; range 2-25 days); frequency volume charts for 2 days; ultrasound abdomen and pelvis; post-void residual estimation; urinary tract infection excluded.	-	1 year	Early catheter removal in patients with normal urodynamic study; appropriate management if abnormal study	none stated

Results: 3 patients had unstable bladder with multiple involuntary contractions in the filling phase, all with no post-void residue; 2 had catheter is situ and 1 had frequency/urgency; 1 had amplitude of contraction >40cm H2O and was started on anticholinergics (significant improvement allowed withdrawal of drug at 2 months). Urodynamic studies repeated after cessation of symptoms were normal; at 1 year follow up all had normal voiding and upper tracts normal.

Other 8 patients had normal urodynamic studies and catheter-free trials in these patients were successful.

Authors concluded that head-injury-induced bladder hyperreflexia had a good prognosis and in all cases (but n=only 3) resolved at 2 months; at 1 year, none of the 11 patients had urinary symptoms; none required neurosurgical intervention, although anticholinergics may be required for some months.

2

1 High risk – managed with urodynamic-directed protocols

<table>
<tr><th>Reference</th><th>Study type</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr><td>Chao R, Mayo ME. Long-term urodynamic follow up in pediatric spinal cord injury. Paraplegia. 1994; 32(12):806-809. Ref ID: CHAO1994</td><td>Retrospective review of patient charts, video urodynamic studies and radiographs</td><td>N=40</td><td>Inclusion: children <18 years old with spinal cord injury.
Exclusion: none stated
Baseline characteristics:
Overall mean age at presentation: 9.0 years (range newborn to 17 years). By lesion level:
<table>
<tr><td></td><td>Cervical</td><td>Thoracic</td><td>Lumbar</td></tr>
<tr><td>n</td><td>22</td><td>13</td><td>5</td></tr>
<tr><td>Male</td><td>15</td><td>11</td><td>3</td></tr>
<tr><td>Female</td><td>7</td><td>2</td><td>2</td></tr>
<tr><td>Mean age</td><td>7.8yr</td><td>9.4yr</td><td>9.8yr</td></tr>
<tr><td>Mean follow up</td><td>56.7 months</td><td>52.9 months</td><td>28.8 months</td></tr>
</table></td><td>Yearly physical examination, 1-2 year upper tract examinations (intravenous pyelogram or renal ultrasound) and video urodynamic investigation</td><td>-</td><td>Mean 46.1 months (range 1 to 240 months)</td><td>Identify patients with high-pressure bladders and detrusor-sphincter dyssynergia who are at risk of upper tract damage and recommend anticholinergic drugs and intermittent catheterisation in these patients</td><td>none stated</td></tr>
<tr><td colspan="9">Reflex voiding (spontaneous detrusor contraction to empty the bladder at acceptable voiding pressure) or catheterisation was recommended depending on the patient's bladder voiding pressure, on urodynamics, the child's age, and the family situation. Those patients having moderate to severe trabeculation and correspondingly high pressures (detrusor >40cmH2O), or any patients exhibiting detrusor-sphincter dyssynergia on video urodynamics, were placed on anticholinergic drugs and intermittent catheterisation (ICP). Patients and families desiring continence also started ICP, with medications if indicated.
<table>
<tr><td></td><td>Cervical spinal cord injury</td><td>Thoracic spinal cord injury</td><td>Lumbar spinal cord injury</td></tr>
<tr><td>Urodynamic studies</td><td>All patients had a hyperreflexic bladder; mean appearance smooth to slightly trabeculated</td><td>11 hyperreflexic bladders; 2 areflexic</td><td>All areflexic</td></tr>
<tr><td>Voiding:
Reflex
ICP/drugs</td><td>
8 (including 1 vesicotomy)
14</td><td>
2
11</td><td>
2 (Valsalva manoeuvre)
3</td></tr>
</table></td></tr>
</table>

26/28 patients following recommended voiding protocols have maintained their urinary tracts, while patients who did not comply with a recommendation to start ICP/anticholinergics had moderate or severe trabeculation at follow up.

The authors concluded that periodic urinary tract assessment with renal ultrasound or intravenous pyelogram and video urodynamics is essential to monitor urinary tract morphology and renal function; intermittent catheterisation and anticholinergic drugs were recommended if bladder wall changes occurred, and this regimen maintained urinary tracts.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Generao SE, Dall'era JP, Stone AR et al. Spinal cord injury in children: long-term urodynamic and urological outcomes. Journal of Urology. 2002; 172(3):1092-1094. Ref ID: GENERAO2002	Retrospective observational study	N=42	Children with spinal cord injury. Children 14 yrs old and younger with a minimum of one year follow up from the date of injury were included. Patient population: mean age 5.3 yrs (range 1 day to 14 yrs). Females:males 23:19. Etiology: 20 motor vehicle accidents, 4 automobile vs pedestrians, 6 postoperative spinal injuries, 5 falls, 2 post-intrathecal methotrexate injections, 2 spinal cord infarcts, 1 gunshot wound, 1 neonatal epidural hematoma and 1 all-terrain vehicle accident. No patient suffered concomitant brain injuries. No patient exhibited latency between injury and onset of symptoms. Patients were divided into 3 groups based on level of injury – cervical (24%), thoracic (62%) and lumbar	Multichannel urodynamic studies	-	Mean 5.5 yrs (range 1 to 15.5 yrs)	Urodynamics Upper tract deterioration	None reported

			(14%).					

Effect

Cervical group

In two patients initial video urodynamics showed a small capacity, hyperreflexic and trabeculated bladder. One had mild hydronephrosis and detrusor sphincter dyssynergia (DSD). Both patients underwent ileocystoplasty. Both are managing their augmented bladders without antibiotic or anticholinergic medication and both are dry. Both patients have normal renal sonograms.

Of the remaining 8 patients with cervical injuries six use anticholinergics and two use prophylactic antibiotics. Six patients manage their bladder with clean intermittent catheterisation (CIC) and four are dry. Two patients are damp and have persistent compliance issues with medication and catheterisation. Two children and spontaneous voiders and are dry.

Of these eight patients six have smooth bladders on fluoroscopy. The bladder of one patient using CIC has changed from mildly trabeculated to smooth and one from smooth to mildly trabeculated after one year of non-compliance with CIC. Four patients have hyperreflexia, 2 with DSD. Five patients have at least two urodynamic studies performed and the safe capacity is smaller than expected but is increasing with time. Of the three patients undergoing one urodynamic evaluation two have a safe capacity equal to expected capacity and one has a smaller than expected capacity. One case of vesicoureteral reflux resolved with time. No patient had development of upper tract deterioration.

	Cervical	Thoracic	Lumbar
No patients	10	26	6
Average age at injury (yrs)	4.8	5.9	3.4
Clean intermittent catheterisation	80%	96%	100%
Dry	80%	54%	33%
Detrusor sphincter dyssynergia (DSD)	30%	31%	0
Hyperreflexia*	60%	38%	17%
Anticholinergics	60%	100%	83%
Safe capacity less than expected capacity	80% (8/10)	58% (15/26)	50% (3/6)
Safe capacity increasing with age**	100% (5/5)	76% (13/17)	67% (2/3)

*Includes 2 children who initially had hyperreflexia but subsequently underwent augmentation ** Includes patients with two or more urodynamic studies

Thoracic group

All patients use anticholinergic medication and 3 (12%) require prophylactic antibiotics for recurrent infection. CIC is used by 25 patients and 1 had a suprapubic tube placed after development of a false passage in the bulbar urethra. 14 (54%) are dry, 11 (42%) are damp, one three yr old is still in diapers and none is continuously wet.

Bladder contour was smooth is 24 patients (92%) and because mildly trabeculated in 2 during follow up. Detrusor hyperreflxia was seen in 10 patients (38%) and areflexia in 12 (46%). Two cases (8%) changed from hyperreflexic. DSD was noted in 8 patients (31%), all of whom had hyperreflexia. Two or more urodynamic studies were performed in 17 patients. Four of these patients have a safe capacity equal to expected capacity and nine have a smaller than expected safe capacity but capacity in all 13 of these patients is increasing with time. Of the nine patients undergoing a single urodynamic evaluation safe capacity was equal to that expected in 7 and smaller than that expected in 2. No patient had development of upper tract deterioration or underwent bladder augmentation.

Lumbar grou

In the lumbar group anticholinergic medication was used by five patients and antibiotics by one patient. All six patients used clean intermittent catheterisation, although two were not always compliant. Two patients are dry, two are damp and two patients with compliance issues are wet. All lumbar patients had smooth bladders and one had hyperreflexia. No patient had DSD. Two or more urodynamic studies were performed in three patients and one had safe capacity equal to expected and two a smaller than expected safe capacity. Two had an increasing and one had a decreasing capacity with time. Of the three patients undergoing urodynamic evaluation two had safe capacity equal to expected capacity based on age and one had smaller capacity than expected. No patient had development of upper tract deterioration.

Conclusions

For children on a clean intermittent catheterisation (CIC) regimen the level of injury did not have a significant impact on upper tract outcome. Early bladder management with CIC and anticholinergics appears to prevent hydronephrosis, scarring, reflux and trabeculation. Serial urodynamics have shown that safe capacity increases in most children with SCI as they grow. Urodynamic patters may improve or deteriorate with time, especially in the thoracic group. We have seen changes in trabeculation and hyperreflexia despite CIC compliance. These findings underscore the importance of close regular follow up with urodynamic studies and upper tract imaging.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kessler TML. Predictive value of initial urodynamic pattern on urinary continence in patients with myelomeningocele. Neurourology and Urodynamics. 2006; 25(4):361-367. Ref ID: KESSLER2006B	Retrospective study	N=123	Inclusion: patients with meningomyelocoele; older than 7 years at last assessment and with complete initial evaluation and follow-up data Exclusion: none stated apart from 29 of original 157 excluded for age <7 years or incomplete data Baseline characteristics: 56 females and 67 males; mean age at last follow up 17 years	History, neurological examination, urinalysis, urine culture, excretory urography, sonography of kidneys and bladder, video urodynamics at birth or 2 weeks after closure of defect; those at risk of upper tract damage or with abnormal imaging had nuclear renal	-	10 years (range 2-27 years)	Primary: Continence status at last follow up (continent = completely dry day and night with therapy; socially dry = dry during a minimum of 3 hours with therapy;	none stated

			(range 7-33 years). Divided on basis of urodynamic pattern at initial evaluation into: Group 1: overactive detrusor + overactive sphincter (upper urinary tract at risk due to high pressures) Group 2: overactive detrusor + underactive sphincter Group 3: underactive detrusor + overactive sphincter Group 4: underactive detrusor + underactive sphincter	scan. Periodic reassessment every 3-6 months to age 2 and yearly thereafter. Treatment strategy: patients with overactive sphincter had intermittent catheterisation; those with overactive detrusor treated with anticholinergics. When continence not achieved, surgery considered (artificial urinary sphincter, bladder augmentation or orthoptic bladder substitution).			incontinent = involuntary loss of urine in intervals <3 hours with therapy). Secondary: surgical interventions	

	Group 1	Group 2	Group 3	Group 4	Total	p
Treatment used:						-
Intermittent catheterisation (IC)	0	0	7	7	14	
IC + anticholinergics	33	4	0	0	37	
IC + drugs + surgery	2	8	0	0	10	
IC + surgery	6	0	0	9	15	
Anticholinergics only	0	20	0	0	20	
Surgery only	1	2	0	0	3	
No treatment	1	3	1	19	24	
Number of patients undergoing surgery*	9	10	0	9	28	-
Type of procedure:						
Bladder augmentation only	3	0	0	0	3	
Orthoptic bladder substitution	1	0	0	0	1	
Artificial urinary sphincter only	2	8	0	6	16	
Bladder augmentation + artificial urinary sphincter	3	2	0	3	8	

Continent or socially dry	37 (86%)	21 (57%)	7 (87%)	26 (74%)	91 (74%)	0.023
Incontinent	6 (14%)	16 (43%)	1 (13%)	9 (26%)	32 (26%)	
Continence by treatment used:						-
Intermittent catheterisation (IC)	-	-	7/7	6/7	13/14	
IC + anticholinergics	28/33	3/4	-	-	31/37	
IC + drugs + surgery	2/2	8/8	-	-	10/10	
IC + surgery	6/6	-	-	9/9	15/15	
Anticholinergics only	-	8/20	-	-	8/20	
Surgery only	1/1	2/2	-	-	3/3	
No treatment	0/1	0/3	0/1	11/19	11/24	

* In some patients, more than one procedure was necessary

Main aim of the management strategy (use of drugs and/or surgery, based on neurological examination, urodynamic investigation and imaging studies) was to preserve renal function and achieve urinary continence.

Group 1 at high risk of upper urinary tract damage due to high pressures, but high chance of continence: convert overactive to underactive detrusor with drugs and use intermittent catheterisation.

Group 2 at high risk of detrusor overactivity incontinence and stress incontinence: use anticholinergics and if necessary electrostimulation of pelvic floor musculature or artificial urinary sphincter.

Group 3: Continent as long as controlled fluid intake prevents overflow incontinence: use intermittent catheterisation.

Group 4: Risk of stress incontinence: use artificial sphincter (may also require bladder augmentation). Empty bladder using intermittent catheterisation. Avoid passive voiding using Valsalva manoeuvre or compression of lower abdomen as increased pressure risks upper renal tract and pressure on urethra can cause inefficient emptying (unless pressure shown to remain <40cm H2O).

The authors concluded that initial urodynamic pattern is useful for counselling families on the likelihood of achieving continence, and that serial urodynamic studies thereafter are a pre-requisite for an adequate treatment strategy (e.g. to monitor the effectiveness of current management and assess whether a change in strategy, e.g. change of drug dose or use of surgery, is required).

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Wang SC, McGuire EJ, Bloom DA. A bladder pressure management system for	Prospective observational study	N=114	Patients with neurogenic bladder and myelodysplasia	In 1983 a protocol was instituted based on the assumption that intravesical		Minimum 18 mths to a maximum of 40 mths	3 monthly urodynamic studies involved	

myelodysplasia--clinical outcome. Journal of Urology. 1988; 140(6):1499-1502. Ref ID: WANG1988			Patient population: 69 girls and 45 boys from newborn to 23 yrs old. Nine newborns were studied urodynamically and radiographically before and immediately after closure of the myelomeningocele defect, and thereafter they were followed with periodic urodynamic studies as described for other subjects.	pressure was the underlying problem requiring treatment in myelodysplastic patients. Patients with bladder filling pressures or pressures at the time of urinary leakage greater than 40 cm water determined by water cystometry were treated to reduce vesical pressure			measurement of vesical storage pressure during bladder filling and bladder pressure at the time of leakage Ultrasound every 6 mths Excretory urogram (IVP), serum creatinine measurement and voiding cystourethrogram yearly	
Effect The patients were group into two categories: group A – bladder pressure during storage or leakage was greater than 40 cm water and group B – bladder pressure during storage or leakage was always less than 40 cm water. These groupings were based on the results of initial fluoroscopically guided urodynamic evaluation of bladder and sphincter. There were 48 patients (42%) In group A, Of these 38 patients (79%) showed an areflexic bladder with an open, nonfunctional internal sphincter. Filling and leak point pressures were greater than 40 cm waterm and mean maximum pressure was 52 cm water with a range of 40 to 78 cm water. Ten patients (21% of group and 9% overall) showed reflex vesical contractility and a reflex increase in external sphincter at the same time as the increase in intravesical pressure. These findings are consistent with detrusor external sphincter dyssynergia. All patients with detrusor external sphincter dyssyenrgia had a functional (closed) internal sphincter mechanism at rest. There were 66 patients (58%) in group B. Of these 62 (94%) showed an areflexic bladder with an open, non-functional sphincter with some function of the external sphincter mechanism and 4 (6%) were urodynamically normal. In this group, including those with a normal bladder, bladder pressure during filling, voiding and/or leakage was well below 40 cm water. The mean maximum filling pressure was 18 cm water and the mean maximum leak point pressure was 18 cm water (range 0 to 24 cm water). Management								

Immediate treatment with intermittent catheterisation was instituted in every patient in group A regardless of age or upper tract status. Volumes recovered at the time of catheterisation were recorded and a repeat urodynamic study was done to document that at those volumes pressures after treatment were less than 40 cm. For those patients with poor compliance and high pressure at low volumes anticholinergic agents were instituted as they were for patients with a reflex vesical contractility and a dyssynergix sphincter. If a sufficient decrease in measured bladder pressure was not achieved by these measures, urethral dilation or vesicotomy was performed to achieve leak point and storage pressures of less than 20 cm water.

In group B patients intermittent catheterisation was instituted in those with chronic or symptomatic infection, in older patients to improve continence or as a method of delivery of antimicrobial agents to control bacteriruria. If in all patients measures pressures with time increased to greater than 40 cm water, intermittent catheterisation was instituted immediately.

Clinical outcome

Of the 48 patients in group A 22 (48%) had ureteral dilation when first evaluated. The degree of dilation diminished in 5, resolved in 3 and stabilised in 6 patients after institution of intermittent catheterisation and anticholinergic agents. Eight girls less than 3 yrs old failed to achieve sufficient reduction in bladder pressure with intermittent catheterisation and medication, and they underwent urethral dilation to reduce leak point pressure, following which all showed resolution or improvement in upper tract dilation. No patients in this group showed progressive upper tract changes by radiographic criteria. Eighteen patients (37.5%) and 21 ureters showed reflux on the initital voiding cystourethrogram and all were managed by intermittent catheterisation and anticholinergic agents. Four required urethral dilation. Reflux did not progress in any of these patients. Reflux ceased in 8 ureters, improved in 3 and remained unchanged in 10. In 3 patients a symptomatic febrile urinary tract infection developed within a short period after the initiation of intermittent catheterisation but this resolved rapidly with treatment by antimicrobial agents.

There were no patients in Group B in whom upper urinary tract abnormalities developed. Seven patients (10.7%) had grades I to V reflux on voiding cystouethrography and all were managed by intermittent catheterisation. Reflux ceased in 2 ureters and 4 remained unchanged but stable. The remaining patient had grade V low pressure reflux and a single symptomatic febrile urinary tract infection. He underwent ureteral reimplantation

Continence

Of 57 children older than 5 yrs in whom continence could be assessed perfect urinary control was achieved in 19 (33%) and socially acceptable continence was achieved in 20, with an overall rate of acceptable urinary control in 39 (68%) patients. 18 patients with areflexic detrusor dysfunction remained wet. None of the patients with a normal internal sphincter mechanism at rest was wet. Of note, not all patients with intractable wetting were in the group with a non-functional vesical outlet and all patients with true reflex detrusor-sphincter dyssynergia were dry with anticholinergic agents and intermittent catheterisation.

Authors conclusions

Treatment with intermittent catheterisation and anticholinergic agents, which reduce bladder pressure in a substantial majority of patients, resulted in perfect urinary control in only 33% and improved urinary control in only 68% of our cases.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Nosseir M, Hinkel A, Pannek J.	Retro-spective	80	Inclusion: neurogenic lower urinary tract dysfunction due to spinal cord injury; presenting for urodynamic examination at least once a year for at least 5 consecutive years; urinary tract	Interview with standard questionnaire;	-	At least 5 years;	"Treatment success" on urodynamic	

<table>
<tr>
<td>Clinical usefulness of urodynamic assessment for maintenance of bladder function in patients with spinal cord injury. Neurourology & Urodynamics. 2007; 26(2):228-233. Ref ID: NOSSEIR2007</td>
<td>study</td>
<td></td>
<td>infection excluded.
Exclusion: "patients with a low risk profile"

Baseline characteristics:
60 male and 20 female patients; mean age at presentation 29.6 years; 30 cervical, 36 thoracic and 14 lumbar injuries. Mean time injury to presentation 77.4 months (range 1 to 611 months).

<table>
<tr><th></th><th>Inter-mittent catheter</th><th>indwell catheter</th><th>reflex void</th><th>abdo strain</th><th>Brindley stimulator</th></tr>
<tr><td>n</td><td>51</td><td>6</td><td>11</td><td>10</td><td>2</td></tr>
<tr><td>Incontinent</td><td>12</td><td>0</td><td>not stated</td><td>not stated</td><td>0</td></tr>
<tr><td>4+ UTI/ year</td><td>10</td><td>2</td><td>4</td><td>4</td><td>0</td></tr>
<tr><td>Median bladder capacity</td><td>466cc</td><td>307cc</td><td>256 cc</td><td>456 cc</td><td>500cc</td></tr>
<tr><td>Median storage pressure</td><td>24cm H2O</td><td>17cm H2O</td><td>31cm H2O</td><td>22cm H2O</td><td>11cm H2O</td></tr>
</table>
</td>
<td>urines microbiologically assessed; renal and bladder ultrasound, urodynamic testing. If results favourable, further visits every 6-12 months; if unfavourable, treatment strategy modified and urodynamic examination 6 weeks to 6 months after change (depending on severity of dysfunction).

If >4 urinary tract infections/year, screening for renal or bladder stones (removed if detected); if neither urodynamic examination</td>
<td></td>
<td>mean 67.3 months (range 60-103 months)</td>
<td>testing (i.e. detrusor storage pressure <40cm H2O in the absence of autonomic dysreflexia; or in the case of reflex voiding or anterior root stimulation, leak point pressure of 40cm H2O or less in the absence of autonomic dysreflexia combined with maximum detrusor pressure <90cm H2O).

Urinary tract infection rate (significant bacteriuria + leucocyturia or + symptoms) of 3/year or less considered</td>
<td></td>
</tr>
</table>

				nor additional screening abnormal, long-term antibiotic treatment initiated.			acceptable; 4 or more/year and/or febrile infections considered treatment failures. Continence status (in patients performing intermittent catheterisation or anterior root stimulation, no pad or one pad/day = socially continent; other pad use = incontinence). Renal status (normal = absence of dilatation or scarring on ultrasound). Bladder ultrasound (abnormal if stones,	

							tumours or thickened bladder wall).	

Effect

At the end of 5 years, no patient had developed signs of renal damage. To achieve this, 8 patients had sphincterotomy; 3 received a Brindley stimulator; 3 underwent bladder augmentation; 1 underwent cystectomy and Koch pouch continent urinary diversion; 12 patients treated with Botulinum-A toxin injections into detrusor muscle; 22 received intravesical anticholinergic therapy. In only 3 patients was therapy unchanged.

Treatments used	success rates
Oral anticholinergics: Baseline Initiated or modified	 36 25 (16 satisfactory results)
Intravesical oxybutinin Baseline Initiated	 2 22 (16 successful)
Botulinum-A toxin	12 (8 successful)
Detrusor myectomy (augmentation)	3 (0 significant improvement at 1 year)
Collagen injections or artificial sphincter	2 (both successful)
Sacral intradural deafferentation	3 (all successful)
Koch pouch	1 (successful)
Sphincterotomy	8 (7 successful)

An elevated storage pressure or urinary tract infection are risk factors for renal deterioration. At presentation, 15% of patients were at risk of renal damage and 15% were incontinent. Overall, treatment was successful in 92.5% of patients.

In 25 patients, clinical symptoms and/or results of ultrasound indicated that treatment was not sufficient; in all these patients urodynamic testing revealed the dysfunction; relying solely on clinical symptoms, 68.75% of treatment failures would not have been detected.

The authors concluded that, based on the results of scheduled urodynamic testing, oral anticholinergic treatment and intermittent catheterisation are the first-line treatment. If this is not successful or not well tolerated, intravesical anticholinergic treatment is initiated. If this is not successful, use Botulinum-A toxin into the detrusor muscle. If none of these is successful, consider surgery. Performing urodynamic testing only "on demand" carries a significant risk of missing changes in bladder function.

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F.5 What criteria or signs/symptoms should be used to refer patients for specialist assessment?

No search was undertaken for this question

F.6 What is the safety and efficacy of intravesical botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in neurological disease

Children

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Neel KF, Soliman S, Salem M et al. Botulinum-A toxin: solo treatment for neuropathic noncompliant bladder. Journal of Urology. 2007; 178(6):2593-2597. Ref ID: NEEL2007	RCT Randomisation – unclear (occurred post operation) Allocation concealment – closed envelope Blinding – not specified	N=23	Children with neuropathic bladder after repair of myelomeningocele. Inclusion criteria were age range 1 to 14 yrs with urodynamic evidence of high intravesical leak point pressure greater than 40 cm H20 resistant to the maximal tolerable dose of anticholinergics without significant side effects, and fully compliant to an every 4 to 6 hr program (clean intermittent catheterisation). Patient population: mean age 5.6 yrs (SD 2.5 yrs)	BTX-A 12 IU/kg (Dysport) N=12 Maximum 300 IU General anaesthesia Plus oxybutynin continued at the same preinjection dose	BTX-A 12 IU/kg N=11 Maximum 300 IU Oxybutynin was discontinued on the day of the BTX-A injection	One mth and six mths	Maximal bladder capacity Vesicoureteral reflux Renal function Side effects	None reported
Effect BTX-A plus oxybutynin								

Maximum bladder capacity ml
Mean (SD)
Before vs one month
96 (66) vs 155 (73); p<0.013
Before vs six months
96 (66) vs 141 (62); p<0.024
BTX-A
Maximum bladder capacity ml
Before vs one month
96 (71) vs 172 (119); p<0.02
Before vs Six months
96 (71) vs 143 (72); p<0.007
The difference between the groups was not statistically significant
Vesicoureteral reflux (VUR)
Of the 4 patients with VUR only 1 patient showed initial improvement (later relapsed)
Incontinence
Clinically of the 16 incontinent patients (8 in each group), 9 (56.2%, 5 in group 1 and 4 in group 2) showed complete continence after treatment, 4 (25%, 2 in each group) reported mild to moderate improvement and 3 (18.8%, 1 in group 1 and 2 in group 2) showed no improvement.
Renal
Of the 46 renal units 25 had renal dilation from the 15 units dilated in group 1, 5 improved after treatment, none from the other 10 renal units deteriorated over the period of treatment. In group 2 of the 10 dilated renal units, 3 had improvements and none of the other 7 units had deterioration during the treatment period. None of those without dilation became hydronephrotic during followup
Side effects
None reported

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Altaweel W, Jednack R, Bilodeau C et al. Repeated intradetrusor	Prospective observational study	N=20	Children and young adults with neurogenic bladder due to myelomeningocele	BTX-A 5 IU/kg to a maximum of 300 IU (unclear manufacturer)	BASELINE In all cases conservative managements with anticholinergics and	Mean 17.2 mths (SD 2 months)	Continence Maximal bladder capacity	None repored

botulinum toxin type A in children with neurogenic bladder due to myelomeningocele. Journal of Urology. 2006; 175(3):1102-1105. Ref ID: ALTAWEEL2006			Patient population: 8 males and 12 femals. Mean patient age 13 yrs (range 8 to 20)	Give in different locations General anaesthesia No. of Injections 1 injection n=13, 2 injections n=3, 3 injections n=1 Postoperatively, anticholinergics were discontinued at 3 weeks after BTX-A but parents were advised to resume anticholinergics progressively if incontinence persisted or reoccurred.	clean intermittent catheterisation had failed. All patients were catheterised or self-catheterised at least 4 times daily, and urinary incontinence was resistant to high dose anticholinergic therapy			
Effect Adverse events None reported Continence Total urinary continence was restored in 13 patients (65%) after the first injection. Before vs after 1st injection Maximal bladder capacity cc mean (SD) Continent (n=13) 215.6 (58.8) vs 338.3 (98.4) p<0.01								

Incontinent (n=7)
146 (44.4) vs 164.2 (48.2) p=0.1

Before vs after 2nd injection
Maximal bladder capacity cc mean (SD)
Continent (n=13) (figures contradict text – '3 had received 2 reinjections'
200.5 (41.6) vs 404.2 (57.8)
Incontinent (n=6)
153.2 (44.1) vs 162.5 (56)
Hydronephrosis
There were no observed changes

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Akbar M, Abel R, Seyler TM et al. Erratum: Repeated botulinum-A toxin injections in the treatment of myelodysplastic children and patients with spinal cord injuries with neurogenic bladder dysfunction (BJU International (2007) 100 (639-645)). BJU Int.	Retrospective observational study	N=19	Patients with myelodysplasia (MDP). Treatment required to treat neurogenic lower and upper urinary tract dysfunction (detrusor overactivity, low compliance, reduced bladder capacity, incontinence and upper urinary dilation) resistant to anticholinergic medication and/or because anticholinergic drugs caused unacceptable side effects Patient population: 13 girls, six boys, mean age 9.87 yrs (range 1.5 to 15.0)	BTX (Dysport) injections in conjunction with clean intermittent catheterisation (CIC). Anticholinergics tapered. 20 units/kg to a maximum of 400 units Injected in upto 20 sites Local	BASELINE CIC plus anticholinergics if tolerated	Urodynamics once or twice a year for upto 12 mths	Maximal bladder capacity Continence Muscle weakness	None reported

2007; 100(3):719. Ref ID: AKBAR2007A				anaesthesia or analgosedation Not able to extract no. of injections given but a minimum of 2 given				
Effect Before BTX vs after 1 injection vs after 2 injections vs after 3 injections Maximal bladder capacity mL mean (SD) 180.58 (128.60) (n=19) vs 290.42 (169.47)* (n=19) vs 292.68 (169.29)* (n=19) vs 346.81 (147.79)* (n=16) * p<0.001 vs before injection Continence Not able to extract outcomes for children. 3/19 stopped BTX-A treatment due to persisting incontinence and underwent augmentation surgery								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Deshpande AV, Sampang R, Smith GH. Study of botulinum toxin A in neurogenic bladder due to spina bifida in children. ANZ Journal of Surgery. 2010; 80(4):250-253. Ref ID: DESHPANDE2010	Prospective observational study	N=7	Patients with neurogenic bladder caused by spina bifida and had uncontrolled incontinence while on clean intermittent catheterisation (CIC) and anticholinergic therapy Urodynamic criteria included significantly reduced bladder capacity at pressures of 40 cm H2O	Botulinum toxin A (Botox) (Allergan)10 IU/kg to a maximum dose of 300 IU Injected into 20 to 30 sites in three or four rows above the trigone General	BASELINE All patients included in the study had uncontrolled incontinence whilst on clean intermittent catheterisation and oxybutynin.	1,3-6 and 9 mths	Incontinence (No. of pads used per patient per day) Patient/carer satisfaction (distress caused by urinary incontinence rated on a scale of 1 to 10, higher	Toxin supplied by Allergan

			Patient population: seven patients (one female, six males), median age 16 yrs (range 11 to 17 yrs)	anaesthesia CIC and anticholinergic therapy were left unchanged in all patients after the BTX-A treatment during the period of the study			score indicates greater distress) Side effects including urinary tract infections, muscle weakness	
Effect Side effects One case of mild microscopic haematuria for several hours after cystoscopy and injection. This did not have any clinical consequences. Urinary tract infection One patients suffered a single urinary tract infection during follow up PreBotox vs 1 mth vs 3-6 mths vs 9 mths Bladder capacity mean mL (% improvement and range) 257 (140-400) vs 344 (134%, 180-700) vs 312 (121%, 200-390) vs 306 (119%, 170 to 400) Continence score median (range) 3 (1-5) vs 1 (0-3) vs 3 (0 to 5) vs 3 (1-7) Satisfaction score median (range) 7 (3-8) vs 3 (1-8) vs 3 (1-9) vs 5 (2 to 10)								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Do N, Audry G, Forin V. Botulinum toxin type A for neurogenic detrusor	Retrospective observational study	N=7	Patients with neurogenic detrusor overactivity due to spinal cord lesions in children (n=3 sacral birth defects, n=4 acquired thoracic lesions)	Botulinum toxin A (BTX-A) (Allergan) 6-11 IU/kg to a maximum of 300	BASELINE 6/7 patients using CIC and oxybutynin 1/7 intolerant to oxbutynin and continuously incontinent	Variable	Adverse events	None reported

overactivity due to spinal cord lesions in children: A retrospective study of seven cases. Journal of Pediatric Urology. 2009; 5(6):430-436. Ref ID: DO2009			Patient population: Patients ranged in age at the first injection from 6.5 to 15.5 yrs	UI General anaesthesia				
Effect Lower urinary tract infections The only adverse events were lower urinary tract infections. Adverse events None of the patients experienced generalised muscle weakness								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kajbafzadeh AM, Moosavi S, Tajik P et al. Intravesical injection of botulinum toxin type A: Management of neuropathic bladder and bowel dysfunction in children with myelomeningocele. Urology. 2006; 68(5):1091-1096. Ref ID: KAJBAFZADEH2006	Prospective observational study	N=26	Children with urodynamically proven detrusor hyperreflexia caused by myelomeningocele. All patients had stable neurological status and had not undergone surgery during the previous 2 yrs. The exclusion criteria consisted of coagulopathy,	Botulinum toxin A (BTX-A) (Botox, Allergan) Anticholinergic medication was discontinued at least 10 days before urodynamic assessment In children with bowel dysfunction,	BASELINE All patients had been taking anticholinergic medications since birth and underwent clean intermittent catheterisation every 3 to 4 hrs, with unacceptable adverse effects or little or no	Urodynamic and VUR – after 4 months Daytime continence monthly? (unclear) Adverse event monthly	Maximum bladder capacity Daytime continence (Voiding diary – episodes of wetness during the 4 hrs between two consecutive catheterisations. Daily incontinence score 0 to 3. 0 = completely dry, 1 = wet once a day, usually at night, 2	None reported

			inflammation of the injection site and urinary tract infection Patient population: 20 boys and 6 girls with mean age of 6.9 yrs (range 3.5 to 13 yrs)	suppositories or enema protocols were discontinued, but the usual diet maintained. Preoperative antibiotic therapy BTX-A 10 IU/kg injected intravesically into at least 40 sites, sparing the trigone and ureteral orifices. General anaesthesia	success from treatment		= wet for less than 50% of the time between catheterisations, 3 = wet for more than 50% of the time between catheterisations). Presence and grade of vesicoureteral reflux (VUR) Systemic muscle weakness Urinary tract infection	
Effect Systemic muscle weakness None reported Urinary tract infection None reported Before vs after Incontinence score 2.5 vs 0.3 (p<0.001) Of the 26 patients, 19 (73%) became completely dry between two consecutive clean intermittent catheterisations and 4 of the remaining 7 patients had improved from score 3 to 1. Total improvement rate 88% Mean bladder capacity ml Mean (SEM) 102.8 (6.3) vs 270.2 (9.5); p<0.01 Mean VUR grade Mean								

1.7 vs 0.7; p<0.01 VUR grade decreased in 11 patients (73%)								
1								
Reference	**Study type Evidence level**	**Number of patients**	**Patient characteristics**	**Intervention**	**Comparison**	**Length of follow-up**	**Outcome measures**	**Source of funding**
Riccabona M, Koen M, Schindler M et al. Botulinum-A toxin injection into the detrusor: A safe alternative in the treatment of children with myelomeningocele with detrusor hyperreflexia. Journal of Urology. 2004; 171(2 I):845-848. Ref ID: RICCABONA2004	Prospective observational study	N=15	Children with myelomeningocele (MMC). All children had bladder dysfunction with radiologic sigms of trabeculation and cellules. Three patients had reflux and 4 kidneys in three patients had hydronephrosis Patient population: 10 boys and 5 girls, mean age 5.8 yrs (range 2.3 to 7.7 yrs)	10 U/kg botulinum-A toxin (BTX-A) (unclear manufacturer) Injected into 25 to 40 sites all over the bladder, randomly, including the dome and just sparing the trigon. 10 U/kg to a maximum of 360 U. General anaesthesia Medications including anticholinergics were discontinued 2 wks before urodynamic	BASELINE All patients had been on anticholinergic medication since birth and received clean intermittent catheterisation every 4 hrs, showing little or no success. 14/15 were nonresponders to orally administered anticholinergic medication. Even the subsequent intravesical administration of oxybutynin in 14 patients proved to be insufficient with a leak point pressure still exceeding 40 cm H20	3 months, 9 months and 12 months	Daytime incontinence (voiding diary for 3 days recording any episodes of wetness during the 4 hrs between 2 consecutive catheterisation. Daily incontinence score 0 to 3. 0 = completely dry, 1 = wet once a day, usually at night, 2 = wet for less than 50% of the time between catheterisations, 3 = wet for more than 50% of the time between catheterisations), maximum cystometric bladder capacity	None reported

				assessment Second injection at one year				
Effect Adverse events 1/15 asymptomatic urinary tract infection Vesicoureteral reflux was successfully treated in three patients Before vs 3 mths vs 9mths vs 12 mths Treatment 1 Maximum bladder capacity mean (ml) 136.34 vs 297.02 vs 284 vs 154 Incontinence score 2 vs 0.47 vs 0.67 vs 2.7 Treatment 2 Maximum bladder capacity mean (ml) 154 vs 295 vs 241 vs 161 Incontinence score 2.7 vs 0.45 vs 0.64 vs 2.7 Mean durability of the effect of the toxin was 10.5 mths after the first treatment. The same value was obtained after the second intravesical injection.								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schulte-Baukloh H, Knispel HH, Stolze T et al. Repeated botulinum-A toxin injections in treatment of children with neurogenic detrusor overactivity. Urology. 2005; 66(4):865-870. Ref ID:	Retrospective observational study	N=10	Children with neurogenic detrusor overactivity who had recevid at least three BTX-A injections. To be included the drug	Botulinum-A-toxin injections BTX-A (Botox Allergan) 12 U/kg	BASELINE Bladder emptying occurred through intermittent catheterisation four or five times daily plus anticholinergics	Initially 1, 3 and 6 mths then twice yearly Outcomes compared	Maximal bladder capacity Serious side effects	None reported

SCHULTEBAUKLOH2005A			regimen before and after every injection had to be the same throughout the 6 mths of follow up. The anticholinergic medication could be changed afterward if necessary. Patient population: 6 boys and 4 girls, mean age 11.2 yrs (range 2.9 to 15.3) when they received the first injection. 8 myelomeningolcele, 1 intraspinal astrocytoma, and 1 spinal cord injury The children had high detrusor pressure – more than 40 cm H2O – despite high doses of anticholinergic drugs	Injected into 30 to 50 sites Anaesthesia/sedation not specified BTX-A injections were given an average of every 7.8 mths (range 4 to 18). Mean injection interval in any given patients was between 6.3 (SEM 1.5 mths) and 9.6 (4.2 mths)		3rd vs 1st (3TI group) (all 10 children) 5th vs 1st injection (5TI group) (n=4 children)		
Effect Serious side effects During 5 yrs of experience no patient experienced any serious side effects (one epileptic attack in known epileptic but no further problems with later injections) Maximal bladder capacity mL Mean (SEM) Three times injected group (n=10) 6 months follow up Baseline vs after 1st injection 111.9 (15.3) vs 231.3 (40.5) Before and after 3rd injection 214.6 (39.3) vs 220.8 (64.1) Five times injected group (n=4) 6 months follow up								

Baseline vs after 1st injection 160.3 (17.8) vs 301.0 (49.8) Before and after 5th injection 235.3 (46.4) vd 403.7 (63.6)								

1

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schulte-Baukloh H, Michael Th, Sturzebecher B, Knispel HH. Botulinum-A toxin detrusor injection as a novel approach in the treatment of bladder spasticity in children with neurogenic bladder. European Urology 2003; 44: 139-143.	Prospective observational study	N=20	Inclusion criteria: 1-16 years old; neurogenic bladder and detrusor hyper-reflexia; respond poorly to anticholinergic drugs; vesical pressure >40 cm H20 or be intolerant to anti-cholinergic drugs. Exclusion: None Baseline characteristics: NA (see effect size section below) Children of mean age 12.2 years (11 boys, 9 girls). All had neurogenic bladder. Cause was myelomeningocele in 16 cases, intraspinal astrocytoma in 2, trauma in 1 and unknown in 1. All manifesting with upper motor neurone lesions with hyper-reflexive detrusor muscle, with detrusor-	Botulinum A toxin (Botox, Allergan)injected intramurally to 30-50 sites, at a dosage of 12 U / kg up to a maximum of 300U. Toxin diluted with 15-20 ml normal saline and each injection contained 0.3-0.5 ml.	Baseline All but one had to use CIC at least 4 times a day. N=13 had anticholingergic therapy stopped on receiving botulinum toxin. N=7 remained on anticholinergic therapy	4 weeks, 3 months and 6 months.	Maximal bladder capacity (mL) using video cystometry Incontinence score, based on the scale: 0=completely dry; 1=wet only once a day; 2=wet <50% of episodes between catheterisation; 3= wet more than 50% of episodes between catheterisation	None given.

			sphincter-dyssynergia All but one child emptied their bladder with clean intermittent catheterisation at least four times a day. Anticholinergic medication was stopped at least 10 days before baseline urodynamic measurements, except that in 1 case, anticholinergic medication was maintained before and after injection.					

Effect size : NB: SE were given in the paper and these have been converted into sds.

	Pre treatment	4 weeks	3 months	6 months	sig
Maximal bladder capacity (mL)	163.05 (93.4)	219.85 (134.5)	200.60 (108.5)	222.38 (166.9)	All 3 follow up measures significantly ($p<0.01$) different to baseline
Incontinence score	2.4 (0.80)	1.1 (1.2)	1.7 (1.4)	-	No significant changes

Authors' conclusion: Botulinum toxin is effective when injected into the hyper-reflexive detrusor muscle. It is a valuable option in the management of neurogenic bladder. The effects last about 6 months, and then re-injection is necessary.

1

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schulte-Baukloh T, Scobert J, Stolze, Knipsel HH. Efficacy of Botilinum-A toxin in children with detrusor hyper-reflexia due to	Prospective observational study .	N=17	Inclusion criteria: 1-16 years; detrusor hyperreflexia and high intravesical pressure >40cm H20 or unacceptable side	Injection of Botulinum A toxin (Botox, Allergan) cytoscopically, to 30-40 sites of the	Baseline All but one child emptied their bladder with clean intermittent catheterisation at least	Unclear. Probably 2-4 weeks.	Maximal bladder capacity (mL) using video cystometry Incontinence score, based on the scale:	None stated

myelomeningocele: preliminary results. Urology 2002; 59;: 325-327			effects of anticholinergic medication. Exclusion: None Baseline characteristics: NA (see effect size section for baseline values). Age: 10.8 (mean), 10.7 (median) (9 boys, 8 girls). All had myelomeningocele, with lesions at the thoracolumbar (2), lumbar (5), lumbosacral (5) and sacral 95) levels. All manifested upper motor neurone lesions, including hyper-reflexive detrusor muscles. All but one had to use CIC at least 4 times a day. N=13 had anticholingergic therapy stopped on receiving botulinum toxin. N=7 remained on anticholinergic therapy	bladder. Dosage was 12U/kg of body weight, up to a maximum of 300 U, diluted in 15-20mL of normal saline. Done under LA, and balloon catheter inserted for 12 hours post injection. Anticholinergic medication was stopped at least 10 days before the injection.	four times a day. Anticholinergic medication was stopped at least 10 days before baseline urodynamic measurements, except that in 1 case, anticholinergic medication was maintained before and after injection.		0=completely dry; 1=wet only once a day; 2=wet <50% of episodes between catheterisation; 3= wet more than 50% of episodes between catheterisation	

Effect size

SD or SE not stated in the paper

	Pre treatment	Post treatment	sig

Maximal bladder capacity mean (mL)	137.53 (59.96)	215.25 (96.36)	P<0.005
Incontinence score	2.36 (0.74)	1.43 (1.02)	NS

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schurch B, Schulte-Baukloh H. Botulinum Toxin in the Treatment of Neurogenic Bladder in Adults and Children. European Urology, Supplements. 2006; 5(11):679-684. Ref ID: SCHURCH2006	Prospective observational study	N=24	Children with neurogenic bladder, who required clean intermittent catheterisation (CIC) and were at high risk of impaired kidney function due to neurogenic detrusor overactivity and high bladder pressure despite maximum anticholinergic medication	Botulinum toxin A (BOTOX, Allergan) 12 U/kg to a maximum dose of 300 U Anaesthesia or sedation not specified	BASELINE CIC and maximum doses of anticholinergic medication	1,3 and 6 months	Maximal bladder capacity Incontinence score Adverse events	One author has a consultancy agreement with Allergan
Effect 1 vs 3 vs 6 mths Maximum bladder capacity % increase from baseline 35 vs 23 vs 36% Incontinence score % (lower score the better) 46 vs 15 vs 13 Adverse effects None reported including muscle weakness. One epileptic seizure in known epileptic Urinary tract infection 4/24 reported throughout the study								

2 **ADULTS**

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-	Outcome measures	Source of

						up		funding
Cruz F, Herschorn S, Aliotta P et al. Efficacy and safety of onabotulinumtoxinA in patients with urinary incontinence due to neurogenic detrusor overactivity: a randomised, double-blind, placebo-controlled trial. Eur Urol. 2011; 60(4):742-750. Ref ID: CRUZ2011	RCT	N=275 (ITT) N=270 (safety pop) Cycle 1 N=230 (available case) Cycle 2 N=130 (available case)	Patients with incontinence due to neurogenic detrusor overactivity Patient population: mean age 45.77 yrs, male % 43.6, duration of neurogenic detrusor overactivity 7.97 yrs, UI episodes per week 33.5, current anticholinergic use % 58.9%, using clean intermittent catheterisation % 52%	Botulinum toxin A (Botox) 200U N=92 300U N=91 Injections were performed with no anaesthesia, local anaesthetic, or under general anaesthesia	Placebo N=90	12 weeks	No of weekly urinary incontinence episodes Incontinence Quality of Life (I-QOL) Adverse events	Allergan
Effect Urinary incontinence episodes per week (ITT population) Baseline vs change at week 2 vs week 6 vs week 12 mean (SD) Placebo (n=92) 36.7 (30.7) vs -9.7 (17.9) vs -13.2 (20.0) vs -12.2 (22.2) Botulinum toxin 200 U (n=92) 32.5 (18.4) vs -18.8 (16.7) vs -21.8 (18.1) vs -20.5 (18.9) 300 U (n=91) 31.2 (18.1) vs -15.8 (25.8) vs -19.4 (25.7) vs -19.8 (18.6) Patients with no incontinence Placebo vs 200 U vs 300 U 17.4% vs 64.4% vs 59.5% Maximum cystometric capacity Baseline vs change at week 6 mean (SD) Placebo 249.4 (139.3) vs 6.5 (144.8) Botulinum toxin 200 U 247.3 (147.6) vs 157.0 (164.8) 300 U 246.8 (149.1) vs 157.2 (185.2)								

Incontinence - Quality of life (total score)
Change from baseline
Placebo vs 200 U vs 300 U
Week 6
11.7 vs 24.4* vs 24.3*
Week 12
8.6 vs 25.1* vs 25.9*
*p<0.01 vs placebo

Adverse events
During first 12 wk, n (%)
Placebo (n=90) vs botulinum toxin 200 U (n=92) vs 300 U (n=89)
All adverse events
50 (55.6) vs 63 (69.2) vs 68 (76.4)
Urinary tract infections
20 (22.2) vs 25 (27.5) vs 34 (38.2)
Muscle weakness
1 (1.1) vs 6 (6.6) vs 4 (4.5)

Longer-term efficacy (repeat injections)
Botulinum toxin 200 U(n=42), 300 U (n=32)

Urinary incontinence episodes per week
Mean (SD)
Baseline vs change at week 6
200 U
37.2 (20.0) vs -20.4 (26.4)
300 U
31.5 (16.6)
-19,7 (20.2)

Maximum cystometric capacity ml

Mean (SD)
Baseline vs change at week 6
200 U
221.7 (151.1) vs 123.5 (154.4)
300 U
232.4 (159.3) vs 147.3 (156.3)

Incontinence-Quality Of Life
Mean (SD)+
Baseline vs change at week 6
200 U
34.6 (20.7) vs 21.2 (25.3)
300 U
36.6 (21.6) vs 20.2 (30.4)

1

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Ehren I, Volz D, Farrelly E et al. Efficacy and impact of botulinum toxin A on quality of life in patients with neurogenic detrusor overactivity: A randomized, placebo-controlled, double-blind	RCT, placebo controlled, double blind. No details of randomisation procedure. No evidence of allocation concealment. Blinding	N=31	Inclusion criteria: age >18 years; urodynamically verified detrusor over-activity with urinary leakage for at least 1 year; inadequate response to oral anticholinergics; ability to perform clean intermittent catheterisation. Exclusion: None	500 U of BTX-A (Botox, Dysport), made up with 0.9% preservative free saline to a total volume of 25ml. 25 2ml aliquots injected intramuscularly into detrusor. Done under LA or GA. Allowed to use a	Unclear if the injections were of the same total volume – no details of placebo injection explicitly given, although it may be tentatively assumed that it was an injection of 25ml saline.	6, 12 and 26 weeks	Cystometric bladder capacity Number of days of leakage per unit time (6 weeks for 6 and 12 week follow ups, and 14 weeks at 26 weeks). Quality of life: 13 QoL questions	Ipsen Scandinavia A/S (pharmaceutical company)

study. Scand J Urol Nephrol. 2007; 41(4):335-340. Ref ID: EHREN2007	unclear		Baseline characteristics: "There were no statistically significant differences in demographics or baseline characteristics between the two groups. Mean age of the patients was 36 years (range 21-66). The majority of the 20 patients with SCI were male, while all 6 MS patients were female". SCI in 20, myelomeningocele in 2; birth trauma in 2; MS in 6; myelitis in 1.	maximum of 4mg (2 tabs) of tolterodine daily. N=17	Allowed to use a maximum of 4mg (2 tabs) of tolterodine daily. N=14		(see "effect size" section below), with Likert scale responses varying from, "Not at all" to "extremely". This was described as the Qualiveen scale, but that should have 30 items, not the 13 reported in this paper. Adverse effects Treatment continuance	

Effect size:

Maximum cystometric capacity

The botulinum-A toxin group had a significantly higher bladder capacity than placebo at 6 ($p<0.001$) and 12 weeks ($p=0.026$) but not at 26 weeks (ns)

No. of days with urinary leakage

The botulinum-A toxin group had significantly fewer days with leakage at 0 to 6 weeks ($p<0.001$), 7 to 12 weeks ($p=0.002$) and 13 to 26 weeks ($p=0.010$)

For QoL data, counts are presented, and there were significant differences between groups for all QoL variables at all time points, with the treatment group always showing better QoL.

	Placebo 6 weeks	Treatment 6 weeks	Placebo 12 weeks	Treatment 12 weeks	Placebo 26 weeks	Treatment 26 weeks
QoL 1: Are you bothered by urine leaks during the day?	Not at all: 1 Slightly: 1 moderately: 3 Quite a bit: 4 Extremely: 1	Not at all:16 Slightly:0 moderately:1 Quite a bit:0 Extremely:0	Not at all: 2 Slightly:0 moderately:2 Quite a bit: 5 Extremely:1	Not at all: 11 Slightly: 4 moderately: 1 Quite a bit:0 Extremely:0	Not at all:1 Slightly:2 moderately:1 Quite a bit:5 Extremely:1	Not at all:11 Slightly: 3 moderately:2 Quite a bit: 1 Extremely:0

QoL 2: Are you bothered by urine leaks at night?	Not at all: 2 Slightly: 1 moderately: 2 Quite a bit: 3 Extremely: 2	Not at all:15 Slightly:2 moderately:0 Quite a bit:0 Extremely:0	Not at all: 1 Slightly:3 moderately:2 Quite a bit: 3 Extremely:1	Not at all: 13 Slightly: 2 moderately: 1 Quite a bit:0 Extremely:0	Not at all:1 Slightly:2 moderately:3 Quite a bit:3 Extremely:1	Not at all:11 Slightly: 2 moderately:3 Quite a bit: 1 Extremely:0
QoL 3: Are you bothered by having a set timetable for passing urine during your activities?	Not at all: 1 Slightly: 0 moderately: 2 Quite a bit: 3 Extremely: 2	Not at all:14 Slightly:2 moderately:0 Quite a bit:0 Extremely:0	Not at all: 3 Slightly:0 moderately:2 Quite a bit: 2 Extremely:1	Not at all: 13 Slightly: 2 moderately: 0 Quite a bit:0 Extremely:0	Not at all:2 Slightly:0 moderately:1 Quite a bit:4 Extremely:1	Not at all:13 Slightly: 1 moderately:2 Quite a bit: 0 Extremely:0
QoL 4: Are you bothered by having a set timetable for passing urine during your activities?	Not at all: 1 Slightly: 1 moderately: 3 Quite a bit: 4 Extremely: 1	Not at all:9 Slightly:4 moderately:2 Quite a bit:1 Extremely:0	Not at all: 1 Slightly:0 moderately:1 Quite a bit: 7 Extremely:1	Not at all: 9 Slightly: 5 moderately: 1 Quite a bit:2 Extremely:0	Not at all:2 Slightly:1 moderately:4 Quite a bit:2 Extremely:1	Not at all:6 Slightly: 7 moderately:3 Quite a bit: 1 Extremely:0
QoL 5: Are you bothered because your nights are disturbed?	Not at all: 2 Slightly: 3 moderately: 0 Quite a bit: 1 Extremely: 4	Not at all:9 Slightly:4 moderately:2 Quite a bit:2 Extremely:0	Not at all: 2 Slightly:2 moderately:3 Quite a bit: 1 Extremely:2	Not at all: 9 Slightly: 4 moderately: 3 Quite a bit:1 Extremely:0	Not at all:2 Slightly:1 moderately:1 Quite a bit:5 Extremely:1	Not at all:10 Slightly: 2 moderately:3 Quite a bit: 2 Extremely:0
QoL 6: Are you bothered when travelling?	Not at all: 1 Slightly: 1 moderately: 2 Quite a bit: 2 Extremely: 4	Not at all:9 Slightly:3 moderately:4 Quite a bit:0 Extremely:0	Not at all: 1 Slightly:1 moderately:2 Quite a bit: 2 Extremely:4	Not at all: 9 Slightly: 3 moderately: 3 Quite a bit:1 Extremely:0	Not at all:1 Slightly:1 moderately:0 Quite a bit:5 Extremely:2	Not at all:5 Slightly: 4 moderately:5 Quite a bit: 2 Extremely:0
QoL 7: Do your bladder problems complicate your life?	Not at all: 2 Slightly: 1 moderately: 1 Quite a bit: 4 Extremely: 2	Not at all:9 Slightly:3 moderately:4 Quite a bit:1 Extremely:0	Not at all: 2 Slightly:1 moderately:1 Quite a bit: 4 Extremely:2	Not at all: 9 Slightly: 3 moderately: 2 Quite a bit:3 Extremely:0	Not at all:1 Slightly:0 moderately:1 Quite a bit:5 Extremely:3	Not at all:6 Slightly: 4 moderately:4 Quite a bit: 1 Extremely:1
	Placebo 6 weeks	Treatment 6 weeks	Placebo 12 weeks	Treatment 12 weeks	Placebo 26 weeks	Treatment 26 weeks

QoL 8: Can you go out without planning anything in advance?	Not at all: 4 Slightly: 3 moderately: 1 Quite a bit: 1 Extremely: 1	Not at all:1 Slightly:1 moderately:3 Quite a bit:8 Extremely:4	Not at all: 3 Slightly:2 moderately:4 Quite a bit: 0 Extremely:1	Not at all: 2 Slightly: 2 moderately: 1 Quite a bit:5 Extremely:7	Not at all:4 Slightly:1 moderately:3 Quite a bit:0 Extremely:0	Not at all:1 Slightly: 3 moderately:3 Quite a bit: 8 Extremely:2
QoL 9: Is your life regulated by your bladder problems?	Not at all: 1 Slightly: 1 moderately: 6 Quite a bit: 1 Extremely: 1	Not at all:7 Slightly:7 moderately:1 Quite a bit:1 Extremely:1	Not at all: 1 Slightly:1 moderately:3 Quite a bit: 2 Extremely:2	Not at all: 9 Slightly: 3 moderately: 2 Quite a bit:1 Extremely:2	Not at all:0 Slightly:3 moderately:3 Quite a bit:2 Extremely:2	Not at all:4 Slightly: 6 moderately:4 Quite a bit: 1 Extremely:1
QoL10: Do you have to plan everything?	Not at all: 0 Slightly: 1 moderately: 5 Quite a bit: 2 Extremely: 2	Not at all:4 Slightly:7 moderately:3 Quite a bit:2 Extremely:1	Not at all: 1 Slightly:0 moderately:4 Quite a bit: 1 Extremely:4	Not at all: 6 Slightly: 5 moderately: 4 Quite a bit:0 Extremely:2	Not at all:1 Slightly:0 moderately:2 Quite a bit:5 Extremely:2	Not at all:2 Slightly: 7 moderately:5 Quite a bit: 1 Extremely:1
QoL11: Do you have to think about taking a change of clothes and/or continence pads/penile sheaths with you?	Not at all: 0 Slightly: 2 moderately: 3 Quite a bit: 0 Extremely: 5	Not at all:12 Slightly:1 moderately:3 Quite a bit:1 Extremely:0	Not at all: 0 Slightly:1 moderately:3 Quite a bit: 0 Extremely:6	Not at all: 11 Slightly: 2 moderately: 3 Quite a bit:0 Extremely:1	Not at all:0 Slightly:1 moderately:2 Quite a bit:1 Extremely:5	Not at all:10 Slightly: 2 moderately:3 Quite a bit: 1 Extremely:1
QoL12: Do you have to wear continence pads/ penile sheaths as a precaution?	Not at all: 3 Slightly: 1 moderately: 1 Quite a bit: 0 Extremely: 5	Not at all:14 Slightly:3 moderately:0 Quite a bit:0 Extremely:0	Not at all: 2 Slightly:0 moderately:3 Quite a bit: 0 Extremely:5	Not at all: 13 Slightly: 2 moderately: 1 Quite a bit:1 Extremely:0	Not at all:2 Slightly:0 moderately:2 Quite a bit:0 Extremely:6	Not at all:12 Slightly: 3 moderately:1 Quite a bit: 0 Extremely:1
QoL13: Do you have to be careful about how much fluid you drink?	Not at all: 0 Slightly: 1 moderately: 2 Quite a bit: 3 Extremely: 4	Not at all:9 Slightly:1 moderately:5 Quite a bit:2 Extremely:0	Not at all: 0 Slightly:1 moderately:1 Quite a bit: 5 Extremely:3	Not at all: 8 Slightly: 3 moderately: 4 Quite a bit:1 Extremely:1	Not at all:0 Slightly:0 moderately:2 Quite a bit:3 Extremely:5	Not at all:5 Slightly: 2 moderately:8 Quite a bit: 1 Extremely:1
Summary Qualiveen	Not at all: 15	Not at all: 131	Not at all: 17	Not at all: 127	Not at all: 13	Not at all: 97

score (not provided by paper, but has been calculated here, based on the 13 items reported (there should be 30 items). This has been calculated by summing the counts in each category across all questions, but reversing the order of the responses to Q8 to reflect the opposite meaning of responses to that question (ie extremely for * 8 represents a good outcome, but is the worst outcome for all other Qs).	Slightly: 15 moderately: 31 Quite a bit: 30 Extremely: 37	Slightly: 45 moderately: 28 Quite a bit: 11 Extremely:3	Slightly: 10 moderately: 31 Quite a bit: 34 Extremely:35	Slightly: 43 moderately: 26 Quite a bit: 12 Extremely:8	Slightly: 11 moderately: 25 Quite a bit: 41 Extremely:34	Slightly: 51 moderately: 46 Quite a bit: 15 Extremely:7
Dichotomised summary scores (note that there are missing data in the tables in the paper)	Slightly or not adversely affected:30 Extremely - moderately adversely affected:98	Slightly or not adversely affected:176 Extremely - moderately adversely affected:42	Slightly or not adversely affected:27 Extremely - moderately adversely affected:100	Slightly or not adversely affected:170 Extremely - moderately adversely affected:46	Slightly or not adversely affected:24 Extremely - moderately adversely affected:100	Slightly or not adversely affected:148 Extremely - moderately adversely affected:68
Treatment continuance	10/14	17/17				
Adverse effects	1	0				

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2

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Herschorn S, Gajewski J, Ethans K et al. Efficacy of botulinum toxin A injection for neurogenic detrusor overactivity and urinary incontinence: a randomized, double-blind trial. Journal of Urology. 2011; 185(6):2229-2235. Ref ID: HERSCHORN2011 Quality of life data: Herschorn S, Gajewski J, Ethans K et al. Efficacy of botulinum toxin A injection for neurogenic detrusor overactivity and urinary incontinence: a randomized double-blind trial. Neurourol Urodyn. 2009; 28(7):608-609. Ref ID:	RCT Randomisation: No details Allocation concealment: Sequential Patients randomised using sequential treatment assignment numbers linked to treatment codes allocation at random by a randomisation schedule prepared on a balanced 1:1 basis Double blind No drop outs reported	N=58 N=57 analysed (ITT analysis, one withdrew consent before receiving study drug) Drop-outs n=6 wk 36	Patients with neurogenic detrusor overactivity and urinary incontinence secondary to spinal cord injury or multiple sclerosis Inclusion criteria: Urinary incontinence minimum of one occurrence per day despite anticholinergic treatment Patient population: 34 male, 23 female, mean age 42.8 yrs (range 32 to 50), spinal cord injury 38, multiple sclerosis n=19	BoNTA (Allergan) 300U injected into 30 sites N=28 At 36 weeks all subjects were offered open label BoNTA	Placebo N=29 At 36 weeks all subjects were offered open label BoNTA	36 weeks	Frequency of incontinence episodes I-QOL	Allergan

HERSCHORN2009A								

Effect

Quality of life

Botulinum toxin was associated with improved quality of life on the ICIQ and I-QOL

Treatment group comparisons: *p<0.05 **p<0.01 ***p<0.001

Compared to baseline + p<0.01 ++ p<0.001

	Frequency of incontinence episodes		
	Daily frequency mean (SD)	% change from baseline (median)	I-QOL Change from Baseline mean (SD)
Baseline BoNTA Placebo	 3.06 (1.69) 4.03 (2.36)		
Week 6 BoNTA Placebo	 1.31 (1.25)*** 4.76 (2.91)	 -57.1*** 12.5	 19.52 (22.93)*** -2.23 (13.24)
Week 24 BoNTA Placebo	 1.56 (1.52)*** 3.98 (2.71)	 -47.5*** 0.0	 16.27 (22.72) 0.44 (16.73)
Week 36 BoNTA Placebo	 2.37 (1.92)* 4.21 (2.70)	 -25.0* 0.0%	 7.9 (10.84)* -1.91 (15.39)
Week 48 BoNTA Placebo	 1.56 (1.69)++ 1.86 (2.19)++	 -55.0++ -57.14++	 21.5 (23.81)++ 21.64 (25.73)++
Week 60 BoNTA Placebo	 1.43 (1.21)++ 1.54 (1.82)++	 -50.45++ 66.25++	 15.36 (20.98)+ 16.44 (21.13)+

Maximum cystometric capacity ml

Median (IQR)

Botulinum toxin
Baseline vs wk6 vs wk24 vs wk36
297.5 (147.5, 518.5) vs 521.5 (384.0, 703.5) vs374.5 (227.5, 661.5) vs 361.5 (167.0, 586.0)
Placebo
270.0 (139.0, 370.0) vs 241.0 (143.0, 358.0) vs 246.0 (129.0, 418.0) vs 211.0 (137.5 to 333.0)
Wk 6 botulinum toxin vs placebo p=0.0002, wk 12 p=0.031 wk 36 ns
Adverse events
Adverse events were similar between treatment groups. 3/28 reported mild transient upper body weakness

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schurch B, de S, Denys P et al. Botulinum toxin type a is a safe and effective treatment for neurogenic urinary incontinence: results of a single treatment, randomized, placebo controlled 6-month study. Journal of Urology. 2005; 174(1):196-200. Ref ID: SCHURCH2005A	RCT, Multicentre Randomised blocked design Allocation concealment: unclear Double blind	N=59 Withdrawals 2/59 (200 U BTX-A)	Patients with urinary incontinence caused by neurogenic detrusor overactivity with spinal cord injury (n=53) or multiple sclerosis (n=6). Inclusion criteria: aged 18 yrs or over, urinary incontinence of > 6 wk duration and regularly performed CIC Patient population: Age range 21 to 73 yrs, duration of neurogenic detrusor overactivity 3 mths to 24 yr	BoNTA (Botox, Allergan) 200 U (n=19) or 300 U (n=19) 30 injections into the detrusor sparing the trigone Patients performing CIC. Also, they had experienced inadequate response to oral anticholinergics, however concomitant use of these agents was	Placebo (n=21) Patients performing CIC. Also, they had experienced inadequate response to oral anticholinergics, however concomitant use of these agents was allowed during study	26 wks	Daily incontinence episodes (bladder diary) Maximum cystometric capacity (MCC) Adverse events	Two authors have consultant agreement with Allergan

				during the study				

Effect

300 U extracted for evidence report

Involuntary urine loss frequency

	Mean Daily Value (mean change from baseline)		
	300 U BTX-A (n=19)	200 U BTX-A (n=19)	Placebo (n=21)
Baseline	2.8 (1.86)	1.9 (1.78)	3.0 (3.29)
Wk2	-1.3 (1.39)	-1.0 (1.67)	-0.2 (1.02)
Wk6	-1.5 (2.33)	-0.9 (1.84)	-0.2 (1.45)
Wk12	-1.2 (1.66)	-0.9 (2.14)	-0.3 (1.46)
Wk18	-1.2 (1.16)	-0.8 (2.75)	-0.3 (1.59)
Wk 24	-0.9 (1.34)	-1.1 (1.92)	-0.1 (1.09)

Maximum cystometric capacity

	Mean Daily Value (mean change from baseline) ml		
	300 U BTX-A (n=19)	200 U BTX-A (n=19)	Placebo (n=21)
Baseline	293.6	260.2	254.6
Wk 2	479.6 (186.1)	482.5 (215.8)	282 (27.4)
Wk 6	462.7 (169.1)	448.8 (182.1)	299.6 (45.0)
Wk 24	398.2 (92.9)	440.9 (174.2)	301.0 (41.6)

Urinary tract infection

300 U BTX-A vs 200 U BTX-A vs placebo

4/19 vs 6/19 vs 3/21

Adverse events

The overall incidence of patients experiencing at least one adverse events was not significantly different among the treatment groups and no adverse events were considered to be related to the study drug.

Discontinuations

One patient in the BTX-A 200 U group discontinued the study during the study injection procedure prior to the administration of study drug due to urethral stricture.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
SAME STUDY AS Schurch et al.(2005) Schurch B, Denys P, Kozma CM et al. Botulinum Toxin A Improves the Quality of Life of Patients with Neurogenic Urinary Incontinence. Eur Urol. 2007; 52(3):850-859. Ref ID: SCHURCH2007	RCT, Multicentre Randomised blocked design Allocation concealment: unclear Double blind	N=59	Patients with urinary incontinence caused by neurogenic detrusor overactivity with spinal cord injury (n=53) or multiple sclerosis (n=6). Inclusion criteria: aged 18 yrs or over, urinary incontinence of > 6 wk duration and regularly performed CIC Patient population: Age range 21 to 73 yrs, duration of neurogenic detrusor overactivity 3 mths to 24 yr	BoNTA (Botox, Allergan) 200 U (n=19) or 300 U (n=19) 30 injections into the detrusor sparing the trigone Patients performing CIC. Also, they had experienced inadequate response to oral anticholinergics, however concomitant use of these agents was during the study	Placebo (n=21) Patients performing CIC. Also, they had experienced inadequate response to oral anticholinergics, however concomitant use of these agents was allowed during study	26 wks	Quality of life (Incontinence quality of life questionnaire, score 0 (poor self-perceived quality of life due to incontinence) to 100 (incontinence does not negatively affect quality of life)	Two authors have consultant agreement with Allergan
Effect Total I-QOL score (median score) Placebo vs BoNTA 200U vs 300U 2 weeks 49.4 vs 79.5* vs 72.7** 6 weeks 56.3 vs 84.1** vs 77.3** 24 weeks								

44.3 vs 86.4** vs 67.0*
* p<0.05 ** p<0.01

1 **LONG TERM FOLLOW-UP DATA**

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Del P, Filocamo MT, Li M et al. Neurogenic Detrusor Overactivity Treated with English Botulinum Toxin A: 8-Year Experience of One Single Centre. Eur Urol. 2008; 53(5):1013-1020. Ref ID: DEL2008	Retrospective observational study	N=199	Patients with spinal cord lesions with neurogenic detrusor overactivity (September 1999 and December 2005) resistant to conventional antimuscarinic therapy Patient population: 39/199 lesion above T5, mean age 42.5 (range 18 to 74)	BoNTA (Dysport) 1000, 750, 500 IU (used at the beginning) 750/500 IU (used thereafter) Local anaesthesia Detrusor muscle injections were performed in 20 sites (trigone and bladder neck sparing) Repeat injection on deterioration	Before 1st injection Resistant to conventional antimuscarinic therapy. Practising clean intermittent catheterisation Following injections Gradually reducing antimuscarinic therapy from the first week until the third week after the drugs, until the complete suspension of the drugs. Therapy reintroduced if deterioration despite injection	Variable range after 1 to 8 injections No. of injections N=1 n=199 N=2 n=160 N=3 n=90 N=4 n=51 N=5 n=49 N=6 n=12 N=7 n=6 N=8 n=2 N=9 n=1	Visits at 3, 6 and 12 months after each treatment. VAS and bladder diary checked one week before each visit. Urinary incontinence (bladder diary) Maximum cystometric bladder capacity Side effects Quality of life (visual analogue scale)	None reported
Effect No. of people by injection and dose.								

Dose	No. of injections									
	1	2	3	4	5	6	7	8	9	Total
Dysport 500	46	41	22	10	9	2	2	1	-	133
Dysport 750	106	85	65	41	41	10	4	1	1	353
Dysport 1000	47	34	3	-	-	-	-	-	-	84
Total	199	160	90	51	49	12	6	2	1	570

Non-responders

20/199 (15 after the first injection and 5 after repeated injections) showed poor clinical improvement (non-responders). 9/20 underwent augmentation cystoplasty. The remaining 11 patients went back to reflex voiding. 39/199 (19.5%) patients had a mean duration of efficacy after each injection > 12 months (very good responders), 80/199 (40.2%) with a mean duration 10-12 months (good responders), 60/199 (30.5%) with < 10 months (responders) and 20/199 (10%) with < 6 months (low responders). Analysing bladder diaries we found 30/199 (15%) patients with inadequate management of bladder voiding, who had frequent long periods (5-8 hr) between intermittent catheterisations, and high voided urine volume of a mean of 700 ml (range 600 to 1000). We found a significant correlation between these patients with inadequate management of their bladder and low results in terms of botulinum efficacy duration (Spearman correlation coefficient $p < 0.0001$). In three women after 2, 3 and 5 yr of BoNTA treatment, respectively, stress urinary incontinence developed. No male patients had stress urinary incontinence, but the voiding pressure showed a general trend to diminish when neurogenic detrusor overactivity reappeared. No patient had a sphincterotomy.

Maximum cystometric bladder capacity

		Injection						
	Baseline	I	II	III	IV	V	VI	VII
Mean ml	226.04	407.69	405.9	400.4	412.4	405.6	393	380
SD	22	26.8	37.5	34.4	21.0	35.6	33.6	26.0

Difference baseline vs after injection $p<0.001$. No statistically significant changes in the improvement were found after each retreatment

Side effects

5 patients who were treated with a high dose of intravesical BoNTA injections (1000 IU Dysport) experienced hyposthenia. This was transient, disappearing 2-4 wk after the injection.

Quality of life and incontinence

Significant improvements were seen in the quality of life symptoms score and in the bladder diary (frequency of urge urinary incontinence) after BoNTA injections. These improvements remained stable with reinjections. A significant improvement in patient satisfaction was found after each retreatment (VAS), with an improvement of a mean of 4 points (median 5, range 2 to 8 points). Mean VAS scores were highest in the Dysport 750 IU dose subgroup, but the difference for all three doses versus

baseline scores was statistically significant (p<0.001). These were significant reductions in the frequencies of incontinence episodes.

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Giannantoni A, Mearini E, Del Z et al. Six-Year Follow-Up of Botulinum Toxin A Intradetrusorial Injections in Patients with Refractory Neurogenic Detrusor Overactivity: Clinical and Urodynamic Results. Eur Urol. 2009; 55(3):705-712. Ref ID: GIANNANTONI2009A	Prospective observational study	N=17	Patients with neurogenic detrusor overactivity. Subgroup of spinal cord injury followed up for > 6 yrs Patient population: 11 males and 6 females, mean age 39.7 (SD 8.4), mean disease duration 62.3 mths.	300 U BoNTA (Botox, Allergan) Injected into the detrusor muscle (30 sites) sparing the trigone Spinal anaesthesia or sedation Mean no. of injections 7.2 (SD 1.3) Mean interval between two consecutive injections 11.0 mths	BASELINE N=8 oral anticholinergics N=9 had stopped taking anticholinergics due to intolerable side effects	QoL 4 mths and every year during follow-up Urodynamics 4 mths, 1, 3 and 6 yr Voiding diary for 2 days/per week during follow up	Quality of life (Incontinence quality of life questionnaire, score 0 (poor self-perceived quality of life due to incontinence) to 100 (incontinence does not negatively affect quality of life)	None reported
Effect Baseline vs 4 mths vs 1 yr vs 3 yr vs 6 yr No, of incontinence episodes per day mean (SD) 4.8 (2.7) vs 2.4 (1.0) vs 2.1 (2.1) vs 1.8 (0.9) vs 1.8 (1.1); baseline vs 6 yr p=0.01 Maximum cystometric capacity ml mean (SD) 243 (64.7) vs 390 (51.8) vs 389.4 (45.9) vs 439.4 (41.6) vs 420.8 (55.7) baseline vs 6 yr p=0.001								

Urinary tract infections per year
6.7 (2.1) vs 1.6 (1.3) vs 3.3 (2.1) vs 1.7 (2.0) vs 1.8 (0.5) baseline vs 6 yr p=0.001
Quality of life mean (SD)
Baseline vs 4 mths vs 12 vs 24 mths vs 36 mths vs 72 mths
22.4 (18.6) vs 77.7 (20.9) vs 85.7 (16.8) (p<0.001) vs
83.5 (22.1) (p<0.001) vs 80.6 (15.4) (p<0.001) vs 83.9 (17)

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Grosse J, Kramer G, Stohrer M. Success of repeat detrusor injections of botulinum A toxin in patients with severe neurogenic detrusor overactivity and incontinence. Eur Urol. 2005; 47(5):653-659. Ref ID: GROSSE2005	Prospective observational study	N=66	Patients with repeat BTX-A injections for neurogenic lower urinary tract dysfunction (detrusor overactivity, low compliance, reduced bladder capacity – with or without incontinence), unmanageable by anticholinergic treatment and able to practice intermittent (self-)catheterisation Exclusion criterion included: patients with coagulation disorders,, or patients unable to practice intermittent catheterisation, patients with congenital spinal cord conditions	Initially 200 UI or 250 UI Botox Allergan) (n=5) and 500 UI Dysport (n=7) Then 300 UI Botox and 750 or 1000 UI Dysport No. of injections: 2 or more N=66 3 or more N=34 4 or more N=17 5 or more N=5 6 or more N=3 7 N=1	BASELINE Intermittent self catheterisation 53/66 (24 also had spontaneous or triggered voiding) Anticholinergic medication 53/66. 13/66 did not anticholinergics because of adverse effects or ineffectiveness	Variable	% Major improvement Treatment failures Adverse events	None reported

			Patient population: 43 men and 23 women mean age at first BTX-A treatment was 38.5 (14 to 77) yrs. Traumatic spinal cord injury 54/66, multiple sclerosis 4/66, myelitis and brain defects in 2/44, and aneurysm, dysmelia, hernia, iatrogenic, spinal cord tumour and spinal cord ischemia in 1 each. Average duration of the condition at the first injection 9.2 Intermittent self catheterisation 53/66 (24 also had spontaneous or triggered voiding) Anticholinergic medication 53/66. 13/66 did not anticholinergics because of adverse effects or ineffectiveness					
Effect Major improvement (%) (satisfied plus very satisfied) Post 1st injection vs 2nd vs 3rd vs 4th 73 vs 71 vs 96 vs 89 Treatment failures Eight patients were injected for the second time within three months since the first injection (one Dysport, seven Botox). Four patients refused a second injection for a period of 2 to 4 yrs because of lack of effect of the first injection. Adverse events Four patients observed transient muscular weakness in the trunk and/or extremities, all after Dysport								

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Karsenty G, Reitz A, Lindemann G et al. Persistence of therapeutic effect after repeated injections of botulinum toxin type A to treat incontinence due to neurogenic detrusor overactivity. Urology. 2006; 68(6):1193-1197. Ref ID: KARSENTY2006	Prospective observational study	N=17	Patients with neurogenic detrusor overactivity and incontinence Patients had to have received at least two repeat injections. Patient population: 16/17 spinal cord injury and 1/17 multiple sclerosis. 13/17 performed intermittent self catheterisation and 4/17 voluntary voiding	300 U Botulinum toxin type A (Botox) (Allergan) Injected at 30 sits sparing the trigone Mean no. of injections 5.4 (range 3 to 9)	BASELINE Anticholinergic use not specified	Not specified Mean no. of injections 5.4 (range 3 to 9)	Mean no. of incontinence episodes per day Maximum cystometric capacity	None reported
Effect Incontinence mean no. of episodes per day First injection vs last injection 2.6 vs 0 Maximum cystometric bladder capacity mean (SD) mL Baseline vs first injection vs last injection 348.8 (115.8) vs 499.1 (3.6) vs 461.8 (63.7)								

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Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Khan S, Game X, Kalsi V et al. Long-term effect on quality of life of repeat detrusor	Prospective observational study	N=137	Patients with multiple sclerosis and neurogenic detrusor	300 U Botulinum toxin type A (Botox)	Pre-treatment Patients had not responded to	Mean 29 mths (range 9 to 80	Continence, Mean Urogenital Distress Inventory (UDI),	Multiple Sclerosis Society, Pfizer, Guy's and St Thomas' Charity, The Urological

injections of botulinum neurotoxin-A for detrusor overactivity in patients with multiple sclerosis. Journal of Urology. 2011; 185(4):1344-1349. Ref ID: KHAN2011			overactivity. Patient must have been willing to perform CIC. Patient population: female: male 77:32%, mean age 47.8 yrs.	(Allergan) Injected into 30 sites on outpatient basis Injections repeated on return of symptoms (no minimum period) 1st injection N=137 2nd injection N=99 3rd injection N=47 4th injection N=25 5th injection N=14 6th injection N=5	behavioural therapy or to pharmacotherapy of at least two medications.	mths)	Incontinence Impact Questionnaire (IIQ) 4 weeks after treatment	Foundation, Prostrate UK, Dept of Health National Institute for Health Research Comprehensive Biomedical Research Centre Award
Effect Continence Before vs after treatment (1st injection implied)								

17% vs 76%
Urogenital Distress Inventory (UDI), Incontinence Impact Questionnaire (IIQ)
UDI
mean (SD)
before vs after
1st injection 61.8 (1.4) 1 vs 23.0 (1.7)
2nd injection 55.5 (2.2) vs 24.0 (2.3)
3rd injection 56.4 (3.4) vs 8.6 (1.6)
4th injection 57.2 (5.0) vs 19.8 (3.6)
5th injection 54.6 (5.8) vs 8.6 (4.0)
6th injection 67 (3.4) vs 12.2 (7.5)

IIQ
mean (SD)
before vs after
1st injection 65.1 (2.2) vs 21.9 (2.1)
2nd injection 58.2 (3.1) vs 11.0 (2.3)
3rd injection 55.9 (5.1) vs 5.2 (1.6)
4th injection 59.0 (5.5) vs 9.5 (3.6)
5th injection 47.7 (7.5) vs 7.5 (3.4)
6th injection 58.0 (12.3) vs 6.6 (6.6)

Adverse events
Urinary tract infections
Antibiotics required after 30/327 treatment sessions
Long term antibiotics treatment was required 23/137 (17%)

Exacerbations of MS
8/137 (5.8%)

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Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kuo H-C, Liu S-H. Effect of repeated detrusor onabotulinumtoxina injections on bladder and renal function in patients with chronic spinal cord injuries. Neurourol Urodyn. 2011; 30(8):1541-1545. Ref ID: KUO2011	Prospective case series	N=38 (N=5 drop-outs)	Patients with more than one year history of chronic suprasacral cord injury. All patients were diagnosed with detrusor sphincter dyssynergia by videourodynamic study. In addition, all patients voided by reflex or abdominal stimulation with or without clean intermittent catheterisation, were free of indwelling catheter or cystostomy, and were free of urinary tract infection. All patients had been treated with anticholinergics for at least one year and failed to resolve their urinary incontinence. Exclusion criteria included patients with detrusor underactivity and large bladder compliance, patients proven to have intrinsic sphincteric deficiency and patients with grade 2 or higher vesicoureteral reflux Patient population: 21 men and 17 women. Mean age 37. Median duration of spinal cord injury 7 yrs	200 U Botulinum toxin type A (Botox) Injected into 40 sites under light general anaesthesia Injections were repeated every 6 mths Antimuscarinics were discontinued	Pre-post injection	24 months	Maximum bladder capacity Quality of life – Quality of Life index adapted from the International Prostatic Symptom Score	None reported
Effect Maximum bladder capacity ml Baseline vs 6 mths vs 12 mths vs 18 mths vs 24 mths								

Mean (SD) p<0.05 for all comparisons
207.1 (111) vs 306.4 (186) vs 376.9 (180) vs 369.7 (129) vs 411.7 (32.9)

QoL-I
Baseline vs 6 mths vs 12 mths vs 18 mths vs 24 mths
Mean (SD) p<0.05 for all comparisons
4.51 (1.34) vs 2.31 (1.28) vs 2.29 (1.49) vs 2.30 (1.23) vs 2.26 (1.68)

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Pannek J, Gocking K, Bersch U. Long-term effects of repeated intradetrusor botulinum neurotoxin a injections on detrusor function in patients with neurogenic bladder dysfunction. BJU Int. 2009; 104(9):1246-1250. Ref ID: PANNEK2009B	Retrospective case series	N=27	Patients with neurogenic detrusor overactivity due to spinal cord lesions Inclusion criteria: minimum of five treatments of BoNT-A Patient population: males 15, females 12, complete spinal cord lesion 15, incomplete spinal cord lesion 12, median age 34.5 (17-62), interval from lesion to 1st injection 62.9 mths (2-234)	BoNT-A injection (unclear manufacturer) Mean no. of treatments 7.1 (range 5 to 11)	BASELINE All patients failed to respond sufficiently to anticholinergic treatment	Not specified Mean no. of treatments 7.1 (range 5 to 11)	Continence Adverse effect	One author consultant of Allergan

Effect
Continence
Before the first BoNT-A treatment, 24 patients performed intermittent catheterisation whereas three patients emptied their bladders by triggered voiding. From the first BoNT-A treatment, all patients performed intermittent catheterisation throughout the entire observation period.
Baseline vs after 1 injection N (%)

4/27 vs 25/27; <0.002
Before final injection vs after final injection
5/27 vs 20/27; ns
Adverse effect
4/27 complained about temporary muscular weakness either localised in the limbs (two patients) or generalised (two patients).

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Reitz A, Denys P, Fermanian C et al. Do Repeat Intradetrusor Botulinum Toxin Type A Injections Yield Valuable Results? Clinical and Urodynamic Results after Five Injections in Patients with Neurogenic Detrusor Overactivity. Eur Urol. 2007; 52(6):1729-1735. Ref ID: REITZ2007	Prospective observational study	N=20	Patients with neurogenic detrusor overactivity Patients who received at least five intradetrusor injections and who were followed by clinical and urodynamic evaluation after at least four injections	Botulinum toxin A (Botox, Allergan) 300 units 30 injections into the detrusor muscle sparing the trigone Local anaesthesia Injections repeated every 7 months	BASELINE Concomitant anticholinergic medications were allowed	For a minimum of 4 injections	Maximum Cystometric capacity	Three authors consultants for Allergan
Effect Maximum cystometric bladder capacity ml Baseline vs Injection 1 vs 2 vs 3 vs 4 vs 5 mean (95%CI) 216.5 (187.5 to 395) vs 500 (500 to 576.5) vs 500 (500 to 520) vs 490 (415 to 500) vs 500 (402.5 to 512.5) vs 500 (435 to 500)								

F.7 What are the long term risks (renal impairment, hydronephrosis, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? What is the quality of life associated with the above?

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bennett CJ, Young MN, Adkins RH et al. Comparison of bladder management complication outcomes in female spinal cord injury patients. Journal of Urology. 1995; 153(5):1458-1460. Ref ID: BENNETT1995	Retrospective observational study Birmingham, Alabama	N=70	Female patients with spinal cord injury undergoing follow-up by a urology service Intermittent catheterisation (N=23): 18 paraplegics and 5 tetraplegics, mean 8.5 yrs (± 4,7 yrs) Reflex voiding and padding (N=25): 7 paraplegics and 18 tetraplegics, mean 15.8 yrs (± 7.3 yrs) Indwelling catheter (N=22): 11 paraplegics and 11 tetraplegics, mean 16.7 yrs (± 9.0 yrs) (no patient was maintained on a suprapubic catheter)	Intermittent catheter Indwelling catheter	Reflex voiding and padding	Years of bladder management ranged from 2 to 33 yrs Frequency of follow up not stated	Reflux Hydronephrosis Bladder calculi Renal calculi	None reported
Complications reported by duration of follow-up								

Complication	Intermittent catheterisation (n=23)	Padding (n=25)		Indwelling catheter (n=22)		
Duration of follow-up	2-10 yrs (n=17)	2-10 yrs (n=7)	11-23 (n=14)	2-10 yrs (n=7)	11-23 (n=9)	24-33 (n=6)
Reflux	1	-	-	2	4	4
Hydronephrosis	-	1	-	4	2	-
Bladder calculi	1	-	-	1	3	12
Renal calculi	-	-	3	-	1	2

None of the 6 patients on intermittent catheterisation for 11 to 23 yrs or the 4 on padding for 24 to 33 yrs reported any complications.

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Cameron AP, Wallner LP, Forchheimer MB et al. Medical and psychosocial complications associated with method of bladder management after traumatic spinal cord injury. Archives of Physical Medicine and Rehabilitation.	Retrospective observational study USA	N=24762 N=1564 excluded	Patients with new spinal cord injury (SCI) entered in the National SCI database Patient population: mean time post injury (psychosocial outcomes) ranged from 6.3 to 11.1 yrs. Age at injury ranged from mean 27.8 to 37.0 yrs	At discharge: 18.2% voiding, 23.9% used indwelling catheterisation, 12.7% condom catheterisation, and 45.1% intermittent catheterisation	Different bladder management techniques	1 to 30 yrs	Incidence of stones SWLS (5 item measure of life satisfaction) Self perceived health status	National Institute on Disability and Rehabilitation Research

2011; 92(3):449-456. Ref ID: CAMERON2011								

Effect

Variable	Odds of stone ≥ 1 (OR 95%CI)
Year 1	
Indwelling catheter	1
Voiding	0.48 (0.39 to 1.28)
Condom	0.71 (0.39 to 1.28)
Clean intermittent catheterisation	0.92 (0.59 to 1.42)
Year 5	
Indwelling catheter	1
Voiding	0.42 (0.21 to 0.85)
Condom	0.68 (0.40 to 1.16)
Clean intermittent catheterisation	0.56 (0.34 to 0.94)
Year 30	
Indwelling catheter	1
Voiding	N?A
Condom	0.18 (0.011 to 2.85)
Clean intermittent catheterisation	2.15 (0.28 to 17.0)

Variable	SWLS	Perceived health status
Indwelling catheter	18.56 (SD0.44) (reference)	2.83 (SD0.06) (reference)
Voiding	19.96 (0.46) (p<0.0005)	2.98 (0.06) (p<0.0005)
Condom	18.75 (0.50) (p=0.56)	2.74 (0.07) (p=0.03)
Clean intermittent catheterisation	18.77 (0.44) (p=0.39)	2.76 (0.06) (p=0.04)

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2

<table>
<tr><th>Reference</th><th>Study type
Evidence level</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr><td>Cardenas DD, Mayo ME. Bacteriuria with fever after spinal cord injury. Archives of Physical Medicine and Rehabilitation. 1987; 68(5 Pt 1):291-293. Ref ID: CARDENAS1987</td><td>Prospective case study
Country:USA (Seattle)</td><td>N = 705

Loss to follow up:
371 turned up to the 1 year follow up appointment (53%)

All patients treated at the Northwest Regional Spinal Cord Injury Center between 1974 and 1984.

Of all patient 64 (9.1%) had normal voiding at discharge from</td><td>557 /705 (79%) were men: 51% quadriplegic, 49% paraplegic

Number of patients by system of drainage at discharge from hospital
<table>
<tr><td></td><td>N(%)</td></tr>
<tr><td>Intermittent catheterisation</td><td>259(36.8)</td></tr>
<tr><td>Indwelling catheter</td><td>114(16.2)</td></tr>
<tr><td>Voiding: external collector</td><td>110(15.6)</td></tr>
<tr><td>Voiding: no external collector</td><td>102(14.5)</td></tr>
<tr><td>Normal voiding</td><td>64(9.1)</td></tr>
<tr><td>Other*</td><td>35(4.9)</td></tr>
<tr><td>Diversion**</td><td>21 (3.0)</td></tr>
</table>
* Other includes cystocath and suprapubic catheter
** Diversion = ileal conduit and vesicostomy.</td><td>n/a</td><td>n/a</td><td>1 year</td><td>Bacteriuaria with fever (BWF)</td><td>Spinal Cord Grant from th e National Institute of Handicapped Research, Department of Education Washington</td></tr>
</table>

		hospital						

Effects

At discharge there was no significant difference in rate of bacteriuria with fever (BWF) between those with self intermittent catheterization, those with intermittent catheterisation by someone else and those with an indwelling catheter.

Rates of BWF at hospital discharge and at 1 year follow up N (%):

	At discharge	At 1 year follow up
Self intermittent catheterisation	77/155 (50)	33/62 (53)
Intermittent catheterisation by other	60/103 (58)	20/24 (83)
Indwelling catheter	48/114 (42)	25/57 (44)

Examining only those who were on the same system of drainage at discharge from the initial rehabilitation and at year 1 follow-up, the patients on intermittent catheterisation by someone else (ICO) were more likely to have experienced at lease one episode of BWF than the group on self intermittent catheterisation and patients with indwelling catheter ($p<0.025$).

Authors' conclusions:

Those patients unable to perform their own intermittent catheterisation appeared to be at greater risk to develop episodes of bacteriuria with fever.

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chen Y, DeVivo MJ, Roseman JM. Current trend and risk factors for kidney stones in persons	Prospective observational study, USA	N=8314	Patients entered into a National spinal cord injury database 1986-1999 Inclusion criteria included: admission to a	Abnormal concretion in either the kidney or ureter documented by x-ray evidence of its	na	Mean 3 yrs (range 7 mths to 13 yrs) Annual	Stones in the kidney or ureter	National Institute on Disability and Rehabilitation Research, Office of Special Education and

with spinal cord injury: A longitudinal study. Spinal Cord. 2000; 38(6):346-353. Ref ID: CHEN2000			model system of care within 365 days of injury, clinically discernible degree of spinal cord neurologic impairment on admission Patient characteristics: Women 18.5%: men 81.5%, age: 15-24 35.5%, 25-34 26.3%, 35-44 16.9%, 45-54 9.5%, 55-80 11.8%, neurologic level: minimal deficit 5.5%, paraplegic (incomplete) 20.4%, paraplegic (complete) 27.9%, tetraplegic (incomplete) 27.8%, tetraplegic (complete) 18.1%, unknown 0.2%	location' Stones that were passed spontaneously before x-ray evidence could be obtained were excluded		check		Rehabilitation Services, United States Department of Education, Washington DC

Effect

Incidence of stones in the kidney or ureter

Bladder management at discharge	N	%	No. of stones 5-yr cumulative incidence	%	P
Catheter-free	1710	20.6	20	1.6	0.002
Indwelling uretheral catheter	1027	12.4	49	6.9	
Condom catheter	563	6.8	25	5.1	
Intermittent catheter	4407	53.0	179	5.0	
Suprapubic catheter	296	3.6	8	2.7	
Other	248	3.0	5	3.4	
Unknown	63	0.8	0		

Risk factors for kidney stones occurring before and after the first year post injury
Multivariate cox regression model

	Year one RR (adjusted) (95%CI)	Year 2 and later RR (adjusted) (95%CI)
Catheter-free	1.0	1.0
Indwelling uretheral catheter	1.3 (0.6 to 2.7)	2.5 (1.1 to 5.7)
Condom catheter	1.3 (0.6 to 2.8)	2.0 (0.9 to 4.6)
Intermittent catheter	1.2 (0.6 to 2.1)	2.4 (1.2 to 5.2)
Suprapubic catheter	0.3 (0.1 to 1.3)	2.6 (1.1 to 6.3)
Other	0.6 (0.1 to 2.6)	4.2 (1.7 to 10.6)

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dahlberg A, Perttil I et al. Bladder management in persons with spinal cord lesion.	Cross-sectional study. Finland	N=129	Patients with traumatic spinal cord injury leading to permanent neurological deficits	Clean intermittent catheterisation Mixed Catheter or	Normal voiding, controlled voiding, suprapubic tapping, compression or straining	One year	Urinary tract infections (with symptoms, confirmed by urinary culture	None reported

Spinal Cord. 2004; 42(12):694-698. Ref ID: DAHLBERG2004			Normal voiding 14 (11%), controlled voiding, 15 (12%), clean intermittent catheterisation 16 (12%), mixed (clean intermittent catheterisation in daily use) but subjects also used other methods, suprapubic tapping 31 (24%), compression or straining 16 (12%), catheter or conduit 7 (5%)	conduit			and treated with antibiotics)	

Effect

Urinary tract infection

Data extracted from graph

Bladder management	Urinary tract infection % (95%CI)
Normal voiding	6 (2 to 36%)
Controlled voiding	20 (5 to 50%)
Clean intermittent catheterisation	70 (43 to 90)
Mixed (using clean intermittent catheterisation plus other method)	72 (58 to 90)
Suprapubic tapping	48 (30 to 68)
Compression or straining	31 (11 to 59)

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
D.M. Dewire, R.S. Owens, G.A. Anderson, M.A. Gottlieb, H. Lepor, "A Comparison	Retrospective cohort study. USA.	N=57 (n=32 with catheter and n=25 non catheter.)	Medical records of 57 consecutive patients who sustained a traumatic cervical spinal cord injury between 1970 and 1980 included. Note: no patients lost to follow-up.	Chronic indwelling catheter.	No chronic indwelling catheter.	Mean follow-up 12 years Frequency of follow up one yeR	Urological Complications.	None reported

of the Urologic Complications Associated with Long-Term Management of Quadriplegic Patients with and without Chronic Indwelling Urinary Catheters," Journal of Urology, 147: 1069-1072, 1992 REF ID DEWIRE 1992			Patient characteristics: mean age of the patient population at injury was 36 yrs. The majority of the patients sustained spinal cord injury after a motor vehicle accident (31), diving accident (10) or fall (8).					

Effect

Urological complications:

Complication	Total (n=57)	Catheterised group (n=32)	Non-catheterised group (n=25)	p-value (diff b/w catheterised and non catheterised group)
Renal stone	14	8	6	0.93
Bladder stone	18	13	5	0.10
Pyelonephritis	13	8	5	0.66

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Suzanne L. Groah, , David A. Weitzenkamp, Daniel P. Lammertse, Gale G. Whiteneck, Dennis C. Lezotte, Richard F. Hamman. Excess risk of bladder cancer in spinal cord injury: Evidence for an association between indwelling catheter use and bladder cancer. Archives of Physical Medicine and Rehabilitation Volume 83, Issue 3, Pages 346-351, March 2002.	Historical cohort study. Denver, Colorado, USA	N=3670 (n=1628 in NIDC, n=314 in multi and n=1728 in IDC)	Participants included listed in the database who incurred spinal cord injury (SCI) between 1950 and 1997 and who were known to have survived at least 1 year. Inclusion criteria: Participants were eligible for the study if initial screening cystoscopy, performed at any time post- SCI, documented the presence or absence of bladder cancer. Patient characteristics: Mean age at SCI (yrs) – 30 years (in NIDC); 29 years (in multi); 29 years (in IDC). Mean age at diagnosis of bladder cancer: 48 years. Mean duration of SCI at time of diagnosis was 20 years. Median duration of	groups: Indwelling catheter (IDC). Non indwelling catheter (NIDC). Multi (using both dwelling and non dwelling)	See interventions	Mean follow-up: 2 years.	Diagnosis of bladder cancer. Death from any cause.	None reported

REFID GROAH 2002			bladder management: NIDC- 9.8 years (in NIDC); 7.3 years (in multi). IDC - 6.9 years (in NIDC); 11.8 years (in IDC). American spinal injury classification (ASIA): A- 47 % (NIDC); 60% (multi); 65% (IDC) B-14% (NIDC); 18% (Multi); 20% (IDC) C- 13% (NIDC); 9% (Multi); 11% (IDC). D- 25%(NIDC); 13% (Multi); 4% (IDC) E- 1% (NIDC); 0%(Multi); 0% (IDC).					

Effect

Analyses of potential risk factors for bladder cancer revealed a significantly greater proportion of participants who used IDC (46% of IDC group, 39% of multi group) developed bladder calculi compared with 10% in the NIDC group (x^2 =537.64, $p<0.001$) . Thirty one (31%) of the IDC group had a history of pyelonephritis, compared with 33% of the NIDC group(x^2 =1.4,p=0.24). There were no documented cases of bladder schistosomiasis in any of the cohorts.

Age- adjusted analyses revealed that increasing exposure to IDC use was associated with bladder cancer in SCI. The IDC group had an age –adjusted rate of 77 per 100,000 person-years, compared with rates of 56.1 and 18.6 per 100,000 person-years in the multi and NIDC groups, respectively.

Age and gender adjustment for development of bladder cancer:

After age and gender adjustment, participants with SCI were 15.2 (95% CI, 9.2 -23.3) times likely to develop bladder than the general population. Of those using IDC only as their method of bladder management, the observed 15 cases of bladder cancer were compared with an expected 0.6 cases, yielding a ratio of 25.4 (95%, 14.0 -41.9).

Bladder management method	Observed	Expected	Observed/expected	95% CI
NIDC	3	0.6	5.0	1.1- 14.6
Multi	3	0.2	15.8	3.6-46.1
IDC	15	0.6	25.4	14.0-41.9
All SCI	21	1.4	15.2	9.2-23.3

Cox regression models to independently examine bladder management method, age at SCI, gender, ASIA classification, level of SCI and history of bladder calculi.

Risk factor	RR (95% CI)	P –value
Bladder management technique IDC use: Multiple catheter use:	 4.9 (1.3-13.8) 4.0 (0.8-20.2)	 0.02 0.49
Age at SCI	1.1 (1.1-1.2)	0.01
Male gender	1.9 (0.6-6.8)	0.83
History of bladder calculi	1.1 (0.5-2.9)	0.34
Cervical level of SCI	0.5 (0.1-4.2)	0.76
ASIA impairment scale class A	Not reported due to high variability	Not significant

Calculations of attributable risk (AR) revealed that IDC was responsible for 34.1 cases of bladder cancer per 100,000 person-years of SCI. This yielded an AR percentage of 55.8% for IDC use, whereas male gender and bladder calculi were responsible for fewer cases of bladder cancer, at 32.9% and 10.7% respectively. In those using IDC only, IDC was responsible for 58.4 cases per 100,000 person-years, or 64.8% of all bladder cancer occurring in the IDC population.

At the completion of the study, 13 persons with bladder cancer had died, with the cause of death identified as bladder cancer in 12.
Of the 12, 10 had solely used IDC, where as 2 used multiple techniques. There were no bladder cancer deaths in the NIDC group.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hansen RB,	Retrospective	N=235	Patients from the	Data	na	Duration of	Renal calculi	Medicon

Biering S, Kristensen JK. Urinary calculi following traumatic spinal cord injury. Scandinavian Journal of Urology & Nephrology. 2007; 41(2):115-119. Ref ID: HANSEN2007	observational study, Copenhagen	(patients with urological investigations)	Clinical for Spinal Cord Injuries, Copenhagen with a traumatic spinal cord injury (SCI) contracted before January 1991 who were still alive at the time of receiving a follow-up questionnaire in 2001 Patients characteristics: Mean age 50.5 yrs (range 28 to 84) and mean follow-up time was 24.1 yrs (range 10 to 45 yrs. 126 paraplegic and 110 tetraplegic	collected from medical records. Results included plain radiography of the abdomen and i.v urography		bladder management 24.1 yrs (range 10 to 45 yrs) Frequency of follow-up 70% yearly or every other year		Valley Academy and Coloplast A/S

Effect

	Participants with renal calculi (%)		Participants without renal calculi (%)	
	Initial discharge (n=46)	Follow-up (n=47)	Initial discharge (n=186)	Follow-up (n=188)
Normal bladder emptying	13	9	12	8
Suprapubic tapping	54	28	58	32
Abdominal pressure	17	19	19	15
Crede manoeuvre	2	23	6	19
Intermittent catheterisation	11	40	13	39
Indwelling catheter	7	19	9	15

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Ku JH, Jung TY,	Retrospective	N=140	Inclusion criteria: Men	Clean	Spontaneous voiding,	Annually	Kidney, ureter or	None

Lee JK et al. Risk factors for urinary stone formation in men with spinal cord injury: a 17-year follow-up study. BJU Int. 2006; 97(4):790-793. Ref ID: KU2006	observational study Korea		with an age at injury of ≥ 18 yrs, discernible neurological lesion, traumatic spinal cord injury (SCI), voiding spontaneously or a neurogenic bladder managed by clean intermittent catheterisation, suprapubic cystomy or indwelling urethral catheter, injured before 1987, and followed from 1987 to 2003. Exclusion criteria: If patients missed two or more consecutive annual visits, or had an ileal conduit or bladder augmentation	intermittent catheterisation, Indwelling urethral catheter	suprapubic cystostomy	for 17 yrs (between 1987-2003)	bladder stones (first occurrence)	reported

Effect

Bladder stone

	Spontaneous voiding (SV)	Clean intermittent catheterisation (CIC)	Suprapubic cystostomy (SPC)	Urethral catheter (UC)
Accumulated incidence (%)	14 (30)	5 (15)	15 (42)*	5 (21)
Episodes/100 person-years	2.0	0.89	5.1	1.7

Renal stones

	Spontaneous voiding	Clean intermittent catheterisation	Suprapubic cystostomy	Urethral catheter
Accumulated incidence (%)	6 (13)	3 (9)	4 (11)	8 (33)**

Episodes/100 person-years	0.88	0.54	0.65	2.5

* <0.05 in the CIC vs SPC group by chi-square test

** <0.05 in the SV vs the UC group, the CIC vs UC group, and the SPC vs the UC group by Fisher's exact test

Multivariate analysis

Bladder management	Bladder stone OR adjusted (95%CI)	p	Renal stone OR adjusted (95%CI)	p
Spontaneous voiding (SV)	1.0		1.0	
Clean intermittent catheterisation	0.53 (0.16 to 1.8)	0.30	0.89 (0.17 to 4.6)	0.89
Suprapubic cystostomy	1.5 (0.56 to 3.9)	0.43	0.71 (0.16 to 3.2)	0.66
Urethral catheter	0.89 (0.24 to 3.3)	0.86	5.7 (1.3 to 25)	0.021

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Ku JH, Choi WJ, Lee KY et al. Complications of the upper urinary tract in patients with spinal cord injury: a long-term follow-up study. Urol Res. 2005; 33(6):435-439. Ref ID: KU2005	Retrospective observational study Korea	N=179	Inclusion criteria: male patients, age at injury 18 yrs or above, neurologic lesion, traumatic spinal cord injury, follow up for 10 yrs or longer from date of injury, follow up until 2003 Patient characteristics: age at injury range 22-24 yrs, duration of follow up 29-35 yrs	Follow up included microbiological confirmation of significant bacteria in the presence of relevant symptoms and plain film radiographs	na	Yearly follow-up for at least 10 yrs	Pyelonephritis Renal calculi	None reported
Effect								

Incidence of the complications of upper urinary tract

	Urethral catheter	Intermittent catheterisation	Suprapubic cystostomy	Crede manoeuvre or reflex voiding	Condom catheter
Pyelonephritis	12 (41.4%)	20 (41.7%)	13 (31.0%)	10 (26.3%)	6 (27.3%)
Renal calculi	6 (20.7%)	6 (12.5%)	15 (35.7%)	13 (34.2%)	4 (18.2%)
Upper tract deterioration	15 (51.7%)	18 (37.5%)	11 (26.2%)	9 (23.7%)	5 (22.7%)

Multivariate risk factors for complications of the upper urinary tract

Adjusted odds ratio (95% CI)

	Pyelonephritis	Renal calculi	Upper tract deterioration
Urethral catheter	1.0	1.0	1.0
Intermittent catheter	0.930 (0.352-2.455)	0.526 (0.147 to 1.888)	0.330 (0.114 to 0.958)
Suprapubic catheter	0.532 (0.186 to 1.519)	1.827 (0.581 to 5.745)	0.097 (0.026 to 0.359)
Crede manoeuvre or reflex voiding	0.464 (0.158 to 1.366)	1.856 (0.579 to 5.955)	0.123 (0.035 to 0.428)
Condom catheter	0.502 (0.148 to 1.704)	0.746 (0.177 to 3.137)	0.200 (0.051 to 0.780)

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Larsen LD, Chamberlin DA, Khonsari F, Ahlering TE. Retrospective	Retrospective cohort study. USA Groups well	N=204 (142 were followed up).	Male; mean age 34; All receiving continuous long term medical care at a veterans centre. n: Indwelling catheter 56; No catheter 86	Chronic indwelling catheterisation (n=56)	No indwelling catheter (n= 86). [spontaneous voiding 54, clean	Mean 12 years Frequency of follow-up	Symptomatic UTIs Bladder stones Renal stones Renal dysfunction	None reported.

analysis of urologic complication in male patients with spinal cord injury managed with and without indwelling urinary catheters. Adult urology 1997; 50: 418-422	matched for age and years of follow up, but differed for existence of an external sphincterotomy which could confound. Patients given choice of the 2 treatment options, with advice on the best option for their particular problems. This would also create a bias between groups.		<table><tr><td>Age at injury</td><td>33</td><td>35</td></tr><tr><td>Years of follow up</td><td>12</td><td>12</td></tr><tr><td>Cx SCI</td><td>36/56</td><td>48/86</td></tr><tr><td>ThLx SCI</td><td>20/50</td><td>38/86</td></tr><tr><td>External sphincterotomy</td><td>16</td><td>47</td></tr></table>		intermittent catheterisation 14, external striated sphincterotomy coupled with condom catheter drainage 16]	unclear		

Effects

Adverse event	Indwelling catheter	Non catheterised	p
All complications	49/56	28/86	Not stated
Symptomatic UTIs (1 episode)	6/56	35/86	0.0001
Symptomatic UTIs (> 1 episode)	42/56	11/86	0.0001
Urosepsis Leading to death	12/56 2/56	7/86 0/86	0.023
Bladder stones	34/56	10/86	0.0001
Renal stones	18/56	6/86	0.0001
Recurrent pyelonephritis	7/56	2/86	0.015
Parenchymal thinning	13/56	4/86	0.0009

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lindehall B, Moller A, Hjalmas K, Jodal U, Abrahamson K. Psychosocial factors in teenagers and young adults with myelomeningocele and clean intermittent catheterisation. Scandinavian Journal of Urology and Nephrology 2008; 42: 539-544	Qualitative. Semi structured interviews. Sweden. Two people analysed tapescripts, and a thematic approach was used.	N=22	26 were selected at random from 41 eligible myelomeningocele patients who had been using Clean Intermittent catheterisation (CIC) for at least 5 years and were at least 13 years old. 26 rather than all 41 were included because of the time-consuming nature of the qualitative analysis. The 41 eligible patients were all those complying with inclusion criteria who had been part of a cohort of children with myelomeningocele (MMC) followed from birth and taught CIC from an early age. 4 of the 26 were not included because of problems understanding the questions. 15 females and 7 males. Age range 13-26 yrs. Age at which CIC began was 6-15 yrs. The follow up period to the interview was 5-12 years. 12 were in wheelchairs permanently, 3 occasionally, 3 used crutches and 4 walked without support. 12 were at mainstream schools, 2 in special schools for learning difficulties and 8 were working.	The experience of the use of CIC.	NA	NA	Semi-structured interviews (conducted by the urotherapist), according to an interview protocol, elicted thoughts and feelings on the following: To whom, and what, information was given to others. Attitude to be being catheterised by someone else. Attitude to their and other disabilities Attitudes towards friendship, aspects of sexuality and fertility.	
Effects: The participants perceived the experience of long term CIC use as follows: Telling peers of their use of CIC was deemed as difficult but important and satisfying. Peer reactions ranged from disgust (catheter insertion) to childish (use of diapers) to admiration. Those not in wheelchairs experienced less belief from others about their CIC use, and some of these wished they were in a wheelchair to increase								

acceptance of their CIC use. Lack of medical staff understanding of CIC was perceived as a major problem.

All disliked being catheterised by someone else, but in medical appointments most were reticent at stating this, and the clinician would do the catheterisation.

Most of the participants rated their incontinence as a mild disability, and rated non-MMC disabilities they didn't have, such as blindness, as more severe.

8 participants had no friends at all. Two others spoke of friends, but on later investigation these were really casual acquaintances. 12 had a best friend. 15 found it easy to make friends but harder to keep them. Barriers to friendship were perceived as an inability to run, the use of crutches or the need for diapers. 12 were currently involved with a partner. Finding a partner was strongly desired by 17, but they found it difficult to realise this wish. None knew of the effects of their condition on sexual function, and felt that a medical professional should give them more information on this. Some could not imagine a future without children of their own. 19 were preoccupied with thoughts of parenthood in the future, but 9 were unsure if they would be able to do this. Of the 3 female adults in a relationship, one had had a healthy baby. At the end of the interview the participants were invited to ask anything. 2 males and 2 females asked: "How am I going to find someone to marry?".

Overall all participants were satisfied with CIC and would not want to return to their previous voiding technique. Most, after 5 years experience, did not find it a problem in daily life. Overall, CIC was regarded as positive and most of the children's negative experiences were related to their overall disability, independent of CIC.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Maynard FM, Diokno AC. Clean intermittent catheterization for spinal cord injury patients. Journal of Urology. 1982; 128(3):477-480. Ref ID: MAYNARD1982	Retrospective observational study USA	N=65 N=28 with complete urologic follow up (outcomes extracted for this group only)	Patients with traumatic spinal cord injury who were discharged from hospital between 1972 and 1977 on clean intermittent catheterisation for the management of neurogenic bladder Patient characteristics: 50 men and 15 women, 36 paraplegia (23 complete and 13 incomplete) and 29 with quadriplegia (13 complete and 16 incomplete). The period after injury until	Excretory Urography		Mean 3.7 yrs (range 1 to 7.5 yrs) Frequency of follow up unclear	Cystolithiasis Urinary tract infections Hydronephrosis	None reported

			clean intermittent catheterisation was started was > 6 mths in 11 patients and < 6 months in 54.					
Effect Urinary tract infections 12/28 patients had received treatment for one or more urinary tract infection Hydronephrosis 0/28 of the patients had hydronephrosis								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
McGuire EJ, Savastano J. Comparatiive urological outcome in women with spinal cord injury. Urological neurology and urodynamics 1986; 135: 730-731	Propsective observational study. No rationale for grouping of patients given.	N=35	Female; age range 19-76. SCI. n: Indwelling catheter 13; Intermittent catheterisation 22 Level of SCI C5-C7: 8/13; 6/22 T1-T12: 4/13; 9/22 T12 and below: 0/13; 7/22 Myelomen-Ingocele: 1/13; 0/22 incomplete: 1/13; 1/22	Foley catheter (indwelling)	Intermittent catheterisation .	Mean 6 years (range 2-12 years) Frequency of follow up 6 monthly for two years then yearly	Symptomatic UTIs Recurrent bladder stones	None reported .
Effects								

Adverse event	Indwelling catheter	Intermittent catheterisation	p
Symptomatic (febrile) UTIs	12/13	7/22	Not stated
Recurrent bladder stones	13/13	0/13	Not stated
Upper tract abnormalities (bilat pyelonephritic scarring with clubbing)	7/13	0/22	Not stated

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Nwadiaro H C; Nnamonu M I; Ramyil V M; Igun G O. Comparative analysis of urethral catheterization versus suprapubic cystostomy in management of neurogenic bladder in spinal injured patients. Nigerian journal of medicine : journal of the National Association of	Retrospective and prospective cohort study . Retrospective study spanned from Jan 1 1984 to Dec 1989 while the prospective study was undertaken from Jan 1990 to June 2005 Nigeria.	N=125 (n=85 UC and n=40 SPC) .	A total of 125 patients with complete spinal cord lesion managed between Jan 1 1984 and June 30, 2005. Patient characteristics: The median of presentation for UC was 28 years vs. 32 for SPC. Male to female ratio compared was 13:1 for UC vs. 19:1 for SPC. The three commonest causes of SCI were road traffic accident (58%) resulting in 60% of injuries in UC vs. 61% in SPC, falls (36%) 36% vs. 35% respectively and cave-in injuries (4%) 35 vs. 2% respectively. In UC, 26% were stable injuries vs. 25% in SPC. Injury to the cervico-thoracic spine is 41% vs. 45% for UC and SPC groups respectively. Injuries	Urethral catheterisation (U.C) Supra-pubic cystostomy (SPC).	see interventions.	1 year	Episodes and timings of UTI. Urinary /blood culture Mortality.	None reported

Resident Doctors of Nigeria 2007;16(4):318-21. REF ID ARO 2007			involving the thoraco-lumbar spine in UC were 59% vs. 555 in SPC group.					

Effect

Episodes and timing of urinary infections post admission

Timing (weeks)	Urethral catheterisation (n=85)	Supra-pubic cystostomy (n=40)	Total (n=125)
1,2	12 (20%)	6 (14%)	16 (13%)
2,4	10(16%)	3 (21%)	13 (10%)
4,6	33(52%)	1 (7%)	34 (27%)
6,8	4 (6%)	2 (14%)	6 (4%)
8,10	2 (3%)	1 (7%)	3 (2%)
10,12	2(3%)	1 (7%)	3 (2%)

Urinary tract infection occurred relatively late at 4-6 weeks in UC compared to 2-3 weeks in SPC.

Organisms cultured from urine/blood in SCI patients :

Bacteria	U.C (n=85)	SPC (n=40)	Total (n=125)
Klebsiella	22 (6) (26%)	6 (2) (12%)	28 (8) (22%)
E.coli	17 (3) (20%)	2 (1) (4%)	19 (4) (15%)
Proteus	14 (3) (16%)	1 (0) (2%)	15 (3) (12%)
Pseudomonas	4 (1) (5%)	1 (0) (2%)	5 (1) (4%)

Staph.aureus	3 (0) (4%)	4 (0) (8%)	7 (0) (6%)

Note: blood culture results are in brackets.

Mortality: SPC was associated with significantly lower mortality figure at one year, 9% vs. 36% for UC (P<0.05).

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Oh SJ, Ku JH, Jeon HG et al. Health-related quality of life of patients using clean intermittent catheterization for neurogenic bladder secondary to spinal cord injury. Urology. 2005; 65(2):306-310. Ref ID: OH2005	Prospective observational study, Korea	N=132	Patients who were neurologically stable and using clean intermittent catheterisation because of neurogenic bladder secondary to spinal cord injury Patient population: mean age 41.8yrs (SE 1.4), male:female 81:51, duration of injury 67.8mths (SE 8.6), injury level cervical: noncervical 36:96, paraplegic: tetraplegic 24: 108, duration of catheterisation 24.2 mths (SE 3.1), catheterisation type caregiver n=44, self n=88	Na	Na	Duration of catheterisation 24.2 months	SF-36 (Health-related QoL). Eight dimensions: physical function, role limitations owing to physical health problems, bodily pain, general health perception, energy and vitality, social function, role limitations owing to emotional problems and mental health. Greater scores representing	None reported

							better health	

Effect

Comparison of SF-36 scores of patients and controls (general population) with respect to sex.

	Male mean (SE)			Female mean (SE)		
Domain	Patients (n=81)	Controls (n=90)	P value	Patients (n=51)	Controls (n=60)	P value
Physical functioning	18.4 (3.2)	85.3 (1.7)	<0.001	28.3 (4.4)	72.0 (2.3)	<0.001
Role-physical functioning	26.2 (4.5)	81.8 (2.9)	<0.001	30.9 (5.7)	71.2 (3.6)	<0.001
Role-emotional functioning	29.2 (4.8)	70.2 (3.4)	<0.001	38.6 (6.4)	60.8 (3.9)	0.002
Vitality	43.6 (2.4)	52.7 (2.0)	0.005	42.3 (3.0)	48.8 (1.9)	0.064
Mental health	55.6 (2.4)	67.2 (1.7)	<0.001	51.9 (3.1)	64.6 (1.7)	<0.001
Social functioning	49.5 (2.9)	85.2 (1.8)	<0.001	54.4 (4.0)	81.7 (2.1)	<0.001
Bodily pain	62.4 (3.3)	81.4 (1.8)	<0.001	60.5 (4.0)	70.9 (2.1)	0.025
General health	46.9 (2.1)	54.7 (1.5)	0.002	44.0 (2.3)	51.7 (1.8)	0.013

Comparison of SF-36 scores of patients and controls (general population) with respect to age

	< 50 yr			≥ 50 yr		
Domain	Patients (n=90)	Controls (n=100)	P value	Patients (n=41)	Controls (n=50)	P value
Physical functioning	20.1 (3.0)	83.5 (1.7)	<0.001	27.1 (5.1)	74.9 (2.3)	<0.001
Role-physical functioning	28.3 (4.2)	81.0 (2.9)	<0.001	27.4 (6.6)	73.0 (3.6)	0.001
Role-emotional functioning	32.6 (4.7)	66.9 (3.4)	<0.001	33.3 (7.0)	64.4 (4.0)	<0.001
Vitality	46.8 (2.1)	51.0 (1.9)	0.146	34.9 (3.5)	50.9 (2.1)	<0.001
Mental health	56.2 (2.2)	63.7 (1.7)	0.005	49.7 (3.7)	68.4 (1.8)	<0.001
Social functioning	54.0 (2.8)	84.2 (1.7)	<0.001	45.7 (4.3)	83.3 (2.2)	<0.001
Bodily pain	64.4 (2.9)	80.0 (1.7)	<0.001	55.7 (5.2)	72.7 (2.3)	0.004
General health	47.1 (1.8)	54.4 (1.6)	0.003	42.9 (3.2)	52.1 (1.6)	0.006

The patient SF-36 scores were significantly lower than those of the general population. When both patients and controls were divided into two subgroups according to

sex, male patients had significantly lower scores for all dimensions than did male controls. Significant differences in all dimension scores, except in the energy and vitality scores, were also observed between the female patients and female controls.

When patients and controls were subdivided into two groups according to age, patients younger than 50 yrs had significantly lower scores for all dimensions, except for energy and vitality, than did controls younger than 50 yrs. Significant differences in all dimension scores were also found between patients and controls 50 yrs old or older.

1

<table>
<tr><th>Reference</th><th>Study type
Evidence level</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr><td>J. Ord, D. Lunn, J. Reynard
Bladder management and risk of bladder stone formation in spinal cord injured patients.

The Journal of urology, Vol. 170, No. 5. (November 2003), pp. 1734-1737.

REF ID : ORD 2003</td><td>Retrospective cohort study

United Kingdom.</td><td>N=457</td><td>Patients included were those admitted to Stoke Mandeville Hospital Spinal injuries centre between 1985 and 1990 with greater than 6 months follow-up.

Patient characteristics:
<table>
<tr><th></th><th>Exp. voiding</th><th>Catheter</th><th>sphinct</th><th>ISC</th></tr>
<tr><td>No. of pt episodes</td><td>240</td><td>162</td><td>55</td><td>70</td></tr>
<tr><td>Av. Age</td><td>34</td><td>40</td><td>33</td><td>29</td></tr>
<tr><td>% male</td><td>88</td><td>70</td><td>100</td><td>57</td></tr>
<tr><td>AV injury level</td><td>T6</td><td>T5</td><td>T3</td><td>T9</td></tr>
<tr><td>%complete spinal injury</td><td>41</td><td>65</td><td>84</td><td>78</td></tr>
</table></td><td>Expression voiding with or without condom.

Indwelling catheters.

Sphincterotomy.

Intermittent self-catheterisation (ISC)</td><td>See interventions.</td><td>Median follow-up: 60 months

Frequency of follow up yearly</td><td>Risk of bladder stone formation .</td><td>None reported .</td></tr>
<tr><td colspan="9">Effect</td></tr>
</table>

A total of 327 patients remained on definitive management for the full duration of follow-up, while 100 changed management during follow-up, some more than once (expression voiding and condom drainage 27%, condom drainage and external sphincterotomy 11% and indwelling catheter 13%). Thus, the catheter and sphincterotomy groups were more likely to remain on definitive treatment, whereas those starting on expression voiding with condom drainage were more likely to change.

Risk of bladder stones:

Bladder management type	Mean follow-up(years)	No. of bladder stones/no. of pts	% forming bladder stones (no./ total no.)	Total group follow-up (years)	% absolute annual risk stone formation
Condom+sphincterotomy	8.4	0	0 (0/55)	463	0
ISC	6.75	1/1	1.5 (1/70)	480	0.2
Expression voiding with or without condom	6.3	7/7	3 (7/240)	1,515	0.5
Indwelling catheter	5.9	59/35	23 (35/152)	789	4% (first stone), 16% (subsequent stones)

Results of Cox- regression analysis: Although age, sex, and injury level were not significantly explanatory variables, degree of injury was considered (p=0.02) in the model. After correcting for degree of injury, both forms of indwelling catheter was found to have a high risk of bladder stone formation compared with ISC or condom drainage with or without sphincterotomy.

The hazard ratio was 10.5 (p<0.0005, 95% CI 4.0-27.5) for patients with supra pubic catheters and 12.8 (p<0.005, 95% 5.1-31.9) for those with indwelling catheters. Bladder stones were no more likely to form in patients with supra pubic catheters than in those with indwelling urethral catheters (hazard ratio 1.2, p=0.6).

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Pannek J, Kullik B. Does optimizing bladder	Prospective observational study, Germany	N=41	Patients with neurogenic lower urinary tract dysfunction due to a spinal cord lesion who	Urodynamically assessed as a "treatment success".	Urodynamically assessed as a "treatment failure". Failure was diagnosed	Mean time between spinal cord injury and	Qualiveen questionnaire (quality of life). Four scales:	None reported

management equal optimizing quality of life? Correlation between health-related quality of life and urodynamic parameters in patients with spinal cord lesions. Urology. 2009; 74(2):263-266. Ref ID: PANNEK2009			were performing intermittent self-catheterisation Inclusion criteria: interval between the occurrence of the spinal cord injury and examination of ≥ 1yr Patient population: male: female 31:10, injury level cervical 9, thoracic 23, lumbar 9, age at examination mean 39.5 yrs (range 18 to 72), age at spinal cord lesion mean 27.0 yrs (range 14 to 61), spinal cord lesion duration mean 14 yrs (range 1 to 22)	Success was defined as a bladder capacity of ≥ 360 mL, a maximum detrusor pressure ≤ cmH2O, the absence of autonomic dysregulation, and continence	when any of the "success" criteria were not satisfied	examination 4 yrs	constraints, limitations, fears and feelings. The greater the score of a scale, the worse the perception of the items on the scale	

Effect

All patients were performing intermittent self catheterisation and receiving anticholinergic treatment. Bladder management was classified as successful in 14/41 (34%) and unsuccessful in 27/41 (66%). Of the 14 patients classified as having successful treatment, 10 were treated with oral anticholinergic drugs, and 4 had received additional intradetrusor botulinum toxin (BTX-A) injections. The 27 patients with treatment failure had either presented because of decreasing efficacy of BTX-A injections (n=16) despite anticholinergic medication or had demonstrated significant detrusor overactivity despite maximal oral anticholinergic treatment (n=11).

Qualiveen scale scores in relation to bladder function after correction for depression

	Bladder management mean (SD)		
Scale	Success (n=14)	Failure (n=27)	P value
Limitations	37.2 (22.10)	48.6 (18.29)	.0544
Constraints	39.2 (21.44)	52.9 (25.68)	.0377
Fears	20.0 (16.40)	44.7 (19.65)	.0014
Feelings	12.7 (15.22)	39.8 (27.69)	.0182

1

2

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sugimura T, Arnold E, English S, Moore J. Chronic suprapubic catheterisation in the management of patients with spinal cord injuries: analysis of upper and lower urinary tract complication. BJU Int. 2008; 101: 1396-1400	Retrospective observational study. New Zealand.	N= 149	Inclusion: Patients attending a hospital in New Zealand with SCI who continued to use the suprapubic catheter for >3 months. Patient characteristics: Newly diagnosed SCI patients with either paraplegia or quadriplegia. 25 patients had used some other form of bladder emptying before changing to a suprapubic catheter (urethral catheter – 12, ISC – 7, external sphincterotomy – 3, bladder neck incision – 1, coposuspension – 1, urethral stent – 1).	A strict protocol to minimise complications was followed. The suprapubic catheter was irrigated weekly with normal saline, and the catheter was changed every 2 weeks while the patient was in hospital. This was continued at home, through close surveillance from the medical team.	NA	68 (3-179) months Frequency of follow up variable	Existence of caliectasis Existence of hydronephrosis Existence of renal scarring Vesiculoureteral reflux Symptomatic UTIs Existence of calculi	None reported.

Effects

Adverse event	Number with adverse effect
All complications	76/149
Symptomatic UTIs	45/149
Bladder stones	33/149
Low grade superficial TCC (?transitional cell carcinoma)	1/149
All renal complications Renal calculi Renal scarring	20/149 12/149 9/149
All vesicoureteral reflux (VUR) VUR with renal stones VUR with renal scarring VUR with renal stones and scarring	21/149 (bilateral in 5) 3/149 1/149 1/149
Urethral incontinence	11/149

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Waites KB, Canupp KC, DeVivo MJ. Epidemiology and risk factors for urinary tract infection following spinal cord injury. Arch Phys med Rehabil 1993;	Prospective observational study.	N=64	Traumatic SCI patients with neurogenic bladder and discharged from the initial hospitalisation. No age given. Exclusion: severe concurrent illness; known vesicoureteral or intrarenal reflux; urinary calculi; severely dimished renal function; indwelling or suprapubic catheters.	Intermittent Catheterisation	Condom with urine bag	1 year Frequenct of follow up monthly	Incidence of UTIs	None stated

74: 691-695.

Effects

Adverse event	Intermittent catheterisation	Condom and collection bag	p
Urinary tract infection	17.2 infections/ person-year	18.9 infections/ person-year	NS

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Weld KJ, Dmochowski RR. Effect of bladder management on urological complication in spinal cord injured patients. The Journal of Urology. 2000; 163: 768-772	Retrospective (chart review) observational study. USA.	N=316	313 males and 3 females with post-traumatic SCI. All receiving continuous long term physical care at a SC unit. Groups equivalent for all variables below (P>0.05)	All were on some form of bladder management. Although some patients changed their method during their stay, the predominant method used was chosen.	NA	18.3 (12.4) yrs since injury. Frequency of follow up unclear	Pyelonephritis VUR Renal stones Bladder stones	Not given

	Urethral n=114	CIC n=92	Spontaneous n=74	Suprapubic n=36
age	36.8 (10.4)	41.0 (12.6)	38.1 (11.8)	33.9 (13.8)
Follow up (yrs)	18.1 (12.1)	18.0 912.6)	19.3 (13.0)	17.8 (12.4)
Suprasacral (%)	89	79	85	89
Complete (%)	21	12	10	9

Effects: Estimated from figures, but all likely to be accurate to within 1%.

Complications	Urethral n=114	CIC n=92	Spontaneous n=74	Suprapubic n=36	p

All	61/114	25/92	24/74	16/36	
pyelonephritis	8%	1%	1.5%	3%	<0.001
Renal stone	55%	22%	20%	36%	<0.001
Bladder stone	28%	0%	8%	22%	<0.001
VUR	23%	7%	8%	28%	0.001
Upper tract deterioration	30%	16%	27%	39%	0.038

F.8 Does monitoring or do surveillance protocols improve patient outcomes?

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bodner DR, Witcher M, Resnick MI. Application of office ultrasound in the management of the spinal cord injury patient. Journal of Urology. 1990; 143(5):969-972. Ref ID: BODNER1990	Prospective observational study USA	N=86 N=171 kidneys N=83 bladders N=106 office ultrasound scans N=68 excretory urography (IVP)	Asymptomatic patients with spinal cord injury undergoing routine urological follow up Patient population: 85 men, 1 woman, mean age 41.7 yrs, mean duration since injury 8.75 yrs	Standard radiology imaging study (excretory urography, computerised tomography (CT) or radiology performed and interpreted ultrasound) Frequency: routine	Office ultrasound	Na	Ultrasound findings	None reported
Effect Diagnosis from office ultrasound and IVP in 68 patients (135 kidneys)								

	No.	Diagnosed by ultrasound	Diagnosed by IVP
Renal obstruction	2	2	2
Kidney stones	3	2	2*
Chronic pyelonephritis	8	0	8
Bladder stones	3	3	2**
Bladder diverticula	3	3	3

* IVP inadequate; stone confirmed by radiologist-performed ultrasound

** IVP inadequate; stone confirmed by cystoscopy

Diagnosis from office ultrasound and CT or radiologist performed ultrasound in 18 patients who did not undergo an IVP (36 kidneys)

	No	Diagnosed by ultrasound	Diagnosed by CT or radiologist-performed ultrasound
Renal obstruction	4	4	4
Kidney stones	3	3	3
Renal cyst	6	4*	6
Renal tumour	1	1	1

* office ultrasound inadequate in 1 patient; CT confirmed bilateral renal cysts

Summary of diagnosis from office ultrasound compared to IVP, CT or radiologist-performed ultrasound in 86 patients (171 kidneys and 83 bladders)

	No.	Diagnosed by office ultrasound (167 kidneys)*	Diagnosed by IVP, CT or radiologist-performed ultrasound
Renal obstruction	6	6	6
Kidney stones	6	5	6
Chronic pyelonephritis	8	0	8 (by IVP)
Renal cysts	6	4**	6
Renal tumour	1	1	1
Bladder with stones	3	3	2***
Bladder with diverticula	3	3	3

* Office ultrasound inadequate in 2 patients (4 kidneys) because of obesity

** Office ultrasound inadequate in 1 obese patients with bilateral renal cysts noted on CT

*** IVP inadequate because of poor preparation; bladder stones confirmed by cystoscopy

Authors conclusions 'Outpatient ultrasonography performed by the urologist proved to be a cost effective and sensitive screening examination for urological disorders'

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Calenoff L, Neiman HL, Kaplan PE et al. Urosonography in spinal cord injury patients. Journal of Urology. 1982; 128(6):1234-1237. Ref ID: CALENOFF1982	Prospective observational study	N=54	Patients with spinal cord injury. Patient population: age range 16 to 63 yrs, male:female 34:20, quadriplegic 31/54, paraplegic 23/54	Ultrasound Frequency: once	Excretory urogram (IVP) and/or voiding cystourethrogram	Na	Ultrasound findings	None reported

Effect

Kidneys: For 15/54 there were concerns regarding renal abnormalities based on the excretory urogram (IVP). Of these 15 patients ultrasound confirmed the radiographic findings in five (two with renal calculi, one with chronic pyelonephritis, one with peripelvic cyst and one with focal pyelonephrtitis), ruled out questionable radiographic findings in six and revealed abnormalities not present radiographically in four (one with renal cyst, one with hydronephrosis, one with cortical atrophy and one with renal calculi). Ureters: Of the 15 patients in whom the ureters were examined nine had different degrees of vesicoureteral reflux on voiding cystourethrography, which was confirmed by ultrasound in five (56%) and not demonstrated in four. The remaining 6 patients had ureterctasis on an IVP, which was confirmed by ultrasound in two (33%) and not noted successfully in 4. In two patients with a known allergy to the contrast medium ultrasound demonstrated vesicoureteral reflux in one, and hydroureter and hydronephrosis in one. Bladder: The bladder was examined in 32 patients during ultrasound voiding cystourethrography but was imaged adequately in only 30. Ultrasound confirmed the positive radiographic findings in 23 (six with bladder calculi, three with trabeculated bladders and 12 with normal bladders), ruled out questionable radiographic findings in three and yielded additional information in four (one with bladder calculi, two with lithogenic bladder sediment and one with calcific crust on the Foley catheter balloon)

Authors conclusion 'It is recommended that spinal cord injury patients undergo a baseline excretory urogram followed by periodical ultrasound examinations to detect hydronephrosis, renal parenchymal disease, and renal and bladder calculi, and to measure bladder volume and residual urine. Whenever real-time equipment and experienced ultrasonologists are available ultrasound can be used as an alternate to voiding cystourethrography to detect vesicoureteral reflux.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Gousse AE, Meinbach DS, Kester RR et al. Renal ultrasound correlates with renal nuclear scan in upper tract surveillance of spinal cord-injured patients. TOP SPINAL CORD INJ REHABIL. 2003; 8(3):1-7. Ref ID: GOUSSE2003	Retrospective observational study USA	N=178 (N=162 patients included with 478 paired and matched renal ultrasound (RUS) and renal nuclear scan (RNS)	Patient with spinal cord injury Patient population: mean age 56 yrs (range 22 to 89), bladder management: spontaneous voiding with or without Crede N=91, clean intermittent catheterisation N=42, sphincterotomy N=30 and indwelling catheter N=40, mean time elapsed since injury 23.9 yrs	Renal ultrasound (RUS) Frequency: Annual routine surveillance scan. Scans performed generally within 48 hrs of each other and within the preceding 5 yrs (1996 to 2001) Average of 2.95 paired study comparisons per patient	Renal nuclear scan (RNS) Data not reported	mean time elapsed since injury 23.9 yrs	Renal impairment	None reported
Effect A RUS scan was judged to be positive if it demonstrated any degree of caliectasis or pyelocaliectasis; parenchymal disease; or the presence of complex cysts, calculi, solid masses, or other renal and/or peri-renal processes. Simple renal cysts were not considered an abnormality because they did not dictate any change in patient management. RUS abnormalities were found in 57 patients (35.2%). Of the 75 positive ultrasound studies, 39 were positive for hydronephrosis, 39 revealed parenchymal disease, 22 revealed renal stones, and 8 revealed solid renal mass (renal malignancy found in 2 of these 8 patients). Many ultrasounds had								

more than one pathologic finding.

Authors conclusions 'Upper tract surveillance of spinal cord injury patients can be performed solely with RUS, which is non invasive, widely available, and less costly than RNS'

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Gupta S, Chawla JC. Review of urinary tract abnormalities in 100 patients with spinal cord paralysis. Paraplegia. 1994; 32(8):531-539. Ref ID: GUPTA1994	Retrospective and prospective observational study	N=100	Patients with spinal cord injury Patient population: paraplegics (n=49), age range 19 to 64 yrs, male:female 40:9, paralysis duration one years or less 12/49, duration 1 to 10 yrs 23/49, duration > 10 yrs 14/49 Tetraplegics (n=51), age range 19 to 64, male:female 44:7, duration of paralysis one year or less 11/51, duration 1 to 10 yrs 21/51, duration > 10 yrs 19/51	Routine radiological screening	Na	Mean time since injury 2 months to 20 yrs	Upper tract changes (reflux, hydroureter and or nephrosis, clayceal clubbing, shrunken kidneys, cortical atrophy, scarring); calculi (renal and/or upper tract, lower tract; bladder abnormalities (contracted bladder, trabeculae/diverticulae; persistent post-voidal residual urine > 100 ml	None reported

Effect

In paraplegics, 26/47 patients had abnormalities (upper tract changes, calculi, bladder abnormalities, persistent post-voidal residual urine > 100 ml) detected on routine radiological screening. 24/26 were detected 0 to 10 years after the injury compared with only 2/26 after 10 yrs of injury. For tetraplegics, 35/50 abnormalities were detected. All of these were detected within 10 yrs after the injury.

Authors conclusion '…it is suggested that patients with spinal cord paralysis should have surveillance or urinary tract annually for 10 yrs and that the follow up beyond 10

yrs should be determined by clinical necessity rather than a fixed protocol'

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lemack GE, Hawker K, Frohman E. Incidence of upper tract abnormalities in patients with neurovesical dysfunction secondary to multiple sclerosis: analysis of risk factors at initial urologic evaluation. Urology. 2005; 65(5):854-857. Ref ID: LEMACK2005	Retrospective observational study USA	N=113 (referred and evaluated) N=66 (completed both urodynamic testing and renal ultrasonography)	Patients with multiple sclerosis (MS) who were referred to the neurourology clinic for evaluation of lower urinary tract symptoms Included: patients with completed urodynamics and renal ultrasonography Patient population: mean age 50.7 yrs, mean time since diagnosis 12.9 yrs, male 10.2%, secondary progressive 44.0%	Renal ultrasound Frequency: once	Na	Na	Renal ultrasound findings	None reported

Effect

Radiologic findings in patients with abnormal renal ultrasound findings

Radiologic findings	Patients (n)
Unilateral focal caliectasis	6
Bilateral focal caliectasis	1
Unilateral cortical scarring	1
Unilateral mild hydronephrosis	1

Bilateral stones (5 mm) mild hydronephrosis	1
Unilateral stone (<5 mm)	1

Authors conclusion: 'No patients in this series had any indication of obstructive uropathy more severe than mild hydronephrosis. Of the 16.7% of patients with any abnormal findings, most were noted to have minor caliectasis, likely to be of little clinical significance…'

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
MacDiarmid SA, McIntyre WJ, Anthony A et al. Monitoring of renal function in patients with spinal cord injury. BJU Int. 2000; 85(9):1014-1018. Ref ID: MACDIARMID2000	Prospective observational study New Zealand	N=36	Consecutive patients presenting to the spinal cord injuries unit for their annual routine evaluation Patient population: 29 men, 7 women, mean age 38 yrs (range 24 to 68 yrs)	Serum creatinine level Measured at the time of the 24 hr urine collection Frequency: once	Na	Na	Creatinine clearance	None reported

Effect

Creatinine clearance was determined in all patients by three methods:

i) The mean of two consecutively measured 24 hr endogenous creatinine clearances using standard clearance techniques. Urine was obtained by indwelling urethral or intermittent catheterisation, or by voiding or condom collections. All patients were catheterised at the beginning and end of each 24 hr period in an attempt to ensure complete urine collection. The absolute mean percentage change between the measurements was also calculated.

ii) The single-shot 99mTc-DTPA clearance technique using multiple blood samples. 99mTc-DTPA (18 MBq) was injected into an antecubital vein and 10 mL blood samples taken from the opposite arm 2, 4 and 6 hr after injection.

iii) The Cockcroft-Gault formula

Of the 36 patients 11 (31%) had a measured creatinine clearance of <100 mL/min (mean 84.8) and a corresponding normal serum creatinine level. Creatinine clearance calculated by the Cockcroft-Gault formula did not correlated well with that measured by the 24 hr endogenous clearance (r=0.426) and 99mTc-DTPA clearance (r=0.366), overestimatimg creatinine clearance in all but three patients. The mean (SD) difference between the creatinine clearance measured by the 24 hr and DTPA clearance technique was 17.7 (16.5%) and the correlation between these techniques was good (r=0.71)

Authors conclusion: Serum creatinine level is not sensitive in detecting early deterioration of renal function in patients with spinal cord injury. The Cockcroft-Gault

formula generally significantly overestimates the true creatinine clearance and is not recommended. The 24 hr endogenous creatine clearance measured on appropriately collected urine samples is an acceptable accurate and practical method of determining glomerular filtration rate in patients with spinal cord injury.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Morcos SK, Thomas DG. A comparison of real-time ultrasonography with intravenous urography in the follow-up of patients with spinal cord injury. Clin Radiol. 1988; 39(1):49-50. Ref ID: MORCOS1988	Prospective observational study UK	N=75	Consecutive patients with spinal cord injury. The indication for the examination in all patients was routine assessment of the upper urinary tract. Patient population: 69 male, 6 female, mean age 35.9 yrs, mean duration of paralysis 10.5 yrs	Renal ultrasonography Frequency: routine assessment	Intravenous urography	Mean duration of paralysis 10.5 yrs	Renal abnormalities	None reported

Effect

Normal IVU and abnormal ultrasound

Ultrasound findings	No. of patients
A simple renal cyst of a left kidney	1
Bilateral multiple renal cysts and simple cysts in the spleen; appearance is consistent with adult polycystic disease	1
A small right kidney (7cm in length)	2
Mild dilatation of the calyces of a left kidney	1
Left kidney not clearly seen	2
Total	7

Abnormal IVU and normal ultrasound

Intraveous urogram findings	No. of patients
Mild dilatation of the calyces of a left kidney	1
Scar of the upper pole of left kidney with blunting of the upper calyx	1
Scar of the upper pole of the right kidney with mild dilatation of the right ureter and lower third of the left ureter	1
Dilatation of the lower third of the ureters	1
Dilatation of the left ureter	1
Dilatation of the right ureter	1
Poor visualisation of right kidney	1
Total	7

Abnormalities which were demonstrated by IVU and also indicated or shown by ultrasound

Dilatation of calyces and renal pelvis	5
Cortical scarring and small kidneys	7
A renal calculus and mild hydronephrosis of a kidney	1
Total	13

Authors conclusion 'The combination of a plain radiography of the abdomen and ultrasound scan of the kidneys was found to be a cheap, safe and reliable alternative to intravenous urography for the regular follow up of these patients'

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Persun ML, Ginsberg PC, Harmon JD et al. Role of urologic evaluation in the	Retrospective observational study	N=40	Adults (aged 18 to 37 yrs) with a history of lumbar myelomeningocele, all of whom performed CIC	Patients with normal ultrasounds/creatinine Ultrasound, serum creatinine	Na	Na	Ultrasound Serum creatinine	None reported

adult spina bifida patient. Urologia Internationalis. 1999; 62(4):205-208. Ref ID: PERSUN1999			and were dry between catheterisations. Patients with conditions predisposing them to renal insufficiency were excluded (12/52)	Cystometry Frequency: once				
Effect In patients with normal ultrasound and normal serum creatinine (1.5 mg/dl), there were no individuals (0/20) whose average catheterised volume corresponded to a bladder pressure of >40 cm H2O on cystometry. However, in patients with hydronephrosis and/or elevated creatinine, 30% (6/20) had average catheterised volumes corresponding to a bladder pressure of >40 cm H2O Author's conclusion 'Many spina bifida patients receive urologic care only as children, and those without urinary calculi or urinary incontinence are assumed to be urologically stable. However, certain patients have urodynamic parameters which put them as risk for renal deterioration even if they appear to be problem-free. We recommend a yearly renal ultrasound and serum creatinine determination in all adult spina bifida patients with immediate urologic consultation and urodynamics if either is abnormal'.								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sepahpanah F, Burns SP, McKnight B et al. Role of creatinine clearance as a screening test in persons with spinal cord injury. ARCH PHYS MED REHABIL. 2006; 87(4):524-528. Ref ID: SEPAHPANAH2006	Retrospective observational study USA	N=70	Patients with spinal cord injury who had annual inpatient evaluations for 5 separate years. Inclusion criteria: only patients admitted to the hospital in each of 5 consecutive annual evaluations were included Patient population:	Annual evaluation including ultrasound and serum creatinine	na	Mean interval (SD) between the first and fifth test 5.57 yrs (2.13)	Serum creatinine Renal ultrasound	None reported

			bladder management at time 5 58.6% indwelling catheter, 18.6% condom catheter, 12.9% spontaneous voiding, 7.1% intermittent catheterisation, 2.9% ileal conduit					

Effect

For individual patients, the results of 24 hr Ccr were highly variable from one evaluation to the next; the within-subject standard deviation (SD) for Ccr was 25.9 mL/min. The within-subject SD for serum creatinine was 0.12 mg/dL. For all comparisons of repeatedly, variability and reliability, serum creatinine was superior to Ccr. No medical management decisions were made based on the result of the 24 hr creatinine clearance.

Renal ultrasound

58 patients had bilateral normal kidneys on 5 consecutive annual evaluation ultrasounds. Four had kidney stones on 1 or more ultrasound studies and 5 patients had at least one renal ultrasound that showed hydronephrosis. For the 3 patients who had normal renal utrasounds at time one, but developed abnormalities over subsequent studies (hydronephrosis for 2, cortical scarring for 1), the largest change in Ccr was 19.7% which is less than the mean variability between serial Ccr measurements. The remaining two patients who developed new renal ultrasound abnormalities had changes in Ccr of less than 1%.

Authors conclusion 'The Ccr test has little value as a screening measure for renal disease in spinal cord injury patients because of its variability in serial testing'

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sliwa JA, Bell HK, Mason KD et al. Upper urinary tract abnormalities in multiple sclerosis patients with urinary symptoms. Archives of Physical Medicine and Rehabilitation.	Prospective observational study	N=48	Patients with multiple sclerosis with symptoms of neurogenic bladder dysfunction Inclusion criteria: Exacerbation-free MS for 6 months Patient population: mean age 44.3 yrs, 75% female, disease duration 13.4 yrs,	Ultrasound Frequency: once	Na	Na	Ultrasound findings	None reported

1996; 77(3):247-251. Ref ID: SLIWA1996			spontaneous voiding 81%, intermittent catheterisation 8%, indwelling catheter 21%					
Effect Renal ultrasound examination showed significant MS-related upper urinary tract abnormalities in 10 patients (21%). These abnormalities included renal stones in five patients, grade one hydronephrosis in two patients, cortical atrophy in two patients, and a reflecting pattern in the renal pelvis of one patient representing an early stone or vascular calcifications. In addition, 14 ultrasounds identified bladder trabeculation (29%), which was considered a non-significant MS-related change. Only five of these were associated with abnormal upper tract findings. Eight patients had incidental findings. Authors conclusion 'Routine screening for upper urinary tract complications appears indicated in a select group of MS patients with urinary symptoms'								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tarcan T, Bauer S, Olmedo E et al. Long-term followup of newborns with myelodysplasia and normal urodynamic findings: Is followup necessary? Journal of Urology. 2001; 165(2):564-567. Ref ID: TARCAN2001	Retrospective observational study	N=25	Patients with myelodysplasia Inclusion criteria: normal urodynamics at birth (defined as normal bladder capacity and compliance, no hyperreflexia or unihibited contractions	Ultrasound Frequency: routine	Na	(Age) Mean 9.1 yrs (SD 5.5 yrs) (range 1 to 18.6 yrs)	Ultrasound findings	None reported
Effect No child had hydronephrosis or reflux								

2

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tins B, Teo HG, Popuri R et al. Follow-up imaging of the urinary tract in spinal injury patients: is a KUB necessary with every ultrasound? Spinal Cord. 2005; 43(4):219-222. Ref ID: TINS2005	Prospective observational study	N=100	Consecutive patients with spinal cord injury attending for routine follow-up imaging on the urinary tract Patient population:80 men and 20 women, mean age 46 yrs, mean time since injury 11 yrs	Kidney, Ureter, Bladder (KUB) radiograph Frequency: routine	Ultrasound	Mean time since injury 11 yrs	KUB findings	None reported
Effect A total of 199 kidneys and 99 urinary bladders were examined. On average, less than 50% of the renal area and about 70-75% of the urinary bladders were visualised. Five patients had renal stones identified on KUB radiograph, and of these two were seen on ultrasound. There were no stones seen on ultrasound only. The patient history was not helpful to identify patients with renal stones. Ultrasound identified renal abnormalities in a further 14 patients. There were seven patients with renal scarring in eight kidneys. There were five patients with hydonephrosis in six kidneys; all cases were mild to moderate. There were two patients with a small kidney with thinned cortex. The KUB identified none of these patients. Ultrasound identified a number of other abnormalities. There was one patient with a duplex renal collecting system, one case of nephrectony, one case of adrenal myolipoma, one situs inversus, one case of abnormally high echogenicity of the liver and two cases of gallstomes. In one of these an additional gallbladder polyp was seen. One of the cases of gallstones was also identified on the KUB; all other abnormalities were not seen on the radiographs. Abnormalities of the urinary bladder were seen in 20 cases. A total of 19 cases showed evidence of bladder wall hypertrophy, and one case of incomplete bladder emptying. There was one case of previous cystectomy and a neobladder. KUB did not identify any of the abnormalities. Therefore, apart from the renal stones and one patients with gallstones, KUB did not identify any of the other abnormalities seen on ultrasound.								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-	Outcome measures	Source of funding

						up		
Tsai SJ, Ting H, Ho CC et al. Use of sonography and radioisotope renography to diagnose hydronephrosis in patients with spinal cord injury. Archives of Physical Medicine and Rehabilitation. 2001; 82(1):103-106. Ref ID: TSAI2001	Prospective observational study Taiwan	N=109 N=235 kidneys	Patients with spinal cord injury undergoing annual urologic surveillance Patient population: 88 men and 21 women, mean age 33.7 yrs (range 9 to 64 yrs), mean duration of injury 45 months	Intravenous urography Frequency: routine	Renal ultrasound	na	Diagnostic accuracy	None reported

Effect

Of 235 kidneys studied, 43 kidneys in 23 patients showed hydronephrosis on the final findings. The estimated prevalence was 21% (23/109) in the study.

Authors conclusion 'Sonography and renal scan are safe, sensitive and specific for detecting hydronephrosis. Combined use of both methods appears to be a reliable alternative to intravenous urography in the long-term follow-up for patients with spinal cord injury with neurogenic bladder dysfunction'.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Sonography	0.96	0.90	0.68	0.99
Renal scan	0.91	0.84	0.56	0.98

1

Reference	**Study type Evidence level**	**Number of patients**	**Patient characteristics**	**Intervention**	**Comparison**	**Length of follow-up**	**Outcome measures**	**Source of funding**
Vaidyanathan S, Hughes PL, Soni BM. A comparative study of ultrasound examination of urinary tract performed on spinal cord injury patients with no urinary symptoms and spinal cord	Retrospective observational study	N=108	Patients with spinal cord injury who underwent ultrasound examination of the urinary tract during the past 6 yrs	Ultrasound in spinal cord injury patients who had symptoms related to the urinary tract (passing	Ultrasound in spinal cord injury patients with no urinary symptoms when they underwent ultrasound examination N=87	Na	Ultrasound findings	None reported

injury patients with symptoms related to urinary tract: do findings of ultrasound examination lead to changes in clinical management? TheScientificWorldJournal. 2006; 6:2450-2459. Ref ID: VAIDYANATHAN2006				purulent urine, temperature, rigors, passing blood in urine, severe kidney/bladder pain, recurrent urine infections) N=21 Frequency: once				

Effect

Asymptomatic group

No abnormalities were reported in 63 patients. The following findings were reported in 24 patients

Abnormal findings	No. of patients
Simple cyst in the kidney	4
Reduced size of a kidney	3
Some increased echogenicity of the left kidney	1
Primineny extrarenal pelvis and mild calyceal dilation	1
Slightly dilated renal pelvis and calyceal system	1
Right pelvic kidney showing mild hydronephrosis	1
Foetal lobulation of kidney	2
Multicystic kidney (no interval changes since last examination)	1
Small (2 cm diameter) parapelvic cyst	1
Small (4 mm) renal calculus in the lower pole	2
4 mm calculus in the upper pole of kidney	1
5 mm renal calculus in the mid pole	2
A little cortical scarring bilaterally	1

Focal renal scar	2
Generalised renal cortical thinning	3
Some increase in renal sinus fat	3
Trabeculated bladder	2
Small vesical diverticulum	1
Mild generalised bladder wall thickening	1
Small residual urine in postvoid scan	2

Symptomatic group

There were 21 spinal cord injury patients who exhibited urinary symptoms (passing purulent urine, temperature, rigors, passing blood in urine, severe kidney/bladder pain, recurrent urine infections) when they underwent ultrasound examination of the urinary tract. Abnormalities such as hydronephrosis, pyonephrosis, vesical calculi, or vesical polyp were detected in 20 of 21 patients and, subsequently, all 20 patients required therapeutic intervention on the basis of ultrasound findings.

Authors conclusions 'Routine ultrasound examination of the urinary tract in spinal cord injury patients who have no urinary symptoms may not be justifiable in terms of cost effectiveness…'

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Waites KB, Canupp KC, DeVivo MJ et al. Compliance with annual urologic evaluations and preservation of renal function in persons with spinal cord	Prospective observational study	N=160	Patients who had received inpatient treatment for spinal cord injury sustained between 1977 and 1986 Inclusion criteria: renal scintigraphic scan performed within one year post-injury and that the person had two kidneys	Patients who had missed two or more consecutive annual examinations N=59 Mean no. of years missed 6.6 yrs (range 3 to 15)	Patients who were compliant with routine annual examinations for the previous three consecutive years Patients underwent renal scintigraphic scanning	Na	Mean-adjusted Effective Renal Plasma Flow	The Centers for Disease Control and Prevnetion Cooperative Agreement, The National Institute on Disability and Rehabilitation, Medical Rehabilitation Research and Training Center

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
injury. J Spinal Cord Med. 1995; 18(4):251-254. Ref ID: WAITES1995			Patient population: Subjects: completed annual investigations 44%, mean yrs of age 26, mean yrs post injury 12 Controls: completed annual investigations 87%, mean yrs of age 28, mean yrs post injury 11	Patients underwent renal scintigraphic scanning Frequency:once				in Secondary Complications in Spinal Cord Injury, UAB Spinal Cord Injury Care System and National Spinal Cord Injury Statical Center Grant
Effect Follow-up mean-age adjusted Effective Renal Plasma Flow There were no significant differences on mean-age adjusted ERPF between subjects and controls (left kidney 311 vs 308 mL/min, right 301 vs 276)								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Yang CC, Clowers DE. Screening cystoscopy in chronically catheterized spinal cord injury patients. Spinal Cord. 1999; 37(3):204-207. Ref ID: YANG1999	Retrospective observational study USA	N=59 N=156 cystoscopy procedures	Chronically catheterised spinal cord injury patients. Number of screening cystoscopies performed per patient, over 6 yr period No. Performed: 1 No. of Patients: 27	Annual health maintenance evaluation to include cystoscopy on patients who were continuously catheterised for 10 more years, or were smoker and catheterised	na	6 year period (1992 to 1997)	Incidence of bladder cancer	None reported

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
			2 13 3 6 4 13 5 7 6 1	for 5 or more years. Majority were performed on quadriplegics as risk for autonomic dysreflexia so a spinal anaesthetic was used				
Effect Ninety three bladder biopsies and 18 urine cytologies were obtained, none of which demonstrated malignant changes. No bladder cancers were diagnosed through screening. During the same six year period four spinal cord injury patients were diagnosed at the hospital with bladder cancer, all outside of the surveillance protocol. Authors conclusion 'Cystoscopy does not fulfil the accepted criteria for screening for primary bladder cancer in spinal cord injury patients. The disease does not seem amenable to screening'								

1

F.9 What is the safety and efficacy of augmentation cystoplasty compared with usual care in neurological disease?

F.9.1 Children (aged <19)

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Arikan N, Turkolmez K, Budak M, Gogus O. Outcome of	Prospective observational study.	18	Inclusion: Consecutive patients undergoing augmentation cystoplasty for neuropathic bladder	Sigmoid augmentation cytoplasty performed in all. Modified clam	Compared to pre-treatment	41 months Range	Existence of incontinence	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
augmentation sigmoidocystoplasty in children with neurogenic bladder. Urologia Internationalis 2000; 64: 82-85	Turkey.		problems, with small capacity or severe hyper-reflex bladder without response/intolerance to conservative treatment. Exclusion: None Patient characteristics: 10 boys and 8 girls with an average age of 10.3 years (range 16-70 months). Spinal trauma (n=7), spinal dysraphism (9), myelitis sequele (2). All had been on a course of intermittent catheterisation and anticholinergics.	technique used, with 20-25 cm section of detubularised sigmoid colon used to augment bladder. In 4 subjects ureteroneocystostomy also performed (in 2, was bilateral), using Leadbetter technique.		16-70 months)	Adverse events Use of intermittent catheterisation urodynamics	

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Adverse events (early post-operative period)		0/18
Adverse events (later) – pyuria		10/18
Clinical acidosis		1/18
Renal function deterioration, ureteral stenosis, or pyelonephritis		0/18

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
	Artificial urinary sphincter fitting Removal of the above due to infection Malignancy, stone formation, or kidney failure				3/18 1/3 0/18			
Incontinence				unclear	3/18 secondary to sphincter deficiency (in the 15 continent patients, use of Clean intermittent catheterisation required)			
Use of intermittent catheterisation				18/18	unclear			
Urodynamics Functional bladder capacity (FBC) Compliance, cm3/cm H20				 86 (7) 3.2 (0.9)	 370 (52) 13.7 (2.9) (p<0.001)			

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Fiorica VM, Barnes WF. Augmentation Enterocystoplasty in children with Myelomeningocele. JOSMA1987; 80: 236-238	Retrospective observational study. USA.	12. One lost to follow up after being followed for 3 years post-operatively.	Patient characteristics: 5 boys and 7 girls; age range 6-16. Diagnoses: thoracolumbar or lumbar level myelomeningocele (n=8) and sacral lesions or sacral agenesis (n=4). Indication sfor operation were undiversion (n=5), improvement of continence (n=6), correction of reflux (n=2), recurrent UTI (n=2) and deterioration of renal function (n=1).	Bladder reconstruction was performed with ileocecocystoplasty (n=4), cecocystoplasty (n=3), ileocystoplasty or ileal cup patch cystoplasty (n=4) or sigmoid patch cystoplasty (n=1). Additional procedures done concurrently included: vesicopexy/urethropexy (n=3),	Compared to pre-treatment	6 – 66 months	Existence of incontinence Adverse events Use of intermittent catheterisation urodynamics	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
				transureteroureterostomy (n=2), ureterneocystostomy (n=1), resection of diverticulum (n=1), takedown of reservoir/conduit (n=4), implantation of artificial urinary sphincter (n=20 and takedown cutaneous ureterostomies (n=1)				

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Adverse events arising from enterocystoplasty procedure itself		0/12
Incontinence	6/12	2/12 (1 needs pads and oxybutynin and 1 not “satisfactory”)
Use of intermittent catheterisation	Not fully reported	
Urodynamics Functional bladder capacity (FBC) Compliance, cm3/cm H20	Bladder volume increased from 55% to >1000% over baseline, and compliance also markedly improved. No other data provided.	

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Mitsui T, Tanaka H, Moriya K, Matsuda M,	Retrospective observational study, with	22 (15 for incontinence and quality of	Inclusion: Patients undergoing augmentation cystoplasty at a Japanese hospital between 1991	Augmentation ileocystoplasty performed alone or in	Compared to pre-treatment	Median 5.2 years	Existence of incontinence	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Nonomura K. Outcomes of lower urinary and bowel function in meningomyelocele patients with augmentation enterocystoplasty. Spinal Cord 2008; 46: 432-437	the incontinence and quality of life questionnaire mailed after a recent follow up (n=15). Japan	life questionnaire).	and 2005. Minimum of 1 year since augmentation. Exclusion: None Patient characteristics: 11male, 11 female. Mean age 14.4 years. Myelomeningocele.	conjunction with continence or antireflux techniques. Three methods were used: Hautmann (n=18), Goodwin (3) and hemi-Kock (1). Two patients had a concomitant antireflux procedure with construction of a hemi-Kock afferent nipple valve with uteroileal reimplantation. Urethral fascial sling (n=10) and Malone's appendicocecostomy procedure (n=4) were also used.		(range 1.1 – 17.5 years)	Adverse events Quality of life Urodynamics	
Results: No statistical analysis performed								

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
			Pre-treatment	Post-treatment				
Adverse effects Bowel obstruction Febrile UTI Bladder stone Metabolic derangement Bladder perforation Bowel urgency (a lot/extremely) Bowel frequency (a lot/extremely) Watery faeces (a lot/extremely) Faecal incontinence (a lot/extremely)			17/22	2/22 0/22 1/22 0/22 0/22 8/15 7/15 6/15 9/15				
Incontinence 1 episode per week 2-3 episodes per week Several episodes per day Small amount Moderate amount High negative impact on quality of life (“a great deal”)			20/22	3/15 1/15 1/15 1/15 2/15 1/15 1/15				
Quality of life – satisfaction with the surgery				14/15				
Bladder capacity			186 (21)	380 (25)				

1

2

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kass EJ, Koff SA. Bladder augmentation in the paediatric neuropathic bladder. The journal of Urology 1983; 129: 552-555			Inclusion: Neurogenic bladder dysfunction. Exclusion: none Patient characteristics: 9 girls (4-17 years) and 5 boys (8-16 years). All had recurrent febrile UTIs and high grade vesicoureteral reflux. 12 had undergone urinary diversion 3-14 years previously, and 2 had bilateral vesicoureteral reflux but yet to undergo urinary diversion. Bladder capacity 15-75 ml. Stable renal function. All had received conservative treatment with no effect (anticholinergics and hydraulic bladder distension).	The 2 without prior urinary diversion had a colonic augmentation (6 months after initial antireflux surgery). Those with previous urinary diversion surgery had the colonic or intestinal conduits opened along the antimesenteric border and anastomoased to the bladder.	Compared to pre-treatment	Mean 2.6 years (range 1-5)	Existence of incontinence Adverse events	Not stated

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	Not clear	0/14 (provided self catheterisation performed every 4 hours)
Adverse events		
Mild metabolic acidosis		2/14
Mechanical small bowel obstruction		1/14
Renal failure and severe metabolic acidosis		1/14

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lopez Pereira P, Moreno Valle JA, Espinosa L, Alonso Dorrego JM, Martinez Urrutia MJ, Lobato Romera R, Jaureguizar Monereo E. Are urodynamic studies really needed during bladder augmentation follow up? Journal of Pediatric Urology 2009; 5: 30-33.	Retrospective observational study.	32	Inclusion: Neuropathic bladder with at least 10 years of follow up after bladder augmentation. Exclusion: Patient characteristics: 20 female, 12 male, mean age 11 (range 2.5 – 18) years at augmentation. Underlying aetiology was myelomeningocele (n=30), sacral agenesis (1) and sacrococcygeal teratoma (1). 17 had vesicoureteral reflux. All but one had normal renal function. Mean (sd) bladder capacity was 106 (52) ml, with a detrusor pressure of 50 (32) cm H20.	Bladder augmentation used the Bramble technique (as popularised by Mundy and Stephenson). No antireflux procedures were additionally carried out. 22 carried out with ileum, 7 with sigmoid and 3 with ureter.	Compared to pre-treatment	12 years (range 10-14.5).	Existence of incontinence Need to have intermittent catheterisation Adverse events Urodynamics	Not stated

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Adverse events		
Bladder stones requiring surgery		3/32
Symptomatic UTI (noncompliant with self catheterisation)		1/32
Intestinal obstruction		1/32
Mild metabolic acidosis		2/32
Incontinence	Not clear	0/32

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Need for catheterisation					Not clear		29/32	
Urodynamics Bladder capacity at end Bladder capacity at 1 yr Detrusor pressure at end Detrusor pressure at 1 yr					 106 (52) 106 (52) 50 (32) 50 (32)		 507.8 (165) p<0.002 396 (125) p<0.0001 10 (4) unclear 7 (4) p<0.0001	

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lopez Pereira P, Moreno Valle JA, Espinosa L, Alonso Dorrego JM, Burgos Lucena L, Martinez Urrutia MJ, Lobato Romera R, Luz Picazo M, Viguer JM, Jaureguizar Monereo E. Enterocystoplasty in children with neuropathic bladders: long term follow up. Journal of Pediatric Urology 2008; 4:27-31	Retrospective observational study.	29	Inclusion: Patients who had undergone enterocystoplasty before or at puberty and with a minimum follow-up of 8 years. Exclusion: Patient characteristics: 18 females, 11 males. Mean age 11.8 (range 3-18) years. Underlying aetiology was myelomenigocele (27), sacral agenesis (1), sacrococcygeal teratoma (1). 21 had an abnormal upper urinary tract and 21 had vesicoureteral reflux and/or ureterohydronephrosis. All had had a course of anticholinergics and intermittent catheterisation without effect since a mean age of 4.4 years (range 8 months to 9 years). Mean bladder capacity was 89.8 ml.	Bladder augmentation used the Bramble technique (as popularised by Mundy and Stephenson). No antireflux procedures were additionally carried out. 22 carried out with ileum, and 7 with sigmoid.	Compared to pre-treatment	11 years (8-14.5).	Existence of incontinence Need to have intermittent catheterisation Adverse events urodynamics	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Adverse effects		
Bladder stones requiring surgical intervention		3/29
Symptomatic UTI because of non compliance with intermittent catheterisation		1/29
Intestinal obstruction		1/29
Problems with catheterisation through the urethra		
Mild metabolic acidosis		1/29
Increased serum cystatin C levels		1/29
Significant proteinuria		2/29
Increased urinary calcium excretion		20/25
Hypocitraturia		27/29
Reduced serum rennin and aldosterone concentrations		17/24
malignancy		14/17
Urodynamics		0/29
Bladder capacity		
Detrusor pressure	89.8 (range 58-252) 44.8 (22-150)	521 (300-1000) 10 (5-15)
Incontinence	Not clear	0/29
Need for clean intermittent self catheterisation	Not clear	26/29 `
Urodynamics		
Bladder capacity	89.8 (range 58-252)	521 (300-1000)
Detrusor pressure	44.8 (22-150)	10 (5-15)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Pereira PL, Martinez Urrutia MJ, Romera RL, Jaureguizar E. Should we treat vesicoureteral reflux in patients who simultaneously undergo bladder augmentation for neuropathic bladder? The Journal of Urology 2001; 165: 2259-2261.	Prospective observational study. Spain.	16	8 boys and 8 girls. Underlying pathology was myelomeningocele. All had high pressure, noncompliant bladder. All had not responded to CIC and anticholinergic therapy. All had vesicoureteral reflux on cystogram.	Augmentation carried out with detubularised section of sigmoid colon (n=3) or ileum (n=11) was used in 14 patients, and teh distal part of the ureter was used in the other two combined with transureterouresterostomy. All patients continued with CIC and anticholinergics during the 6 months to 1 yr post-op.	Pre-op.	5.2 years (range 2.8-7.5).	Urodynamics Adverse effects	Not stated

Results: No statistical analysis performed

	Pre-op	Post op
Bladder capacity	83 (range 50-110)	429 (range 260 – 550)
Adverse effects Hydronephrosis UTI		 0/16 1/16

2

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Beseghi U, Casolari E, Del Rossi C, Ghinelli C. Enterocystoplasty with a sigmoid patch in children with neurogenic bladder dysfunction. Paediatric Surgery 1994; 9: 82-85	Retrospective observational. Italy.	15	Inclusion: Patients with neurogenic bladder dysfunction having bladder augmentation with a sigmoid patch. Exclusion: Patient characteristics: Age 3-18 years. 8 had a ventriculoperitoneal shunt. 3 had had previous urinary diversions. All had normal renal function. Background etiology was meningocele (n=13) and sacral agenesis (n=2). All had had 1-2 years of intermittent catheterisation and oxybutynin with little effect. Bladder capacity of 126 ml.	Augmentation cystoplasty performed with a sigmoid section 15-20 cm long, which was anastomosed to the bladder. Concurrent procedures were transureteroureterostomies, urethral taperings, ureteral reimplantations, bladder neck reconstructions, and continent diversions.	Compared to pre-treatment	1-4 years	Existence of incontinence Adverse events urodynamics	Not stated

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Adverse events Leakage of a transureteroureterostomy Stenosis of reimplanted ureter Spontaneous bladder rupture		 1/15 1/15 0/15
Incontinence	Not clear, but “urinary incontinence improved in all patients”.	3/15
Bladder capacity	126	372

1

2

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Marte A, Di Meglio D, Cotrufo AM, Di Iorio G, De Pasquale M, Vessella A. A long term follow- up of autoaugmentation in myelodysplastic children. BJU International 2002; 89: 928-931.	Retrospective observational case series	11	Mean age 12.8 years. 8 boys and 3 girls. Neuropathic bladder secondary to myelomeningocele.	Autoaugmentation involves the excision of th anterior, lateral and superior surfaces of the detrusor muscle, to allow the inner mucosa to form a diverticulum. None had VUR at surgery, as 5 with grade II or IV VUR had undergone endoscopic correction in a day surgery procedure using a suburethral collagen injection 1-3 weeks previously.	Pre-operative	Mean 6.6 years	Urodynamics Adverse events	Not stated
Results: No statistical analysis performed								

	pre	Post (1 year)
Bladder capacity (leak point volume)	94	297

3

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Stothers L,	Retros	12	All had low capacity, hypertonic, poorly compliant	Autoaugmentation involves	Pre-			Not

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Johnson H, Arnold W, Coleman G, Tearle H. Bladder autoaugmentation by vesicomyotomy in the pediatric neurogenic bladder. Urology 1994; 44: 110-113	pectiv e oserva tional case series		bladders. Age range of 4-14 years. 8 myelomeningocele, 2 SCI, 1 posterior erethral valves and 1 unknown.	the cutting of the detrusor muscle, to allow the inner mucosa to form a diverticulum.	operativ e		Adverse events urodynamics	stated

Results: No statistical analysis performed

	pre	post
Adverse effects Post operative fever Mucosal tears		 1/12 2/12
Bladder capacity		“mean increase in capacity of 40%”.[no numeric data provided]

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
MacNeily AE, Afshar K, Coleman	Retrospective oservational	17	9 boys and 8 girls with neurogenic bladder secondary to spinal	Autoaugmentation involved the excision of	Pre-operative	75 months	Urodynamics	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
GU, John son HW. Autoaugmentation by detrusor myotomy: its lack of effectiveness in the management of congenital neuropathic bladder. The Journal of Urology 2003; 170: 1643-1646.	case series		dysraphism. Median age 10.2 (range 2.2 to 13.2). All had upper tract deterioration and/or incontinence secondary to hyper-reflexic small capacity hypocompliant bladders. All had failed to respond to anticholinergics and CIC.	part of the detrusor muscle, to allow the inner mucosa to form a diverticulum.		(range 4-126)	Adverse events incontinence	

Results: No statistical analysis performed

	pre	post
Bladder capacity Detrusor pressure	198ml (range 55-575) 51 (range 24-100)	291ml (range 102-500) 54.4 (25-100)
Adverse events Progressive pyelonephritis		 5/17
incontinence	13/17	8/17

1 # Adults (aged ≥19)

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
DeLong J, Tighiourt H, Stoffel J. Urinary diversion/reconstruction for cases of catheter	Retrospective chart review study	In the study there were 26 patients, but only 7	Secondary progressive multiple sclerosis patients with refractory	An enterocystoplasty was carried out. Stoma applied in	Pre-post comparison	3 weeks, 3 months and every 6 months postoperatively.	Adverse events symptomatic	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
intolerant secondary progressive multiple sclerosis with refractory urinary symptoms. The Journal of Urology 2011; 185: 2201-2206		underwent augmentation cystoplasty. The other 19 underwent an ileal loop procedure. (n=4) or ileovesicostomy (n=15) which are not described further here.	urinary symptoms. EDSS score >4. Indications for surgery included refractory urinary incontinence, chronic symptomatic UTIs and/or catheter related complications. All had tried multiple pharmacological and conservative treatments. All had tried catheterisation prior to surgery but were not candidates for continued clean IC or indwelling catheterisation because of refractory symptoms, unfavourable physiology/anatomy and patient unwilling ness to continue with this modality. All patients (including those not having the ileal loop diversion) had: symptoms for 24 (10) yrs and mean EDSS of 7. But there is no baseline data appropriate to the cystoplasty patients.	6/7. No details given in the paper.		Mean follow up 16 months.	UTIs Incontinence	

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Results:

	pre op	post op
Incontinence	4/7	0/7
Symptomatic UTIs requiring antibiotics (3 or more in a 6 month period)	4/7	3/7
Adverse events mortality Other adverse events reported but not specific to those undergoing cystoplasty		1/7

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Nomura S, Ishido T, Tanaka K, Komiya A. Augmentation ileocystoplasty in patients with neurogenic bladder due to spinal cord injury or spina bifida. Spinal cord 2002; 40: 30-33	Retrospective observational study. No comparison group Japan.	21	Inclusion: neurogenic bladder due to SCI or spina bifida. Exclusion: none Patient characteristics: 11 patients with SCI (10 males; mean age 29 (9.6); mean period from injury to Rx 73.5 (87.6) months), and 10 patients with spina bifida (3 males; mean age 16 (3.9)). Mean vesical pressure of SCI patients was 150.9 (47.4) ml and of spina bifida patients was 148.5 (52) ml. Previous micturitional management was clean intermittent catheterisation for 11 and Crede's manoeuvre for 10.	Augmentation ileocystopathy was performed according to Bramble's method. Bladder opened transversely in the coronal plane like a clam. Incision made laterally between the main branches of the inferior vesical vessels anterior to the trigone and ureteric orifice to a point approximately 2 cm from the internal urethral meatus. A 20cm length of ileum was	Compared to pre-treatment	SCI patient: Mean 66 (43) months (range 8-135 months). Spina bifida patient: 51.8 (32.4) months (range 12.4 –	Existence of incontinence Need for catheterisation Adverse events urodynamics	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
				isolated with its own blood supply, and sutured in to the bladder.		111 months)		

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Urinary incontinence	21/21	1/21
Need for catheterisation	11/21	21/21
Adverse events (all were SCI patients)		
Paralytic ileus		4/21
Contralateral occurrence of vesicourethral reflux		3/21
Recurrence of operated side vesicourethral reflux		1/21
Wound infection		1/21
Liver dysfunction		1/21
Urethral stricture		1/21
Bladder capacity	148.5 (52)	315 (36)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sidi AA, Becher EF, Reddy PK, Dykstra DD. Augmentation enterocystoplasty for the management of	Prospective observational study No comparison group.	12	Inclusion: High pressure neurogenic bladder caused by detrusor-sphincter dysynergia or poor bladder compliance. Exclusion: none	Bladder was bivalved in the sagittal plane, and detubularised section of the sigmoid colon was sutured to the bladder. 3 patients also had an artificial urinary	Compared to pre-treatment	15 months (4-34 months)	Existence of incontinence at 4 months post-op Adverse events	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
voiding dysfunction in spinal cord injury patients. The Journal of Urology 1990; 143: 83-85	USA		Patient characteristics: 11 female, 1 male; SCI injured patients (C5 to L2) aged 33.5 years (range 22-53 years); bladder capacity was 134 (range 70-220) ml. All had recurrent UTIs.pre-operatively managed by anticholinergics and intermittent catheterisation (for 7 patients), indwelling catheter (3 patients) and urinary diversions (2 patients).	sphincter implanted as well.			urodynamics	

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	10/12	3/12 at 4 months post-op (Only 1/12 were incontinent, but 2/12 were incontinent until artificial sphincter implantation)
Adverse effects Symptomatic UTIs Autonomic dysreflexia	12/12	 4/12 0/12
Bladder capacity	134 (range 70-220)	562 (300-900)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Herschorn S and Hewitt RJ. Patient perspective of long-term outcome of augmentation	Retrospective observational study No comparison	59	Inclusion: Neurogenic bladder Exclusion: None Patient characteristics: 37 women and 22 men; mean age 30.56	For augmentation cystoplasty, bladder clammed in the midline and bowel segment used was selected by surgical reasons specific to the patient. Ileum used in	Compared to pre-treatment	Mean 73 (range 2 – 175) months after surgery.	Existence of incontinence Need to have intermittent catheterisation	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
cystoplasty for neurogenic bladder. Urology 1998; 52: 672-678.	group. Canada		(range 19-56) years; pre-operative bladder capacity was 220 (920-550) ml. Diagnosis of spina bifida (49%), SCI (31%), sacral dysgenesis (5%), MS (5%), Muscular dystrophy (3%), Spinal cord tumour (3%),Friedrich's ataxia (2%), Cerebral palsy (2%).	49, sigmoid in 8, transverse colon in 1 and ileocecum in 1. There were also 46 associated continence procedures carried out, including ureteral continuity, bladder neck tapering, hemi-kock continence stoma, and hemi-kock with urethral continence procedure.			Adverse events Patient satisfaction urodynamics	

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Existence of incontinence Mild incontinence Moderate-severe incontinence	42/59 (unclear, as there is the implication that the 15 with a prior diversion did not have incontinence prior to surgery)	20/59 17/59 3/59
Need to have intermittent catheterisation	59/59	56/59
Adverse events Bowel dysfunction	7/59	24/59 11/59
Patient satisfaction		41/59 – delighted; 12/59 – pleased; 6/59 – mostly satisfied. Mean response was 0.42 (range 0-2, with 0 the best). All but one would go through the surgery again.
Bladder capacity Detrusor pressure	220 (range 20-550) 48.9 (20-113)	531.2 (350-1000) 15.8 (10-50)

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2

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Zachoval R, Pitha J, Medova E, Heracek J, Lukes M, Zalesky M, Urban M. Augmentation cystoplasty in patients with multiple sclerosis. Irologia Internationalis 2003; 70: 21-26	Propsective observational study. Czech Republic.	9	Inclusion: The presence of a detrusor hyper-reflexia; stablised MS with favourable prognosis. Exclusion: None Patient characteristics: 7 females and 2 males. Mean age 39.1 (range 23-57). All with MS. Mean Expanded Disability Status Scale score was 4.4 (range 3-6.5). 7 with relapse remitting and 2 with secondary-progressive form. Mean duration of MS was 6.8 (range 3 months – 17) years. Duration of micturition symptoms was 3.4 years (range 1-8 years). Mean maximum bladder capacity was 105 ml, with a maximal detrusor pressure of 53 cm H20.	Augmentation ileocystoplasty performed using Goodwin technique. Patch of detubularised ileum used. Hospitalization for 7 days.	Compared to pre-treatment	11 months (range 6-19)	Existence of incontinence Quality of life Adverse events urodynamics	Not stated

Results: No statistical analysis performed and no variances given.

	Pre-treatment	Post-treatment
Quality of life (0=excellent, 6=unbearable)	5.0	0.7
Incontinence		0/9
Incontinence scores (scored from 0-5, with 0=no problems and 5=great problems)		
Pollakisuria	4.8	1
Nycturia	3.9	0.7

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Urgency			4.0	0.6				
Urge incontinence (pads/day)			2.3	0				
Need for abdominal straining			2.3	3.9				
Adverse events								
Metabolic acidosis				0/9				
Mild hyperchloremia				1/9				
Intermittent community UTI			5/9	3/9				
Intermittent nosocomial infection			1/9	3/9				
Abscessing orciepididymitis				1/9				
Recurrent cystitis				1/9				
Need for clean intermittent catheterisation			2/9	6/9				
Bladder capacity			105	797				
Detrusor pressure			53	30				

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chen JL, Kuo HC. Long term outcomes of augmentation enterocystoplasty with an ileal segment in patients with spinal cord injury. J Formos med	Retrospective observational study. Taiwan	40	Inclusion: 40 consecutive adults with SCI and recurrent UTI, urinary incompetence or upper urinary tract dysfunction. Exclusion: none Patient characteristics: 4 women and 36 men. Mean (range) age: 36.3 (20-56). SCI level was suprasacral in 33 and	Augmentation performed using a terminal ileal segment in a modified Hautmann's procedure. Ureteral reimplantation carried out concurrently if there was any vesicoureteral reflux.	Compared to pre-treatment	7.8 years (range 1-14 years)	Existence of incontinence Need to have intermittent catheterisation Adverse events	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Assoc 2009; 108: 475-480			sacral in 7. All treated with medications and self catheterisation but without effect. Bladder capacity <150ml.					

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	38/40	4/40 (unclear)
Adverse events Wound infection Bladder stone UTI (required admission) Reservoir calculi Diarrhoea Malabsorbtion Recurrent epididymitis (due to catheterisation)		 1/40 13/40 26/40 13/40 3/40 0/40 2/40
Need for intermittent catheterisation Need for long term indwelling catheter	40/40 (but unclear)	31/40 5/40
Bladder capacity	115 (16.3)	513 (31.4)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sutton MA, Hinson JL, Nickell KG,	Retrospective observational study.	19. The total study size was 23, but 4 of these	Inclusion:	Augmentation performed using detubularised right	Compared to pre-treatment	Mean 29.8 months	Existence of incontinence	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Boone TB. Continent ileocecal augmentation cystoplasty. Spinal Cord 1998; 36: 246-251	USA.	did not have problems with a low capacity bladder and so not considered in this summary. All data provided in this table only relate to the 19.	Exclusion: Patient characteristics: 7 females and 12 males; mean age (range): 41.8 (27-64); aetiology – 12 SCI, 4 MS, non neurogenic 3. Bladder capacity was 179.2 ml.	colon. In addition a stoma was created to promote easy catheterisation, sparing the urethra. Other concurrent surgeries included a pubovaginal sling (n=2), urethral closure (6), right nephrectomy (1) and a collagen injection (1).		(range 3-67 months).	urodynamics	

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	Not clear	1/18
Bladder capacity	179.2	495.1

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chancellor MB, Erhard MJ, Strup S, Tammela TLJ. Bladder augmentation using the stomach in spinal cord injured	Prospective observational study. USA.	2	Adult SCI patients with small capacity poorly compliant neurogenic bladders, impaired renal function, VUR and recurrent UTIs.	Stomach segment excised with gastroepiploic artery in situ, and apex of the stomach segment was rotated 180 degrees to lay facing the bladder neck before suturing.		12-18 months	Bladder capacity	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
patients with impaired renal function.								

Results: No statistical analysis performed

	pre	post
Bladder capacity	97.5 (range 75-120)	540 (range 500-580)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Stohrer M, Kramer G, Goepel M, Lochner-Ernst D, Kruse D, Rubben H. Bladder autoaugmentation in adult patients with neurogenic voiding dysfunction. Spinal Cord 1997; 35: 456-462.	Retrospective oservational case series	36	Adults with neurogenic voiding dysfunction. Mostly SCI but other diagnoses as well, as well as interstitial cystitis.	Autoaugmentation involves the excision of part of the detrusor muscle, to allow the inner mucosa to form a diverticulum.	Pre-operative	Up to 80 months	Urodynamics Adverse events	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Results: No statistical analysis performed

	pre	post
Bladder capacity	121ml	406ml
Detrusor pressure	86.4	50.9
Adverse events		
Mucosal perforation		23/36
Failures		5/36
Mucosal fibrosis		0/36

1 # Mixed age groups

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lockhart JL, Bejany D, Politano VA. Augmentation cystoplasty in the management of neurogenic bladder disease and urinary incontinence. The Journal of Urology 1986; 135: 969-971	Prospective observational study USA No comparison group	15	Inclusion: Urinary incontinence secondary to neurogenic bladder disease, presenting with small capacity bladder, and having failed previous therapy with drugs and intermittent catheterisation (IC). Exclusion: none Patient characteristics: Age range 4-48 years (only one adult, who was female). 6 female and 9 male subjects. All had been followed conservatively (drugs such as propantheline, bromide, oxybutynin and	Augmentation cystoplasty was performed with ileum in 9 patients, cecum in 3 and sigmoid in 3. Other surgical procedures were applied concurrently: 7 patients had antirefleux uretosigmoid reimplantation, 7 had uretovesical reimplantation, 5 had a psoas hitch, 2 had urethral lengthening, 2 had direct uretoileal reimplantation with ileococcal valve nipple, and 1 had	Compared to pre-treatment	Not stated	Existence of incontinence Need to have intermittent catheterisation Adverse events urodynamics	Not stated

			imipramine, and intermittent catheterisation) for many years, and such treatment had failed. All patients had also failed a programme of clean intermittent self-catheterisation. All had a low bladder capacity of <150ml. Main etiology was myelomeningocele (10 patients). Others included cord lipoma, Riley-Day syndrome, MS and SCI.	periurethral polytetraflouroethylene injection.				

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	15/15	2/15
Need to have intermittent catheterisation	15/15	14/15
Adverse event Persistent mucus secretion Recurrent UTIs Reflux or obstruction at ureterosigmoid, ureteroileal or ureterovesical reimplantation Reflux at ileocecal valve		 1/15 2/15 0/15 1/15
Bladder capacity Detrusor pressure	<150 >40 for 86%	480 18

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Quek M, Ginsberg DA. Long term urodynamics	Retrospective observational study	26	Inclusion: Diagnosis of neurogenic bladder dysfunction due to traumatic spinal cord injury (18), myelomeningocele (6) or transverse myelitis (2).	Augmentation cystoplasty was performed using "clam-shell" ileocystoplasty in 23 cases and the "star"	Compared to pre-treatment	Mean follow up of 8 years	Existence of incontinence Need to have	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
follow up of bladder augmentation for neurogenic bladder. The Journal of Urology 2003; 169: 195-198	USA No comparison group		Exclusion: None Patient characteristics: 29 years (range 11-53); 18 male and 8 female; All had failed prior drug therapy (mostly oxybutynin). Main methods of pre-operative bladder management were clean intermittent catheterisation (13 cases), reflex voiding (60, and indwelling urethral catheterisation (4). Bladder capacity was 201 (106) ml.	modified method in one case. Two others received an unspecified method of augmentation. Concomitant procedures included an antireflux procedure with construction of a hemi-Kock afferent nipple valve with unilateral or bilateral ureterileal reimplantation. Other concomitant procedures included bladder neck closure, urethral sling, hemi-hock continent cutaneous efferent nipple valve and a Mitrafanoff appendicovesicostomy.		(range 4-13).	intermittent catheterisation Adverse events Patient perceptions urodynamics	

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence Leak continuously Leak 1 x per week Leak 1 x per month	26/26 (not clear)	8/26 1/26 4/26 3/26
Need to have clean intermittent catheterisation	13/26 (unclear)	26/26

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Adverse event Significant changes in bowel function Problems with symptomatic urinary infections Autonimic dysreflexia Periodic episodes of sweating Cancer Perforation of augmented bladder Metabolic disturbances				17/26 3/26	3/26 2/26 1/26 1/26 0/26 0/26 0/26			
Patient perceptions					"Nearly all patients expressed extreme satisfaction" and all but one would recommend the procedure to a friend. Mean satisfaction score out of 10 was 8.7			
Bladder capacity Detrusor pressure				201 (106) 81 (43)	615 (204) 20 (12)			

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Nasrallah PF, Aliabadi HA. Bladder augmentation in patients with neurogenic bladder and vesicoureteral reflux. The Journal of Urology 1991;	Prospective observational study No comparison group. USA	14	Inclusion: High pressure noncompliant neurogenic bladder. Exclusion: none Patient characteristics:5 male and 9 female. Age from 3-20 years.All had varying degrees of vesicoureteral reflux (grade II in 5, grade III in 6, grade IV in 8 and grade V in 1). Myelodysplasia was underlying cause for all except one (SCI).	Augmentation performed with detubularised section of sigmoid colon.	Compared to pre-treatment	Mean 28 months (range 3 – 72 months).	Existence of incontinence Need to have intermittent catheterisation Adverse events urodynamics	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
146: 563-566			Pre-operative treatment included anticholinergics and intermittent catheterisation. Despite this 9 remained incontinent, 2 were incontinent with progressive hydronephrosis and 3 had upper tract dilatation and infection. Bladder capacity was 40-210 ml at a pressure of 30 cm water.					

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	11/14	2/14 (all dry by day)
Intermittent self-catheterisation	14/14	14/14
Adverse effects Hydronephrosis pyelonephrosis		0/14 0/14 0/14
Bladder capacity	40-210	Improved by average of 286ml

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Simforoosh N, Tabibi A, Basiri A, noorbala MH, Danesh AD, Ijadi A. Is ureteral	Prospective observational study No	130	Inclusion: High pressure, non-compliant neurogenic bladder and vesicoureteral reflux. Exclusion: none	Augmentation cystoplasty using detubularised section of bowel (ileum 82 cases, ileocecal segment 23, sigmoid 20, stomach 5).	Compared to pre-treatment	21-108 months (mean 44.5)	Existence of incontinence Adverse effects	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
reimplantation necessary during augmentation cytoplasty in patients with neurogenic bladder and vesicoureteral reflux? The journal of Urology 2002; 168: 1439-1441	comparison group. Iran		Patient characteristics: mean age 21.6 years (range 1.5 to 57). 112 male, 18 female. SCI – 102 patients; neuro-spinal dysraphism – 26; transverse myelitis – 1; posterior urethral valve – 1. Vesicoureteral reflux present in all patients: grade 1 3% of all 197 refluxing units, grade II 9%, grade III 20%, grade IV 61% and grade V 7%. Hydronephrosis observed in 173 renal units. Pre-operatively, all patients treated with meds and clean intermittent catheterisation for at least 6/12, with poor response.	No efforts made to correct existing reflux				

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	86/130	9/130
Adverse effects Clinical pyelonephritis Pouch perforation Bowel obstruction		 8/130 2/130 1/130

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Radomski SB, Herschorn S, Stone AR. Urodynamic comparison of ileum versus sigmoid in augmentation cystoplasty for neurogenic bladder dysfunction.Neurology and Urodynamics 1995; 14: 231-237	Prospective observational study No comparison group. Canada	26	Inclusion: Patients with neurogenic bladder dysfunction. Exclusion: None Patient characteristics:11 females, 15 males. Age range: 8-43yrs. 19 with spina bifida, 3 SCIs, 2 spinal cord tumours, 1 cauda equina tumour, 1 spinal cord abscess.	Bowel segment detubularised, reconfigured into a U shape and implanted into bladder. 14 patients had distal ileum, and 12 patients had sigmoid colon. The choice of bowel was based on surgical reasons.	Compared to pre-treatment	18 months (range 6-50) in ileum group and 37 months (range 6-108) in the sigmoid group	Existence of incontinence	Not stated

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	Not stated	8/26 postoperatively (5 later became continent with anticholinergics)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Linder A, Leach GE, Raz S. Augmentation cystoplasty in the treatment of neurogenic bladder dysfunction.	Retrospective observational study. USA. No comparison	18 (17 patients attended follow up)	Inclusion: Severe urinary incontinence after failed conventional therapy, including meds, intermittent self-catheterisation and hydraulic distension. Exclusion: none	Augmentation was performed with cecocystoplasty (83%) or ileocystoplasty (17%). Associated surgical procures included ureteroneocystostomy, intussusceptions of the ileocecal valve, bladder	Compared to pre-treatment	Mean 38 (range 12-120) months	Existence of incontinence Adverse events Need for intermittent catheterisation	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Journal of Urology 1983; 129: 491- 493	group used.		Patient characteristics:7 female, 11 male; mean age 31 (range 10-68) years. Underlying pathology was spina-bifida-myelomeningocele in 22%, neurogenic bladder secondary to multiple previous pelvic lesuions in 22%, sacral agenesis in 17%, spinal cord trama in 17 %, severe hyperreflexia in 17 percent and cerebral palsy in 5.5%	neck operations, and artificial urinary sphincter cuff insertion.				

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	18/18	3/17
Early post-operative adverse effects Pulmonary atelectasis Late complications Mucous plug retention		 2/17 1/17
Need for intermittent catheterisation	unclear	6/17 (unclear)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sidi AA, Aliabadi H, Gonzalez R. Enteroplasty	Prospective observational study	18 (only 17 followed up – no	Inclusion: Documented neurovesical dysfunction	When one or both ureters were of normal size or only minor dilation (n=12), the procedure involved tubular	Compared to pre-treatment	20.4 months (range 7-42	Existence of incontinence	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
in the management and reconstruction of the pediatric neurogenic bladder. Journal of Pediatric Surgery 1987; 22: 153-157		reasons given for loss to follow up)	Exclusion: none Patient characteristics:9 males, 9 females; age 14.4 (range 5-31) years; aetiology: myelodysplasia – 12, SCI – 2, sacral agenesis – 2; postpelvic surgery – 1, medulloblastoma – 1. 11 patients undertook intervention as part of urinary undiversion, and 7 for Rx of incontinence with or without progressive upper tract deterioration. Cystography under fluoroscopic control showed detrusor sphincter dyssynergia in 5 children, reduced bladder compliance in 7, and absent detrusor contraction with atonic bladders in 6.	sigmoid enterocystoplasty with transuteroureterostomy, and the ureter of smaller diameter was implanted into the bowel tenia in an anti-reflux manner. In 2 children with marked ureter dilation, the ileocecal segment was used with the intussusception of the ileocecal valve to prevent reflux, and the ureters were anastomosed to the ileum. In 4 children who did not require ureteral re-implantation, the cecum or sigmoid colon fashioned into a patch was anastomosed onto the bladder. No bladder resection was undertaken in any patient. In 8 patients a high resistance continence zone was constructed using the Young-Dees technique in the males, with additional suspension to the symphysis pubis or Cooper ligament in the females.		months)	Adverse events Need for intermittent catheterisation	

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	Probably 17/17 (but unclear)	1/17 (the 16 continent patients must have clean self-intermittent catheterisation every 3-4 hours to stay continent).
Adverse events Perioperative death (ARDS) Mechanical bowelobstruction Ureteral obstruction Obstruction of the Young-Dees bladder tube Enterourinary fistula Symptomatic UTI Asymptomatic bacteriuria		 1/17 3/17 1/17 2/17 1/17 2/17 12/17
Need for intermittent catheterisation	unclear	17/17

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Metcalfe PD, Cain MP, Kaefer M, Gilley DA, Meldrum KK, Misseri R, King SJ, Casale AJ,Rink RC. What is	Retrospective observational study, using patient records. USA	500. First 500 augmentation patients studied.	Inclusion: First 500 patients undergoing bladder augmentation surgery between 1978 and 2003 at hospital in USA. Exclusion: Patient characteristics: 258 males and	The 500 augmentations had been performed over 25 years by 8 surgeons. 297 performed with ileum, 85 with sigmoid, 8 with ileal-	Compared to pre-treatment	Mean 13.3 years (minimum 2 years).	Adverse events	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
the need for additional bladder surgery after bladder augmentation in childhood? The journal of Urology 2006; 176: 1801-1805			242 females. Mean age 11.8 years. Myelomeningocele most common primary disease (n=272), sacral agenesis (25), other spinal dysraphism (39), SCI (17), SC tumour (6), Non-neuropathic causes occurred in 107.	sigmoid composite, 38 gastric, 7 composite ileal or sigmoid gastric, 46 ceceal or ileocecal, 8 ureter, 3 ureter and ileum, and 8 unknown. 207 also underwent bladder neck surgery at augmentation, and 46 had had prior bladder neck surgery.				

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Adverse effects		
Complications requiring additional surgery		169/500 (mean of 1.5 extra surgeries per 169 patients)
Deaths due to malignancy		4/500
Deaths due to bladder perforation		1/500
Bladder perforation		43/500
Bowel obstruction		16/500
Need for repeat augmentation		47/500
Bladder stones requiring surgery		75/500

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Reyblat P, Chan KG, Josephson DY, Stein JP, Freeman JA, Grossfield GD, Esrig D, Ginsberg DA. Comparison of extraperitoneal and intraperitoneal augmentation enterocystoplasty for neurogenic bladder in spinal cord injury patients. World Journal of Urology 2009; 27:63-68.	Retrospective observational study. USA.	73 (49 with an extraperitoneal technique and 24 with an intraperitoneal approach)	Inclusion: Known diagnosis of neurogenic bladder dysfunction Exclusion: Patient characteristics: 55 male and 18 female; median age 34 (range 17-66); aetiology of bladder neurogenic dysfunction: trauma (n=63), tumour (2), infection (2), MS (2), transverse myelitis (1), spina bifida (3). All had persistent incontinence secondary to uninhibited bladder contractions and/or urodynamic evidence of high detrusor pressures, despite maximal anticholinergic therapy and the use of intermittent catheterisation.	Two different versions of augmentation enterocystoplasty were used. In the extraperitoneal approach, the peritoneum was completely detached from the posterior surface of the bladder, whereas in the intraperitoneal approach peritoneum was not dissected. Otherwise the two approaches were identical, involving the anastomosis of ileum (n=64) or colon (n=9), using the Bramble approach.	Compared to pre-treatment	Mean 2.5 years (range 25 days – 5.6 years)	Adverse events Existence of incontinence	Not stated

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Adverse events		
Overall		28/73
Early		15/73
Late		13/73

Ileus Bowel obstruction Wound infection Wound dehiscence Stomal stenosis stones		12/73 2/73 4/73 1/73 4/73 5/73
Incontinence Mild incontinence Severe incontinence	64/70	15/70 12/70 3/70

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Khastgir J, Hamid R, Arya M, Shah N, Shah PJR. Surgical and patient reported outcomes of 'Clam' augmentation ileocystoplasty in spinal cord injured patients. European Urology 2003; 43: 263-269.	Retrospective observational study. UK.	34. 2 lost to follow up and only the 32 remaining included.	Inclusion: Urodynamically proven detrusor hyper-reflexia with incontinence, and with failure to respond to conservative therapy. Exclusion: None Patient characteristics: 25 males and 7 females. Mean age (range): 36.2 (11-52). All had suprasacral SCI. Normal upper urinary tracts. Bladder capacity 143 (81) ml.	Augmentation followed the Bramble technique using detubularised ileal patch. Concurrent procedures included the Mitrofanoff formation (n=3), colposuspension (1), bilateral ureteric re-implantation (1) and insertion of an artificial urinary sphincter (1).	Compared to pre-treatment	6 (3.6) years (range 2.4 – 9.6).	Existence of incontinence Need to have intermittent catheterisation Adverse events Patient perception urodynamics	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Results: No statistical analysis performed

	Pre-treatment	Post-treatment
Incontinence	32/32 (not clear)	0/32
Adverse events		
Persistent VUR		1/5
New recurrent UTIs		2/32
Initial recurrent catheter blockages		9/32
Bladder stones		2/32
Residual hyper-reflexia		1/32
Delayed bladder rupture		1/32
Bowel obstruction		1/32
Minor bowel dysfunction		6/32
Questionnaire results		
Excellent QoL and overall improvement in the management of the UT		26/27
Need to use pads		2/27
Would recommend to others		27/27
Deterioration in sexual dysfunction		0/27
Reduction in UTIs		5/7
Mean reduction in self catheter use		4-6 per day
Use of catheterisation		
Self catheterisation	21/32	27/32
Suprapubic long term catheter	6/32	5/32
Reflex voiding	5/32	0/32
Bladder capacity	143 (range 62-224)	589 (401-777) <0.01
Detrusor pressure	108 (65-151)	19 (4-34) <0.01

1

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Medel R, Ruarte AC, Herrera M, Castera R, Podesta ML. Urinary continence outcome after augmentation ileocystoplasty as a single surgical procedure in patients with myelodysplasia. The Journal of Urology 2002; 168: 1849-1852	Retrospective observational study.	26	14 girls and 12 boys (age range 5-19 years). No previous vesicostomy drainage, with myelodysplasia and neurogenic bladder refractory to conservative management (anticholinergics and CIC). Indications for augmentation were upper urinary tract deterioration in 7 patients, upper urinary tract deterioration and incontinence in 8 and urinary incontinence only in 11. 11 patients (16 renal units) had VUR.	Detubularised augmentation ileocystoplasty performed as a single procedure. The 11 with VUR had ureteral reimplantation carried out concurrently.	Compared to baseline.	Followed up 1-10 years post-op.	Incontinence CIC Adverse effects	Not stated

Results: No statistical analysis performed

	Pre-operative	Post operative
Incontinence	19/26	4/26
Need for IC	26/26	26/26
Adverse effects Renal insufficiency VUR	 2/26 11/26	 2/26 3/26 (includes 2 new cases)

2

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
McInferney PD, DeSouza N, Thomas PJ, Mundy AR. The role of urodynamic studies in the evaluation of patients with augmentation cystoplasties. British Journal of Urology 1995; 76: 475-478	Retrospective observational study.	100	50 consecutive patients with detrusor instability and 50 consecutive patients with neuropathic bladder dysfunction. Age 15-50 years. Only those with neuropathic bladder dysfunction had reported underlying neurological disease, as follows: Spina bifida 18/50, SCI 10/50, MS 9/50, Transverse Myelitis 4/50, other spastic paraplegia 9/50. Only these 50 are reported below.	Clam ileocystoplasty	Compared to baseline	2 years	Need for CIC Bladder capacity	Not stated

Results:

	Pre-operative	Post operative
Incontinence	100/100	0/100
Need for CIC	6/100	27/100
Bladder capacity Detrusor hyperreflexia (n=50)	 196	 496

2

3

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Arikan N, Ozdiler E, Yaman O, Gogus O. Augmentation duracystoplasty in neurogenic bladder dysfunction. Int J Urol 1995; 2: 172-175.	Retrospective oservational case series	10	Patients with neurogenic bladder dysfunction. 4 females and 6 males with ages 9-51 years. SCI – 7, operated Myelomeningocele – 3. 5 had hyper-reflexic neurogenic bladder and the other 5 had hypocompliant neurogenic bladder. All had detrusor-sphincter dyssynergia and had not responded to previous pharmacological treatment and used indwelling catheters at teh time of surgery. Exclusion: Severely fibrotic and diseased detrusors, and those with high grade VUR.	Augmentation using the modified Bramble-Clam technique (not described).	Pre-operative		Urodynamics	Not stated

Results:

	pre	post
Bladder capacity	88.7 (19.1)	227.2 (83.8) p<0.0001
Detrusor pressure	72.5 (15.9)	35.3 (6.9) p<0.0001

F.10 2 Do behavioural management programmes (timed voiding, voiding on request, bladder retraining, habit retraining,) compared with a) each other b) usual care, improve outcomes?

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Eustice S, Roe B, Paterson J. Prompted voiding for the management of urinary incontinence in adults	Systematic review with meta-analysis.	This included 9 trials, with a total	Average age was 84 years, and women predominated.	Prompted voiding. This is used to encourage people to initiate their	No prompted voiding. These	Interventions lasted from 20 days to 32 weeks, but	Numbers with no improvement of wet episodes	Not stated

(review). Cochrane Database of Systematic reviews 2000, Issue 2, Art No: CD002113. DOI: 10.1002/14651858.CD002113	This was a Cochrane review, with clearly defined search criteria, and criteria for study inclusion.	participant number of 674.	Many were from nursing homes, and some were cognitively impaired and/or not independent in ADLs.	own toileting. It usually involves positive reinforcement. It involves the use of a carer to take the person with incontinence to the toilet, and so involves education of both the person with incontinence and the carer.	patients were not given any placebo treatment or alternative treatment.	only two studies looked at longer term effects after cessation of intervention (12 and 22 weeks).	Proportion of hourly checks that were wet Reduction in the mean proportion of hourly checks Incontinent episodes in 24 hours Self initiated toileting	

Effect size: RR or mean differences given, with respect to the comparison group [referent].

Numbers with no improvement of wet episodes (lower better):RR: 0.7 (0.41-1.19)

Proportion of hourly checks that were wet (lower better): MD: -12 (-18.79, -5.21)

Reduction in the mean proportion of hourly checks (higher better): MD: 17.6 (-14.58, 49.78)

Incontinent episodes in 24 hours (lower better): MD: -0.92 (-1.32, -0.63)

Self initiated toileting (higher better): MD: MD: 1.9 (1.51, 2.29)

Reporting of the outcome of proportion of hourly checks that were wet was not reported adequately to allow meta-analysis in 4 RCTs (Ouslander 2005, Schnelle 1983, Smith 1992, Surdy 1992), as they lacked measures of variance and some used medians. These studies all found that the median or mean number of hourly checks that were wet were numerically greater in the control group, weakly suggesting a beneficial effect of prompted voiding (table 2). No statistical analysis was performed, but it can be seen that the probability of all 4 studies showing this trend by chance alone is only 6.25% (50%4).

Mean or median proportion of hourly checks that were wet

Study	Treatment	Control
Ouslander 2005	25%	50%

Schnelle 1983	15%	25.5%
Smith 1992	21%	85%
Surdy 1992	13.25%	49.95%

Authors' conclusion: The limited evidence suggested that prompted voiding increased self-initiated voiding and decreased incontinent episodes in the short term. There was no evidence about whether these effects are sustained over a long period of prompted voiding, or persist after stopping prompted voiding.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Ostaszkiewicz J, Chestney T, Roe B. Habit retraining for the management of urinary incontinence in adults (review). Cochrane Database of Systematic Reviews 2004, Issue 2. Art. No.: CD002801. DOI: 10.1002/14651858.CD002801.pub2	Systematic review with meta-analysis. This was a Cochrane review, with clearly defined search criteria, and criteria for study inclusion.	378 participants from 4 trials	Mean age was 80 years, and they were all physically and/or mentally impaired. They were mostly in nursing homes and dependent in ADLs.	Habit training + other treatment. Habit retraining involves working out an individual's toileting pattern and then developing a personalised toileting schedule, to prevent involuntary voiding. Other treatments combined with it include: education to staff and caregivers, toileting prompt, electronic monitoring devices, fluid manipulation, environmental modification and support.	Usual care	Only 1 study stated any longer term FU: at 12 weeks. Interventions lasted from 6 weeks to 6 months	Incontinent episodes in 24 hours Voided volume and incontinent volume Prevalence of bacteriuria Prevalence of skin rash Prevalence of skin breakdown Impact on caregivers	Not stated
Effect size: RR or mean differences given, with respect to the comparison group [referent].								

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Incontinent episodes in 24 hours (lower better). Standardised MD: -0.12 (-0.47, 0.23) Voided volume and incontinent volume (lower better): MD: 99 (-17.57, 215.57) Prevalence of bacteriuria (lower better): RR: 1.88 (0.40, 8.85) The following are reported narratively, as the results were not suitable for meta-analysis. Prevalence of skin rash Colling 2003 reported a significant decrease in skin rash prevalence from 17.7% at baseline to 9.4% at the end of the intervention period. No data are provided for the usual care group, other than the information that a non-significant increase occurred. Prevalence of skin breakdown Colling 2003 reported a significant decrease in skin breakdown prevalence from 11.6% at baseline to 2.3% at the end of the intervention period in the intervention group. In the control group two patients had skin breakdown at baseline and none at the end of the study period. The prevalence figures for the intervention group appear to be counts of the episodes of skin breakdown rather than counts of participants having at least one episode, as 11.6% of the group size of 32 and 2.3% of the control group size of 24 yield non-whole numbers (3.7 and 0.6 respectively). Thus they cannot be analysed with a meta-analysis. Impact on caregivers Colling 2003 reported that caregivers found management of incontinence less stressful at the end of the intervention. A greater number of carers felt more prepared to care for their patient's incontinence needs than at baseline. No significant changes were reported. Different comparison It should be noted that one other study (Nikoletti 2004) in one of the Cochrane reviews compared habit retraining plus an electronic device with habit retraining alone, but the results are not presented here, as the comparison does not seem to have the potential to yield any information relevant to the guideline question. Authors' conclusion: The review findings of inadequate evidence to support habit retraining as a specific type of toileting assistance should not be interpreted as evidence of no effect, or lead to its dismissal.								

1

Reference	Study type	No pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
van Houten P, Achterberg W,	RCT. Single blinded. Block	57	Inclusion: Dependent elderly women >65 years with a mild or moderate mobility	Intervention provided by PTs or OTs on an	Usual	Up to 8 weeks	Average weight of pads over 24	Not

Reference	Study type	No pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Ribbe M. Urinary incontinence in disabled elderly women: a randomised clinical trial on the effect of training mobility and toileting skills to achieve independent toileting. Gerontology 2007; 53:205-210	randomisation used (thus predictability of last participant in each block, potentially). Stratified for toilet timing test level – i.e. ability to perform tasks needed to toilet independently. No mention of allocation concealment.		disorder (able to go to the toilet through walking, in a wheelchair independently, or with the aid of one person) who were suffering from chronic urinary incontinence (incontinence episodes 2x per week for at least 3 months). Exclusion: Severe mobility disorders. Dementia. Currently on other treatment for incontinence. Surgery within past 6 months for incontinence. UTI not responding to treatment. <18 on MMSE. Indwelling catheter. Post void residue of >150ml. Heamaturia. The participants were recruited from nursing homes, homes for the elderly and day care centres for non-demented elderly people.	individual basis, and aimed at training mobility and toileting skills. The therapy was focussed on those aspects of toileting that took longer than a threshold time. The tasks were practiced 3x per week for 30 mins, for a minimum of 1 week and a maximum of 8 weeks. Once the participant could achieve all tasks under the threshold time the intervention was allowed to be terminated.	care	(immediately post intervention). No long term follow up	hours Micturitions on toilet compared to total micturitions Change from dependent to independent toileting Change from independent to dependent toileting	stated
Effect size Average weight of pads over 24 hours The intervention group had a trend (p=0.07) for an 8% lower weight of pads over 24 hours compared to the comparison group. No further data were given in the paper. Micturitions on toilet compared to total micturitions The intervention had no significant effect on the number or percentage of micturitions on the toilet. No data were given in the paper. Change from dependent to independent toileting In the intervention group 6 changed from dependent to independent, compared to 2 in the comparison group (p=0.14). The lack of data on the number who were initially dependent in each group makes this data inappropriate for GRADE.								

Reference	Study type	No pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Change from independent to dependent toileting In the intervention group 4 changed from independent to dependent, compared to 3 in the comparison group (p=0.70). The lack of data on the number who were initially independent in each group makes this data inappropriate for GRADE. Authors' conclusion: This study suggests that it is possible to influence long-standing incontinence in dependent elderly women by training mobility and toileting skills.								

F.11 Does pelvic floor muscle training with or without electrical stimulation or biofeedback compared with treatment as usual, improve outcomes?

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lucio AC, Campos RM, Perissinotto MC, Miyaoka R, Damsceno BP, D'Ancona CAL. Pelvic floor muscle training in the treatment of lower urinary tract dysfunction in women with multiple sclerosis. Neurourology and urodynamics	RCT. Brazil. Patients blinded to treatment or sham. No details of randomisation or allocation concealment. Single (patient blind) No drop-outs	N=27	Inclusion: women with MS that had been stable for the previous 4 months; relapsing remitting form of MS; >18 years; EDSS score < 6.5; cognitive capacity to complete assessment and treatment protocol, ability to contract the pelvic floor muscles, and at least 3 of the following urinary tract symptoms: urgency, urge incontinence, daytime frequency, nocturia, and nocturnal enuresis Exclusion: Pregnancy, previous gynaecologic surgery, cearian section or vaginal delivery within 6 months previously to time of enrolment, history of MS relapse during treatment, pelvic organ prolapsed at vaginal examination, UTI and menopause. Baseline characteristics: PFMT / Sham / P value	Pelvic floor muscle training 2x per week 30 minute sessions over 12 weeks, presided over by the same physiotherapist. In each session the patient performed 30 slow pelvic floor muscle contractions and 3 mins of fast contractions in supine with the assistance of a perineometer.	This sham procedure consisted solely of the introduction of the perineometer inside the vagina. They were asked to keep the device in for 30 minutes, with no contractions required. No home exercises were given and the	Post-treatment (12 weeks)	Incontinence symptoms Treatment adherence	Not stated

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
2010; 29: 1410-1413				The patients were also instructed to carry out the same exercises daily at home, but without any assistance from any device, in various positions such as sitting and standing. They were also told to integrate the exercises into their daily life activities N=13	physiotherapist was present. N=14			

age	36 (7.2)	34.7 (8.8)	>0.05
BMI	23.4 (3.1)	23.8 (3.6)	>0.05
Parity	1.3 (1.3)	1.1 (1.2)	>0.05
Duration of urinary disorder (months)	36.5 (37.4)	31.5 (20.8)	>0.05
Duration of MS since onset	9.1 (5.8)	6.8 (3.5)	>0.05
Maximum cystometric capacity	254.9 (92.9)	212.7 (116.4)	>0.05

Results:

	PFMT baseline	PFMT final	Sham baseline	Sham final
Incontinence variables (counts)				
Frequency	13/13	4/13	14/14	14/14
Urgency	13/13	4/13	14/14	13/14
Urge incontinence	12/13	4/13	13/14	13/14
Nocturnal enuresis	8/13	2/13	9/14	10/14
Nocturia	12/13	2/13	12/14	11/14
Incomplete emptying	8/13	3/13	7/14	7/14
Mean (sd) Treatment adherence (sessions attended out of a maximum of 24)		21.5 (1.8)		21.5 (1.8)

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Author's conclusions: PFMT is an effective approach to treat LUTD in females with MS								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
McClurg D, Ashe RG, Lowe-Strong AS. Neuromuscular electrical stimulation and the treatment of lower urinary tract dysfunction in multiple sclerosis--a double blind, placebo controlled, randomised clinical trial. Neurourol Urodyn. 2008; 27(3):231-237. Ref ID: MCCLURG2008	RCT Randomisation: unclear Allocation concealment: unclear (sealed envelope technique) Double blind except for pelvic floor muscle assessment ITT analysis	N=74 N=2 withdrawals	Patients with multiple sclerosis Inclusion criteria: diagnosed with clinically definite or laboratory supported diagnosis of MS with disease stabilised for the previous 3 mths, over 18 yrs old, an EDSS ≤ 7.5 and sufficient dexterity enabling completion of assessment and treatment protocol. Lower urinary tract dysfunction was confirmed after a clinical assessment. Inclusion criteria: presented with at least one of the following: any involuntary leakage of urine, voiding frequency > 8 per 24 hr, nocturia, and/or reported voiding dysfunction such as hesitancy, straining, poor stream and incomplete emptying demonstrated during uroflowmetry with	Pelvic floor muscle exercises Plus electromyography (EMG) feedback Plus neuromuscular electrical stimulation (NMES) One session a week for nine weeks	Pelvic floor muscle exercises Plus electromyography (EMG) feedback Plus placebo One session a week for nine weeks	24 weeks	Bladder diary (leakage episodes, frequency, nocturia) Portable bladder scanner (post-void residual) Incontinence Impact questionnaire, Urogenital Distress Inventory, visual analogue scale	None reported

			measurement of post-void residual. Exclusion criteria: MS relapse necessitating hospitalisation 3 months prior to or during the study. Other exclusions included symptomatic prolapse, previous or current treatment for prostatic hyperplasia and presence of urinary tract infection Patient population: Placebo - 0 leaks 13/37, 1-2 leaks 12/37, ≥ 3 leaks 12/37, females/males 26/11, mean age 52.0 yrs (range 27 to 72 yrs), years since diagnosis mean 11.0, type of MS relapsing remitting 13/37, primary progressive 8/37, secondary progressive 16/37, intermittent self catheterisation routinely used 8/37 NMES - 0 leaks 12/37, 1-2 leaks 12/37, ≥ 3 leaks 13/37, females/males 31/6, mean age 48.3 yrs (range 27 to 72 yrs), years since diagnosis mean 10.2, type of MS relapsing remitting 20/37, primary progressive 5/37, secondary progressive 12/37, intermittent self catheterisation routinely used 7/37 The groups were well matched					

			at baseline					
Effect Leakage episodes per 24 hr At the end of the active treatment period (week 9), there was a significant difference in treatment effect in favour of the neuromuscular electrical stimulation (NMES) group (p=0.028). At weeks 16 and 24 this significant difference was not maintained (p≥0.535) Post-void residual mean (SD) Week 0 vs 9, 16 and 24 Placebo 69 (76) vs 56 (55)*, 53 (36), 49 (32) NMES 74 (56) vs 38 (18)** vs 35 (16)* vs 38 (23)* * significant difference from week 0 (p<0.005) ** significant difference between group (p<0.005) Visual analogue scale Both groups demonstrated a significant improvement throughout the duration of the study (p=0.001). However, the NMES group demonstrated a superior improvement throughout the study which was statistically significant at weeks 9 and 24 (p ≤ 0.013) when compared to the placebo group. Incontinence Impact Questionnaire (IIQ) and Urogenital Distress Inventory (UDI) There was a significant superior benefit in the NMES group in the irritative subscale of the UDI at weeks 16 and 24 (p≥0.132)								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
McClurg D, Ashe RG, Marshall K et al. Comparison of pelvic floor muscle training, electromyography biofeedback, and neuromuscular electrical stimulation	RCT Randomisation: computer generated Allocation concealment: unclear	N=30 (2 drop outs)	Female patients with multiple sclerosis Inclusion criteria: Patients were included if they presented with at least one of the	Pelvic floor training and advice (PFTA) PLUS Electomyography (EMG)	PFTA 9 wks duration N=9 PFTA plus EMG	24 wks		

for bladder dysfunction in people with multiple sclerosis: a randomized pilot study. Neurourol Urodyn. 2006; 25(4):337-348. Ref ID: MCCLURG2006	Drop-outs 2/30 ITT analysis Blinding: unclear		following: an involuntary leakage of urine, voiding frequency >8 per 24 hr, nocturia, and/or voiding dysfunction Exclusion criteria included: MS relapse requiring hospitalisation 3 months prior to or during the study, symptomatic prolapse, severe cognitive impairment Patient population: PFTA: mean age 49.5, yrs since diagnosis 6.0 yrs, relapse remitting MS 6/10, Intermittent self catheterisation routinely used 3/10, anticholinergic therapy 2/10 PFTA+EMG: mean age 52.1, yrs since diagnosis 10.2 yrs, relapse remitting MS 6/10, Intermittent self catheterisation routinely used 1/10, anticholinergic therapy 2/10	PLUS Neuromusclar electrical stimulation (NMES) N=9 9 wks duration	9 wks duration N=10			

			PFTA+EMG+NMES: mean age 49.9, yrs since diagnosis 11.3 yrs, relapse remitting MS 6/10, Intermittent self catheterisation routinely used 2/10, anticholinergic therapy 1/10					

Effect
Leakage episodes per 24 hr
Week 0 vs 9
PFTA reduction 12 % (week 0 vs 9; p=0.687)
PFTA + EMG 45% (p=0.074)
PFTA + EMG + NMES 68% (p=0.002)
Group 1 vs 3 (p=0.014)
Week 0 vs 24
PFTA reduction minimal
PFTA + EMG 58% (p=0.028)
PFTA + EMG + NMES 75% (p=0.003)
Group 1 vs 2 (p=0.007); Group 1 vs 3 (p=0.001)

No. incontinence
Week 0 vs 9 vs 24
PFTA 6/10 vs 9/10 (RR0.67 (95%CI0.39 to 1.15) vs 8/10 (RR0.75 (0.41 to 1.36)
PFTA + EMG 8/10 vs 7/10 (RR1.14 (0.69 to 1.90) vs 5/10 (RR1.60 (0.80 to 3.20)
PFTA + EMG + NMES 9/10 vs 7/10 (RR1.29 (0.82 to 2.03) vs 5/10 (1.80 (0.94 to 3.46)

Nocturia
Nocturia was reduced in all groups by week 9 (p=0.035) maintained, albeit by varying degrees, by week 24

Post-void residual volume ml
Week 0 vs 9 vs 24
PFTA 90 vs 60 vs 80
PFTA + EMG 160 vs 60 vs 60
PFTA + EMG + NMES 84 vs 60 vs 30
No significant between groups

Kings Health Questionnaire (KHQ)
Throughout the duration of the study, results for the KHQ were variable both within and between groups, however significant improvements were demonstrated in the Symptom Severity Scale in the PFTA + EMG and PFTA + EMG + NMES groups at all time points ($p \leq 0.034$)

Incontinence Impact Questionnaire (IIQ) (higher score indicates worse outcomes)
Total score mean (SD)
Week 0 vs 9
PFTA vs PFTA + EMG + NMES (p=0.027)
PFTA vs PFTA + EMG (p=0.036)

Week 0 vs 24
PFTA vs

Multiple sclerosis quality of life (MSQoL-54)
Throughout the duration of the study, results for the MSQoL-54 were variable both within and between groups, however significant improvements were demonstrated in the cognitive function sub-scale at all time points in PFTA + EMG + NMES ($p \leq 0.016$). In addition, statistically significant improvements were also observed in the emotional well-being sub-scale in PFTA + EMG and PFTA + EMG + NMES (week 24; $p \leq 0.027$)

Compliance
Attendance at the weekly clinic sessions averaged 78% in all groups. Home of the EMG unit was 75% recommended. No major effects or problems with usage were indicated.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tibaek S, Gard G, Jensen R. Pelvic floor muscle training is effective in women with urinary incontinence after stroke. A Randomised, Controlled and Blinded Study. Neurourol Urodyn. 2005; 24(4):348-357. Ref ID: TIBAEK2005	RCT Randomisation: mathematical tables Allocation concealment: sealed numbered envelope by physiotherapist without any further relation to the study prior to the inclusion of the subjects States 'Single blind' (but no sham procedure?). No ITT	N=32 N=24 completed treatment	Inclusion criteria: 1) women, diagnosed with first ever ischemic stroke according to the definition and verified by CT scan. Stroke was defined as focal neurological deficits of acute onset, lasting >24 hr, due to brain ischemia as shown by CT scan or of presumed ischemic nature after appropriate clinical and neuroradiological work up 2) stroke symptoms in at least one month 3) normal cognitive function 4) Urinary incontinence according to the definition of ICS with start in close relation to the stroke 5) independent walking abilities	Pelvic floor muscle training Introduction – 1 hr Group treatment – 6-8 patients/group Frequency – 1 hr/week Duration – 12 wks Attendance in group treatment sessions – min 8 times Vaginal palpation – 2/3 times Home exercises ½ times daily	Control group General rehabilitation without any specific treatment of urinary incontinence	4 weeks	Voiding diary (time and frequency of voiding, the no. of incontinence episodes) 24-hr home pad test (pad number and weight)	None reported

			indoors >100 m with/without aids 6) independence in toilet visits 7) age between 40 and 85 yrs Exclusion criteria included: urinary tract infection Patient population: treatment – mean age 59 yrs (range 56 to 72), gynaecological surgery none 58% one or more 42%, urinary incontinence type stress 8% urge 42% mixed 50% , time since stroke 12 mths Control - mean age 62 yrs (range 52 to 75), gynaecological surgery none 42% one or more 58%, urinary incontinence type stress 17% urge 25% mixed 58%, time since stroke 13 mths					
Effect Voiding diary Pelvic floor muscle training (PFMT) Median, quartile range								

	2 days (PFMT: n=11 Control n=10)			3 days (PFMT: n=10 Control n=8)		
Recording period	Pre-test	Post-test	P	Pre-test	Post-test	P
Voiding frequency, daytime/24 hr						
PFMT	7 (6-11)	5 (5-7)	0.021	7 (5-11)	6 (5-7)	0.107
Control	8 (7-10)	6 (5-10)	0.074	8 (6-10)	9 (7-13)	0.753
Voiding frequency, nighttime/ 24 hr						
PFMT	2 (1-3)	1 (1-2)	0.234	1 (1-3)	2 (1-2)	0.733
Control	1 (1-2)	1 (1-3)	0.348	2 (1-2)	2 (1-3)	0.605
No. of incontinence episodes/24 hr						
PFMT	0 (0-2)	0 (0-0)	0.518	0 (0-1)	0 (0-0)	0.680
Control	0 (0-2)	0 (0-1)	0.102	1 (0-3)	0 (0-1)	0.285
No. of pads used/24 hr						
PFMT	0 (0-2)	1 (0-2)	0.176	1 (0-1)	1 (0-1)	0.10
Control	2 (0-5)	1 (0-4)	0.573	1 (1-5)	1 (0-3)	0.674

Pad test

The within subject comparison was not significant for either group

There was a significant difference in favour of the PFMT group for post-test values (p=0.013). PFMT pre vs post test median 8 to 2 g/24-hr control median 12 to 8 g/24-hr.

Treatment adherence (no. of patients who dropped out)

PFMT vs control

2/14 vs 0/12

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tibaek S, Jensen R, Lindskov G et al. Can quality of life be improved by pelvic floor muscle training in women with urinary incontinence after ischemic stroke? A randomised, controlled and blinded study. International Urogynecology Journal. 2004; 15(2):117-123. Ref ID: TIBAEK2004	Details as for Tibaek S, Gard G, Jensen R. Pelvic floor muscle training is effective in women with urinary incontinence after stroke. A Randomised, Controlled and Blinded Study. Neurourol Urodyn. 2005; 24(4):348-357. Ref ID: TIBAEK2005					6 mths	SF-36 (0 worst case 100 best case) Incontinence Impact Questionnaire (IIQ) (0 best case 100 worst case)	The Foundation of Danish Physiotherapists Research, The Foundation of 1870 and Director Jacob Madsen og hustrus Fond
Effect SF-36 There were no significant differences between the treatment group and control group on any of the sub-scales (physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations because of emotional problems, mental health) Total score Treatment group (n=12) vs control group (n=12) follow-up median (quartile range) (0 worst case, 100 best case) 563 (430-682) vs 623 (494-676) (ns) IIQ There were no significant differences between the treatment group and control group on any of the sub-scales (physical activity, travel, social relationships, emotional health) Total score								

Treatment group (n=12) vs control group (n=11) median (quartile range) (0 best case, 100 worst case)
20 (1-50) vs 27 (6-93) (ns)

1

<table>
<tr><th>Reference</th><th>Study type</th><th>No. pts</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr>
<td>Vahtera T, Haaranen M, Viramo-Koskela AL, Ruutiainen J. Pelvic floor rehabilitation is effective in patients with multiple sclerosis. Clinical Rehabilitation 1997; 11: 211-219</td>
<td>RCT. Finland.
Stratification for sex.
No other details of randomisation procedure or allocation concealment.
Open trial. No drop-outs reported</td>
<td>80</td>
<td>Inclusion: MS patients admitted for a 21 day comprehensive rehabilitation period. Stable phase of the disease; EDSS < 6.5; symptoms of lower urinary tract disorder; post void residual volume of <100ml.
Exclusion: pregnancy, cardiac pacemakers or any metallic plates near the treated area, history of pelvic malignancy, dementia or any nervous system disorder other than MS.
Baseline characteristics: NSD observed
<table>
<tr><th></th><th colspan="2">Female</th><th colspan="2">Male</th></tr>
<tr><th></th><th>PFMT</th><th>Con</th><th>PFMT</th><th>Con</th></tr>
<tr><td>Age</td><td>42.2 (8.9)</td><td>45.7 (10.7)</td><td>45.3 (6.3)</td><td>41.8 (11.8)</td></tr>
<tr><td>Time after MS onset</td><td>14.7 (6.6)</td><td>13.4 (10.3)</td><td>11.6 (9.4)</td><td>12.7 (9.7)</td></tr>
<tr><td>Time after urinary symptoms onset</td><td>5.8 (6.1)</td><td>5.6 (4.4)</td><td>5.9 (4.7)</td><td>5.7 (4.7)</td></tr>
<tr><td>EDSS</td><td>4.4 (1.8)</td><td>4.3 (2.1)</td><td>4.4 (1.5)</td><td>4.4 (2.2)</td></tr>
<tr><td>Post void residual volumes</td><td>48 (25.4)</td><td>44 (22.5)</td><td>49 (26.9)</td><td>58.6 (27.9)</td></tr>
</table>
</td>
<td>Pelvic floor muscle training + electrical stimulation Sessions were given for 6 sessions over 2 weeks. This gave awareness of the sensation of the contractions. The ES was treated with a carrier frequency of 2000Hz, and Rx frequencies of 5-10, 10-50 and 50Hz. Each session consisted of 10 mins at each frequency followed by 3 mins rest. All ES given at maximally tolerated level.</td>
<td>Untreated group.
N=40</td>
<td>6 months</td>
<td>Incontinence severity
Subjective handicap
Treatment adherence</td>
<td>Not stated</td>
</tr>
</table>

				In the final session the patients were taught by biofeedback with EMG to exercise, as well as relax, their pelvic floor muscles. Patients were told to perform the exercises for at least 6 months 3-5 times a week. These were to be done in the sitting and standing positions as well as during ADL. N=40				

Results:
Mean (SD)

	PFMT 0 weeks	CON 0 weeks	PFMT 3 weeks	CON 3 weeks	PFMT 2 months	CON 2 months	PFMT 6 months	CON 6 months
Leakage of urine in absence of effort (score 0-2, 0=never, 1=occ, 2=often)	0.35 (0.5)	0.23 (0.4)	0.23 (0.4)	0.33 (0.5)	0.05 (0.2)	0.23 (0.4)	0.05 (0.2)*	0.38 (0.5)
Leakage of urine on minimal effort (score 0-2, 0=never, 1=occ, 2=often)	0.60 (0.7)	0.50 (0.6)	0.23 (0.5)***	0.75 (0.6)	0.15 (0.4)*	0.35 (0.5)	0.08 (0.3)***	0.55 (0.6)

Leakage of urine on heavy effort (score 0-2, 0=never, 1=occ, 2=often)	0.80 (0.6)	0.63 (0.6)	0.43 (0.6)**	0.83 (0.6)	0.20 (0.4)**	0.68 (0.6)	0.23 (0.7)**	0.60 (0.6)
Nocturia (0-none, 1=0-1 times, 2=2-3 times, 3= > 3 times)	1.45 (0.6)	1.40 (0.63)	0.98 (0.6)*	1.35 (0.7)	0.68 (0.7)***	1.35 (0.8)	0.70 (0.7)***	1.43 (0.8)
Regular pelvic floor exercises carried out Irregular adherence Exercises not done					31/40 7/40$ 2/40$$		25/40 12/40 3/40$$$	
Subjective handicap – 5 questions asked about how symptoms influenced: ADL, travelling, social activities, social shame and need for diapers.							"Less handicap than control group (P<0.05) in terms of travelling, social shame and need of diapers"	

* p<0.05, ** p<0.01, ***p<0.001, for diff between groups at each time point

$ - due to improvement in symptoms after ES; $$ - due to emergency admission; $$$ - 1 gave up as symptomless, 1 gave up after hosp discharge at 2 months, and 1 had MS relapse.

Author's conclusions: " The present study indicates that pelvic floor muscle exercises combined with electrical stimulation of the pelvic floor constitute an effective treatment for lower urinary tract dysfunction at least in male patients with MS"

F.12 What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease?

No papers were identified for this question

F.13 What is the safety and efficacy of urethral tape and sling surgery compared with usual care in neurological disease?

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Abdul-Rahman A, Attar KH, Hamid R et al. Long-term outcome of tension-free vaginal tape for treating stress incontinence in women with neuropathic bladders. BJU Int. 2010; 106(6):827-830. Ref ID: ABDULRAHMAN2010	Details as for Hamid R, Khastgir J, Arya M et al. Experience of tension-free vaginal tape for the treatment of stress incontinence in females with neuropathic bladders. Spinal Cord. 2003; 41(2):118-121. Ref ID: HAMID2003					Mean 10 yrs	Continence Health-related quality of life	None reported

Effect

	Pre-surgery	Post-surgery
Continence	0/12 implied – 5 yr follow up 0/9 implied – 10 yr follow up	10/12 7/9
Health-related quality of life 'satisfied'	- -	11/12 5 yrs 9/9 10 yrs

1

2

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Albouy B, Grise P, Sambuis C et al. Pediatric urinary incontinence: evaluation of	Prospective observational study	N=14	Patients with neurogenic bladder resulting from spinal dysraphism Patient population: mean age 14 yrs (range 8 to 22 yrs)	Bladder wall wraparound sling procedure Plus bladder	Pre surgery	Mean 5 yrs (range 2 to 8 yrs)	Continence Urinary tract infections Problems with long term catheterisation	None reported

bladder wall wraparound sling procedure. Journal of Urology. 2007; 177(2):716-719. Ref ID: ALBOUY2007			Incontinent despite anticholinergic therapy and clean intermittent catheterisation 7 females and 7 males	augmentation				

Effect

	Pre-surgery	Post-surgery
Continence	0/14	13/14 (results very good or good)
Urinary tract infections	-	0/14
Problems with catheterisation	-	0/14

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Austin PF, Westney OL, Leng WW et al. Advantages of rectus fascial slings for urinary incontinence in children with neuropathic bladders.	Retrospective observational study	N=18	Children with neuropathic bladder secondary to myelodysplasia or traumatic spinal cord injury Patient population: mean age 14 yrs (range 8 to 18 yrs), myelodysplasia n=16 8 males:10 females	Fascial sling surgery	Pre-surgery	Mean 21.2 mths	Continence Repeat surgery	None reported

Journal of Urology. 2001; 165(6 Pt 2):2369-2371. Ref ID: AUSTIN2001								

Effect

	Pre-surgery	Post-surgery
Continence	0/18 implied	14/18
Reoperation to repair sling	-	2/18

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Barthold JS, Rodriguez E, Freedman AL et al. Results of the rectus fascial sling and wrap procedures for the treatment of neurogenic sphincteric incontinence. Journal of Urology. 1999; 161(1):272-274. Ref ID: BARTHOLD1999	Retrospective observational study	N=27	Children with neurogenic sphincter incontinence Patient population: Myelomeningocele 21/27 7 boys and 20 females	Rectus fascial sling (N=10 procedures) and wrap (N=18 procedures) (one patient underwent both procedures) N=22 bladder augmentation	Pre-surgery	Minimum 1 yr	Continence (completely dry day and night) Difficulty with catheterisation	None reported

Effect

	Sling (N=10 procedures)		Wrap (N=18 procedures)	
	Pre-surgery	Post-surgery	Pre-surgery	Post-surgery

Continent	0/10 implied	5/10 (completely dry)	0/18	5/18 (completely dry)
Difficulty with catheterisation	-	0/10	-	0/18

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bauer SB, Peters CA, Colodny AH et al. The use of rectus fascia to manage urinary incontinence. Journal of Urology. 1989; 142(2 Pt 2):516-519. Ref ID: BAUER1989	Retrospective observational study.	N=11	All female. Age range 6-22 yrs (mean 14 yrs). All had urinary incontinence. Underlying cause of incontinence was myelodysplasia (8), sacral agenesis (1) and non-neurogenic etiology (2). 3 had undergone prior bladder neck reconstruction, and 2 had previous augmentations.	Rectus fascia sling 4/11 underwent augmentation (plus n=2 had previous augmentation)	None. Pre-op to post-op was compared.	3-24 months (mean 12 months)	Continence Adverse events	Not stated.

Effect

	Pre-surgery	Post-surgery
Continence	0/11	8/11 completely continent on IC 1/11 dry for 2-3 hrs between IC, but leakage with vols of >250cc. 2/11 improved but damp
Adverse effects (perioperative or late)		0/11

2

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bugg CE, Jr.,	Retrospective	N=15	Children with neurogenic intrinsic	Sling (rectus	Pre-surgery	10 to 36	Continence	None

Joseph DB. Bladder neck cinch for pediatric neurogenic outlet deficiency. Journal of Urology. 2003; 170(4 Pt 2):1501-1503. Ref ID: BUGG2003	observational study		sphincter deficiency and a poorly compliant and/or small capacity bladder Patient population: 14/15 female 1/15 male	fascia) applying circumferential pressure All patients underwent ileal augmentation		mths	(dry between catheterisation and dry at night)	reported

Effect

	Pre-surgery	Post-surgery
Continence	0/15	9/15 (completely dry)
Difficulty with catheterisation	-	0/15

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Castellan M, Gosalbez R, Labbie A et al. Bladder neck sling for treatment of neurogenic incontinence in children with augmentation cystoplasty:	Retrospective observational study	N=58	Patients with neurogenic bladder. Criteria: a detrusor leak point pressure of less than 45 cm H2O, an open bladder neck during bladder filling at low detrusor pressure and clinical evidence of stress incontinence. Patient population: 43 females, 15 males, median age 11.4 yrs (range 4 to 40 yrs). Spina bifida 52/58	Rectus fascial sling neck procedure All patients underwent bladder augmentation	Pre-surgery	Mean 4.16 (range 1 to 10 yrs)	Continence Upper tract deterioration Bladder neck occlusion	None reported

long-term followup. Journal of Urology. 2005; 173(6):2128-2131. Ref ID: CASTELLAN2005								

Effect

	Pre-surgery	Post-surgery
Continence	0/58	51/58 (completely dry)
Upper tract deterioration	-	0/58
Bladder neck occlusion	-	2/58

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Daneshmand S, Ginsberg DA, Bennet JK et al. Puboprostatic sling repair for treatment of urethral incompetence in adult neurogenic incontinence. Journal of Urology. 2003; 169(1):199-202. Ref ID: DANESHMAND2003	Retrospective observational study	N=12	Males with neurogenic bladder due to spinal cord injury (n=9) and spina bifida (n=3)	Autologous fascial sling (rectus fascia) 10/12 underwent simultaneous bladder augmentation	Pre-surgery	Mean 14.25 (1 to 39 mths)		
Effect								

	Pre-surgery	Post-surgery
Continence (completely dry)	0/12	8/12 (completely dry)
Complications	-	0/12
Difficulty catheterising	-	0/12

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dean GE, Kunkle DA. Outpatient perineal sling in adolescent boys with neurogenic incontinence. Journal of Urology. 2009; 182(4 Suppl):1792-1796. Ref ID: DEAN2009	Retrospective observational study	N=6	Patient population: Patients aged 14 to 20 yrs. History of myelomeningocele. Urodynamics showed normal compliance, adequate capacity and sphincter incompetence. Previous surgery: 5/6 (1 appendicovesicostomy and bladder augmentation, 4 bladder neck bulking) 6/6 male	Suburethral sling was placed on an outpatient basis through a small perineal incision	Pre surgery	Median 33 mths (range 27 to 39 mths)	Continence Urethral erosion Re-operation Need for catheterisation	None reported

Effect

	Pre-surgery	Post-surgery
Continence	0/6	5/6 (completely dry)
Re-operation	-	3/6
Urethral erosion	-	0/5*
Need for catheterisation	6/6	5/5*

* one patient had the sling removed and not replaced

2

3

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Decter RM. Use of the fascial sling for neurogenic incontinence: lessons learned. Journal of Urology. 1993; 150(2 Pt 2):683-686. Ref ID: DECTER1993	Retrospective observational study	N=10	Patients with neurogenic incontinence Patient population: 8 patients with meningomyelocele, 2sacral anomalies. Age range 6 to 26 yrs	Fascial sling (n=5 rectus abdominus fasica, n=5 fascia lata) N=6 underwent bladder augmentation	Pre surgery	Mean 2.2 yrs	Continence Erosion Difficulty with catheterisation	None reported

Effect

	Rectus fascia		Fascia lata	
	Pre-surgery	Post-surgery	Pre-surgery	Post-surgery
Continence	0/5	2/5 long term	0/5	2/5 long term

Erosion 1/10

Transient difficulty with catheterisation 3/10

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dik P, Klijn AJ, Van Gool JD et al. Transvaginal	Retrospective observational study	N=24	Female patients with spina bifida and neurogenic sphincter paralysis Patient population: mean age 9 yrs (range	Transvaginal sling suspension (rectus fascia)	Pre-surgery	Mean 3 yrs (range 0.6 to 11	Continence Infections Difficulty with catheterisation	None reported

sling suspension of bladder neck in female patients with neurogenic sphincter incontinence. Journal of Urology. 2003; 170(2 Pt 1):580-581. Ref ID: DIK2003A			1 to 17 yrs)	Adjunct bladder augmentation in a few patients		yrs)	Complications	

Effect

	Pre-surgery	Post-surgery
Continence	0/24 implied	19/24
Infections	-	0/24
Difficulty with catheterisation	-	0/24
Complications	-	1/24 (vesicovaginal fistula)

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dik P, Van Gool JD, de Jong TP. Urinary continence and erectile function after bladder neck sling	Retrospective observational study	N=14	Male patients with neurogenic sphincter incontinence and spina bifida Patient population:mean age 11.7 yrs (range 6.5 to 15.2 yrs)	Puboprostatic sling suspension (recuts fascia) Simultaneous autoaugmentation of the bladder 8/14	Pre-surgery	Not reported	Continence Difficulty with catheterisation Erectile dysfunction	None reported

suspension in male patients with spinal dysraphism. BJU Int. 1999; 83(9):971-975. Ref ID: DIK1999				2/14 simultaneous ileocystoplasty				

Effect

	Pre-surgery	Post-surgery
Continence (daytime)	0/14	10/14
Difficult with catheterisation	-	2/14
Erectile dysfunction	0/14	1/14

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Elder JS. Periurethral and puboprostatic sling repair for incontinence in patients with myelodysplasia. Journal of Urology. 1990; 144(2 Pt 2):434-437. Ref ID: ELDER1990		N=14	Patients with myelodysplasia undergoing periurethral and puboprostatic sling repair None had undergone previous bladder neck surgery or augmentation cystoplasty. All patients had failed pharmacological therapy Patient population: mean age 12.6 yrs (range 7 to 25 yrs) 10 female: 4 male	Female – periurethral sling using rectus fascia N=10 Male – puboprostatic sling N=4 13/14 underwent augmentation	Pre-surgery	Mean 12 months (2 to 27 months)	Continence	None reported

				cystoplasty				

Effect

	Pre-surgery	Post-surgery
Continence	0/14 implied	12/14 (completely dry)

1

2

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Fontaine E, Bendaya S, Desert JF et al. Combined modified rectus fascial sling and augmentation ileocystoplasty for neurogenic incontinence in women. Journal of Urology. 1997; 157(1):109-112. Ref ID: FONTAINE1997	Prospective observational study	N=21	Patients with neurogenic incontinence unresponsive to conservative treatment in whom postoperative volitional voiding was not expected Patient population: 13 patients with congential lesions, 8 with acquired cord lesions. 21/21 female	Rectus fascial sling procedure and augmentation ileocystoplasty	Pre-surgery	28.6 mths (range 6 mths to 5 yrs)	Continence Asymptomatic bacteriuria Bladder calculi Difficulty with catherisation	None reported

Effect

	Pre-surgery	Post-surgery
Continence	0/21	20/21 daytime 18/21 nighttime
Asymptomatic bacteriuria	-	13/21 (4/13 febrile UTI)

Bladder calculi	-	0/21
Difficulty with catheterisation	-	0/21

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Godbole P, Mackinnon AE. Expanded PTFE bladder neck slings for incontinence in children: the long-term outcome. BJU Int. 2004; 93(1):139-141. Ref ID: GODBOLE2004	Retrospective observational study	N=19 N=17 (follow-up data available)	Children with a neuropathic bladder who underwent a Gore-tex bladder neck sling procedure. All patients had a poorly compliant bladder, neurogenic sphincteric weakness with low leak-point pressure. Management consisted of clean intermittent catheterisation, pharmacotherapy and cystoplasty (4/19) 7/19 concomitant bladder augmentation Patient population: median age 10 (2.5 to 17) yrs. 12 boys and 7 girls. Spina bifida 7/17	Gore-tex bladder neck sling 7/19 concomitant bladder augmentation	Pre-surgery	Median 7 yrs	Continence Adverse events	None reported
Effect Continence 15/17 (initially dry) 4/17 (dry long term) Re-operation 14/17 sling removed due to erosion Complications No short-term complications								

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hamid R, Khastgir J, Arya M et al. Experience of tension-free vaginal tape for the treatment of stress incontinence in females with neuropathic bladders. Spinal Cord. 2003; 41(2):118-121. Ref ID: HAMID2003	Retrospective observational study	N=12	Women with neuropathic bladder dysfunction and stress urinary incontinence Patient population: mean age 53.3 yrs (range 41 to 80 yrs) Crede manoeuvre 3/12, clean intermittent catheterisation 9/12	Tension-free vaginal tape	Pre-surgery	Mean 27.1 mths (range 17 to 54 mths)	Continence (videourodynamically confirmed) Adverse events	None reported

Effect

	Pre-surgery	Post-surgery
Continence	0/12	10/12
Detrusor hyperreflexia	-	1/12
Urinary tract infection	-	3/12

2

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Herschorn S,	Retrospective	N=13	Male patients with neurogenic	Urethral sling	Pre-surgery	34.3	Continence	None

Radomski SB. Fascial slings and bladder neck tapering in the treatment of male neurogenic incontinence. Journal of Urology. 1992; 147(4):1073-1075. Ref ID: HERSCHORN1992	observational study		incontinence Patient population: Spina bifida n=10, spinal cord injury n=3, mean age 27 yrs (range 17 to 40 yrs)	plus bladder augmentation 2/13 Marlex mesh 11/13 rectus sheath 12/13 underwent bladder neck tapering		mths (range 5.5 to 49 mths)	Reoperation Symptomatic urinary infection Bladder neck narrowing Wound infection Marlex erosions Bladder stones	reported

Effect

	Pre-surgery	Post-surgery
Continence	0/13	9/13 (completely dry)
Reoperation	-	3/13
Symptomatic urinary infection	-	7/13
Bladder neck narrowing	-	2/13
Wound infection	-	1/13
Marlex erosions	-	2/13
Bladder stones	-	1/13

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
McGuire EJ, Wang CC, Usitalo H et al. Modified	Retrospective observational study	N=8	Female children with myelodysplasia	Pubovaginal sling (rectus fascia)	Pre-surgery	Not reported	Continence Difficulty with catheterisation	None reported

pubovaginal sling in girls with myelodysplasia. Journal of Urology. 1986; 135(1):94-96. Ref ID: MCGUIRE1986A				Simultaneous augmentation cystoplasty 1/8				

Effect

	Pre-surgery	Post-surgery
Continence	0/8	8/8 (dry)
Difficulty with catheterisation	-	0/8

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Misseri R, Cain MP, Casale AJ et al. Small intestinal submucosa bladder neck slings for incontinence associated with neuropathic bladder. Journal of Urology. 2005; 174(4 Pt 2):1680-1682. Ref ID: MISSERI2005	Retrospective observational study	N=36	Patients treated with small intestinal submucosa (SIS) bladder neck sling procedure for neuropathic urinary incontinence (all with myelodysplasia) with a leak point pressure less than 25 cm H2O and a minimum of 6 mths follow up Patient population: 21 females and 15 males, mean age 9 yrs (range 3 to 10 yrs) All had failed on clean intermittent catheterisation and anticholinergic treatment	Small intestinal submucosa (SIS) bladder neck sling N=27 Bladder neck repair with SIS sling N=9 All patients underwent Augmentation	Pre surgery	Mean 15 mths	Continence (requiring no pads and dry underwear) Urinary tract infection Renal complications	None reported

				cystoplasty				

Effect

	Pre-surgery	Post-surgery
Continence	0/36 implied	Sling alone 19/27 (dry) Sling plus bladder neck reconstruction 8/9 (dry)
Urinary tract infection	-	0/36
Renal complications	-	0/36

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Nguyen HT, Bauer SB, Diamond DA et al. Rectus fascial sling for the treatment of neurogenic sphincteric incontinence in boys: is it safe and effective? Journal of Urology. 2001; 166(2):658-661. Ref ID: NGUYEN2001	Retrospective observational study	N=7	Male children with neurogenic sphincteric incontinence Patient population: myelodysplasia 5/7	Fascial sling (rectus fascia) Simultaneous continent stoma (N=4)	Pre-surgery	1 to 9 yrs	Continence, complications, repeat surgery	None reported

Effect

	Pre-surgery	Post-surgery
Continence (completely dry)	0/7	1/7

Occasionally dry		6/7
Complications due to surgery	-	1/7 (wound dehiscence)
Repeat sling surgery	-	1/7
Difficulty with catheterisation	-	0/7

1
2

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Snodgrass W, Barber T, Cost N. Detrusor compliance changes after bladder neck sling without augmentation in children with neurogenic urinary incontinence. Journal of Urology. 2010; 183(6):2361-2366. Ref ID: SNODGRASS2010A	Prospective observational study	N=26	Patients with neurogenic incontinence Inclusion criteria: urodynamics within one yr postoperatively and additional testing at least 18 mths postoperatively Patient population: 21/26 myelomeningocele 15 male and 11 female	360-dregree tight fascial wrap around the bladder neck with appendicovesicostomy but no augmentation	Pre-surgery	Mean 39 mths (19 to 94 mths)	continence	None reported

Effect

	Pre-surgery	Post-surgery
Continence	0/26 implied	16/26 (dry)

2

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Snodgrass W, Keefover-Hicks A, Prieto J et al. Comparing outcomes of slings with versus without	Cohort study	N=41	Children with spina bifida with neurogenic urinary incontinence Bladder neck sling with augmentation: male:female 10:8, ambulatory 7/18, mean age at operation 8.6 (range 3.2 to 13.6) yrs	Bladder neck sling with augmentation N=18	Bladder neck sling without augmentation N=23	Not reported	Continence Health-related quality of life	None reported

enterocystoplasty for neurogenic urinary incontinence. Journal of Urology. 2009; 181(6):2709-2714. Ref ID: SNODGRASS2009			Bladder neck sling without augmentation: male:female 11:12, ambulatory 12/23, ambulatory 12/23, mean age at operation 8.0 (range 4.1 to 14.0) yrs					

Effect

	With augmentation	Without augmentation
	Pre-surgery vs post surgery	Post-surgery
Continence Patient reported Surgeon reported	 0/18 vs 11/18 0/18 vs 13/18	 0/23 vs 12/23 0/23 10/23
Health-related quality of life	Median score 5 (range 2 to 5)	Median score 4 (range 1 to 5) (p<0.019

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Snodgrass W, Barber T. Comparison of bladder outlet procedures without augmentation in children with neurogenic incontinence. Journal of Urology. 2010; 184(4 Suppl):1775-1780.	Prospective observational study	N=35	360-degree tight bladder neck sling for incontinence due to neurogenic bladder outlet incompetence Patient population: 32 male 3/35 female, mean age 8.1 yrs	360-degree tight bladder neck sling	Pre-surgery	Mean 28 mths (6 to 94 mths)	Continence	None reported

Ref ID: SNODGRASS2010								

Effect

	Pre-surgery	Post-surgery
Continence	0/35	16/35 (dry)
Hydronephrosis	-	0/35

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Walker RD, Erhard M, Starling J. Long-term evaluation of rectus fascial wrap in patients with spina bifida. Journal of Urology. 2000; 164(2):485-486. Ref ID: WALKER2000	Retrospective observational study	N=15	Patients with spina bifida who underwent rectus fascial wrap procedure 7 males and 8 females	Rectus fascial wrap Augmentation cystoplasty 14/15	Pre-surgery	Mean 58 mths (Minimum 36 mths)	Continence Patient satisfaction	None reported

Effect

	Pre-surgery	Post-surgery
Continence Mean no. of pads used	5.5	1.1
Continence (completely dry)	0/15 implied	5/15
Would you have the operation again?	-	14/15

2

3

F.14 What is the safety and efficacy of artificial urinary sphincter compared with other treatments in neurological disease?

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Aaronson IA. The AS 800 artificial urinary sphincter in children with myelodysplasia – preliminary results. S Afr Med J 1986; 69: 686-688	Prospective observational study.	10	9 boys and 1 girl with myelodysplasia (age 6-16 years (mean 11 years)). All had severe incontinence despite 2 hourly IC and the use of anticholinergics. 8 had mild bladder hyper-reflexia but abolished by oxybutynin. One child had a VUR in left ureter, which was reimplanted during the stent surgery.	The AS 800's occlusive cuff was placed around the bladder neck and a regulating balloon with 71-80 cm pressure used. Prophylactic antibiotics used for 7 days post operatively, and long term oxybutynin was begun. The device was de-activated at the time of implantation and activated between 4 and 12 weeks later.	Pre to post Rx	12-14 months	Adverse events Incontinence	Not stated

Results:

	Pre-treatment	Post-treatment
Adverse effects Post-op UTI Wound infection Need for revision New VUR		 3/10 0/10 4/10 2/10
Incontinence	10/10 had "severe incontinence"	8/10 dry and 2/10 improved

Author conclusions: The complete urinary incontinence achieved in 8 of the patients is very gratifying and compared favourably with the experience of others.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Aprikian A, Berardinucci G, Pike J, Kiruluta G. Experience with the AS-800 artificial urinary sphincter in myelodysplastic children. JCC 1992; 35: 396-400	Retrospective observational study.	27	Children with sphincteric urinary incontinence secondary to myelomeningocele (n=26) or sacral agenesis (n=1). Children needed to have adequate manual dexterity to operate the sphincter, be refractory to conservative management, be motivated and have a low pressure and compliant detrusor muscle (if hyperreflexive they would need to be responsive to anticholinergics). All male. Median age at implantation 14 (range 9-19). None had had previous urethral surgery or bladder neck reconstruction. One had had a AS-792 sphincter fitted elsewhere, but this had needed to be removed because of erosion. .	AS 800 implanted according to teh standard technique. Sphincters placed around the bladder neck in all but one patient, whose sphincter was implanted at the bulbous urethra.	pre-	6-31 months (median 12 months).		Not stated

Results:

	Pre-treatment	Post-treatment
Incontinence	27/27 (not explicitly stated)	3/25
Adverse effects Erosion Infection without erosion Device-related problems Removal of AUS Revision of AUS		11/27 2/27 2/27 7/27 4/27 7/27

Author conclusions: The AS800 can establish continence in boys with neurogenic bladders. Proper selection of the ideal patient for the artificial sphincter is essential to avoid complications.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Barrett DM and Furlow WL. The management of severe urinary incontinence in patients with myelodysplasia by implantation of the AS791/792 urinary sphincter device. The Journal of Urology 1982; 128: 484-486	Prospective observational study	24	Inclusion: Sphincteric incontinence, detrusor areflexia or manageable bladder neck contractions, urinary flow >10ml/sec, minimal residual urine, no evidence of vesicoureteral reflux, a motivated and co-operative patient and sterile urine. 17 male and 7 female patients with myelodysplasia. Patient age ranged from 7 to 56 years.	The inflatable cuff was placed around the baldder neck in all patients in whom the incontinence was related to myelodysplasia. The pressure regulating balloon reservoir was placed in the prevesical space, and its tubing and the cuff tubing was brought through the anterior abdominal fascia near the internal inguinal ring.	Pre vs post	Up to 40 months	Incontinence Adverse events	Not stated

Results:

	Pre-treatment	Post-treatment

incontinence	24/24	2/24 (1 additional patient had to wear pads for mild stress incontinence, and 1 more developed insidious incontinence at 12 months)
Adverse events Bladder erosion Device failure UTI Upper tract disease		 2/24 (same as the 2 above) 3/24 0/24 0/24

Author conclusions: No deleterious effects on the urinary tract were observed

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Belloli G, Campobasso P, Mercurella A. Neuropathic urinary incontinence in pediatric patients: management with artificial sphincter. Journal of pediatric surgery 1992; 27: 1461-1464	Retrospective observational study.	37	Inclusion:neuropathic urinary incontinence; unable to treat by other conservative methods, >11-12 years; cognitively adequate; good physical condition; no urological complications; acceptable MCC and bladder compliance; absence of hyper-reflexia or pharmacological control; no obstruction to urine flow. Aged 13-19 years. 35 male, 2 female. Underlying pathology – myelomeningocele (33), partial sacral agenesis (3), neuropathic bladder secondary to pelvic surgery (1). Oxybutynin used pre-operatively, and all males had a sphincterotomy. One girl had bladder flap surgery pre-operatively. 1 day before surgery all had prophylactic antibiotics.	The first 2 cases had the AS792 implanted; thereafter, the AS800 was used. The cuff was placed at the bladder neck in 33 cases, and at the urethral bulb in 4. The sphincter was usually activated about 3 weeks after implantation.	Pre to post	Not stated, but approx 1-9 years, based on the years of data collection and the year of paper submission.	Incontinence Adverse effects	Not stated

Results:

	Pre-treatment	Post-treatment
Incontinence in day Incontinence at night	37/37 (not explicitly stated) 37/37 (not explicitly stated)	4/37 15/37
Adverse effects Upper urinary tract dilatation renal impairment Need to operate on late complications Bladder neck lesion Anterior rectum wall lesion Scrotal hematoma		 2/37 2/37 14/37 1/37 1/37 2/37

Author conclusions: Adolescents with an artificial sphincter must be monitored carefully....with at least an annual assessment of the upper tract...

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bersch U, Gocking K, Pannek J. The artificial urinary sphincter in patients with spinal cord lesion: description of a modified technique and clinical	Retrospective observational study	51	Patients with neurogenic bladder dysfunction. 37 had a traumatic SCI (24 complete), 8 myelomeningocele, and 6 had SCI secondary to spinal stenosis and spinal infarction. 4 had Cx lesions, 25 Tx and 22 had a Lx lesion. Mean age was 38.7 (14). 37 males, 14 females. Median time between SC lesion onset and implantation was 50 months. All had bladder neck insufficiency and sphincter weakness. Detrusor overactivity was either not present or suppressed with anticholinergics. Most emptied bladders by CIC, and 10 used	A sphincter cuff was placed at the bladder neck, with an intraperitoneal pressure-regulating balloon. The implant was activated at 6 weeks post surgery. There was no pump; instead a “port” was used (unclear) where inflation occurred.	Pre versus post	60-174 months. Appointments occurred 3,6 and 12 months after implantation and then every 12 months.	Incontinence Adverse events	Not stated

results. European Urology 2009; 55: 687-695			sacral anterior root stimulation.					

Results:

	Pre-treatment	Post-treatment
Incontinence Moderate but bothersome Severe Permanent urine loss	51/51 4/51 24/51 23/51	15/51 (10 minimal leakage seen on video-urodynamics but no need for incontinence aids; 4 needed 1 pad per day; 1 needed > 1 pad per day)
Adverse events Significant hemmorrhage leading to revision within 6 weeks of procedure Infection requiring explantation during whole FU period Revision of sphincter cuff Total patients requiring revisions		 1/51 4/51 (3 received a new implant without further complications) 6/51 16/51

Author conclusions: With a long follow up of 8 years the modification presented by our group proved to be highly successful, reliable, safe and even cost effective. Therefore it seems to be a valuable tool for the treatment of this group of patients.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bitsch M, Nerstrom H, Nordling J, Hald T. Upper urinary tract deteriorationafter implantation of	Observational study	20	20 patients who had had artificial sphincter implantation because of urinary incontinence secondary to myelomeningocele. Age range: 15-47 (median: 22)	Artificial sphincter implantation.	Pre-op to post op	1-13 years	Adverse effects	Not stated

artificial urinary sphincter. Scand J Urol Nephrol 1990; 24: 31-34.								

Results:

	Pre-treatment	Post-treatment
Adverse effects Hydronephrosis and impairment of renal function		4/20

Author conclusions: If the device is implanted, periodic, life long control of the upper urinary tract is recommended.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Brantley Scott F, Bradley WE, Timm GW, Kothari D. Treatment of incontinence secondary to myelodysplasia by an implantable prosthetic urinary sphincter. Southern medical Journal 1973; 66: 987-990	3 case reports	3	Case 1: 26 yr old woman with Spina Bifida and MMC. Past history of bladder-flap urethroplasty, leading to total urinary incontinence. Normal renal function Case 2: 18 year old man with spina bifida and MMC. Total incontinence. Case 3: 16 year old male with spina bifida and MMC. Recurrent UTIs, but no mention of incontinence. However likely to have been incontinent in the context of teh wording of the results.	An implantable artificial sphincter, consisting of an inflatable cuff inserted around the urethra at the level of the bladder neck, was implanted through a lower abdominal incision which exposes the anterior surface of the bladder and bladder neck. Tubing to the inflatable balloons passes to subcutaneous pockets in the scrotum or labium majora, where the ballons can be deflated and inflated externally.	Pre-Rx versus post-Rx	unclear	Incontinence Adverse events	Not stated

Results:

	Pre-treatment	Post-treatment
Incontinence	3/3 (one unclear)	0/3 (one had a lapse due to leakage of fluid from inflation bulb but this was corrected)
Adverse events Urethral injury Leakage of fluid from inflation bulb		 0/3 1/3

Author conclusions: Combining this artificial sphincter with a bladder-volume sensor and a radio-coupled electrical bladder stimulator should restore normal urinary function to those patients who have sustained injury to the lower spinal cord.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Brantley Scott F, Fishman IJ, Shabsigh R. The impact of the artificial urinary sphincter in the neurogenic bladder on the upper urinary tracts. The Journal of Urology 1986; 136: 636-642	Retrospective observational study	120	Inclusion:Charts and X-rays of patients with neurogenic bladder undergoing artificial sphincter implantation between 1973 and 1984. Myelomeningocele in 89 patients, SCI in 20, congenital sacral dysgenesis in 6, and miscellaneous neurogenic etiology in 5. 85 male and 35 female. Mean patient age at implantation was 19.3 yrs (range 3-68). 21 patients had persistent detrusor hyperreflexia and 99 had detrusor atonia. 77 patients (90.6% of all male patients) required sphincterotomy. Bladder falp urethroplasty was also done in 30 female and 2 male patients.	222 devices of different designs were used in the 120 patients. 56 had 1, 34 had 2, 24 had 4, 4 had 4 and 2 had 5 devices implanted. At the time of publication 100 had the AS792/791 and 20 had the AS800 in place. The cuff was placed around the bladder neck in 104 patients and around the bulbar urethra in 16. 77 patients (90.6% of all male patients) also required sphincterotomy. Bladder flap urethroplasty	Pre-op to post op	3-130 months (mean 36.8)	Adverse effects	Not stated

				was also done in 30 female and 2 male patients. Ureteral reimplantation was done before implantation in 8, during implantation in 15 and afterwards in 3.				

Results:

	Pre-treatment	Post-treatment
Adverse effects		
Chronically dilated tracts		6/120
Transient hydroureteronephrosis		8/120
Progressive hydroureteronephrosis		4/120

Author conclusions: The artificial urinary sphincter can be implanted safely in neurogenic bladder patients without adverse impact upon the upper urinary tracts.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chartier Kastler E, Genevois S, Game X et al. Treatment of neurogenic male urinary incontinence related to intrinsic sphincter insufficiency with an	Retrospective observational study	51.	Adult males (18-58 yrs). 16/51 had myelomeningocele, 35/51 had SCI. 24/51 had had previous urological surgery, including: sacral neuromodulation (n=3), peribulbar or periprostatic AUS (n=8), enterocystoplasty 9n=6), botulinum toxin (n=6), ACT balloon (n=1), endoscopic sphincterotomy (n=4), macroplastic injections (n=2). Voiding methods were: IC: 19/51; spontaneous 21/51;	Performed by 10 surgeons working in 4 different Urology wards. Implantation of an AMS800. Midline subumbilical incision, AUS balloon is placed lateral to the bladder. The cuff is at the junction between the bladder neck and the anterior face of the prostate. Cuff sizes ranged from 6-11cm. Post operative catheterisation laster for 2-30 days. AUS activated on average	Pre versus post	early (<30 days), late (6-208 months). The endpoint of the study was 20 years from inception (only 15 had dropped	Incontinence Adverse events	Not stated

artificial urinary sphincter: a French retrospective multicentre study. British Journal of Urology International 2010; 107: 426-432			chronic transurethral catheterisation 1/51.	1 month after implantation. 61 AUS devices implanted into 51 patients.		out).		

Results:

	Pre-treatment	Post-treatment
Incontinence (all) Incontinence of those with AUS still in place at final follow up	not clear	20/50 12/40
Adverse events (<30 days post op) death due to Sx (post op pneumopathy) UTI Acute urinary retention Transient raised ICP Failure to perform IC Complications during later follow up requiring new procedure infections bladder neck erosions mechanical failure urethral stenosis cuff fibrosis initial failure		 1/51 (unclear if this is incidence or number episodes) 8/51 (unclear if this is incidence or number episodes) 3/51 (unclear if this is incidence or number episodes) 1/51 (unclear if this is incidence or number episodes) 1/51 (unclear if this is incidence or number episodes) 5/51 3/51 13/51 1/51 1/51 5/51
Use of self - IC	19/51	44/51

Author conclusions: This procedure was effective in restoring urinary incontinence in the vast majority of our patients with an acceptable morbidity.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
De Badiola FIP, Catro-Diaz D, Hart-Austin C, Gonzalez R. Influence fo preoperative bladder capacity and compliance on the outcome of artificial sphincter implantation in patients with neurogenic sphincter incompetence. The Journal of Urology 1992; 148: 1493-1495	Retrospective observational study.	23	Inclusion: Patients with neurogenic sphincteric incompetence who underwent implanation of an artificial sphincter, with end filling pressures of <50cm H2O, no previous surgery on the lower urinary tract, and who had performed pre and post-operative cystometrography. 20 males and 3 females. Underlying neuropathology: myelomeningocele (18), sacral agenesis (3), SC tumours (2).	6 recieved the artificial urinary sphincter model AS791 and 17 received AS800. No other procedures were performed concurrently.	Pre to post op.	12-160 months	Incontinence Adverse events	Not stated
Results:								

	Pre-treatment	Post-treatment
Incontinence	23/23 (unclear but probable)	7/23 (all had bladder capacity <60% of age expected level)
Adverse events Need for enterocystoplasty Renal insufficiency and hydronephrosis		 7/23 (same patients as above) 1/23

Author conclusions: Our results suggest that all patients with neurogenic sphincter incompetence and a preoperative bladder capacity of >60% of expected capacity...can expect an excellent long-term results for artificial urinary sphincter implantation without augmentation.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Gonzalez R, Garcia Moreno F, Vaughn M. Long term results of the artificial urinary sphincter in male patients with neurogenic bladder. The Journal of Urology 1995; 154: 769-770.	Retrospective observational study	19	Inclusion:males with neurogenic sphincteric incompetence, no previous surgery on the bladder neck, myelodysplasia and >5 years FU. Retrospective record review supplemented by questionnaire and interview. Mean age 8.4 years (range 4-17). Mean age at last FU 16.8 years.	Artificial urinary sphincter implantations (AMS 800 in first 11 patients, and AMS 721 or 792 in 8) done at the bladder neck.	Pre-Rx to post-Rx.	Mean 8 years	Incontinence Adverse events	Not stated

Results:

	Pre-treatment	Post-treatment
All incontinence (unable to stay dry for at least 4 hours between voiding without pads)		3/19

Stress incontinence		1/19
Complete incontinence		2/19
Adverse effects		
Need for bladder augmentation after sphincter implantation		3/19
Erosion		0/19
Need for sphincter revisions (for replacement of older models)		19/19
Upper tract dilatation		
Mild	3/19	2/19
Moderate		1/19
Severe (with loss of renal function)		1/19

Author conclusions: The artificial urinary sphincter is an excellent modality for the initial surgical treatment of neurogenic sphincteric incompetence in male patients. Careful patient selection and lifelong surveillance are essential to success and safety.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Gonzalez R, Sheldon CA. Artificial sphincters in children with neurogenic bladders: long term results. The Journal of Urology 1982; 128: 1270-1272	Prospective observational study.	15	Inclusion: Neurogenic bladder, absence of residual urine, normal renal function and upper tracts, no VUR and functional mobility. In adition the patient and parents had to be enthusiastic about the procedure (the obvious potential for bias here is not mentioned). Detrusor hyper-reflexia and UTIs were controlled pharmacologically before implantation. 10 boys and 5 girls between 5 and 17 years. Underlying pathology was myelomeningocele in 8, spinal cord tumours in 3 and sacral agenesis in 3.	The AS 721 and AS 792 sphincters were placed at the bladder neck. Of the boys, 5 had undergone transurethral external sphincterotomies previously, and of the girls 2 had V-flap urethroplasties performed at the time of implantation.	Pre-op to post-op	Up to 88 months		Not stated
Results:								

	Pre-treatment	Post-treatment
incontinence	15/15 (not stated explicitly)	5/15 (1/10 boys; 4/5 girls)
Adverse effects Device failure of AS721 Device failure of AS792 Bladder erosion		 9/10 (5/6 boys; 4/4 girls) 2/5 (2/4 boys; 0/1 girls) 3/15 (0/10 boys; 3/5 girls)

Author conclusions: The artificial device is useful in boys with neurogenic bladders without residual urine if bladder spasticity is controlled. We use the device in girls only when pharmacological methods and intermittent catheterisation have failed

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Gonzalez R, Dewolf WC. The artificial bladder sphincter AS-721 for the treatment of incontinence in patients with neurogenic bladder. The Journal of Urology 1979; 121: 71-72	Prospective observational study.	12	Inclusion: Normal upper urinary tracts, no VUR and normal renal function in patients with neurogenic bladder. 9 males and 3 females. Mean age was 19 (range 7-32) for females and 17 (range 7 to 45) for males. Causes of neurogenic bladder were myelomeningocele in 7 cases, benign spinal tumour in 2, and sacral agenesis in 1. One had neurological injury secondary to a pelvic fracture, and another had neurogical problems secondary to surgery for hypotonic bladder of unknown cause. Most patients had failed CIC and anti-cholinergics. All patients were ambulatory.	The AS-721 artificial sphincter was implanted around the bladder neck.	Pre-Rx versus post-Rx	Mean 25 months	Incontinence Adverse effects	Not stated

Results:

	Pre-treatment	Post-treatment

Incontinence (not dry for 2 hours)	12/12 (not explicitly stated but implicit in the paper)	4/12 (1 male became continent 8 months post-op, and 1 female became continent after a second op with a smaller cuff, but later failed due to renal complications).
Adverse events		
Bladder neck erosion		3/12
Recurrent UTI		1/12
Persistent incontinence		1/12
VUR, pyelonephritis		1/12
Revision due to inflating mechanism malfunction		1/12
Total failure and need for permanent removal of prosthesis		4/12

Author conclusions: The data presented suggest that in carefully selected incontinent male patients with neurovesical dysfunction the use of artificial bladder neck sphincters is a reasonable alternative to supravesical diversion. In those patients in whom this kind of operative treatment is not successful supravesical diversion can be performed later without added difficulty.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Jakobsen H, Hald T. Management of neurogenic urinary incontinence with AMS artificial urinary sphincter. Scand J Urol nephrol 1986; 20: 137-141	Retrospective observational study	33	Inclusion:Neurogenic urinary incontinence patients treated with AMS artificial sphincter devices between 1974-1984. 15 females of median age 34 (range 10-65) and 18 males of median age 16 (range 9-75). Underlying neurological problem was: myelodysplasia (17), neural tmours (3), traumatic spinal injury (7), lumbar disc pathology (3) and peripheral nerve lesion (3). Criteria for acceptance of patients as candidates for implantation were|: ability to understand and operate the prosthesis, “not too old” and no skin infection or decubitus at the implantation site. Special criteria were:	All types of prosthesis available during the 10 year period were employed, including these models: AS 721, AS 761, AS 742, AS791, AS792 and AS 800, the latest one. In all models the principles of mechanism are the same, with a cuff, a pump and pressure-regulating balloon. Implantation of the cuff around the bladder neck was undertaken with a suprapubic access.	Pre-test to post-test.	Up to 8 years	Incontinence	Not stated

			low urethral closure pressure, unobstructed micturition, no or very slight detrusor hyper-reflexia, no urine and sterile urine at operation.	Implantation around the bulbous urethra was chosen only when the bladder neck was unsuitable due to scarring.				

Results:

	Pre-treatment	Post-treatment
Complete continence (total urine loss <1g during 1 hour)	0/33	19/33
Slight incontinence (not socially inconvenient) on exertion		6/33
Severe stress incontinence		1/33
Adverse events		
Failure of sphincter after 10 years		7/34
Need for phenoxybenzine because of incomplete bladder emptying		2/33
Need for CIC because of incomplete bladder emptying		1/33
UTI	19/33	9/33

Author conclusions: successfull control of voiding function, defined as complete continence or slight but not socially inconvenient incontinence, was obtained in 25 patients (76%).

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Light JK, Scott FB. Use of the artificial urinary sphincter in spinal cord injury patients. The journal of urology 1983; 130: 1127-1129	Prospective observational study	50	Spinal cord injury patients aged 8 to 69 years (mean 34.6 years). 45 paraplegic and 4 incomplete quadriplegia. Interval from injury to implantation ranged from 1-43 years.	No details of the implantation procedure. Male patients had concurrent transurethral sphinterotomy and female patients bladder flap urethroplasty if bladder outflow present.	Pre to post	3-60 months	Incontinence	Not stated

Results:

	Pre-treatment	Post-treatment
Incontinence Sub-group with detrusor hyper-reflexia Areflexia Low compliance	Assumed that all, though unclear.	 4/16 (2 were later continent with further surgery) 17/20 (1 more continent with a tandem device fitted) 3/6
Adverse effects Need for further surgery Need for removal of cuff secondary to infection Renal dysfunction		 26/50 12/50 0/50

Author conclusions: The artificial urinary sphincter should be considered in carefully selected patients with neuropathic bladder dysfunction secondary to SCI

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lopez Pereira P, Somoza I, Martinez Urrutia MJ, Romera L, Jaueguizar E. Can urodynamioc studies predict bladder behaviour changes after artificial urinary sphincter	Retrospective observational study	17	Patients with neuropathic sphincteric incompetence, who had a follow up of > 1 year, did not have early removal of the and who did not have a comcommitant or previous cystoplasty operation. Underlying pathology mostly myelomeningocele. All were initially treated with CIC and /or anticholinergics. 12 male and 5 female, with ages at implantation from 12.5 – 21 years (mean 14.4).	All AUS cuffs were placed around the bladder neck	Pre to post	Mean 7.5 years (range 1.5 – 9.8)	Adverse effects	Not stated

implantation. Journal of pediatric Urology 2005; 1: 397-401								

Results:

	Pre-treatment	Post-treatment
Adverse events Need for augmentation later Bladder neck erosion Renal dysfunction Abnormal upper urinary tract		 6/17 1/17 0/17 1/17 (unilateral renal scarring)
Incontinence	Likely to be 17/17	0/16

Author comments: These patients require long term careful observation to detect any asymptomatic change in detrusor behaviour.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lopez Pereira P, Ariba IS, Martinez Urrutia MJ, Romero RL, Monroe EJ. Artificial urinary sphincter: 11 year experience in adolescents	Prospective observational study	35	Patients with neuropathic sphincteric incompetence. Underlying etiology was myelomeningocele in 27, sacral agenesis in 4, spinal cord lipoma in 3 and sacrococcygeal teratoma in 1. Age 11.5 – 18 (mean 14.4). 21/35 had significant residual urine, necessitating CIC. Detrusor filling pressure of <15 cm H20 at 505 or more of bladder capacity for the patient's age was the criterion for implantation. 13 did not fulfil this, despite ongoing Anticholinergic therapy, and these were included, but also	Prophylactic antibiotics received for 7/7 pre-operatively. Standard and posterior approaches used to dissect the neck of teh bladder. Cuff placed around the bladder neck and the cuff pressure set at 61-70 cm H2O. Activation occurred 6-8 weeks after	Pre-Rx to post-Rx.	0.4 – 11 years (mean 5.5)	Incontinence Adverse effects	Not stated

with congenital neuropathic bladder. European Urology 2006; 50: 1096-1101			received a concurrent augmentation (see intervention).	implantation. For 11 an augmentation was performed at the same time, with a further two having an augmentation on a separate occasion before.				

Results:

	Pre-treatment	Post-treatment
Incontinence	35/35 (but unclear)	2/35
Adverse events		
Bladder neck erosion requiring removal of device		3/35
Mechanical malfunctions		7/35
Need for further surgery		14/35
Worsening of bladder compliance despite anticholinergics and CIC in those who did not have an augmentation (but no clinical signs in these patients)		7/22

Author conclusions: It produces better continence rates than other methods. However these patients need long-term followup....

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Murphy S, Rea D, O'Mahony JK, McDermott TED, Thornhill J, Butler M, Grainger R. A	Retrospective observational study. This study aimed to compare incontinence and adverse events between a group with neurogenic causes of their incontinence (13), and a group with non-neurogenic causes (17).	13	Of 38 patienrs having implantation of the AUS 800 device at ainstitution over a 15 year time period, 13 had neurogenic cause of incontinence and complete records and follow up data. Neurogenic causes included	AUS 800 implanted in standard surgical fashion. Activation was performed a mean of 47 days post surgery (range 31-54).	Pre-test to post test	Mean 6 years.	Incontinence Adverse events	Not stated

comparison of the functional durability of the AMS 800 artificial urinary sphincter between cases with and without an underlying neurogenic aetiology. Irish Journal of medical Science 2003; 172: 136-138.	Only the results pertaining to the neurogenic cases are reported in this summary.		spina bifida (9), SCI (2), and severe pelvic trauma (2).					

Results:

	Pre-treatment	Post-treatment
Incontinence		
Entirely dry	Not given	3/13
Rare dribble		1/13
Need for suprapubic/CSIC		4/13
Convene catheter		3/13
Need for pads		2/13
Adverse events		
Cuff erosion		9/13
Device infection		2/13
Loss of cuff compression		1/13
Device herniation		0/13

Post revisional surgery		1/13
Permanent removal		7/13
Complete replacement		3/13
Re-operation rate		11/13
Original device NOT in situ		11/13

Author conclusions:Inserting an AMS 800 remains a durable means of regaining urinary continence.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Murray KHA, Nurse DE, Mundy AR. Detrusor behaviour following implantation of teh Brantley Scott Artificial Urinary Sphincter for neuropathic incontinence. British Journal of Urology 1988; 61: 122-128	Retrospective observational study	19	Patients undergoing endoscopic sphincterotomy and artificial sphincter implantation for the control of sphincter weakness in continence die to congenital neuropathic bladder dysfunction. None had previous augmentation or substitution procedures. 17 had spina bifida and 2 sacral agenesis. 16 males and 3 females. Age range 5-42.	3 patients received the AS800 device, and the other 16 received the AS 792 device. All patients had sphincter ablation.	none	7-39 months (mean 22.7)	Adverse effects	Not stated

Results:

	Pre-treatment	Post-treatment
Adverse effects		

Vesicoureteric junction obstruction with bilateral hydroureteronephrosis		2/19

Author comments: All patients treated with an AUS require long-term surveillance including videourodynamic studies.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
O'Flynn KJ, Thomas DG. Artificial urinary sphincter insertion in congenital neuropathic bladder. British journal of Urology 1991; 67: 155-157	Retrospective observational study	44	Patients with congenital neuropathic bladder and genuine stress incontinence. Underlying pathology was meningocele (3), lipoma of cauda equina (4), sacral agenesis (2). 37 males and 7 females. Age range of 11-43 (mean 21) years. 39 were ambulatory with/without a walking aid.	In 35 male patients a spincterotomy was performed prior to AUS implantation. Those with a good bladder capacity had an AUS alone (n=18), and those with a low capacity bladder with low compliance and/or hyperreflexia were given AUS combined with cystoplasty (n=22). For these the ballon and control valve were added in a small operation 6/52 later. The other 4 patients had an undiversion and AUS implantation. Early on in the series the cuff was placed around the bladder neck in males and upper urethra in females. Later the cuff was placed around the membranous urethra. The AMS 792 was used for 8 and the AMS 800 for the rest.	Pre versus post	Not stated	Incontinence Adverse effects	Not stated

Results:

	Pre-treatment	Post-treatment
Incontinence at final follow up Damp but leak only on maximal exertion or		

excited Wet – awaiting further procedures		 2/44 2/44
Adverse effects Detrusor hyper-reflexia and incontinence refractory to oxybutynin Erosion Infection Kink System leakage Pump failure Stress leakage Other Need for further surgery Renal deterioration		 5/44 (continent after clam ileocystoplasty) 3/44 2/44 2/44 4/44 1/44 1/44 2/44 16/44 1/44

Author comments: In patients with agood bladder capacity and normal compliance and detrusor hyper-reflexia controlled by Anticholinergic drugs, cystoplasty is not necessary at the time of AUS insertion.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Patki P, Hamid R, Shah PJR, Craggs M. Long term efficacy of AMS 800 artificial sphincter in male patients with	Retrospective observational	9	Inclusion: male SCI patients who had undergone insertion of an AMS 800 artificial sphincter for neurogenic stress incontinence (proved on video cystometrogram). All male, mean age 38.2 years (range 27-47). Mean time with spinal lesion was 13.8 yrs (range 6-26 yrs). 5 thoracic, three lumbar and one cervical. 7 complete lesions and 2 incomplete. Neurogenic detrusor over-activity in 3 cases.	Sphincters implanted with the urethral cuff around the bulbar urethra via a perineal approach. 61-70cm water reservoir used in all patients. At 6/52 into the post-op period, all implants successfully activated. All patients followed up at 3	Pre to post op.	3-133 months (mean 70.2 months)	Incontinence Adverse effects	Not stated

urodynamic stress incontinence due to spinal cord lesion. Spinal Cord 2006; 44: 297-300.			These 3 patients treated with augmentation ileocystoplasty, sacral-anterior root stimulator implant and regular oxybutynin respectively. [Not clear if these treatments had occurred prior to the study, or if they were carried out afterwards.] Pre-operatively 3 used CIC, 1 voided on reflex and 1 on urge. 2 had long-term suprapubic indwelling catheters. One had a SARSI.	months, 6 months and then every year.				

Results:

	Pre-treatment	Post-treatment
Incontinence		At activation point: 0/9 3 months: 2/9 Currently: 3/9 (one of them is very mild leak with no need for pads)
Immediate adverse effects Intra-operative Immediate post-operative Later (3 months+) effects Cuff erosion and infection (3 months) Cuff failure (12 months) Secondary inf of scrotal pump (24 months) Pump failure (36 months) Cuff erosion (53 months) Upper tract damage/ decrease in renal function		 0/9 0/9 1/9 1/9 1/9 1/9 1/9 0/9

Author conclusions: On a long term AMS 8-00 is a viable option to treat USI in men with SCL

1

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sidi AA, Reinberg Y, Gonzalez R. Comparison fo artificial sphincter implantation and bladder neck reconstruction in patients with neurogenic urinary incontinence. The Journal of Urology. 1987; 138: 1120-1122	Prospective cohort study 2 groups: 1 treated with sphincter implantation and other with bladder neck reconstruction. No mention of randomisation – likely this was an observational study of what was done routinely.	27	Inclusion:Children with neurogenic sphincteric incontinence as determined by urodynamic evaluation. Sphincter group mean age (range) 17.2 (5-44) and mean years of follow up 5.7 (1-12) years. Comparison group mean age (range) 16.3 (4-27) and mean years of follow up 3.2 (1-5) years.	Sphincter implantation (AS 800). (n=16). 2/16 had concurrent augmentation cystoplasty.	Young-Dees-Leadbetter operation (n=11). 9/11 had concurrent augmentation cystoplasty.	1-12 years	Incontinence Reoperation rate	Not stated

Results:

	Sphincter implantation	Bladder neck surgery
Postoperative Incontinence score – scored from 1 to 5, with 1=total incontinence (or dry < 2 hours), 2= stress and/or night incontinence, dry 2-4 hours, 3= stress and/or night incontinence, dry >4hrs, 4= minor stress incontinence and/or night dampness, dry >4 hrs, 5= continent day and night, dry > 4 hours) [mean(sd)].	3.62 (0.7)	3.72 (0.9)
Reoperation rate	Unknown the count of patients	5 patients required 9 operations. These

	requiring implantation, but 24 operations in total were required for this group. These were for improving continence, changing malfunctioning devices and removing eroded sphincters.	included repairs of neourethral strictures or obstructions, revisions of the bladder neck tube and 2 artificial sphincter reimplantations. Of these, ione remained dry and the other had to undergo prosthesis removal because of infection.

Author conclusions: Although an equal degree of continence was achieved with both procedures, the reoperation rate was significantly higher in patients who underwent artificial sphincter implantation.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Simeoni J, Guys JM, Mollard P, Buzelin JM, Moscovici JM, Bondonny JM, Melin Y, Lortat-Jacob S, Aubert D, Costa B, Galifer B and Debeugny P. Artificial urinary sphincter implantation for neurogenic bladder: a multi-institutional study in 107	Retrospective observational study, covering 10 pediatric surgery departments in France.	107	Inclusion: children with neurogenic bladder. Exclusion: previous implanted of a AUS, no follow up data ior achievement of continence without activation of the AUS. 74 boys and 33 girls, age range 8-18 9mean 13.7). Underlying causes of the neurogenic bladder were myelomeningocele (92), sacral agenesis (9), medullary lipoma (2), acquired causes (4).	The AS 800 was used. The pre-vesical approach used in 98 patients and the perineal approach in 9. Inflatable cuff placed around the bladder neck in 98 patients and around the bulbar urethra in 9.	Pre versus post test	Mean 5 years	Incontinence Adverse events	Not stated

children. British journal of Urology 1996; 78: 287-293								

Results:

	Pre-treatment	Post-treatment
Incontinence Total Severe (no definition) Totally continent	 100/107 7/107 0/107	 44/107
All adverse events Death Mechanical problems with prosthesis Mechanical problems with prosthesis requiring surgical correction Need for removal of prosthesis Need for surgical revision		9/107 0/107 63/107 20/107 26/107 29/107

Author conclusions: For successful implantation of of an artificial urinary sphincter in children, the pre-operative bladder capacity must be sufficient and previous surgery should bot have been performed on the bladder neck.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Singh G, Thomas DG. Artificial urinary	Retrospective observational study.	90	75 male and 15 female patients with neutropathic bladders. Age range 13-62 (mean 26). 71 congenital (mostly meningomyelocele) and 19 aquired	AUS alone implanted in those with good capacity (>350ml) and compliance (n=38). In patients with hyper-reflexia	Pre vs post	Mean 4 years (range 1-10)	Incontinence Adverse effects	Not stated

sphincter in patients with neurogenic bladder dysfunction. British Journal of Urology 1996; 77: 252-255.			cord lesions. 66 had "intermediate-type" bladder activity and 24 had acontractile bladders.	and/or low compliance a combined cystoplasty and AUS implantation was performed (n=52). For these combined operations the balloon and control valve were added in a second minor operation 6-12 weeks after the first. Pump activated 2-4 weeks after the operation. 8 had the AMS 792 and the other 82 had the AMS 800. Early on in the series the cuff was implanted around the bladder neck but later cuffs were placed around the membranous urethra.				

Results:

	Pre-treatment	Post-treatment
Incontinence	90/90	7/90 (at last follow up, but some had required repeat surgery)
Adverse effects		
Infection		6/90
Erosion		7/90
System fail		8/90
Pump fail		2/90
Sheered tube		1/90
Rectal perforation		1/90
Bladder perforation		1/90
Intermittent catheterisation		70/90
Need for re-operation		25/90
Bulbar conversion		7/90
Higher pressure balloon		6/90

Smaller cuff Third operation		2/90 10/90

Author conclusion: A rate of continence >90% was achieved in these neurogenic patients after implantation of an AUS, and we recommend a simultaneous cystoplasty in patients with detrusor overactivity.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Spiess PE, Capolicchio JP, Kiruluta G, Salle JP, Bernardinicci G, Corcos J. Is an artificial sphincter the best choice for incontinent boys with Spina Bifida? Review of our long term experience with the AS-800 artificial sphincter. 2002; 9: 1486-1491	Retrospective observational study	30	Inclusion: Males under 19 who underwent insertion of the AS-800 for the treatment of urinary incontinence, and who attended follow up. All had congenital neurogenic bladder dysfunction secondary to Spina Bifida. Mean age was 12.6 (9-19 years). 5 had had previous attempts at surgical correction of incontinence – 4 had collagen injections and 1 had a bladder neck reconstruction. Anticholinergic medication was used in 21/30 prior to insertion and CIC in 22/30.	The AS-800 cuff was placed at either the bladder neck or the bulbous urethra at the discretion of the surgeon. Cuff size varied between 4 and 10cm, and the reservoir pressure varied between 51 and 80 cm H2O. Iliocystoplasty was performed prior to insertion in 1, during insertion in 3 and following insertion in 11.	Pre versus post-op	Range 36-177 months (mean 6.5 years)	Incontinence Adverse events	Not stated
Results:								

	Pre-treatment	Post-treatment
Incontinence at most recent follow up Completely continent (dry at least 4 hours) Slightly wet (some leaking but socially continent) Incontinent (patient felt it was socially unacceptable/ uncomfortable)		 19/30 6/30 5/30
Adverse events Revisions required Failure of device by last follow up Post-operative unilateral hydronephrosis		 17/30 5/30 6/30

Author conclusions: The AS-800 model artificial sphincter has a long term survival which rarely exceeds 8 to 9 years.

1

F.15 What is the efficacy of the ileal conduit diversion compared with usual care in neurological disease?

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Guillotreau J, Castel-Lacanal E, Roumiguie M et al. Prospective study of the impact on quality of life of cystectomy with ileal conduit urinary diversion for neurogenic bladder dysfunction. Neurourol Urodyn. 2011; 30(8):1503-1506. Ref ID: GUILLOTREAU2011A	Prospective observational study	N=48	Patients undergoing cystectomy with ileal conduit for neurogenic bladder dysfunction. Multiple sclerosis N=38, spinal cord injury N=7, spina bifida with myelomeningocele in one case and other neurological diseases in two cases Indications for surgery: febrile urinary tract infections 60.4%, chronic urinary retention or indwelling catheter in 54.2% of cases, urinary incontinence in	Procedures were carried out bylaparoscopyUretero-ileal anastomosis were performed over 8Fr ureteric stents using a Wallace I technique. The ileal loop was isolated on its mesentery, bowel continuity restored with staplers and mesenteric window closed.	Na	6 mths	SF 36 Qualiveen	None reported

			37.5% of cases, chronic kidney disease in 22.9% of cases and recurrent urethral bleeding secondary to urethral false passages in patients with indwelling catheter in 6.3% of cases. Mean age 50.6 yrs. Male 79%					

Effect

Qualiveen Quality of Life Scores and Index Before and 6 mths after surgery. SIUP specific impact of urinary problems. Mean (SD)

	Before (SD)	After (SD)	P
Limitations	1.55 (1.35)	0.57 (0.64	<0.001
Constraints	2.64 (1.12)	2.12 (0.83)	0.046
Fears	1.46 (0.91)	1.18 (0.75)	ns
Feelings	1.57 (1.33)	1.52 (1.04)	ns
SIUP	1.79 (0.95)	1.29 (0.65)	0.015
Quality of life	-0.39 (0.86)	-0.26 (0.75)	ns

Comparison of SF36-v2 Quality of Life Scores Before and 6 mths after surgery. Mean (SD). All not significant

	Before	After
Physical functioning	19.7 (10.7)	18.6 (10.4)
Role-physician	26.4 (12.9)	24.2 (10.5)
Bodily pain	38.2 (13.9)	40.5 (11.5)
General health	33.8 (8.9)	31.8 (8.6)
Vitality	36.8 (10.5)	36.9 (9.2)
Social functioning	37.9 (14.4)	32.6 (11.2)
Role-emotional	29.1 (17.4)	24.5 (17.0)
Mental health	38.0 (13.2)	36.3 (12.3)
Physical component summary	27.1 (8.7)	28.0 (7.9)
Mental component summary	40.5 (14.9)	35.4 (14.7)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chartier-Kastler EJ, Mozer P, Denys P, Bitker MO, Haertig A, Richard F. Neurogenic bladder management and cutaneous non-continent ileal conduit. Spinal Cord 2002; 40: 443-448	Retrospective observational study	33	The charts of 33 consecutive patients undergoing cutaneous non-continent ileal conduit surgery were reviewed. 19 women and 14 men. Mean age 40.6 (15.2) yrs. Mean history of neuro-urological disease was 16.1 (10.7) yrs 21 had SCI, 4 had MS, 3 myelitis, 5 CNS diseases. All unable to use CISC, and all incontinent. Indications for surgery were upper UTI protection, perineal dryness and for functional/social reasons.	Cutaneous non-continent ileal conduit surgery was performed alone for 19 patients and with cystectomy in 14. Midline incision made according to Bricker's description. Both ureters asastomosed and attached to the ileal conduit.	Pre to post comparison	Mean 48 months (range 12 to 240 months)	Perceptions of symptoms/ QoL Adverse events	Not stated

Results:

	pre	Post	p
Patient satisfaction/QoL		100% of patients satisfied with stomal appliances. Mean satisfaction score was 9.1 (2.8)/10. 0= worse than before with feelings of regret, 10=high level of satisfaction in terms of QoL	
Adverse events Mortality Stoma leakage Stoma ulceration Ureteral anastomosis Bowel obstruction Incisional hernia		 0/33 0/33 1/33 0/33 0/33 0/33	NA

Early			
Perioperative septic shock		1/33	
Uretero-ileal anastomosis leak		1/33	
Cystectomy wound hematoma		1/33	
Prolonged ileau		1/33	
Lower limb thrombophlebitis		1/33	
Late			
Permanent urethral leak		2/33	
Recurrent suprapubic collection		1/33	
Pyocystitis		4/33	
Re-op for shortened ileal loop		1/33	
Acute non-complicated pyelonephritis		4/33	
Extracorporeal shock wave lithotripsy for renal stones		1/33	

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
DeLong J, Tighiourt H, Stoffel J. Urinary diversion/reconstruction for cases of catheter intolerant secondary progressive multiple sclerosis with refractory urinary symptoms. The Journal of Urology 2011; 185: 2201-2206	Retrospective chart review study	In the study there were 26 patients, but only 4 underwent an ileal loop procedure. The other 22 underwent augmentation cystoplasty (n=7) or ileovesicostomy (n=15) which are not described	Secondary progressive multiple sclerosis patients with refractory urinary symptoms. EDSS score >4. Indications for surgery included refractory urinary incontinence, chronic symptomatic UTIs and/or catheter related complications. All had tried multiple pharmacological and conservative treatments. All had tried catheterisation prior to surgery but were not candidates for continued clean	An ileal loop conduit diversion was carried out. No details given in the paper.	Pre-post comparison	3 weeks, 3 months and every 6 months postoperatively. Mean follow up 16 months.	Adverse events	Not stated

		further here.	IC or indwelling catheterisation because of refractory symptoms, unfavourable physiology/anatomy and patient unwilling ness to continue with this modality. All patients (including those not having the ileal loop diversion) had: symptoms for 24 (10) yrs and mean EDSS of 7. But there is no baseline data appropriate to the ileal loop patients, apart from all patients undergoing ileal loop surgery having bladder capacity <100ml.					

Results:

Adverse events mortality Other adverse events reported	1/4

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Legrand G, Roupret M, Comperat E et al. Functional outcomes after	Retrospective case series	N=44 (9 drop-outs	Patients with multiple sclerosis who underwent cutaneous noncontinent urinary diversion.	Bricker procedure. Cutaneous diversion was	Pre-post comparison	6 mths then yearly	Quality of life - Qualiveen	None reported

management of end-stage neurological bladder dysfunction with ileal conduit in a multiple sclerosis population: a monocentric experience. Urology. 2011; 78(4):937-941. Ref ID: LEGRAND2011		for QoL outcome)	Median age 51 yrs, 6 men and 47 women. Clean intermittent catheterisation was impossible for this population, all patients suffered from urge incontinence, dysuria and recurrent cystitis or pyelonephritis	performed by midline incision and retroperitoneal cystectomy, when requested.				
Effect Mean (SD) Pre vs post (at last follow up) Discomfort 1.2 (0.71) vs 0.48 (0.48) p=0.01; Frequency of stress 2.52 (0.72) vs 2.21 (0.66) ns; Fears 1.31 (0.7) vs 1.04 (0.69) ns; Feeling 2.45 (1) vs 1.31 (0.98) p=0.01; Overall QOL 2.2 (1.18~) vs 1.16 (0.63) p=0.02; Health related quality of life 1.1 (0.31) vs 0.06 (0.61) p=0.03								

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Smith HP, Russell JM, Boyce WH, Alexander E. Results of urinary diversion in patients with myelomeningocele. Journal of Neurosurgery 1979; 50: 773-778	Prospective observational study	46	Children with myelomeningocele undergoing urinary diversion at a North American hospital from 1959-1976. 20 boys and 26 girls. Age range 18 months to 19 years. Lumbosacral level of myelomeningocele in 21, lumbar in 11, sacral in 6, thoracolumbar in 6 and thoracic in 2. All but 2 had had their myelomeningocele treated with excision and closure. Prediversionary management included Credes in 24% and spontaneous or incontinent voiding in 100%. Neurological status was flaccid paraplegia in 28,	An ileal conduit was performed in 43, sigmoid in 2 and transverse colon in one. Ileal conduits were normally supplied with 2 vessel arcades.	Pre-post comparison	12 for 1-4 years, 17 for 5-10 years, 11 for 11-15 years and 4 for > 15 years. 2 were lost to	Adverse events	Not stated

			flaccid paraparesis with hip flexors in 8, weak lower leg muscles with neurogenic bladder in 5, sacral anaesthesia or decreased rectal sphincter tone with neurogenic bladder in 3, and neurogenic bladder only in 2.			follow up review.		

Results:

Adverse events	
Death	0/46
Ureterocutaneous fistula / ureterileal stenosis / subphrenic abscess	1/46
Electrolyte imbalance and acidosis	2/46
SURGICAL COMPLICATIONS	
Stenosis of stoma	2/46
Pyocytosis	1/46
Bilateral ureteroileal stenosis with stones	1/46
Unilateral ureteroileal stenosis with Hydronephrosis	1/46
Leaking distal ureter	1/46
Herniation of loop	1/46
Renal calculi < 5yrs post op	4/46
Renal calculi > 5yrs post op	6/46

1

2

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kato H, Hosaka K, Kobayashi S, Igawa Y, Nishizawa O. Fate of tetraplegic patients managed by ileal conduit for urinary control: long-term follow-up. International Journal of Urology 2002; 9: 253-256.	Retrospective observational	16	Tetraplegic patients who underwent ileal-conduit formation over an 18 year period in Japan. 13 male, 3 female. Age range 19-70 (mean 46) years. All had cervical SCI. Pre-operatively managed by urethral or suprapubic catheter in 10 cases, IC by carers in 4 cases and tapping voiding in 2 cases.	Ileal conduit diversion. Conduit arranged in an isoperistaltic fashion, and a stoma was constructed in the skin of the right lower abdominal wall.	Pre versus post test comparison	2-17 years (mean 8.7)	Patient satisfaction Adverse events	Not stated

Results:

Patient satisfaction	"A few months after the operation....most patients were more satisfied with .....ileal condu formation than with their previous management"
Adverse events	
Death	3/16 [intestinal perforation (2yrs), repeated UTIs (8 years) and unknown(2 yrs)]
Stone formation after diversion in those with native bladders	5/11
Stone formation in those with prior cystectomy	0/5
Serious UTIs after stone formation	3/5
Pyocyst	8/13 (3 had had a cystectomy done at the same time as diversion)
Pyocyst requiring subsequent cystectomy	2/13

1

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Flanigan RC, Kursch ED, Persky L. Thirteen year experience with ileal loop diversion in children with myelodysplasia. The American Journal of Surgery 1975; 130: 535-538	Retrospective observational study	58	Children with myelodysplasia, with incontinence of urine, chronic UTI, progressive Hydronephrosis and/or abnormal renal function. All incontinent and 8 on continuous catheter drainage. 35 had chronic UTIs. 21 had moderate or severe hydronephrosis, but only 6 had uremia. Mean age 4.5 years (range 5 months to 13 years).	Ileal conduit surgery. The standard Bricker technique was used in earlier patients, but later patients used the Albert-Persky conjoined method of ureteroileal anastomosis.	Pre-test versus post-test.	1-13 years (mean 5 years)	Adverse events	Not stated

Results:

Adverse events	
Death	1/58 (non-renal, 8 months after ureteroileostomy)
Early complications	
Ureteroileal obstruction	3/58
Stomal obstruction	3/58
Stomal evisceration	2/58
Small bowel obstruction	1/58
Pyelonephritis	1/58
Strangulation of loop with peritonitis	1/58
Late complications	
Stomal obstruction	36/58
Stomal haemorrhage	8/58
Ureteroileal obstruction	6/58
Pyelonephritis	5/58

Pyocystis	4/58
Renal calculi	3/58
Small bowel obstruction	1/58
	In general early and late non-stomal complications were more frequent with the Bricker anastomosis (Early: 40% compared to 8%; Late: 15% compared to 5%) but these data were not analysed statistically.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Moeller BA. Some observations of 31 spinal cord injury patients on whom the Bricker procedure was performed. Paraplegia 1977-78; 15: 230-237.		31	SCI patients. Indications for diversion were recurrent UTIs with and without reflex, Hydronephrosis and/or deterioration of renal function. Exclusion: markedly incomplete central cord syndrome and all patients with known neoplasm	Bricker ileal conduit surgery	Pre-test versus post test	4.8 years	Adverse events	Not stated

Results:

Adverse events	
Renal insufficiency	4/31
Stones	4/31
Pelvilithiotomy	3/31
IVP	4/31
Death	2/31
Hydronephrosis	2/31
Hypertension	2/31
Pyelonephritis	2/31
Death	2/31

Stenotic ureter	2/31
CVA	1/31
Brain damage	1/31
Kidney excision	1/31
MI	1/31
Pneumonia	1/31
Nephrectomy	1/31
Ureteropyeloectasis	1/31
Caliectasis	1/31
Abdominal/renal thrombosis	1/31
pyohydronephrosis	1/31

F.16 Do prophylactic antibiotics reduce the risk of symptomatic urinary tract infections?

Children

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Clarke SA, Samuel M, Boddy SA. Are prophylactic antibiotics necessary with clean intermittent catheterisation? A	RCT. Random number table used for randomisation. No mention of allocation concealment. No placebo – those discontinuing received	85 entered the study. 4 lost to follow up and 28 excluded as did not comply with the randomisation. Thus 53 finished (37% drop-out rate) with 31 in the continuation group and 22 in the discontinuation group. No intention to treat analysis, nor any analysis of how those dropping out differed, was performed. The attrition bias in	Mean age in continuation group was 12.65 (2.1) and in the discontinuation group was 11.89 (2.3). All had a diagnosis of neuropathic bladder. The primary	The antibiotic used for prophylaxis was not described. It is implied that the patients were all already on prophylaxis with an un-named antibiotic, but this is not at all clear.	Discontinuation of prophylactic antibiotics.	4 months	Existence of a clinical UTI – 100,000 bacteria/cc urine plus fever, nausea, vomiting or abdominal pain. Such events were reported prospectively – ie patients were told	Not stated

randomised controlled trial. Journal of Pediatric Surgery 2005; 40: 568-571	nothing in place. Thus no blinding possible either.	this study was very serious, and might have led to a bias that could have explained the overall results seen (ie poor responders in the discontinuation group were not analysed after they had dropped out). However, it is stated that the 28 exclusions were due to parental refusal to comply with the randomisation, so it is possible that the exclusions may have occurred before the children even started discontinuation. However the paper is not very clear on this issue.	diagnosis in most was Spina bifida secondary to myelomeningocele. M:F ratio was 1.1:1 in the continuation group and 1:1.4 in the discontinuation group.				to contact their doctors if they experienced symptoms. A single symptomatic UTI was the end point for a patient in the study. One major drawback of this study was that the infection status of each group at onset was not recorded.	

Results: The high attrition rate and lack of any intention to treat analysis was a potential confounder. Although the groups were well-matched for age and gender, they differed in the manner of IC – more in the continuation group used non-self IC, which seemed to be associated with infection (though no independent effects of this were presented after analysis). So this could have been a confounder as well. It was stated that a multivariate analysis was performed, but no results describing any adjustments for such a confounder were given.

	Continuation of antibiotics	Discontinuation	p
Confirmed urine infection	20/31	3/22	<0.0001

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of fundin g
Zegers B, Uiterwaal C, Kimpen J, van Gool J et al.	RCT. Computer based randomisatio	176 randomised (88 to each group). None	All patients with Spina Bifida at two children's hospitals who were performing CIC and using low dose chemoprophylaxis (LDCP) during the preceding 6 months.	Continuation of LDCP. This meant continuation	Discontinuatio n of LDCP.	18 month s	Existence of a clinical UTI – significant bacteriuria	Not stated

<table>
<tr>
<td>Antibiotic prophylaxis for urinary tract infections in children with spina bifida on intermittent catheterisation. The Journal of Urology 2011; 186: 2365-2371</td>
<td>n, with concealed allocation. Stratification for age (younger/older than 3 years), gender and participating centre. No use of placebo purposely, to mimic effects of ceasing prophlaxis in clinical practice, and also because it would have been difficult to make different and convincing placebos for all the varying drugs used. But blinded outcome evaluation was used.</td>
<td>were lost to follow up. In the continuation group, none changed treatment. In the discontinuation group, 38 returned to LDCP. However an ITT analysis was used, and these patients were retained into the discontinuation group. Hence zero attrition after ITT.</td>
<td>Exclusion was for refusal of GP / carer consent, language barrier or use of LDCP for <6 months.

Baseline characteristics: None differed between groups.
<table>
<tr><th></th><th>Continuation</th><th>Discontinuation</th></tr>
<tr><td>age</td><td>8.7(6.7)</td><td>9.4(5.9)</td></tr>
<tr><td>males (%)</td><td>42</td><td>45</td></tr>
<tr><td>% overactive detrusor</td><td>31.4</td><td>35.3</td></tr>
<tr><td>% overactive sphincter</td><td>22.1</td><td>25</td></tr>
<tr><td>bladder capacity</td><td>280(161)</td><td>270(143)</td></tr>
<tr><td>mean number UTIs in year before study</td><td>1.82</td><td>1.88</td></tr>
</table>
</td>
<td>of whatever regime the patients were already prescribed, and these included trimethoprim, nitrofurantoin, cefuroxim, co-trimoxazole or a combination. Dosages and types were allowed to differ between patients.</td>
<td></td>
<td></td>
<td>(>10,000 cfu/ml urine; positive reading of leukocyturia on dipstick; clinical symptoms such as increasing incontinence, foul smelling/cloudy urine, with or without fever >38.5C.</td>
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</table>

Results:

	Continuation of antibiotics	Discontinuation	p
Confirmed urine infection during 18 months FU	2/88	4/88	0.42

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Johnson HW, Anderson JD, Chambers GK, Arnold WJD, Irwin BJ, Brinton JR. A short-term study of Nitrofurantoin prophylaxis in children managed with clean intermittent catheterisation. Pediatrics 1994; 93; 5: 752-755	Double blind randomised placebo controlled cross-over study. Cross-over design flawed by lack of ensuring sterility of urine on the second arm (ie placebo or Rx). No mention of randomisation method or allocation concealment.	56. 4 dropped out during treatment but intention to treat principle used.	Inclusion: Children with neurogenic bladder secondary for meningocele, initially free from symptomatic or asymptomatic infection, managed by IC, with surgically closed meningocele, normal renal function and no additional urologic abnormalities. 12 boys and 17 girls, of mean age 12.3 years. A cross-over design so no need for baseline comparison.	Nitrofurantoin (25mg 1xpd for those weighing 12.5-25kg, and 50mg for those weighing >25kg). This was taken for 12 weeks, followed by the placebo; or vice versa for the other randomised group. Patients were allowed to take a 2 week break (for any vacations) within the trial. Compliance with meds assessed with a monthly interview and pill count.	Placebo (matching appearance)	24 weeks	Clinical infection, defined as occurrence of at least one of – flank or abdominal pain, pyrexia, or incontinence.	Not stated

Results: Used a paired t test for cross-over data, but tested for homogeneity of variance.

	Nitrofurantoin	placebo	p
Symptomatic UTIs	4/56	2/56	Not given

2

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schlager TA, Anderson S, Trudell J,	Double blind cross-over placebo	15 completed the study	Inclusion: Children aged 2-18 years with neurogenic bladder receiving CIC 4x	5 months of nitrofurantoin taken 1xpd nightly (50mg	See intervention	11 months	Incidence of symptomatic infections	Not stated

Hendley JO. Nitrofurantoin prophylaxis for bacteriuria and urinary tract infection in children with neurogenic bladder on intermittent catheterisation. The Journal of Pediatrics 1998; 132: 704-708.	controlled trial. No mention of randomisation or allocation concealment. 4 week wash-out period used.	(1 dropout due to torsion of ovarian cyst)	per day with a normal renal US and living at home. Children were not excluded if they had previously been receiving antibiotic prophylaxis, but were required to discontinue any existing prophylaxis 2 weeks before commencing the study. Children continued to be treated by their doctor as normal during the study, and any prophylaxis (or placebo) was temporarily discontinued during treatment of UTIs. 10 female, 5 females. 14 myelomeningocele and 1 traumatic SCI.	tablet if >25 kb body weight, and 25mg tablet if <25kg body weight). 4 weeks washout before receiving the placebo for 5 months. The order of nitrofurantoin and placebo was decided randomly, and patients and those administering drugs were blinded.			Adverse events	

Results: Failure to account for cross-over design in the analysis, using Fisher exact test.

	Nitrofurantoin	Placebo	p
Number of patients developing symptomatic UTI infection	8/15	11/15	0.048
Adverse events Carriage of klebsiella/pseudomonas	140/330 weeks of carriage	43/330 weeks of carriage	0.00004

1 **Adults - new SCI cases**

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Anderson RU. Prophylaxis of bacteriuria during	RCT. Use of a randomisation table to assign groups. No	64, divided into 4 groups.	Inclusion: SCI patients referred to a specialist centre within 30 days of injury. Sterile urine at onset	Nitrofurantoin (100mg 1xpd); nitrofurantoin (100mg 1xpd) with or	Sterile IC only (usual care); genitourinary irrigant (intravesical neomycin/polymyxin	Unclear but probably > 45 days	Symptomatic UTI.	Not stated

intermittent catheterisation of the acute neurogenic bladder. The Journal of Urology 1980; 123:364-366	mention of allocation concealment. No mention of blinding.		of study. Intermittent catheterisation done by trained technicians. Patients catheterised every 4 hours to keep balder volume <500ml.	without 4 ampules of genitourinary irrigant (intravesical neomycin/polymyxin B [160mg neomycin, 800,000 units of polymyxin B per litre of sterile water] injected into the bladder after each IC. Any episodes of significant bacteriuria were treated with an appropriate systemic antibiotic for 5 days (both groups), and the nitrofurantoin was ceased during this period, but intravesical irrigant was continued.	B).	for most.		

Results:

	Nitrofurantoin	nitrofurantoin plus genitourinary irrigant	Sterile IC only (usual care)	genitourinary irrigant only	p
Symptomatic UTIs	1/15	0/16	0/16	0/17	Not given

<table>
<tr><th>Reference</th><th>Study type</th><th>No. pts</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr>
<td>Gribble MJ, Putterman ML. Prophylaxis of urinary tract infection in persons with recent spinal cord injury; a prospective, randomised, double-blind, placebo-controlled study of Trimethoprim-sulphamethoxazole. The American Journal of Medicine 1993; 95: 141-152.</td>
<td>Double blind placebo-controlled randomised trial. Computer-generated randomisation performed. Randomisation stratified for sex and level of baseline bacteriuria, and in blocks of 8. Stated that the randomisation code was not broken until data collection and entry were complete, but this does not completely confirm or ensure true allocation concealment (one person must always have the key to the code, and</td>
<td>131 randomised. 2 placebo subjects resumed spontaneous voiding and so were excluded. 66 randomised to the TMP prophylaxis group and 62 to the placebo group.</td>
<td>Inclusion:
Acute SCI 30 days or less prior to enrolment; neurogenic bladder dysfunction; commencement of IC 72 hours of less prior to enrolment; sterile urine at enrolment (but not enforced as inevitable that some would have some baseline bacteriuria); >18years.
Exclusion:
Known hypersensitivity to TMP, elevated serum creatinine and transaminase levels and pregnancy.

Baseline characteristics (all NS)
<table>
<tr><th></th><th>TMP (n=66)</th><th>Placebo (n=60)</th></tr>
<tr><td>age</td><td>36 (18-79)</td><td>31 (18-64)</td></tr>
<tr><td>M:F</td><td>57:9</td><td>52:8</td></tr>
<tr><td>Quad: Para</td><td>33:33</td><td>26:34</td></tr>
<tr><td>Concurrent major injuries</td><td>17</td><td>25</td></tr>
<tr><td>Duration of IC (days)</td><td>11 (1-29)</td><td>11 (1-29)</td></tr>
<tr><td>Bacteriuria</td><td>33</td><td>30</td></tr>
</table>
</td>
<td>Trimethoprim-sulphamethoxazole (TMP) 40mg given once daily at 10am, and continued until IC was discontinued, or until discharge, or a maximum of 16 weeks.</td>
<td>Identically administered placebo.</td>
<td>Up to 16 weeks</td>
<td>Counts of definite symptomatic bacteriuria, and possible symptomatic bacteriuria.
Adverse events</td>
<td>Not stated</td>
</tr>
</table>

	it is not stated that this person was not involved in allocation to groups).		<table><tr><td>before randomisation</td><td></td><td></td></tr><tr><td>Time on study (wks)</td><td>9 (1-16)</td><td>9 (1-16)</td></tr><tr><td>Total study weeks</td><td>612</td><td>580</td></tr></table> Study was prematurely discontinued in 25 TMP subjects and 19 placebo subjects, but there were no significant differences between groups for each category of reasons for discontinuation.				

Results:

	TMP	Placebo	p
Definite symptomatic bacteriuria	4/66	19/60	P values only reported for males and females separately in the paper
Possible symptomatic bacteriuria	16/66	24/60	ditto
Adverse events			Not given
Epididymo-orchitis	0/66	1/60	
Skin and soft tissue infections	15/66	20/60	
Bacteraemia arising from non-urinary sources	2/66	1/60	
Clostridium difficile diarrhoea	1/66	0/60	
Prolonged and unexplained fever	1/66	0/60	
Severe skin rash	2/66	1/60	

Neutropenia Development of resistant bacteriuria after 3 years FU	2/66 47/66	3/60 45/60	

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lindan R, Joiner E. A prospective study of the efficacy of low dose nitrofurantoin in preventing urinary tract infections in spinal cord injury patients, with comments on the role of pseudomonas. Paraplegia 1984; 22: 61-65	Trial, but unclear if it was randomised, as no mention of randomisation at all.	60	SCI patients. 36 Cx, 13 Tx, 11 Lx. 49/60 male. 45/60 <20 years. Mean time from injury to study entry was 44 days. Groups not well matched (control group were older, more male, more lower spine injury).	50mg nitrofurantoin every 12 hours	No prophylaxis (no placebo)	Mean was 11.8 weeks	Symptomatic UTI - fever and leukocytosis, in the presence of bacteriuria. Adverse events	Not stated

Results:

	Nitrofurantoin	No prophylaxis	
Symptomatic UTIs	1/31	1/29	No statistical tests done
Adverse events Pseudomonas colonisation	 23/31	 17/31	 No statistical tests done

2

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-	Outcome measures	Source of funding

						up		
Maynard FM, Diokno AC. Urinary infection and complications during clean intermittent catheterisation following spinal cord injury. The Journal of Urology 1984; 132: 943-946.	RCT. No mention of randomisation method. No mention of allocation concealment.	50 completed the study, but no mention of how many were randomised. 27 were in subgroup B, which is the only subgroup relevant to this review (see intervention column for explanation)	Patients with SCI who were <6 months post trauma at baseline. Sterile urine was ensured by a pre-study course of antibiotic if any infection was found. All were on clean IC. 27 quadriplegics and 23 paraplegics. 27 complete and 23 incomplete lesions. 32 men and 18 women. Age not given, but almost certainly adults.	Oral 80mg trimethoprim with 400m sulphamethoxazole (TMP/SMX) daily [or 100mg Nitrofurantoin daily if allergic to TMP/SMX]. IMPORTANT: A subgroup (A) in each group also received a 10 day course of therapeutic antibiotic of choice for all episodes of laboratory and clinical infections. The other subgroup (B) only received the 10 day course for any symptomatic infections. Since sub-group A would be less likely to produce symptomatic infections on that regimen (as many pre-clinical infections showing up as asymptomatic bacteriuria would have been treated) that without treatment of asymptomatic infections, the results from that subgroup have been excluded from the first table below. Hence results in the table 1 only relate to the subgroup B, who only received prophylactic/control treatment until the end point of clinical infection. Results in table 2 give insight into the effects of two different strategies – treating when evidence of asymptomatic /symptomatic UTi was found versus treating only when	No antibiotics(no placebo given)	Average of 50 days	Symptomatic UTI infection – 1) temperature >100F orally plus >100,000 org/ml urine or pyuria (>25 WBC per high power field), 2) urethritis, or 3) other signs of abdominal or pelvic irritation. Adverse events	Not stated

				symptomatic UTI was found. This therefore contains all the subjects.				

Results:

TABLE 1.

	TMx/SMP or nitrofurantoin	No prophylaxis	
Symptomatic UTI EPISODES	1	7	
Estimate of Symptomatic UTI COUNT	1/12	5-7/15*	
Adverse events			
Allergy to TMP/SMX	0/12	0/15	
Heamaturia	1/12	0/15	
Bladder stones	0/12	0/15	

*the number of patients suffering clinical UTIs was 11 across all 4 subgroups, but there were 13 separate episodes. But for each subgroup the data given was the number of episodes! We know that one episode means one person (as more than one patients cannot share 1 episode and 0 patients can't have any!) so we know the TMX/SMP count for the B subgroup (1/12). In the other 3 groups there is uncertainty. In the no prophylaxis subgroup B we could therefore have between 5 and 7 patients experiencing the 7 UTIs given. 7 is the maximum number of people as you cannot have 7 infections amongst 8 infected people (and would imply that no one had >1 infection in that subgroup, and that all the multiple infections occurred in the other 2 subgroups). 5 is the minimum, as that would be the number needed to make 11 people with an infection in total if the remaining 2 subgroups had not had anyone having > 1 infection. So we could regard a figure of 5/15 as a conservative estimate of a count that can be used in a meta-analysis.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Mohler JL, Cowen DL, Flanigan RC. Suppression and treatment of urinary tract infection in patients with an	RCT. Use of a random number table to assign patient to the prophylactic Rx (n=25) and placebo (n=21) groups. No mention of allocation concealment.	47	Inclusion: All adult patients admitted to a SCI rehab service, managed on admission by IC (or for whom IC would seem to be the Rx of choice) and with anticipated stays of >1 month, were considered.	Nightly tablet of 160mg Trimethoprim with 800 mg Sulfamethexazole given as prophylaxis.	Identical placebo tablet.	Mean 56.1 days	Infection rate of symptomatic UTI (38C fever, any symptoms or signs of a UTI, with +ve urine culture and WBC	Not stated

intermittently catheterised neurogenic bladder. The Journal of Urology 1987; 138: 336-340	This aspect of the study was double-blinded. There was a further randomised splitting of both groups in terms of whether 1) any infection (n=19) or 2) only symptomatic infections (n=27) were treated (twice the prophylactic dose). Those in the original placebo group were treated with the real medication once found to have an infection. The final randomised splitting concerned the length of treatment (NB not prophlyaxis) – 3 (n=28) or 10 (n=18) days of antibiotic. It was stated that the distribution of patients originally randomised to the active prophylaxis and placebo groups was "identical" across the 2 subsequent groupings, though in reality it seems that there was merely no statistically significant difference.		36 men, 10 women. Mean age 35.7 yrs. 14 Cx (12 complete quadriplegia); 5 T1-T6; 13 T6-T12; 9 Lx At hospitalisation 35 were managed by IC. 6 voided independently, but were incontinent (3 of those required condom catheter drainage, the other 3 having no urological management). The other 5 had had a Foley indwelling catheter in situ for 7-56 days, after which IC was initiated. During the study, all patients were managed by sterile IC. 37 had no Hx of UTI, 6 had had 1 infection and 3 had had 2 or more. 4 patients had received chronic suppressive antibiotics and 3 had had medication to control detrusor instability. All had sterile urine at admission, or entrance into the study was delayed until it was.	For treatment of established infection (symptomatic or asymptomatic) then twice daily treatments were given.			count >10,000/cc).	

	No drop outs reported after inception.							

Results: Results appropriate for meta-analysis were not provided. The comparisons of 3 days vs 10 days and symptomatic vs symptomatic and asymptomatic relate to the second part of the guideline question.

	Active prophylaxis with Trimethoprim/Sulfamethexazole	Placebo	p
Infection rate of symptomatic UTIs (infections/100 days at risk)	1.11	1.86	0.15

1

2

3

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sandock DS, Gothe BG, Bodner DR. Trimethoprim-sulphamethoxazole prophylaxis against urinary tract infection in the chronic spinal cord injury patient. Paraplegia 1995; 33: 156-160	RCT. No mention of randomisation method used.	43	Inclusion Patients with SCI hospitalised in a specialist rehab centre. All were previously on prophylactic Trimethoprim-sulphamethoxazole (TMP-SMX). Exclusion Hospital stay < 3 months, antibiotic therapy for febrile illness other than UTI, peri-operative antibiotics, TMP-SMX allergy or intolerance. Baseline characteristics (sig diff for age, but NSD for all others) Prophylaxis (n=20) / Discontinuation (n=23) age: 46 / 58.3 Male: 20/20 / 23/23 C1-C7: 13 / 12	Continuation of TMP-SMX prophylaxis (TMP 80mg combined with SMX 400mg daily)	Discontinuation of prophylaxis. No placebo given.	Up to 7 months	Symptomatic UTI was defined as a measure of 105 org/cc urine combined with any of fever, pyuria, malodorous urine, suprapubic pain, lethargy, and increasing autonomic dysreflexia.	Not stated

			T1-T6	1	5				Levels of bacterial resistance	
			T7-T12	4	3					
			Lx	2	3					
			Time from injury (yrs)	9.2	14.9					
			Time on study (months)	5.9	7					
			Using IC	15	6					
			Reflex voiding	2	7					
			Indwelling catheter	3	7					
			Suprapubic catheter	0	3					

Results:

	Prophylactic	Discontinuation	p
Number of symptomatic UTIs per week	0.043	0.035	NS
Cultures resistant to TMP-SMX (%)	42.5	37.5	NS

1 **Adults - prior to urodynamics**

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Darouiche RO, Smith MS, Markowski J. Antibiotic	Double blind RCT. No mention of randomisation method or	46 enrolled. 6 missed follow up, but no intention to	Inclusion: Patients hospitalised at a specialised SCI unit. Exclusion:	500mg of Ciproflaxin orally 2x per day. Given 2 days	placebo	18 months, but unclear	Symptomatic UTI defined as 108 org/L in association with at least	Not stated

<table>
<tr>
<td>prophylaxis for urodynamic testing in patients with spinal cord injury: a preliminary study. Journal of Hospital Infection 1994; 28: 57-61</td>
<td>allocation concealment.</td>
<td>treat was used. 18 prophylaxis, 22 placebo.</td>
<td>Patients receiving antibiotics for an infection or unable to give informed consent

Baseline characteristics (all NS)
<table>
<tr><th></th><th>Prophylaxis (n=18)</th><th>Placebo (n=22)</th></tr>
<tr><td>age</td><td>52.9 (18.3)</td><td>46.9 (13.2)</td></tr>
<tr><td>Male</td><td>18</td><td>22</td></tr>
<tr><td>Pre-procedure bacteriuria (>108 org/L</td><td>9</td><td>10</td></tr>
<tr><td>Pre-procedure pyuria (>107 WBC/L</td><td>8</td><td>9</td></tr>
<tr><td>Need for bladder catheterisation</td><td>12</td><td>14</td></tr>
<tr><td>Renal complications</td><td>2</td><td>6</td></tr>
<tr><td>Mean number symptomatic UTI in previous yr</td><td>0.7 (1.0)</td><td>1.4 (2.3)</td></tr>
</table>
</td>
<td>prior to urodynamic testing (aim of study was to assess the effect of prophylaxis on post-investigational infection).</td>
<td></td>
<td></td>
<td>one of: fever, leukocytosis, flank pain, suprapubic discomfort, change in voiding habits, nausea, vomiting, increase in muscular spasm.
Adverse effects</td>
<td></td>
</tr>
<tr>
<td colspan="9">Results:
<table>
<tr><th></th><th>Ciproflaxin</th><th>placebo</th><th>p</th></tr>
<tr><td>Symptomatic UTIs</td><td>0/18</td><td>3/22</td><td>0.24</td></tr>
<tr><td>Adverse events</td><td>0/18</td><td>0/22</td><td>1</td></tr>
</table>
</td>
</tr>
</table>

1 **Adults - established neurological cases with recurrent UTIs**

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Biering-Sorensen F, Hoiby N, Nordenbo A, Ravnborg M, Bruun B, Rahm V. Ciproflaxacin as a prophylaxis for urinary tract infection: prospective, randomised, cross-over, placebo controlled study in patients with Spinal Cord Lesion. The Journal of Urology 1994; 151: 105-108	Prospective, randomised, cross-over, double blind placebo controlled study. Randomisation carried out in blocks of 4. No details of randomisation method given. No details of allocation concealment given. 1 patient is reported to have dropped out. The paper states that "Drop outs were substituted with subjects belonging to the same group". This statement is very unclear, and the extent to which attrition bias was limited or avoided is therefore unclear, but as the dropout rate is <25% this is not a major problem. No washout period described.	22	Inclusion: Age >18 yrs, neurogenic bladder dysfunction due to SCI/cauda equina lesion, a history of recurrent symptomatic UTIs (at least 3x in the past year or 2x in the past 3 months). No significant bacteriuria (>10,000/cc) at entry to the study (though of course at cross-over this could not be assured, especially with no reports of a wash-out period). 18 men and 3 women. Median age at entry: 38 years (range 19-73 years). Median duration of SC lesions was 16 years (range 1 to 31 years). One patient was respirator dependent (complete C1). There were also 2 C4, 4 C6, 2 C7, 1 T2, 3 T4, 1 T7, 2 T10 and 5 L1. In 11 cases lesion was complete. Mean number of symptomatic UTIs per patient in the past 12 months was 5.8 (maximum 14). Bladder emptying methods included suprapubic tapping (n=8), abdominal pressure (n=5), suprapubic tapping, abdominal pressure and IC (n=1), suprapubic tapping and IC (n=2), IC (3), abdominal pressure and IC (n=1) and suprapubic tapping and abdominal pressure (n=1).	100mg ciprofloxacin (each patient was treated with this continuously for 6 months, as well as 6 months continuously on the placebo, the order decided by randomisation). Both given after last bladder emptying at night. Symptomatic UTIs were treated during the study with another antibiotic (in both groups).	See intervention	12 months	Bacterial cultures on mid stream urine were done at 1 month intervals, before treatment, during treatment and whenever a symptomatic UTI was suspected. The end point of the study was the number of treated symptomatic UTIs. Adverse events	Not stated

Results: Unclear statistical methods, and failure to account for cross-over design in the analysis. No counts of patients affected available (unless stated).

	Ciproflaxin	Placebo	p
Number of symptomatic UTIs needing treatment with microbial agents	5	59	<0.00005
Clinical adverse events Laboratory abnormalities Resistant e-coli to cipaloflaxin	0 3 patients showed low Hb values, 2 showed elevated WBC, but all returned to normal during the study. 1	0 0 reported	None given

1 ## Adults – neurogenic bladder clinic cases

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Duffy L, Smith AD. Nitrofurantoin macrocrystals prevent bacteriuria in intermittent self-catheterisation. Urology 1982; 20: 47-49	Double blind cross-over study. Allocation concealment and blinding were rigorous, but no mention of the randomisation procedure.	31	Neurogenic bladder patients with sterile urine at inception. Self catheterising. 28 mean and 3 women. 6 had condom drainage devices. 15 were taking oxybutynin to control urgency and 2 were taking imipramine hydrochloride for nocturia.	100mg 2xpd of nitrofurantoin macrocrystals. Switch to placebo after 3 months	Identical tablet. See intervention.	6 months	Bacterial resistance	Not stated

Results: Unfortunately there is very poor reporting of symptomatic infection, with the only reference being: “symptoms of urinary tract infection were rare, and no patient required hospitalisation. A few complained of mild flank pain unaccompanied by fever, and 3 patients who usually were continent leaked urine”. This cannot be analysed, and gives no useful information about the efficacy of the antibiotic in preventing symptomatic infections. No details of statistical tests used, so unclear if cross-over design accounted for.

	Nitrofurantoin (n=31)	placebo (n=31)	p

Resistant cultures* to nitrofurantoin (resistant/(resistant+sensitive))	2/4	5/21	NS
Resistant cultures* to TMP/SMX (resistant/(resistant+sensitive))	2/4	4/22	NS
Resistant cultures* to carbenicillin (resistant/(resistant+sensitive))	1/4	4/21	NS
Resistant cultures* to aminoglycosides (resistant/resistant+sensitive)	0/4	0/21	NS

F.17 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services?

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Davies H, Rennick J, Majnemer A. Transition from pediatric to adult health care for young adults with neurological disorders: parental perspectives. Canadian journal of neuroscience nursing. 2011; 33(2):32-39. Ref ID: DAVIES201	Observational qualitative study of interviews with parents. Member checking took place through a follow up telephone phone call to five parents who had participated in the interviews. Triangulation was used through the use of field notes, transcriptions, member checks and review with	N=17 parents of 11 young people	Parents of young adults with a complex chronic neurological condition and intellectual impairment.	This study aimed to elicit 1) parents' perceptions of transition of health care from pediatric to adult services 2) what facilitated or hindered these parents' perceptions	None	NA	Patient experience	None reported

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
1	the authors							
Effect Parents reported: Sense of abandonment by the health care system. Parents felt they had received little, if any, preparation for the eventual transition from the pediatric health care setting to the adult health setting. Some pediatric services provided referrals to specialists in the adult setting while others did not. There was limited discussion about the process in the year preceding the transition, and it was generally only at their young adult's last appointment in the pediatric setting that future care was discussed. When a specific referral was not provided, the parents felt abandoned, as the onus was on them to locate adult specialists. There was a gap between two months and two years between their young adult's last pediatric appointment and their first appointment in the adult setting. Fear and uncertaintly during transition. Parents were fearful of the unknown in relation to the availability of appropriate services to address the multifaceted needs of not only the young adult, but the needs of the family, as well. Facilitating transition from the pediatric to adult health care system Establishing relationships within the adult health care setting. Parents felt a tremendous sense of relief following their first appointment with the adult health care professional. They felt reassured that they had begun the process of developing new relationships Parental resourcefulness. Seven parents spoke about their informal support network that they used to help guide them through the process of transition. Family support system. The availability of others within the family to share household responsibilities was perceived as important by all parents Factors perecieved to hinder transition from pediatric to adult health care Inadequate resources, insufficient coordination, compromised parental health, vulnerability of the young adult								

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sawyer SM, Collins N, Bryan D, Brown D, Hope MA, Bowes G. Preliminary report.	Pilot trial of a transistion strategy involving semi-structured interviews to measure the outcome. No	10. Convenience sample from 404 young people with spina bifida aged >18. .	Young spina bifida patients, aged >18 yrs who were not linked to any adult health service. Mean age was 22 yrs. 5 used a wheelchair full time, whilst the rest used callipers/wheelchair. 3 had neurological shunts in situ	A pilot programme, facilitated by a transition co-ordinator, to transfer paediatric patients with spina bifida to the adult setting. A comprehensive case file was assembled by the transition co-ordinator. This	None	Pre and post-transfer interviews were conducted with the subjects,	Semi-structured interviews with the subjects were carried out before and after the transfer. These were aimed at eliciting:	Not stated

Young people with spina bifida: transfer from paediatric to adult health care. J Paediatr. Child health 1998; 34: 414-417.	mention of any attempts to avoid selection bias (ie in terms of selecting those who might respond favourably). No mention of any methods to optimise trustworthiness of the interview data, such as triangulation. No mention of the qualitative analysis methods used (ie thematic analysis)		and 6 were incontinent of urine. 2 had attended a special school while 8 had attended regular school. 4 were studying part-time, 4 in supported employment, one performed voluntary work and one home duties. 9 lived at home with parents, one of these with her partner too. Although most were able to manage their own care independently, almost all relied on parents for psychological support.	included: Transfer summary record Inpatient clinical summaries Operation notes Radiological reports Special investigations Original radiographs The co-ordinator also presented a case presentation to the adult medical centre to where they would be transferred. An initial assessment by the adult medical centre was also carried out by a nurse in the patient's own home. Finally a review was carried out by the medical team at the adult centre.		but it is unclear how long after transfer the post-transfer interviews occurred.	Their expectations of the adult care Their level of satisfaction with the transfer process	

Results:

Patient satisfaction	Pre-transfer interviews suggested anxieties about leaving paediatric care, focussed around concerns about leaving familiar and trusted health care professionals and clinical environments, and about having to meet and develop rapport with, new health professionals. There were specific fears about how well the medical record would be passed to the adult facility. Post-transfer interviews showed there were 3 main sources of dissatisfaction: Time delay between planned transfer date and actual date, which was up to 3 months in 5 cases The assessment and review were regarded as insufficient, and it was believed that the prospect of the annual review was not as good as the paediatric service Uncertainty about future care at the adult institution

1

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Osterlund CS, Dosa NP, Arnott Smith C. Mother knows best: medical record management for patients with spina bifida during the transition from pediatric to adult care. AMIA 2005 symposium proceedings 2005: 580-584.	Observational qualitative study involving focus groups and structured interviews. Grounded theory was used as the analysis technique. High quality methods, using triangulation of findings from 3 investigators. Limitations were that the parents involved represented the most enabling and proactive section of this population	Convenience sample of 6 patients drawn from 34 eligible patients.	Young adults aged 18-21 receiving comprehensive care at a regional referral centre for people with spina bifida and spinal cord injury. 4 male and 2 female patients took part. Also recruited were 6 family members and one private home nurse. The authors stated that highly motivated and high cognitively functioning patients were over-represented in the sample.	There was no real intervention here, but discussion was more about the perceived benefits of better medical record management during transition. So this was less a study about the effects of good medical record management during transition, and more about how the lack of good medical record management would be likely to adversely affect care after transition.	None	Not stated	Patient experience	Not stated

Results:

Patient experience	Patients felt that primary care physicians and school were not good at maintaining records that would be helpful in the transition process. They also saw their parents as essential in managing their records. There was also the perception that no healthcare provider had the whole story of their case. Parents felt that the best documentation of the care their children had received was carried in their own heads, and worried that once their children took over independent responsibility for their own care they would not have this information. The patients were aware they did not carry such detailed memories of all the necessary information as their parents. Parents thus felt compelled to make their own written care records. Medical forms were felt inadequate to capture the rich detail of a true case. Parents felt that they were not given adequate access to their own official medical records, although they felt this should be their right. They

	were enthusiastic about the concept of on-line records that they could access. They felt that having access to certain information, such as a baseline CT scan, would save much time and stress when going to hospital during emergencies, or when away from home. Parents felt that sharing of information between institutions was inadequate, and they often felt that they were the only ones capable of initiating and facilitating that sharing. No patients reported access to transition notes. In summary, parents were most concerned that since medical providers all had incomplete records, with poor communication between them, their children would have to take on the responsibility of managing the information that they, as parents, had painstakingly, memorised and documented. The authors recommended that: Research into electronic health records, and how they could utilise the position of parents as the central information manager, should be carried out. Efforts should be made to help parents transition the information management role to their children Internet accessible records would be very useful Future medical information systems could learn from current parental information strategies.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lotsein DS, McPherson M, Strickland B, Newacheck PW. Transition planning for youth with special health care needs: results from the National survey of children with special health care needs. Pediatrics 2005;	Observational questionnaire study (USA).	5533, taken from a larger nationwide sample of 38,886 children with special health care needs.	Inclusion: Initially, samples of 373,000 children in each of all 50 US states were screened, and 750 Children with special health care needs (CSHCN) were sampled in each state, making a total of 38, 866 CSHCN between 0-17 years. The questions relevant to transition were only asked of those aged 13-17 years, and,	This study aimed to elicit information about the experiences of transitional services already in use. In addition it looked at the existence of a "medical home" – "an approach to providing continuous and comprehensive primary pediatric care from infancy through young adulthood". Criteria for having a medical home	None	NA	Receiving guidance and support in the transition to adulthood. Shown by answering yes to these 3 questions: 1. Have your child's doctors or other health care providers talked to you or your child about how his/her health care needs might change when he/she becomes an adult? 2. Has a plan for	Not stated

115: 1562-1567			furthermore, of a sub-section recruited later. Hence only 5533 were asked the transition questions.	were: Having a usual source of care Having a personal physician or nurse Having no problems obtaining referrals or effective care co-ordination when needed. Having received family-centred care			addressing these changing needs been developed with your child's doctors or other health care providers? 3. Have your child's doctors or other health care providers discussed having your child eventually see a doctor who treats adults?	

Results: having a medical home increased the odds of meeting the goal of getting guidance and support in transition more than twofold [adjusted OR: 2.1 (1.6-2.8)]

	Existence of a medical home	No medical home	
Receiving guidance and support in the transition to adulthood	20.1%	11.4%	adjusted OR: 2.1 (1.6-2.8)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Fiorentino L, Phillips D, Walker A, Hall D. Leaving paediatrics: the experience of service transition for young disabled people and	Qualitative study, using semi-structured interviews (30 mins – 4 hrs). Thematic analysis of transcribed scripts undertaken. No mention of techniques to optimise trustworthiness. A	50 young people with disabilities. 28 were interviewed independently, 16 were interviewed alongside their carer, and for 6 the interviews were	Physically disabled young people from the Sheffield area aged 16-24 years. They were not to have learning difficulties. The patients were divided into 4 groups: Those attending a special school for people with physical disabilities (n=8) Those attending a special school for people with physical and some learning disabilities (n=16) Those attending mainstream schools	The aim of this paper was to describe the procedures already in place to facilitate the transition from child and paediatric services to adult services.	None	NA	Patients and carers perceptions about transition services.	Not stated

their family carers. Health and Social care in the Community 1998; 6: 260-270.	focus group was later used to discuss the findings and policy recommendations.	conducted with the carer and not the young person. 159 eligible young people were identified, and the 109 who did not take part were excluded because of refusal, inability to trace them, or they did not fulfil the inclusion criterion of a physical but not learning disability.	(n=17) Those attending an integrated unit within a mainstream school (n=9)					

Results:

Patient/carer perceptions	None of the young people felt that transition to adult services was smooth. The perception of problems was greater for the carers than the patients, the latter often lacking interest in their health. Carers often felt disturbed by the perceived reduction in service quality and quantity after transition, and the authors suggested that transition should be handled sensitively and gradually. Many young people were also often expected to contact their new consultants independently, which was, in the authors' opinion, often not done through disinterest, lack of confidence or moving away from the area. Often young people were unaware of the name of their new consultant. Carers also felt that this excluded them from the care process. One important feeling was that information about transfer was not communicated smoothly. Children from special units within mainstream schools seemed to have a smoother transition in that those from mainstream schools without a special unit: the former had better continuity of care, and less loss of services such as physiotherapy, and this was attributed by the authors' to being networked better into the services system.

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2

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Reiss JG, Gibson RW, Walker LR. Health care transition: youth, family and provider perspectives. Pediatrics 2005; 115: 112-120	Exploratory qualitative study in 9 cities in South-eastern and mid west USA, involving 30 focus groups, of 60-90 minutes length. Separate focus groups were used for patients, families and health care providers (10 each). There were also individual interviews for 1 young person, and 3 providers. After the focus groups, content analysis was used. Only 1 researcher performed the thematic codings, but the authors' claimed a consensus method was used.	143, consisting of youths and young adults (49), family members (44) and health care providers (50), drawn from 20 states. 81 were white, 56 black, 5 other and 1 mixed/biracial. Health providers were mostly RNs (25), followed by SWs (9) and MDs (7).	Youths and young adults were required to be 13-35 yrs, to have a chronic disability, and to have had treatment initiated before the age of 18. Family members had to have a child who fitted the inclusion criteria, but those children did not have to be in the study. Health care providers had to have knowledge of the transition procedures.	Experiences and perceptions about the transition practices already in use in this area were sought, with the aim of eliciting information that would inform good practice.	NA	NA	Patient, carer and health care provider perceptions	Not stated

Results:

Patient, carer and health care provider perceptions	Cognitive deficits were viewed as making transition even harder, so attention should be given to any cognitive deficits for transfer to work optimally. If a disease were progressive and prognosis were poor, patients should be allowed to stay in paediatrics. Preparatory steps should be taken early to prepare children for the adult world, and specifically for being an adult patient. In the earlier years this should involve asking the parents about their future wishes and desires for the child, thus instilling a sense of the child as on a pathway to adulthood, and thus affirming the importance of teaching independence. Later, children should be given tasks to develop independence and self-care. Transition should be based on maturity, not always age. Adult service providers were often perceived as lacking knowledge about the condition relative to the paediatric provider. Pediatrics was seen as patient and family centred, and warm, but adult care was seen as "quick and dirty" and disease centred. In particular , parents often felt disenfranchised which limited their ability to share important information with providers. There was perceived to be poor communication between the paediatric and adult services. A lack of trust on the part of paediatric providers concerning the ability of adult providers to maintain the progress thay had generated was also evident. There should be a chance for the paediatric provider and the patient/family to say goodbye and to mark the important stage with some kind of rite of passage. Otherwise there is a sense of abandonment that may aggravate negative feelings towards the new provider. Pediatric and adult care are thought to represent two different philosophies, each with their advantages and disadvantages. The need for them to work together was emphasised.

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Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Duke NN, Scal PB. Adult care transitioning for adolescents with special health care	Cross-sectional telephone interview study.	18,198 parents/guardians. These were self identified as knowledgeable about their child's health and care needs. There was	Parents/guardians of youth aged 12-17 years, with special health care needs. This includes allergic disease, congenital disorders and developmental/behavioural conditions.	Medical Home. This is a conceptual framework of care, comprising: 1. Family centred partnerships, 2. Community based systems, such as co-ordinated care networks for the promotion of wellbeing for children and their families.	Higher values of FCC (>3.6) were compared to lower values (< 3.6)	NA	Continuity of Care; has the care provider: Reviewed future health needs? Encouraged	Not stated

needs: a pivotal role for family centred care. Matern child health J 2011: 15: 98-105		a response rate of 56.1%.		3. Transitions – uninterrupted health care services during the move from child to adult services, 4. Appropriate funding to finance all aspect of the Medical Home. Family centred care (FCC): This is a measure of the extent to which the ideal medical home was approached. It is a measure of the visit time adequacy, provider listening quality, provider sensitivity to family issues, receipt of necessary health information, partnering in an adolescent's care, and the presence of interpreting services, if appropriate. This was converted into an overall continuous variable score. There was a regression analysis of the relationship between the outcome measures and FCC values, adjusting for potential confounders.			taking responsibility for care? Transfer to adult providers?	

Results:

	FCC
Reviewed future health need?	OR: 2.3 (2.07-2.57); p<0.001 [Higher levels of FCC led to a 2.3x increased odds of future health needs being reviewed]. Adjusted for all demographic confounders, as well as UCC (a usual place of routine care and a personal provider)
Encouraged taking responsibility for care?	OR: 3.93 (3.51-4.40); p<0.001 [Higher levels of FCC led to a 3.9x increased odds of being encouraged to take responsibility for care]. Adjusted for all demographic confounders, as well as UCC(a usual place of routine care and a personal provider)
Transfer to adult providers?	OR: 1.63 (1.38-1.92); p<0.001 [Higher levels of FCC led to a 1.63x increased odds of transfer to adult providers being arranged]. Adjusted for all demographic confounders, as well as UCC(a usual place of routine care and a personal provider)

Author comment: Family centred care may be the mechanism through which providers are able to address health care transitioning issues for youth with special needs.

1

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Scal P, Ireland M. Addressing transition to adult health Care for Adolescents with special health care needs. Pediatrics 2005; 115: 1607-1612	Cross-sectional interview study (USA).	4332, taken from a larger nationwide sample of 38,886 children with special health care needs.	Inclusion: Initially, samples of 373,000 children in each of all 50 US states were screened, and 750 Children with special health care needs (CSHCN) were sampled in each state, making a total of 38, 866 CSHCN between 0-17 years. The patients in this study were those aged 14-17 years. Hence only 4332 were included.	Health Care Transition. The main explanatory variable in this regression analysis was the Parent provider interaction. This was assessed with 5 questions: how often the providers spent enough time, listened carefully, was sensitive to family values, provided enough information, and made the patient feel like a partner in care. The score form the 5 questions were summed, with a higher score denoting a better parent-provider interaction. Other explanatory variables in the model were demographic and socioeconomic data, and illness severity and complexity.	NA	NA	Receiving guidance and support in the transition to adulthood. Shown by answering yes to these 3 questions: 1. Have your child's doctors or other health care providers talked to you or your child about how his/her health care needs might change when he/she becomes an adult? 2. Has a plan for addressing these changing needs been developed with your child's doctors or other health care providers? 3. Have your child's doctors or other health care providers discussed having your child eventually see a doctor who treats adults? A composite variable representing the adequacy of addressing HCT was created as the sum of the scores on these questions (1= yes, 0=no). Thus the score ranged from 0-3.	Not stated
Results: Linear regression modelling showed a significant relationship between higher provider-parent interaction and higher score of the outcome variable (Regression co-efficient =0.0831, t =7.24, p<0.001) after adjustment for potential confounders. Other significant correlates of outcome were female gender, age and the number of needed services.								

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Stewart DA, Law MC, Rosenbaum P, Willms DG. A qualitative study of the transition to adulthood for youth with physical disabilities. Physical and occupational Therapy in pediatrics 2001; 21: 3-20	Qualitative study, using semi-structured interviews. Focus group interviews were also used. A thematic approach was used on the transcripts. Triangulation and member checking were used to optimise trustworthiness.	Recruitment was from rehabilitation centres in the Ontario area. 34 were interviewed. Data collection ended at saturation. 21 were youth (10 women); 12 were parents (11 mothers); 1 service provider was also interviewed.	Inclusion: Age range 18-30 years; final year or completed high school; physical disabilities; some carers or parents as well. Mean age was 23.2. 54% were women. Main diagnoses were Cerebral Palsy (43%), SCI (10%), Spina Bifida (7%) and head injury (4%). 10 participants had non-neurological conditions, including Muscular Dystrophy, RA, congenital amputation and other deteriorating syndromes (some possibly neurological ,but unclear). Disability varied from total functional dependence (32%) to complete independence (7%). 21.5% could walk independently, and 29% had attended University. 11% were in paid work.	Experiences and perceptions about the transition practices already in use in this area were sought, with the aim of eliciting information that would inform good practice.	NA	NA	Patients and carers perceptions about transition services.	Not stated

Results:

A common theme was the perception that the transition process left patients feeling like they had been left at the edge of a cliff, with a gulf separating them from adult services. There was a feeling of doors being shut, being dropped and feeling cut off. It was felt too abrupt, often when the patients were not ready for it.

In consequence, most respondents wanted the opportunity to build their own bridges between the pediatric and adult services. To do this they needed the help and support of others to assist them in communicating their needs, asking for assistance appropriately and making decisions. This was felt especially important since many had not, because of their condition, had the opportunity to develop these skills throughout childhood.

It was also perceived that service providers should communicate better with each other to improve service co-ordination. Negative attitudes from service providers were also seen as negative.

The participants suggested the following changes to transition services:

- Involve patients and their families in the planning and delivery of transition services
- Shift the focus of services from therapy to supports, including information, advocacy and education, peer support, and sharing knowledge
- Provide individualised services in the local community
- Start early to help a young person develop the skills and supports to lead a full life

- Improve co-ordination and communication among community services
- Share service providers' knowledge and expertise to guide and support the person in transition.

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Young NL, Barden WS, Mills WA, Burke TA, Law M, Boydell K. Transition to adult-oriented health care: perspectives of youth and adults with complex physical disabilities. Phys Occup Ther pediatr 2009; 29:345-61	Qualitative study, using semi-structured interviews. One RA conducted interviews for the patients, and a separate one conducted interviews for the primary carers. The constant comparative method was used between the two interviewers and 2 other investigators. No mention of techniques to optimise trustworthiness.	15 youths and 15 adults with neurological conditions, as well as their primary caregiver.	Patients: Youths aged 15-20 yrs, adults aged 25-33 yrs. Patients had CP (n=13), Spina Bifida (n=9) and acquired brain injuries of childhood (n=8).3 subjects from each category were severe. 5 of the youths had not yet started transition, 3 youths were in the process of transistion and 7 youths and 15 adults who had completed transition. Caregivers: usually parents of the above	Experiences and perceptions about the transition practices already in use in this area were sought, with the aim of eliciting information that would inform good practice.	NA	NA	Patients and carers perceptions about transition services.	Not stated
Results: The main challenges occurring in transition were: Lack of access to health care. In particular the concern was in the loss of access to healthcare providers with whom a relationship had been built up, and who had a historical knowledge of the condition. The sense of being left in the dark, with no knowledge of what health care was available for access out there, was expressed . Lack of professional's knowledge. Adult providers were often viewed as having little relevant knowledge or training, who seemed afraid of treating people with								

disabilities.

Lack of information provided. Many felt that information from someone who knew how the system worked, would have been helpful. Transistion co-ordinators were suggested.

Uncertainty about transition. Many did not know what to expect.

Two solutions were identified:

- Early provision of detailed information. Some youths wanted information to be directed at them and not just their parents. Some felt that the pediatric clinicians should give the information. Those who had already been through transition stated how helpful more information would have been in terms of knowing what to expect and what was available.
- More extensive support throughout the clinical transition process. Again, a transition co-ordinator was suggested. There was also talk of support to help shift the role of advocate from parent to child

1

F.18 Does provision of information about the management of neurological lower urinary tract dysfunction improve patient outcomes?

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Cardenas DD, Hoffman JM, Kelly E, Mayo EM. Impact of a urinary tract infection educational program in persons with spinal cord injury. J Spinal	RCT. Very long 5-6 month baseline period before randomisation, wherein pre Rx data on urine infection and symptoms were collected. No blinding reported. No mention of method of	58 randomised. 2 dropped out after randomisation – 1 from each group. Unclear reasons for withdrawal. 30 randomised to the patient information group and 28	Inclusion: SCI of > 6 months duration; self reported Hx of recurrent UTIs; no plan to change bladder drainage in study period; at least 18 yrs of age. Exclusion: Upper tract abnormalities; renal/bladder calculi; significant bacteriuria Baseline characteristics (only those followed up included): NSD detected for characteristics below but the treatment group had higher UTI incidence at baseline.	Patient information. This consisted of: 1. Provision of the Bladder management Resource Notebook; 2. Self administered tests of bladder management;	Usual care	5 or 6 months	Episodes of symptomatic UTI (defined by urine culture, WBC in urine and 1 self reported symptom).patients were given a list of 17 symptoms to help them know what the symptoms of a UTI would be. Baseline symptomatic UTIs were recorded	Grant from the National Institute on Disability and Rehabilitation Research, USA.

<table>
<tr>
<td>Cord Med. 2004; 27:47-54</td>
<td>randomisation or allocation concealment</td>
<td>to the control group. No ITT performed.</td>
<td>
<table>
<tr><th>Characteristic</th><th>Treatment group (n=29 after 1 drop out)</th><th>Control group (n=27 after 1 drop out)</th></tr>
<tr><td>Age</td><td>40.6 (13.5)</td><td>41.5 (11.0)</td></tr>
<tr><td>male</td><td>22</td><td>20</td></tr>
<tr><td>Cervical</td><td>17</td><td>17</td></tr>
<tr><td>Thoracic</td><td>11</td><td>9</td></tr>
<tr><td>Lumbar/sacral</td><td>8</td><td>8</td></tr>
<tr><td>ASIA impairment score
A
B
C
D</td><td>
20
7
1
1</td><td>
15
8
2
2</td></tr>
<tr><td>Duration SCI yrs</td><td>13.2 (11.8)</td><td>9.7 (7.2)</td></tr>
<tr><td>Non white</td><td>3</td><td>5</td></tr>
<tr><td>>high school</td><td>25</td><td>22</td></tr>
<tr><td>IC</td><td>17</td><td>16</td></tr>
<tr><td>indwelling</td><td>6</td><td>5</td></tr>
<tr><td>Condom</td><td>5</td><td>6</td></tr>
<tr><td>spontaneous</td><td>1</td><td>0</td></tr>
</table>
</td>
<td>3. Counselling on IC technique and fluid management after nurse evaluation of catheter technique and fluid intake/output;
4. Discussion with the physicians on UTI symptoms, the processes of seeking medical Rx for a symptomatic UTI and problems in accessing Rx;
5. A follow-up 15-20 minutes telephone call after the final visit by the nurse to discuss any final questions.

A single educational session lasting</td>
<td></td>
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<td>prospectively during a 5 or 6 month run-in period. Post intervention symptomatic UTIs were recorded prospectively during a 5 or 6 month follow up. (In the latter 2 years of this 5 year long project, the run-in and follow up periods wee shortened from 6 months each to 5 months each)

Health beliefs questionnaire to evaluate perceptions of UTIs.

Multidimensional health locus of control questionnaire, to measure the degree to which the patient perceives him/herself to have control over the situation.</td>
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				2-2.5 hours was also described but it is unclear if this was additional to the above, or related to 4. Also, visits are mentioned but it is unclear when or how long these visits were, and whether these were additional to the interventions described above.			Self efficacy questionnaire, to assess the belief someone has that they can carry out a specific UTI prevention task.	

Results: All incomplete and inappropriate for GRADE

	Information	Usual care	p
Symptomatic UTI (by episodes not participants)	Baseline 41; follow up 32	Baseline 27; follow up 26	Trend for a lower incidence of UTIs in the Rx group (p=0.097), after ANCOVA, with baseline values as a covariate
Health beliefs questionnaire	no data provided	no data provided	Increased perception of severity of UTIs in the Rx group, after ANCOVA (p=0.042)
Multidimensional health locus of control	no data provided	no data provided	Trend for higher locus of control in the Rx group, after ANCOVA (p=0.066)
Self efficacy questionnaire	no data provided	no data provided	Decreased self-efficacy in the Rx group, after ANCOVA (p=0.033)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hagglund KJ, Clark MJ, Schopp LH, Sherman AK, Acuff ME. Consumer-assistant education to reduce the occurrence of urinary tract infections among persons with spinal cord injury. Top Spinal Cord Inj Rehabil 2005; 10: 53-62.	Non randomised trial.	60. 37 to the intervention group and 23 to the control group. Assignment to groups was made on a non-random geographical basis. The two locations chosen were evaluated for similarity of population base, urban/rural clientele and educational characteristics, though results of this are not given.	Inclusion: Diagnosis of SCI, use of a wheelchair for primary mobility, use of personal assistance services (PAS), willingness to complete the study. Mean age 39 (12.9) yrs. 74% were men. 47% reported needing at least a moderate amount of help with ADLs. Average use of PAS was 8 years. Subjects had spent an average of 6.8 days in hospital and 1.2 visits to the ER during the previous 12 months. No baseline characteristics given specific to each group.	6 hour PAS training workshop. The workshop addressed: prevention of common secondary conditions, and was chaired by a SCI physician, who provided information on preventing and treating pressure sores, UTIs, spasms, and autonomic dysreflexia. There was also information on bowel and bladder programs, general nutrition and weight loss strategies. Bladder management topics include types of catheters, proper insertion techniques, sterilisation and handling of reusable catheters, and signs of infection. UTI prevention was discussed with an 8 minute video.	No intervention	6 months	Telephone interviews were conducted before and 6 months after the workshop (unclear, but the control group also appeared to have a 6 month period in between baseline and follow up interviews). These interviews contained questions adapted from the Client Questionnaire. This included: Assistance needed with activities of daily living, and UTIs in the past 6 months	Not stated

Results:

	Information	control	p
Assistance required with activities of daily living	No data provided	No data provided	
UTIs in the past 6 months	Baseline 70%; FU: 40%	Baseline 76%; FU 76%	<0.02 for group effect at 6 months

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Anderson TP, Newman E, Dryja R, Price M. Urinary tract care: Imoprovement through patient education. Arch Phys Med rehabil 1983; 64: 314-316	Non-randomised trial, using two cohorts of patients treated at different times: 1975 and 1979. Although no attempts were made to match the groups, they were reportedly similar in terms of age, sex, proportion of quadriplegics and types of drainage used.	75. 21 patient who had participated in the intervention programme (1979 data) and 54 who hadn't (1975 data).	SCI patients. No other information given. No baseline measures available.	A training program of discussion periods followed by practical workshops. During the rehabilitation phase the patients attended 5 classes of 45 minutes each, on the topics of urinary tract care anatomy and physiology; bacteriology and UTI; monitoring urinary tract, including danger signs and prevention; modes of urinary drainage, disinfection and appliance care; and trial of voiding and intermittent catheterisation. In addition an instruction manual was developed for the patients and their families, who were also invited to join the teaching sessions. Patients were expected to follow the information and advice at home.	An earlier cohort of patients who did not receive an educational programme.	6 months (post discharge)	Symptomatic UTIs, and these data were elicited via a telephone interview. No criteria for being symptomatic are given.	Not stated

Results: Both groups had a similar level of bacteriuria at 6 month follow-up (48% confirmed in controls and 52% confirmed in education group), but differed in terms of symptomatic UTIs as follows:

	Education	No education
Symptomatic UTI at 6 month follow up	6/21 (29%)	37/54 (68%)

1

Reference	Study type	No. pts	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Barber DB, Woodard FL, Rogers SJ, Able AC. The efficacy of nursing education as an intervention in the treatment of recurrent urinary tract infection in individuals with spinal cord injury. SCI Nursing 1999; 16: 54-56	Prospective observational single-group study.	17	Patients at an out-patient SCI clinic with a history of 2 or more UTIs (see definition in outcome measures column), and no additional risk factors for UTI such as increased intravesical pressures and the presence of renal calculi. All patients were using clean intermittent catheterisation, with or without concomitant external condom catheter.	Intensive counselling by the clinic nurse with respect to proper CIC technique, daily external condom catheter application and care, appropriate cleansing of supplies with dilute sodium hypochlorite solution and daily perineal hygiene. Sessions lasted 15-30 minutes. If the patient continued to exceed the threshold of 2 or more UTIs in the following 6 month period then they were either given further intensive counselling sessions, or placed on antibiotic therapy, and this was decided by patient choice (though antibiotic therapy was the default).	The post intervention UTI count was compared to a set threshold (<2 UTIs/6 months period) to define efficacy.	6 months +	UTI, defined as Symptomatic bacteriuria (malaise, foul smelling urine, genital or suprapubic pain, epididymitis, gross hematuria, temperature > 99.5F, increased spasticity), or Bacteriuria with a WBC count > 12,000 Significant pyuria (>20 leukocytes/high power field) A positive outcome was defined as <2 UTIs per 6 month period.	Not stated
Results: 6 months: UTIs dropped from >2 /6months pre-intervention to <2/6 months post intervention after one intervention: 3/17 positive outcomes > 6 months: UTIs dropped from >2 /6months pre-intervention to <2/6 months post intervention after multiple interventions: 8/14 further positive outcomes Overall: 11/17 positive outcomes NB: The 6 “non-responders” may well have responded after multiple interventions, but opted for antibiotic therapy, so it is not possible to know if they would have								

eventually responded. The 11/17 positive outcome figure after multiple interventions is thus a conservative figure.

F.19 For patients and their carers with lower urinary tract dysfunction associated with neurological disorders, what are the experiences of access to and interaction with services, that address these issues?

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
van der Eijk M, Faber MJ, Al SS et al. Moving towards patient-centered healthcare for patients with Parkinson's disease. Parkinsonism and Related Disorders. 2011; 17(5):360-364. Ref ID: VANDEREIJK2011	Qualitative study (focus groups)	N=60	Patients and informal caregivers with Parkinson's disease. Hoehn and Yahr 1 to 3 (all living independently) Patient population: Patients N=40, informal caregivers N=20, female: male 25: 35, mean age 62 yrs, yrs since diagnosis mean 6	Focus groups ranged between 4 and 10 in size (mean 8). Separate group meetings for patients and informal caregivers. Each group lasted approximately 2 hrs. An independent moderator accompanied all focus groups by asking open-ended questions	Not applicable	Not applicable	Experiences of services	Dutch Ministry of Health, Welfare and Sport
Effect Themes Emotional support, empathy and respect Patients and informal care caregivers both expressed the need to be instructed how to cope with the disease in light of the changing roles in their relationship and								

maintaining their job as long as possible. Patients wanted to be treated with respect and taken seriously, Paying attention to the 'person behind the disease' and providing customised care to individual preferences were greatly appreciated. Involvement and support of the informal caregiver was felt to be necessary in order to prevent overburdening.

Knowledge of Parkinson's disease treatment among caregivers

Participants desired to be treated by healthcare providers with specific, adequate knowledge of and experience in Parkinson's disease (PD). According to patients, late recognition of early symptoms and delayed referrals by the general practioner were major problems. Patients who were supported by a specialised Parkinson nurse endorsed their great importance for the treatment.

Involvement in decision making and respecting patients' preferences

Many patients and informal caregivers expressed a desire to be actively involved, and to be able to participate in shared decision making with their professional caregivers. However, they identified a current lack of information to do so. Patients also valued the freedom to request a second opinion, and to self-select their professional caregiver or institution.

Continuity and collaboration of caregivers

Several PD patients identified the lack of multidisciplinary collaboration and communication between healthcare providers as an important bottleneck. They wanted therapists to plan multidisciplinary consultations periodically, where patients would be discussed as a group and informed of the outcome afterwards.

Healthcare accessibility

Participants underscored the importance of a brief access time prior to consultation with their doctor, and the need to have easy access to interim telephone and mail contact. Patients also raised the suggestion for follow-up by telephone whenever medication was changed, to monitor for possible side-effects. The perceived access to hospital care increased considerably by the presence of a specialised nurse in the department.

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Wollin J, Bennie M, Leech C et al. Multiple sclerosis and continence issues: an exploratory study. Br J Nurs. 2005; 14(8):439-440. Ref	Qualitative study (mail survey)	N=11 (phase 2)	Phase 1: Non-random, self-selected sample of English speaking men and women aged 18 yrs and over, living in south-east Queensland, Australia. All participants had a confirmed diagnosis of	Not applicable	Not applicable	8-10 weeks after seeing the continenc e adviser	Impact of intervention on continence	Multiple Sclerosis, Australia

ID: WOLLIN2005			MS. Phase 2: Participant who met with the continence advisor					

Effect

Has your continence status changed since consulting the continence adviser?

Eight participants reported their continence status had improved. Comments included 'problems have eased', 'reassured', 'reduced infections' and 'less accidents'

Have your bladder issues changed since visiting the continence adviser?

Seven of the 11 participants reported that their issues were less troublesome and four stated they were the same

Have your lifestyle activities changed since visiting the continence adviser?

Five participants reported an improvement in most of the variables with six participants reporting no change in lifestyle activities. The one variable that did not improve was 'feeling tired'. The strongest result was an increase in 'self confidence' with six participants reporting an improvement

1

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Davies, A. and Ekers, M. (2010). Quality Neurology http://www.csupport.org.uk/care-professionals/toolkit-professionals/Quality%20Neurology%20Final%20Report%20(Revision%20Aug%202010).pdf	Qualtative study (focus groups)	6 focus groups	Patients and carers with neurological conditions	Not applicable	Not applicable	Not applicable	Experience of services	Funding: Research Initiative for Long Term Conditions, Dept of Health, Neurological Charities

Effect

Experience of staff groups – Neurologists

Those who did have check-ups with their neurologist described them as being very brief and offering no support or information, and only occasional drug reviews. There were a couple of instances of lack of flexibility within neurology services e.g., accessing services outside of their regular visits

Experience of staff groups – General Practioners

GPs were unable to be proactive in their support, relying on the patients to ask for specific treatments, or telling the person to return to their specialist for support. The lack of GP awareness did have particular consequences for some people, with a couple of people being prescribed drugs for other conditions that were not suitable for someone with a neurological condition, or which reacted to existing drugs. GP education was considered to be vital. Continuity of GP was highlighted as important.

Experience of staff groups – Specialist Nurses

Not everyone had access to specialist nurses, but those who did were very positive about them, finding it helpful to have support from someone who knew about the complexities of their condition.

Experience of staff groups – Specialist Teams

People's experiences of specialist teams was positive.

Access to services

Physical access

People reported difficulty physically accessing services e.g., parking was lacking.

Service availability

There were several people who had been helped by specific treatments which they no longer had access to.

Support groups

People talked about the benefit of support groups; findings them a good opportunity to discuss their conditions and a good source of information, friendship and a way of helping them cope with their illnesses

Continuity of care

People mentioned instances of lack of communication and co-ordination between services and that people became lost to services in the transition from child to adult services and also post 65.

Person-centred care

Very few people had care plans, although there was some confusion as to what constituted a care plan. Despite this a number of people felt that they were as involved as they wanted to be in their care. Not many people had a key worker or care co-ordinator but people said they knew who they would contact if their needs changed.

Carers and families

In most areas people said that their carers received little or no support. It was suggested that carers rarely knew they were also entitled to have an assessment of their needs, and were often unaware of the relevant allowances and benefits.

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Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Johnson J., Smith, P and Goldstone, L. (2001). Evaluation of MS Specialist Nurses: A review and development of the role. http://www.mstrust.org.uk/downloads/part2.pdf	Qualitative study (patient survey)	N=24	Patients with multiple sclerosis (MS) spanning the four disease phase/levels of disability (i.e. newly diagnosed, minimal impairment, moderate disability, severe disability) Patients were selected following randomized, stratified sampling from the database of MS patients held in neurology departments Two cohorts of n=12 participants Cohort 1: mean age 50.6 (range 37-67 yrs). Mean Barthel Index mean 16 (range 2 to 20), yrs since diagnosis 5 mths to 26 yrs Cohort 2: mean age 50.5 yrs (range 34 to 66 yrs). Barthel Index mean 14.4 (range 5 to 20), yrs since diagnosis 1 to 33 yrs	Not applicable	Not applicable	Not applicable	Experiences of services	None reported

Effect
The diagnosis, the time leading up to and following it, were for most a very difficult time, arousing strong emotions
Those who had had contact with the MS Nursing Service at or around the time of diagnosis, had found it to be very helpful in terms of both support and information given
Comparative data suggested the concept of “abandonment by the healthcare system” was a prominent feature before the establishment of an MS Specialist Nurse, was mitigated following her appointment
Further comparative data implied there was a growing awareness, contact with and access to the MS Specialist Nurse describing her as:
An ongoing source of support and information for people and their carers at subsequent phases of the disease and not just at diagnosis
An emotional resource for spouses or partners and other family members
Adviser to and educator of non-specialists such as GPs, hospital and community nurses and home care assistants
A “lynchpin” and link with other professionals, who was well placed to act as an overall service co-ordinator
GPs and hospital doctors featured as sources of help throughout the disease trajectory, although mixed experiences were reported
The availability of disabled friendly transport and easy access to public places was viewed as currently restricted but an essential source of help
Education for people with MS, the general public and their lay carers was viewed as very important
The role played by spouses or partners both at the time of diagnosis and later in terms of continued care and support, in some cases over many years, could not be overestimated
More general support for family carers was seen not to be required
Easier access for patients to specialist treatments and care, was said to be needed

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Appendix G: Evidence tables – economic studies

G.1.1 V. Kalsi, R. B. Popat, A. Apostolidis, R. Kavia, I. A. O. Odeyemi, H. A. Dakin, J. Warner, S. Elneil, C. J. Fowler, and P. Dasgupta. Cost-consequence analysis evaluating the use of botulinum neurotoxin-A in patients with detrusor overactivity based on clinical outcomes observed at a single UK centre. European Urology 49(3):519-527, 2006. 445

G.1.2 B. Wefer, B. Ehlken, J. Bremer, H. Burgdorfer, B. Domurath, C. Hampel, J. Kutzenberger, C. Seif, K. D. Sievert, K. Berger, and J. Pannek. Treatment outcomes and resource use of patients with neurogenic detrusor overactivity receiving botulinum toxin A (BTX) therapy in Germany. World Journal of Urology 28 (3):385-390, 2010. 448

1

1 V. Kalsi, R. B. Popat, A. Apostolidis, R. Kavia, I. A. O. Odeyemi, H. A. Dakin, J. Warner, S. Elneil, C. J. Fowler, and P. Dasgupta. Cost-consequence analysis evaluating the use of botulinum neurotoxin-A in patients with detrusor overactivity based on clinical outcomes observed at a single UK centre. European Urology 49(3):519-527, 2006.				
Study details	**Population & interventions**	**Health outcomes**	**Costs**	**Cost effectiveness**
Economic analysis: Cost-consequence analysis **Approach to modelling:** This analysis was conducted alongside an open-label prospective cohort study. **Perspective:** UK NHS **Time horizon:** Unclear; seemingly up to 26 months for the health outcomes;	**Population:** Patients with intractable overactive bladder and urodynamically-proven phasic or terminal detrusor overactivity (based on the definitions published by the International Continence Society) Patients with urodynamically-proven detrusor overactivity of either neurogenic (n=63) or idiopathic (n=38) origin were included Among neurologic patients, 65% had multiple sclerosis, while 14% had spinal injuries and 21% suffered from other underlying conditions. **Interventions:** ***1.BTX*** ***Neurogenic patients:*** 300 units of BoNT/A (BTX) in 30ml normal saline. Local anaesthetic gel was applied to the urethra and the BoNT/A saline solution was injected into the detrusor muscle in 20–30 separate injection sites (1ml per site) using a flexible cystoscope. Patients received oral antibiotic prophylaxis for three days starting immediately before treatment. At	***Neurogenic patients:*** - 25% of clinical improvement at 4 weeks in 84.1% of patients; after 16 weeks in 73.0% of patients - 50% of clinical improvement at 4 weeks in 76.2% of patients; after 16 weeks in 60.3% of patients - Mean time to re-injection (years): 1.438 (1.241-1.633) - Mean duration of clinical improvement (years): i) 25% improvement:	**Total costs:** Initial treatment: - Neurogenic patients: £874.62 - Idiopathic patients: £745.33 **Currency & cost year:** 2003/2004 UK pounds **Cost components incorporated (*see table 1 below*):** ***Neurogenic & Idiopathic patients:*** A) Preoperation: 15 mins initial consultation; 1 cystometry/urodynamics; 1 urinalysis; B) Intra-operation: BoNT/A (300 units for neurogenic; 200 units for idiopathic); saline (30ml for neurogenic; 20ml for idiopathic); 1 needle; 500ml saline irrigation; 30mins theatre	**Cost-effectiveness results:** ***Neurogenic patients:*** Cost per treatment year (cost ÷ time to re-injection): £609 **Sensitivity analysis:** Excluding the cost of BoNT/A, the largest cost components comprise theatre-time and pre-procedure urodynamics. If administering BoNT/A injections took 45 mins (50% longer than was assumed in the base-case scenario – 30mins), the cost of theatre-time would increase of £122. Additionally, at some centres, urodynamics and urinalysis may be conducted routinely on all patients referred to secondary care. This cost was removed from the base case (£130.17). Empirical data suggest that

1 V. Kalsi, R. B. Popat, A. Apostolidis, R. Kavia, I. A. O. Odeyemi, H. A. Dakin, J. Warner, S. Elneil, C. J. Fowler, and P. Dasgupta. Cost-consequence analysis evaluating the use of botulinum neurotoxin-A in patients with detrusor overactivity based on clinical outcomes observed at a single UK centre. European Urology 49(3):519-527, 2006.				
Study details	**Population & interventions**	**Health outcomes**	**Costs**	**Cost effectiveness**
immediate for cost analysis **Discounting:** N/A	follow-up outpatient consultations occurring 4 and 16 weeks after therapy, repeat injections were administered to patients reporting a loss of efficacy that was confirmed by urodynamic investigations. ***Idiopathic patients:*** 200 units in 20ml normal saline. ***2. Standard care*** Comprised of regular checkups in an outpatient setting every 6–12 months (including investigations such as: urinalysis, midstream urine specimen examination, urine cytology, urodynamics, voiding diaries and assessment of post-void residual volume by ultrasound, where appropriate). It was assumed that none of the patients had undergone surgery within the timeframe of the analysis	1.174 (0.941-1.408); 50% improvement: 0.942 (0.708-1.176) ***See table 4 below***	cost; Antibiotic prophylaxis (100mg trimethoprim bd for 3 days); C) Post-operation: 15mins specialist follow-up; 1 hour specialist nurse time; 1 urinalysis. Although previous studies have shown that treatment with BTX reduces the use of anticholinergic medication, NHS savings associated with reduced medication and continence aid usage were, conservatively, not included within the analysis. In addition, BTX may avoid or postpone the need for surgery in some patients, although such savings were assumed to fall outside the timeframe of this analysis. The use of catheters was also excluded from this analysis.	severe urge incontinence is associated with a utility score of 0.61 and that a 25% reduction in frequency produces a 0.11 improvement in utility, while preventing leakage and reducing frequency by 50% produces an improvement of 0.13. This suggests that BTX is likely to be a cost-effective treatment, potentially costing around ***£6,000 per QALY gained*** relative to standard care.
Data sources				
Quality of life data:				

1	V. Kalsi, R. B. Popat, A. Apostolidis, R. Kavia, I. A. O. Odeyemi, H. A. Dakin, J. Warner, S. Elneil, C. J. Fowler, and P. Dasgupta. Cost-consequence analysis evaluating the use of botulinum neurotoxin-A in patients with detrusor overactivity based on clinical outcomes observed at a single UK centre. European Urology 49(3):519-527, 2006.				
	Study details	**Population & interventions**	**Health outcomes**	**Costs**	**Cost effectiveness**
	O'Brien BJ, Goeree R, Bernard L, Rosner A, Williamson T. Cost-Effectiveness of tolterodine for patients with urge incontinence who discontinue initial therapy with oxybutynin: a Canadian perspective. *Clin Ther* 2001;23:2038–49. **Costs:** British National Formulary (BNF) No.49, March 2005); Department of Health reference costs database 2004; Personal and Social Services Research Unit (PSSRU) 2004; Average cost incurred/charged by the National Hospital for Neurology.				
	Comments				
	Source of funding: This project was funded by grants from the Multiple Sclerosis Society of Great Britain and Northern Ireland and Pfizer Inc. Allergan UK Ltd provided gratis BTX for research purposes and funded the data analysis. **Limitations:** Outcome data from a prospective cohort study with a high drop-out. Small cohort size. Only the cost of the initial intervention was calculated; short time horizon; potential effects of the intervention were not captured in the cost analysis (use of antimuscarinic medication, use of pads, surgeries, etc.). Cost per QALY calculation based on limited data.				
	Overall quality*: *Potentially serious limitations*	**Overall applicability**: *Partially applicable***			

1 *Very serious limitations/Potentially serious limitations/Minor limitations; **Directly applicable/Partially applicable/Not applicable.

2 Abbreviations: BoNT/A = Botulinum Neurotoxin-A; QALY = Quality-Adjusted Life-Years; NHS = National Health Service; UK = United Kingdom; NHS = National
3 Health Service.

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B. Wefer, B. Ehlken, J. Bremer, H. Burgdorfer, B. Domurath, C. Hampel, J. Kutzenberger, C. Seif, K. D. Sievert, K. Berger, and J. Pannek. Treatment outcomes and resource use of patients with neurogenic detrusor overactivity receiving botulinum toxin A (BTX) therapy in Germany. World Journal of Urology 28 (3):385-390, 2010.				
Study details	**Population & interventions**	**Health outcomes**	**Costs**	**Cost effectiveness**
Economic analysis: Study assessing the resource use and health outcomes related to the use of BTX; partial cost analysis included. **Approach to modelling:** Analysis based on a retrospective cohort study and assessing the same cohort of patients 12 months before and after the first BTX therapy (cases included from 7 centres, between March 2000 and January 2006) **Perspective:** Germany; third party	**Population:** Patients with neurogenic detrusor overactivity (N=214). 80.8% spinal cord injury; 14.0% myelomeningocele; 5.2% Multiple Sclerosis. 19.6% of patients received BTX therapy because of intolerable side effects of the antimuscarinic treatment. **Intervention:** Botulinum toxin A (BTX) therapy (300 IU diluted in 15ml sodium chloride 0.9%,	***Prior to BTX therapy:*** - Urinary tract infection in 68% of patients (3 per patient in average); - Incontinence episodes in 63%; - Incontinence aids were used in 58%. ***After BTX therapy:*** - Urinary tract infection in 28% of patients (1 in average); - Incontinence episodes in 24%; - Incontinence aids were used in 28%. Mean interval between treatments was 8 months (SD 4.2)	**Resource use:** - Mean of 1.6 (±0.6) treatment within 12 months; - 50.9% received 1 treatment; 41.1% 2; and 8% 3. - Mean dosage of BTX was 291.5 IU ± 57.2 with a mean number of 29 injections per treatment; - 10.1 IU/ml NaCl per injection - Therapy given in an inpatient setting in 95% of patients; - Mean hospital stay due to injection therapy was 4.0 days (SD 2.9 days). - Drug treatment before and after 1st intervention: ***see table 3 below;*** - 20% of patients reduced the use of antimuscarinic drugs; - Use of incontinence devices in 58% before, and in 27% after; - Number of absorbent pads needed from 1.7 to 0.7 per day; - In patients requiring incontinence aids despite treatment, the daily number of absorbent pads decreased from 2.6 to	**Cost-effectiveness results:** None **Sensitivity analysis:** None

2	B. Wefer, B. Ehlken, J. Bremer, H. Burgdorfer, B. Domurath, C. Hampel, J. Kutzenberger, C. Seif, K. D. Sievert, K. Berger, and J. Pannek. Treatment outcomes and resource use of patients with neurogenic detrusor overactivity receiving botulinum toxin A (BTX) therapy in Germany. World Journal of Urology 28 (3):385-390, 2010.				
Study details	**Population & interventions**	**Health outcomes**	**Costs**	**Cost effectiveness**
payer (German statutory sickness funds) **Time horizon:** 12 months post first intervention **Discounting:** N/A	distributed in 30 injections)		2.3 per day. **Total costs:** - Total resource use data for 12 months pre and post 1st intervention were collected in 136 patients (64%); - Direct medical cost was analysed for this subset of patients; - The mean annual drug cost for urinary tract infection decreased from €162.71 to €80.32 (***see table 4 below***) - The incontinence aids per patient per day decreased from €2.11 to €1.05 (***see table 4 below***). **Currency & cost year:** Euro 2006 **Cost components incorporated:** BTX therapy; use of continence aids (absorbing pads and urinary reservoirs); medication for urinary tract infection and neurogenic detrusor overactivity; outpatient visits; hospitalizations due to urinary tract.	
Data sources				

2	**B. Wefer, B. Ehlken, J. Bremer, H. Burgdorfer, B. Domurath, C. Hampel, J. Kutzenberger, C. Seif, K. D. Sievert, K. Berger, and J. Pannek. Treatment outcomes and resource use of patients with neurogenic detrusor overactivity receiving botulinum toxin A (BTX) therapy in Germany. World Journal of Urology 28 (3):385-390, 2010.**			
Study details	**Population & interventions**	**Health outcomes**	**Costs**	**Cost effectiveness**
Treatment effect: From the retrospective cohort study **Costs and resource use:** Medication from the German pharmaceutical index 2006; Outpatient visits and hospitalizations from the participating centres; absorbing pads and urinary reservoirs from the sickness funds of Bavaria and Hamburg 2006.				
Comments				
Source of funding: The study was financially supported by Pharm Allergan, Ettliengen, Germany. **Limitations:** Patients selected were offered BTX therapy as a last alternative to major surgery, possibly leading to a negative selective bias; no quality of life or QALY assessment; partial cost analysis; analysis based on a retrospective cohort study assessing the same cohort of patients 12 months before and after the first BTX therapy; analysis developed in Germany which limits its applicability to the UK NHS.				
Overall quality*: *Potentially serious limitations*	**Overall applicability**: *Partially applicable***			

1 *Very serious limitations/Potentially serious limitations/Minor limitations; **Directly applicable/Partially applicable/Not applicable.

2 Abbreviations: QALY = Quality-Adjusted Life-Years; NHS = National Health Service; UK = United Kingdom; SD = Standard Deviation.

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P. Padmanabhan, H. M. Scarpero, D. F. Milam, R. R. Dmochowski, and D. F. Penson. Five-year cost analysis of intra-detrusor injection of botulinum toxin type A and augmentation cystoplasty for refractory neurogenic detrusor overactivity. World J.Urol. 29 (1):51-57, 2011.				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA **Study design:** Decision analytic model **Approach to analysis:** Decision tree using TreeAGE software. Comparison over 5 years of augmentation cystoplasty (AC) and botulinum toxin (BTX). Successful outcome defined as 1 and all other outcomes defined as 0. Complications, adverse events and what happens when treatment fails modelled. Maintanence and monitoring costs also modelled **Perspective:** US payer **Time horizon:** 5 years **Treatment effect**	**Population:** Individuals with neurogenic bladder and associated detrusor over activity for whom anticholinergics and intermittent catheterisation were not sufficient at maintaining safe bladder pressures and continence. These individuals often have decreased bladder compliance, elevated storage pressures and detrusor over activity associated with upper tract dilation and recurrent UTIs **Intervention 1:** 300 U of Botulinum toxin A: repeat injections every 6 months over 5 year period **Intervention 2:** Augmentation cystoplasty: 1 operation	**Total costs (mean per patient):** Intvn 1: $28,065 Intvn 2 : $33,272 *Incremental: $5,207* **Currency & cost year:** US Dollars 2008-2009 Converted into GBP 2010‡: Intvn 1: £18,597.66 Intvn 2 : £22,048.15 *Incremental:* £3,450.49 **Cost components incorporated:** Facility costs; Surgeon costs; Cost of complications: - UTI	**Primary outcome measure:** *QALYs: N/A* Intvn 1: Successful outcome = 1 All other outcomes = 0 Probability of all complications following BTX = 0.5 Therefore the outcome is 1- complication rate Intvn 2: Successful outcome = 1 All other outcomes = 0 Probability of all complications following AC = 0.4 Therefore the outcome is 1- 0.4 = 0.6	**Primary ICER (Intvn 2 vs Intvn 1):** N/A **Other:** Intvn 1: $28,065 Intvn 2 : $33,272 *Incremental: $5,207 less for BTX per successful intervention* **Subgroup analyses:** N/A **Analysis of uncertainty** Model appears robust Threshold sensitivity analysis on the durability of BTX. If durability of BTX drops below 5.1 months, then BTX no longer favoured Complication rate post augmentation was also analysed: if the complication rate with AC drops below 14% then AC is favoured Facility and surgeon costs of BTX and facility costs of AC also impact the

P. Padmanabhan, H. M. Scarpero, D. F. Milam, R. R. Dmochowski, and D. F. Penson. Five-year cost analysis of intra-detrusor injection of botulinum toxin type A and augmentation cystoplasty for refractory neurogenic detrusor overactivity. World J.Urol. 29 (1):51-57, 2011.				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
duration: 5 years **Discounting:** None		- Urinary retention - Bowel dysfunction - SBO - Stones - Bladder perforation		model: with threshold values of $3,02.74, $1,004.03 and $17,100 respectively No Probabilistic analysis
Data sources				
Health outcomes: 1= successful treatment, 0 any complication **Quality-of-life weights:** NR **Cost sources:** Treatment reimbursement costs from eight insurance carriers | Drug costs from www.drugstore .com | Radiological costs from reimbursements to the Vanderbilt Hospital (US).				
Comments				

P. Padmanabhan, H. M. Scarpero, D. F. Milam, R. R. Dmochowski, and D. F. Penson. Five-year cost analysis of intra-detrusor injection of botulinum toxin type A and augmentation cystoplasty for refractory neurogenic detrusor overactivity. World J.Urol. 29 (1):51-57, 2011.				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Source of funding: Vanderbilt Department of Urological Surgery and the Institute for Medicine and Public Health ; **Limitations:** should match checklist ; **Other:** Dr Dmochowski is a consultant for Allergan (BTX manufacturer)				
Overall applicability*: Partially applicable	**Overall quality**: potentially serious limitations**			

[‡] Converted using 2010 Purchasing Power Parities from Organisation for Economic Co-operation and Development (OECD). OECD Stat Extracts: purchasing power parities for GDP. http://stats oecd org/Index aspx?datasetcode=SNA_TABLE4 [cited 2011 March 2]* Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations

** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

Appendix H: Forest plots

H.1 Do behavioural management programmes (timed voiding, voiding on request, prompted voiding, bladder retraining, habit retraining, urotherapy) compared with a) each other b) usual care, improve outcomes? 455

H.1.1 Comparison of prompted voiding versus no prompted voiding: 455

H.1.2 Comparison of habit retraining versus no habit retraining 456

H.2 What is the safety and efficacy of antimuscarinics compared with a) placebo or treatment as usual b) other antimuscarinics for the treatment of incontinence due to neurological disease/ overactive bladder due to neurological disease? 456

H.2.1 Comparison of Propiverine vs Placebo 456

H.2.2 Comparison of Propiverine vs Oxybutynin 457

H.2.3 Comparison of Tropsium versus Oxybutynin 458

H.2.4 Comparison of Oxybutynin versus Propantheline 458

H.2.5 Comparison of Propiverine versus Oxybutynin 458

H.3 What is the safety and efficacy of detrusor injections of botulinum toxin type A or B compared with a) usual care b) antimuscarinics in neurological disease 458

H.3.1 Comparison of botulinum toxin type A 200 U versus Placebo 458

H.3.2 Comparison of botulinum toxin type A 300 U vs Placebo 460

H.4 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care for the treatment of incontinence due to neurological disease? 462

H.4.1 Comparison of tamsulosin versus placebo 462

H.4.2 Comparison of Indoramin versus placebo 464

H.4.3 Comparison of Prazosin versus placebo 464

H.5 Do prophylactic antibiotics compared with a) no treatment b) other antibiotics reduce the risk of symptomatic urinary tract infections? 465

H.5.1 Comparison: New prophylaxis verus no prophylaxis 465

H.5.2 Comparison: New prophylaxis versus no prophylaxis for adults prior to urodynamics 466

H.5.3 Comparison: new prophylaxis versus no prophylaxis for adults with new SCI 466

H.6 Does the provision of information and support regarding the different management systems improve patient outcomes? 467

H.6.1 Comparison of information versus no intervention 467

H.1 Do behavioural management programmes (timed voiding, voiding on request, prompted voiding, bladder retraining, habit retraining, urotherapy) compared with a) each other b) usual care, improve outcomes?

H.1.1 Comparison of prompted voiding versus no prompted voiding:

Figure 1: Number of people with no improvement in wet episodes

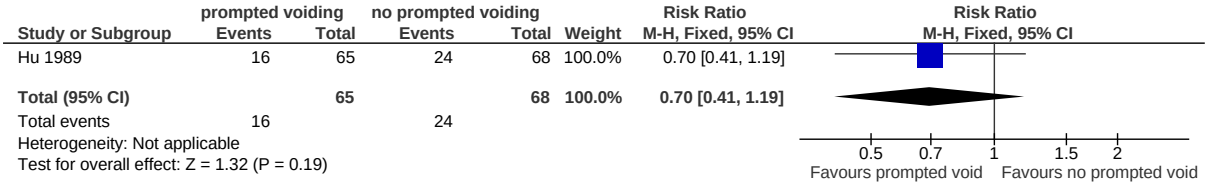


Figure 2: Proportion of hourly checks that were wet

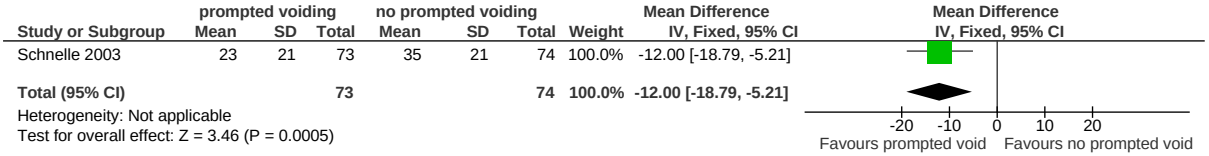


Figure 3: Change in mean proportion of hourly checks that are wet

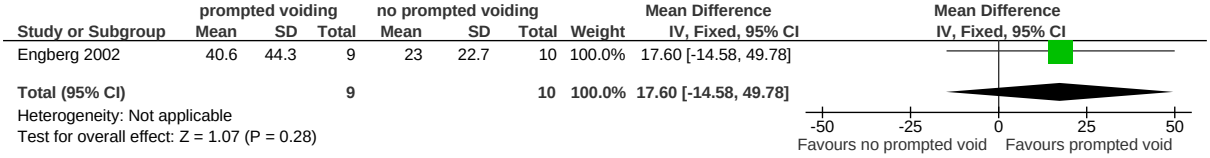


Figure 4: Incontinent episodes in 24 hours

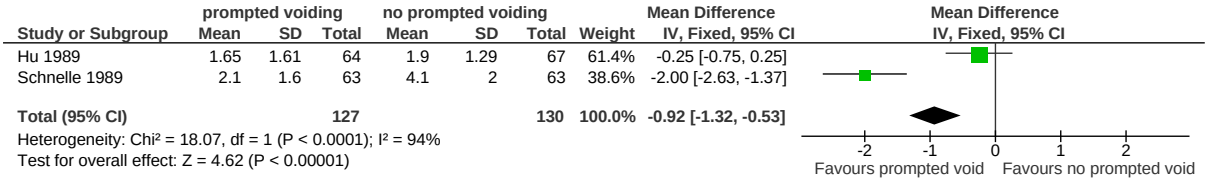
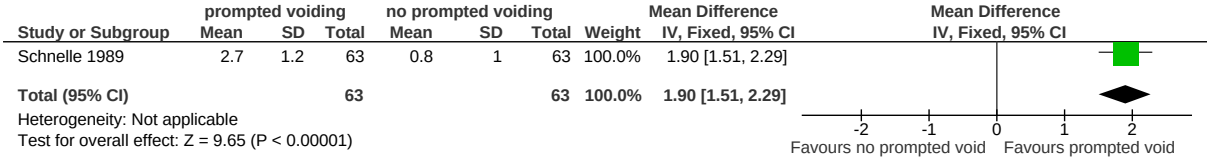


Figure 5: Self initiated toileting



H.1.2 Comparison of habit retraining versus no habit retraining

Figure 6: Number of incontinent episodes per 24 hours

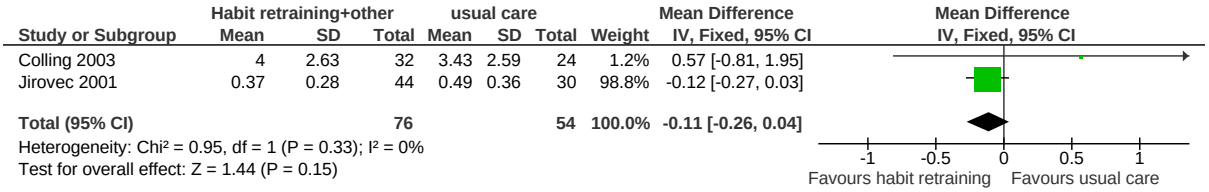


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Figure 7: Incontinent volume

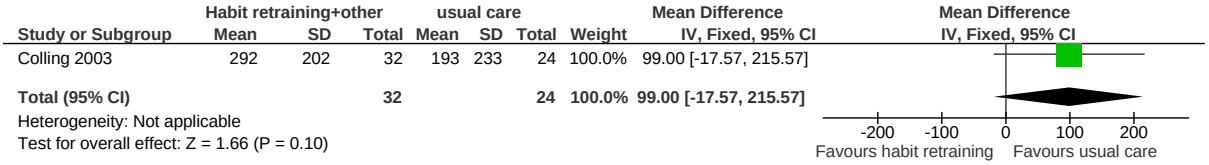

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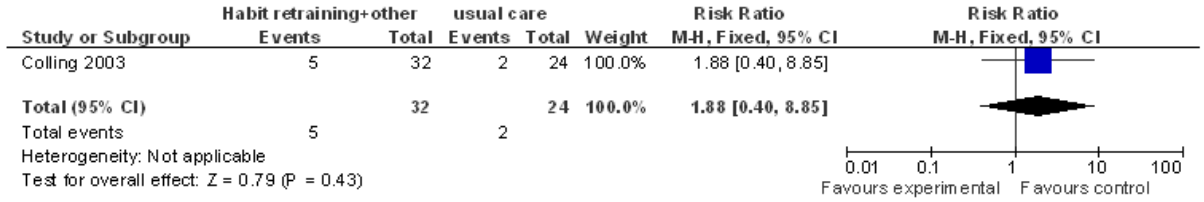
Figure 8: Prevalence of bacteriuria (E coli)



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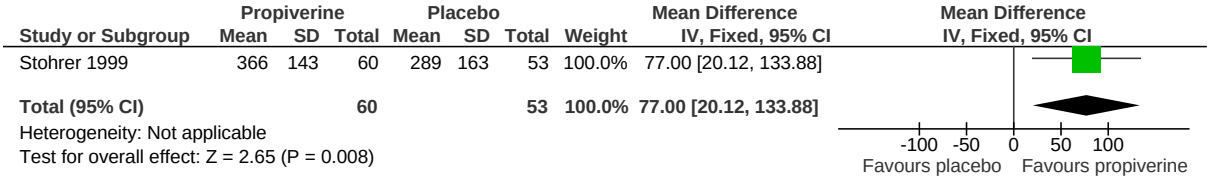
H.2 What is the safety and efficacy of antimuscarinics compared with a) placebo or treatment as usual b) other antimuscarinics for the treatment of incontinence due to neurological disease/ overactive bladder due to neurological disease?

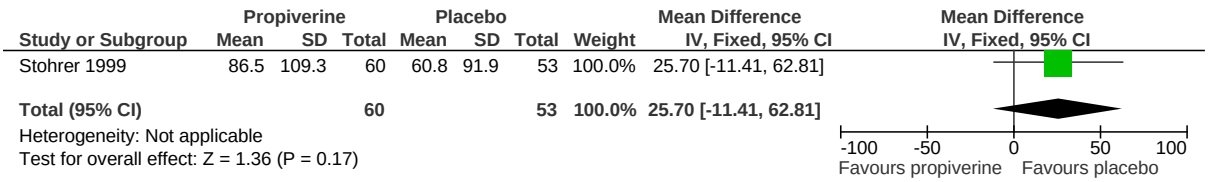
H.2.1 Comparison of Propiverine vs Placebo

Figure 9: Maximum cystometric bladder



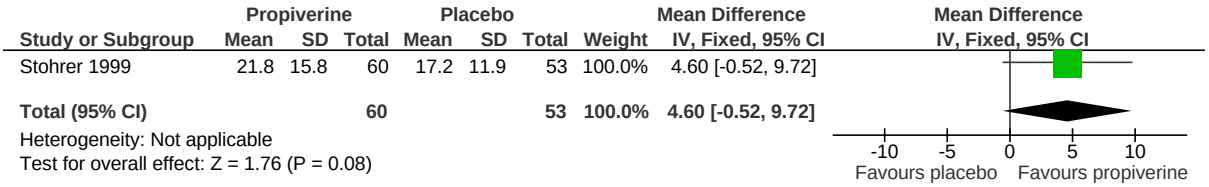
10

Figure 10: Residual urine



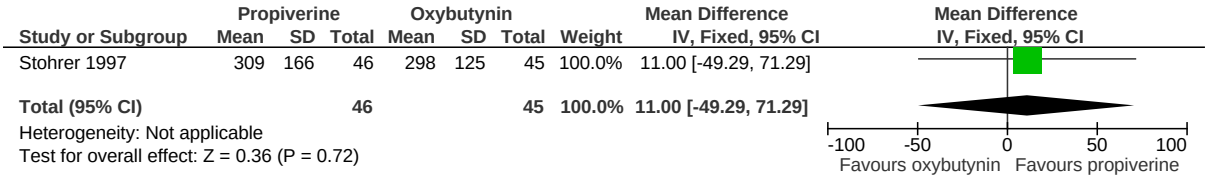
1

Figure 11: Drop-outs due to adverse events



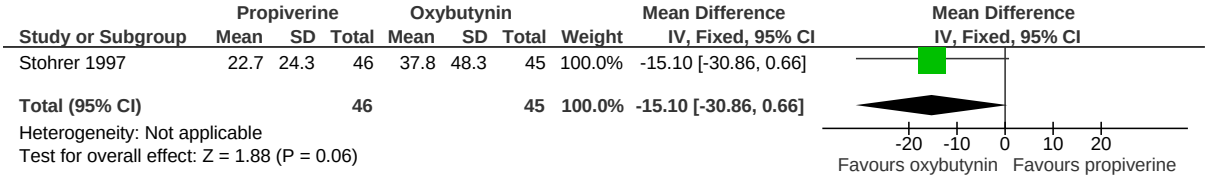
1.2.2 Comparison of Propiverine vs Oxybutynin

Figure 12: Maximum bladder capacity



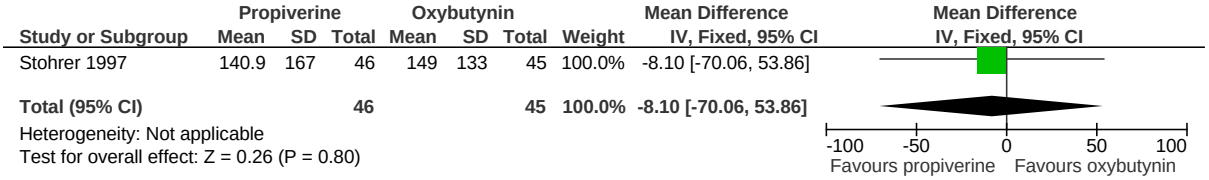
3

Figure 13: Bladder compliance



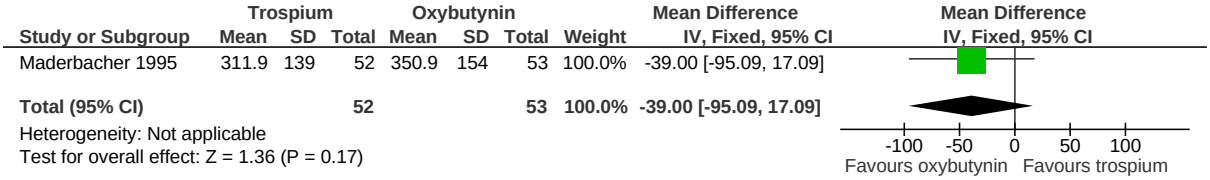
4

Figure 14: Residual urine



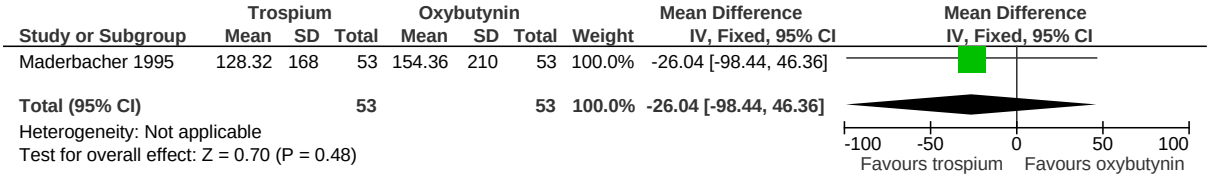
H.2.3 Comparison of Tropsium versus Oxybutynin

Figure 15: Maximum bladder capacity



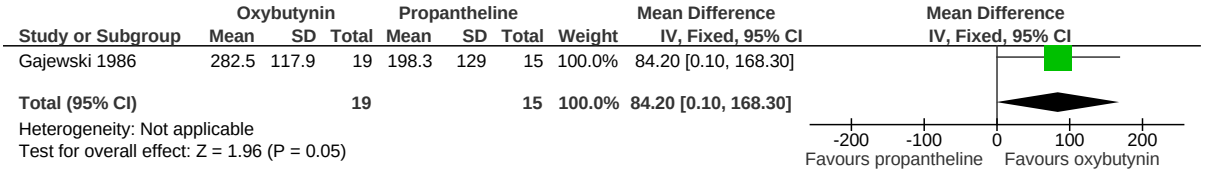
2

Figure 16: Residual urine



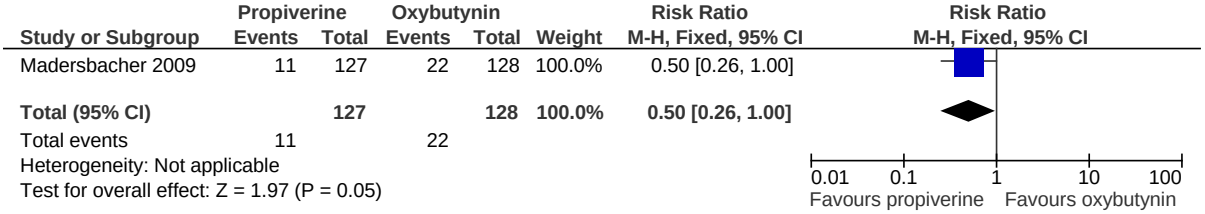
H.2.4 Comparison of Oxybutynin versus Propantheline

Figure 17: Maximum bladder capacity



H.2.5 Comparison of Propiverine versus Oxybutynin

Figure 18: Adverse events

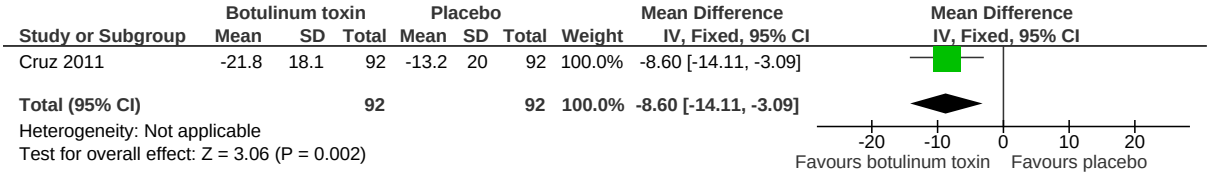


H.3 What is the safety and efficacy of detrusor injections of botulinum toxin type A or B compared with a) usual care b) antimuscarinics in neurological disease

H.3.1 Comparison of botulinum toxin type A 200 U versus Placebo

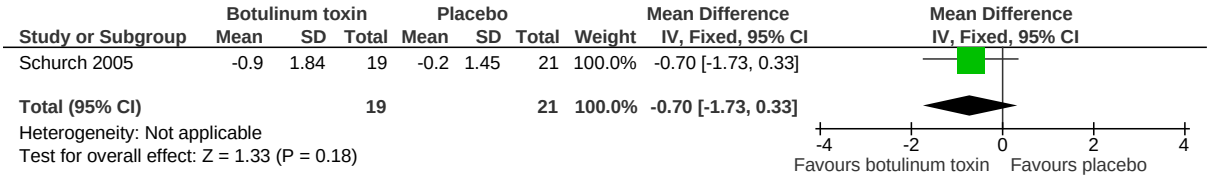
9

Figure 19: Incontinence episodes/week (mean change score) 6 weeks.



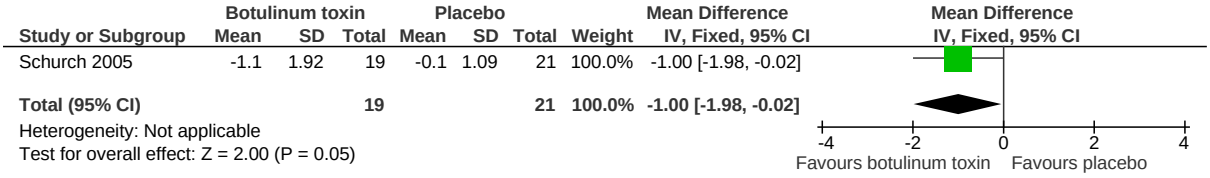
1

Figure 20: Incontinence episodes/day (mean change score) 6 weeks.



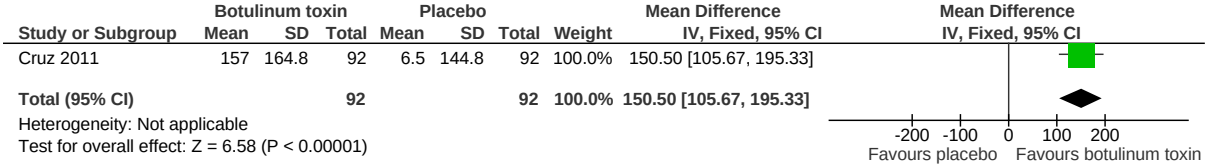
2

Figure 21: Incontinence episodes/day (mean change score) 24 weeks.



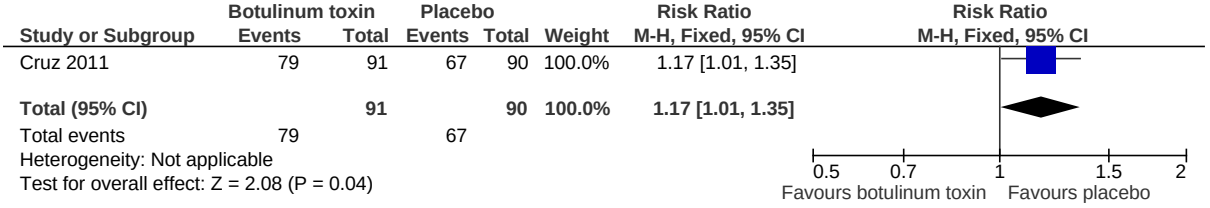
3

Figure 22: Maximum bladder capacity ml (mean change score) 6 weeks.



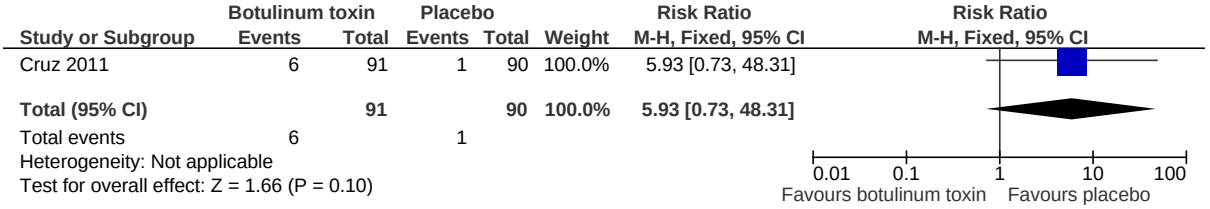
4

Figure 23: All adverse events end of scheduled follow-up.



5

Figure 24: Muscle weakness end of scheduled follow-up.

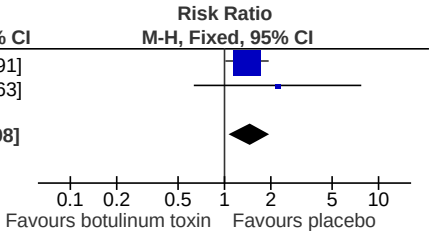


6

Figure 25: Urinary tract infections end of scheduled follow-up.

Study or Subgroup	Botulinum toxin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cruz 2011	51	91	36	90	92.7%	1.40 [1.03, 1.91]
Schurch 2005	6	19	3	21	7.3%	2.21 [0.64, 7.63]
Total (95% CI)		**110**		**111**	**100.0%**	**1.46 [1.08, 1.98]**
Total events	57		39			

Heterogeneity: Chi² = 0.50, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 2.44 (P = 0.01)

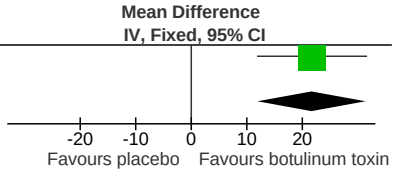


H.3.2 Comparison of botulinum toxin type A 300 U vs Placebo

Figure 26: I-QoL (mean change score) 6 weeks.

Study or Subgroup	Botulinum toxin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Herschorn 2009	19.52	22.93	28	-2.23	13.24	29	100.0%	21.75 [11.98, 31.52]
Total (95% CI)			**28**			**29**	**100.0%**	**21.75 [11.98, 31.52]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.37 (P < 0.0001)

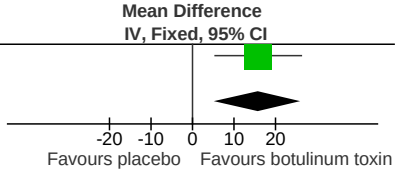


2

Figure 27: I-QoL (mean change score) 24 weeks.

Study or Subgroup	Botulinum toxin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Herschorn 2009	16.27	22.72	28	0.44	16.73	29	100.0%	15.83 [5.44, 26.22]
Total (95% CI)			**28**			**29**	**100.0%**	**15.83 [5.44, 26.22]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.99 (P = 0.003)

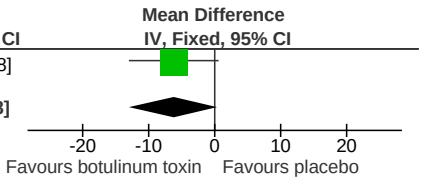


3

Figure 28: Incontinence episodes/week (mean change score) 6 weeks.

Study or Subgroup	Botulinum toxin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Cruz 2011	-19.4	25.7	91	-13.2	20	92	100.0%	-6.20 [-12.88, 0.48]
Total (95% CI)			**91**			**92**	**100.0%**	**-6.20 [-12.88, 0.48]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.82 (P = 0.07)

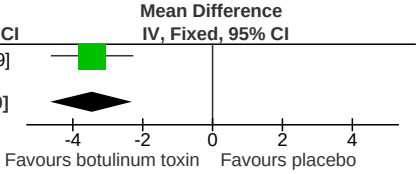


4

Figure 29: Incontinence episodes/day (mean final score) 6 weeks.

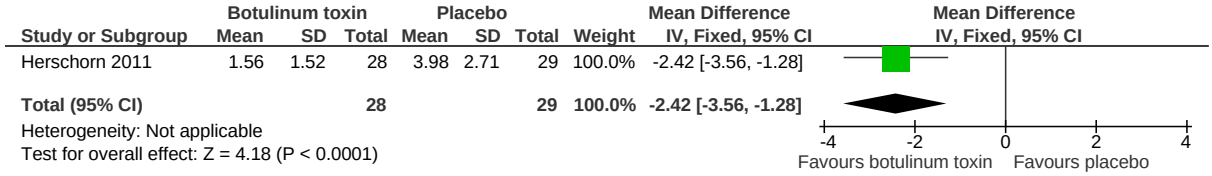
Study or Subgroup	Botulinum toxin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Herschorn 2011	1.31	1.25	28	4.76	2.91	29	100.0%	-3.45 [-4.61, -2.29]
Total (95% CI)			**28**			**29**	**100.0%**	**-3.45 [-4.61, -2.29]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.85 (P < 0.00001)



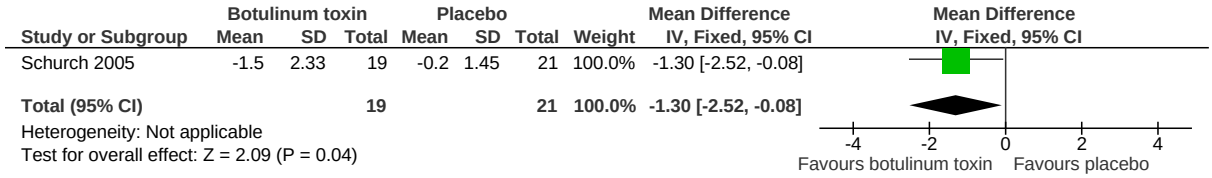
5

Figure 30: Incontinence episodes/day (mean final score) 24 weeks.



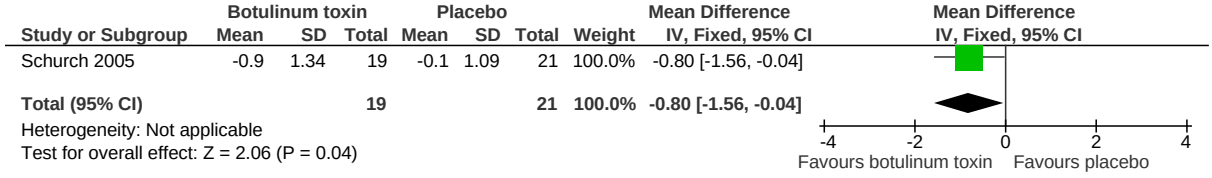
1

Figure 31: Incontinence episodes/day (mean change score) 6 weeks



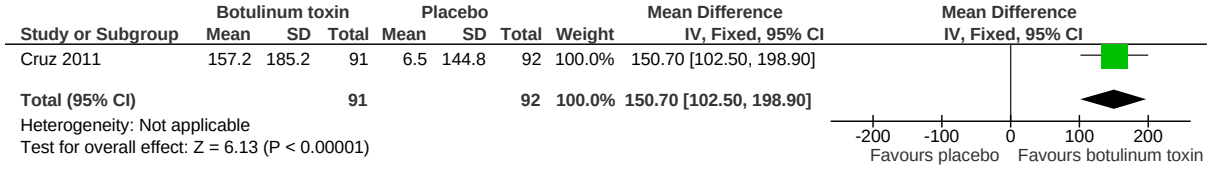
2

Figure 32: Incontinence episodes/day (mean change score) 24 weeks.



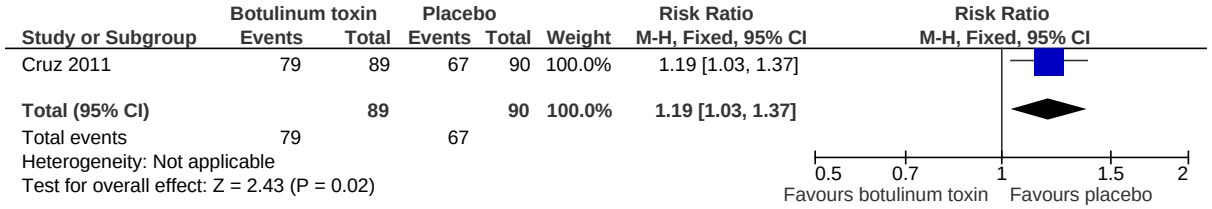
3

Figure 33: Maximum bladder capacity ml (mean change score) 6 weeks.



4

Figure 34: All adverse events end of scheduled follow up.

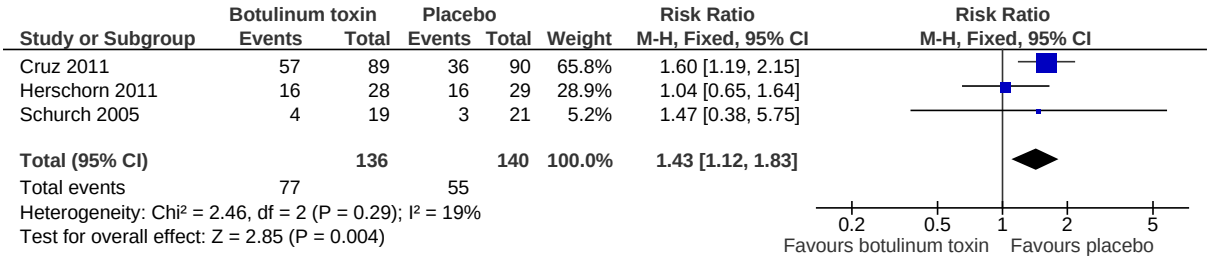


5

Figure 35: Muscle weakness end of scheduled follow up.

1

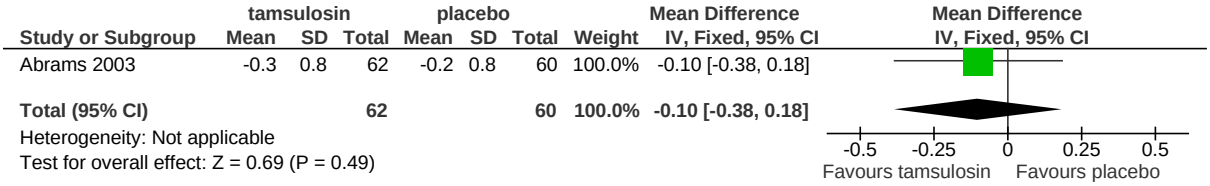
Figure 36: Urinary tract infection end of scheduled follow up.



H.4 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care for the treatment of incontinence due to neurological disease?

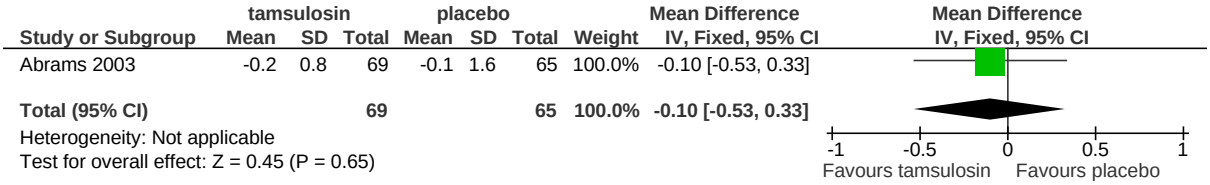
H.4.1 Comparison of tamsulosin versus placebo

Figure 37: Mean frequency of incontinence episodes/24 hrs



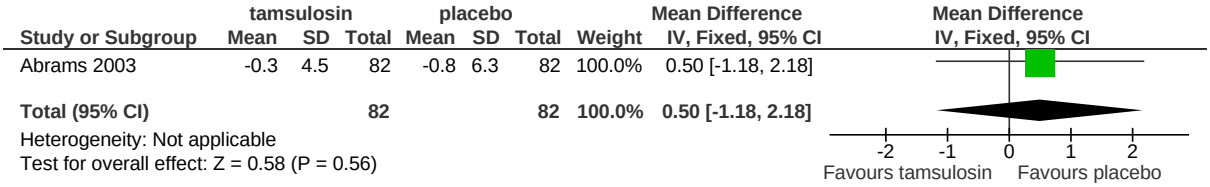
6

Figure 38: Mean frequency of urgency episodes/24 hrs



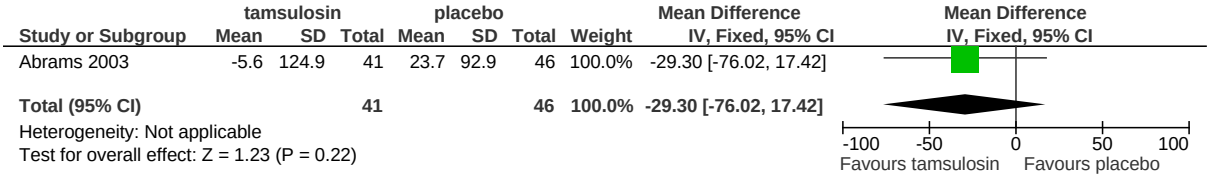
7

Figure 39: Urinary symptoms questionnaire - total subscale score



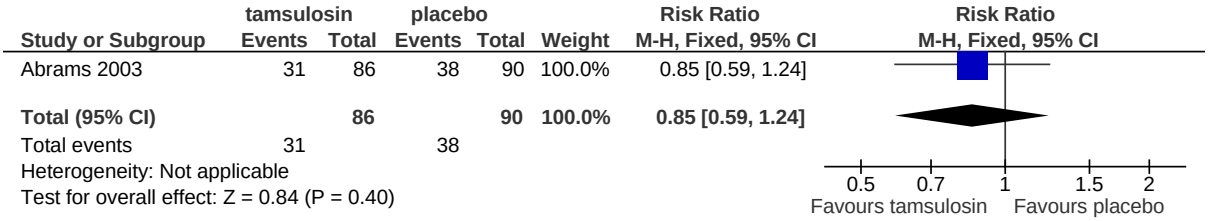
1

Figure 40: Residual urine



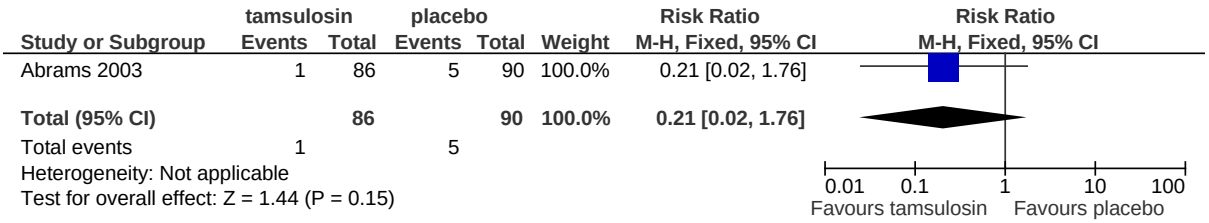
2

Figure 41: Any adverse events



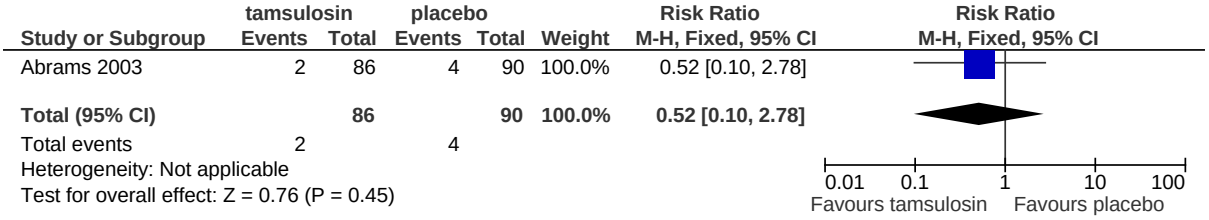
3

Figure 42: Dizziness



4

Figure 43: Discontinuations due to adverse events



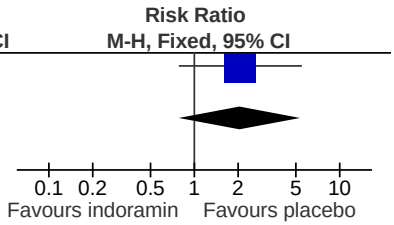
5

H.4.2 Comparison of Indoramin versus placebo

Figure 44: Overall improvement

Study or Subgroup	Indoramin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
O'Riordan 1995	7	9	3	8	100.0%	2.07 [0.79, 5.42]
Total (95% CI)		**9**		**8**	**100.0%**	**2.07 [0.79, 5.42]**
Total events	7		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.49 (P = 0.14)

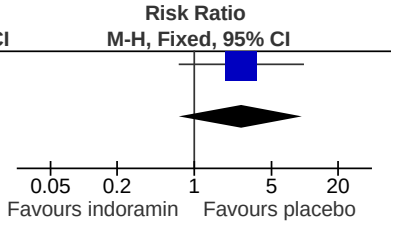


2

Figure 45: Maximum flow rates

Study or Subgroup	Indoramin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
O'Riordan 1995	6	9	2	8	100.0%	2.67 [0.74, 9.65]
Total (95% CI)		**9**		**8**	**100.0%**	**2.67 [0.74, 9.65]**
Total events	6		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.49 (P = 0.13)

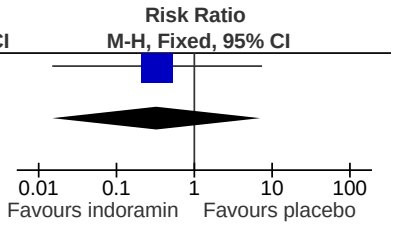


3

Figure 46: Adverse events leading to withdrawal

Study or Subgroup	Indoramin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
O'Riordan 1995	0	9	1	9	100.0%	0.33 [0.02, 7.24]
Total (95% CI)		**9**		**9**	**100.0%**	**0.33 [0.02, 7.24]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.48)

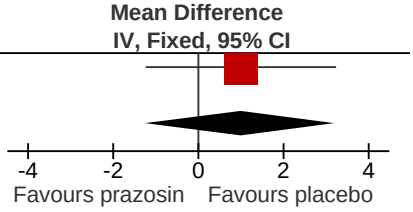


H.4.3 Comparison of Prazosin versus placebo

Figure 44: Maximum flow

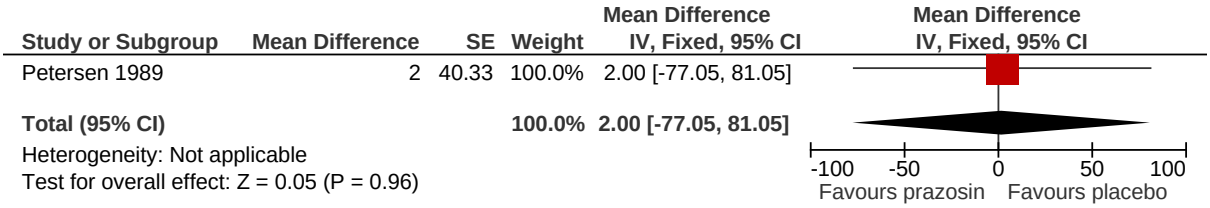
Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Petersen 1989	1	1.13	100.0%	1.00 [-1.21, 3.21]
Total (95% CI)			**100.0%**	**1.00 [-1.21, 3.21]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)



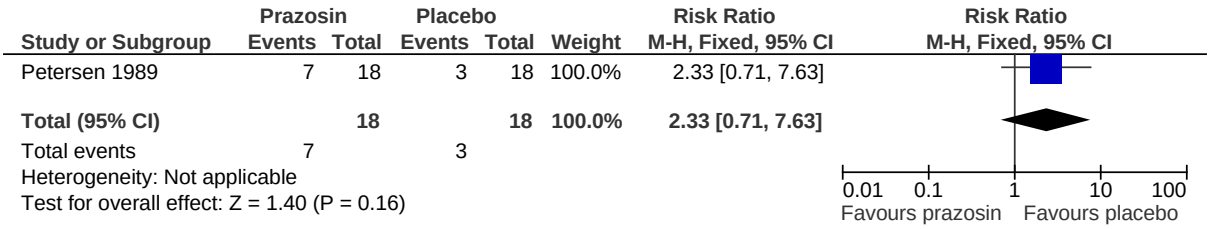
5

Figure 45: Residual urine



1

Figure 46: Adverse events



H.5 Do prophylactic antibiotics compared with a) no treatment b) other antibiotics reduce the risk of symptomatic urinary tract infections?

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H.5.1 Comparison: New prophylaxis verus no prophylaxis

Figure 47: Incidence of symptomatic UTIs for children – new prophylaxis versus no prophylaxis

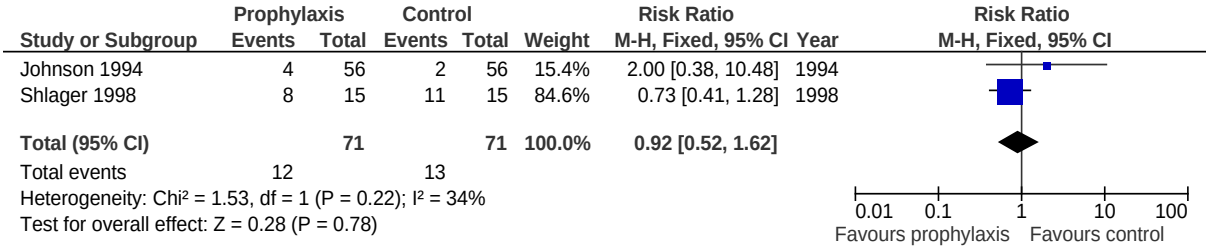

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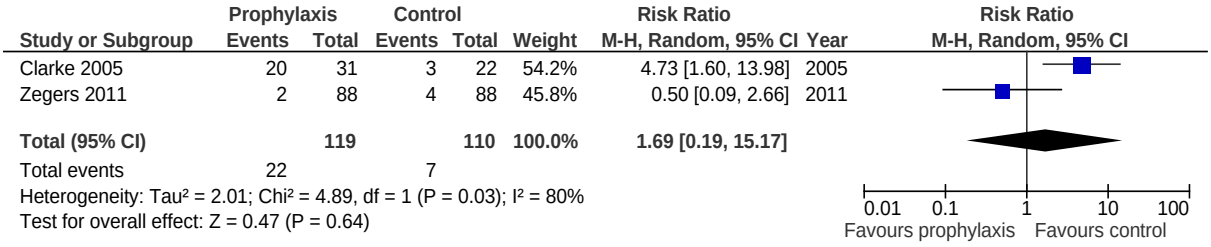
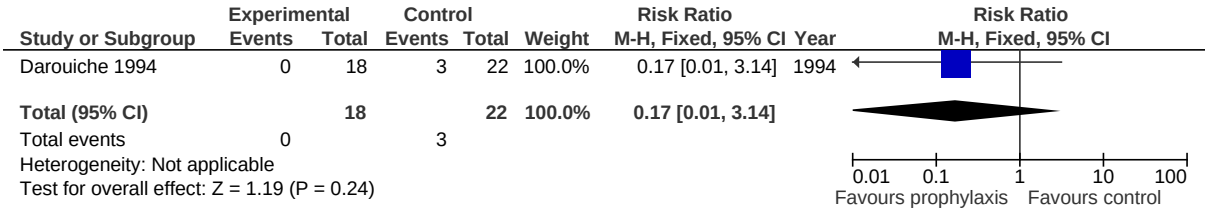
Figure 48: incidence of symptomatic UTIs for children – continue prophylaxis versus discontinue prophylaxis



1.5.2 Comparison: New prophylaxis versus no prophylaxis for adults prior to urodynamics

Figure 49: Incidence of Symptomatic UTIs



1.5.3 Comparison: new prophylaxis versus no prophylaxis for adults with new SCI

Figure 50: Incidence of symptomatic UTIs for Adults by case type.

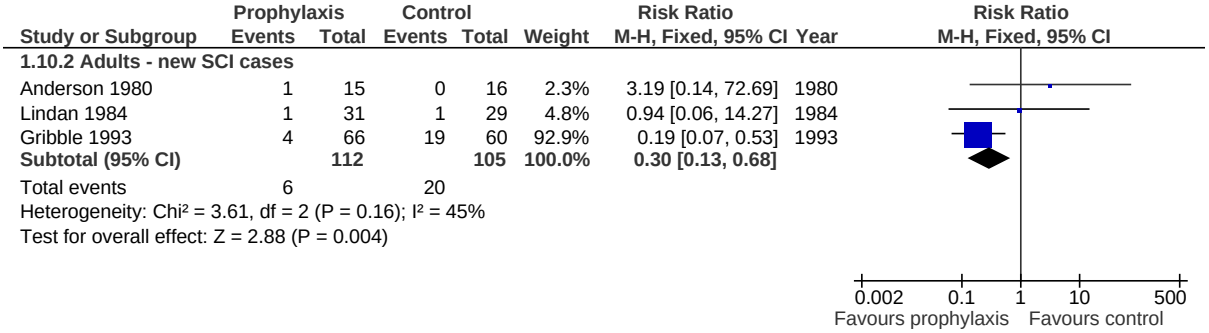


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Figure 51: Adverse events – resistance

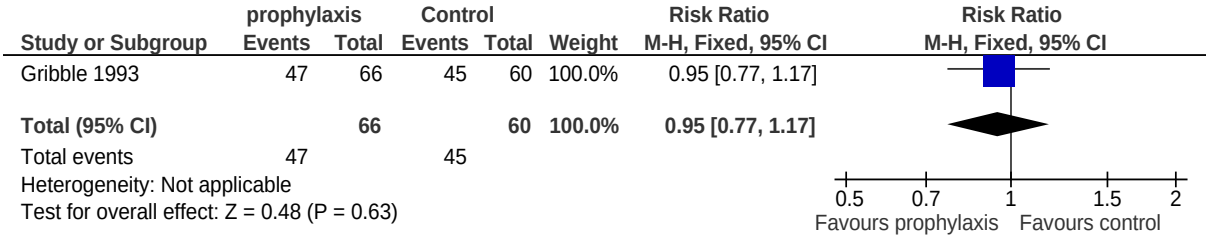

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Figure 52: Adverse events – GI disturbance

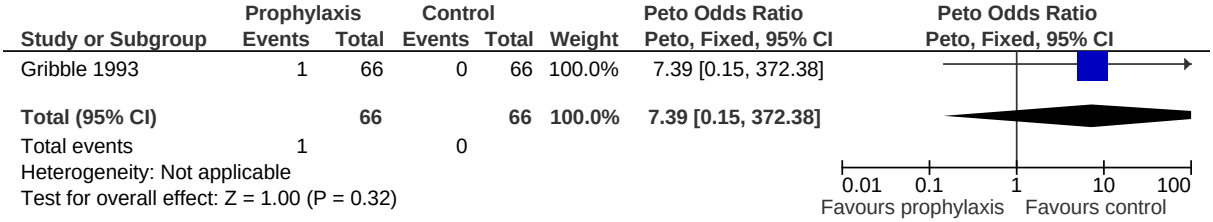

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Figure 53: Adverse events – skin or soft tissue infection

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Figure 54: Adverse events – Pseudomonas colonisation

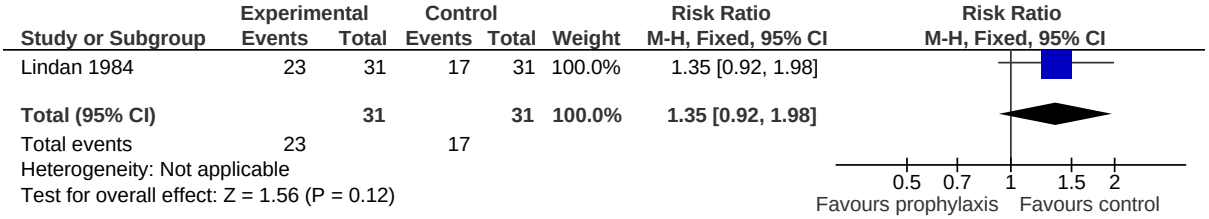

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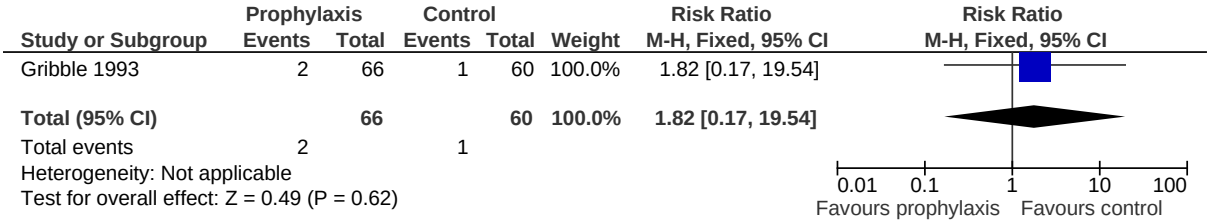
Figure 55: Adverse events – skin rash



H.6 Does the provision of information and support regarding the different management systems improve patient outcomes?

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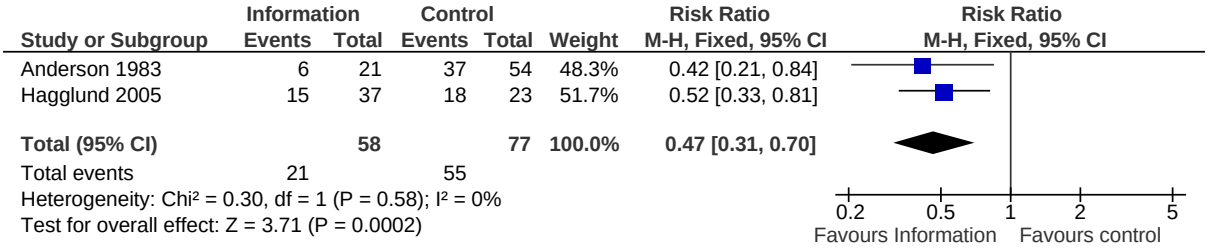
4

H.6.1 Comparison of information versus no intervention

Figure 53: Symptomatic UTIs.



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Appendix I: Cost-effectiveness analysis – Botulinum toxin type A versus Augmentation Cystoplasty

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I.1 Introduction

Dysfunction of the urinary bladder during the storage phase of the micturition cycle can take the form of either involuntary contractions of the bladder (neurogenic detrusor overactivity) or a loss of receptive relaxation of the bladder wall leading to a progressive increase in pressure as the bladder fills (reduced bladder compliance). Both neurogenic detrusor overactivity and impaired bladder compliance can lead to symptoms, such as increased urinary frequency, urinary urgency and incontinence. In both conditions deterioration in renal function may occur due to an inability of the upper urinary tract to expel urine in the face of high pressures within the bladder. Incontinence and urinary frequency in patients with neurological disease also occurs in the context of cognitive impairment as a result of difficulties with the interpretation of urinary tract sensations and a loss of the appreciation of the social context of micturition.

There are a number of treatment options available that seek to improve continence through improving the ability of the bladder to store urine. Less invasive treatments such as drug treatments or behavioural management may be preferred by a patient butwill not be effective in somecases. Surgical treatment of incontinence – augmentation cystoplasty – is permanent and requires major open surgery but has been shown to be effective in reducing incontinence (see clinical review). Other, less invasive treatments such as bladder wall injections of botulinum toxin type A are also available as second line treatments. However there remains uncertainty about the cost effectiveness of this treatment due to the unknown length of time to reinjection, the need for repeat reinjection and its long term efficacy. In this analysis botulinum toxin type A will be compared with augmentation cystoplasty as second-line treatments to establish the most cost effective method for preventing incontinence.

There is no, single best treatment for impaired bladder storage function in neurogenic lower urinary tract dysfunction and, due to the heterogeneity of the diseases analysed in the data, it is impossible to state that any one treatment is optimal even for patients with the same condition.. However, it is important to determine if there are wide differences in cost-effectiveness between the different treatments in the neuropathic population as this will provide valuable information for clinicians in circumstances where there is a choice to be made between different treatment options. This analysis looks at the main issues that will impact on the cost effectiveness of second line treatments.

Length of effect will obviously be an important factor as neurogenic lower urinary tract dysfunction is a long term condition and it is important to establish patient compliance and treatment response. Botulinum toxin has a short effectiveness period and requires frequent re-visits to the hospital wheras augmentation is a one-off operation. The data on the continued effectiveness of botulinum toxin type A is limited as this is a relatively new treatment modality. The invasive nature of the treatment and the quality of life lost to adverse events will also be important considerations. While the available data is limited at best, the construction of an economic model allows us to establish and analyse this uncertainty explicitly.

I.2 Methods

I.2.1 Model overview

I.2.1.1 Comparators

The model compares the cost effectiveness of four strategies for the management of incontinence due to neurogenic lower urinary tract dysfunction (NLUTD):

Augmentation Cystoplasty (AC) is a well established, major, open surgical technique where the bladder is made larger or ‘augmented’ by incorporating a bowel segment into the bladder. Most

commonly an ileal segment is used but alternatives include a section of the large intestine. The incorporation of intestine into the bladder prevents effective bladder contractions from occurring and patients usually cannot void completely following the surgery and therefore need to perform clean intermittent self catheterisation.

The second intervention is the injection of *botulinum toxin* type A *(BTX)* into the bladder wall. BTX is currently not licensed for this indication but various trials have shown it to be effective in reducing the frequency of incontinence episodes[1-3] in patients with incontinence due to NLUTD. The protocol for administration of BTX varies but the method used in this model is 30 endoscopic injections of 300u or 200u into the bladder wall. Patients with neurogenic LUT dysfunction will mostly need to use intermittent catheterisation to empty the bladder effectively following the treatment.

The third strategy is whereBTX is administered for two cycles and then AC is conducted in 100% of those that do not respond to BTX (BTX100AC) BTX continues to be administered in those that do respond.

The final comparator is no treatment or "best supportive care" (No-Rx). This comparator is included as an arm where patients opt to manage their incontinence with a mixture of incontinence appliances: pads, indwelling catheters, sheaths and suprapubic catheters.

I.2.1.12 Population

The population in this model is made up of patients with NLUTD (Myelomeningocele, Spinal Cord Injury, Multiple Sclerosis etc.) and bladder over-activity who are unresponsive or intolerant to anticholinergic medication. The patients in the base case are considered to be adults as the paucity of data on children prevents an adequate analysis for the paediatric age group. However the cost effectiveness in children will be tested in a sensitivity analysis.

The trial that the data for BTX[3] utilises measures effectiveness in patients with an average age of 49. The AC study used patients with an average age of 34. The AC study defined its population with a range, 17-66, as the BTX study falls fairly centrally within this range; the base case age was selected as 49. The distribution of men and women across the studies were also defined. In the Cruz study, there were around 40% men and in the AC study, there were 76% men. If a pooled average is taken this comes to a sex distribution of 53% female and 47% male.

Using this base case patient, it is possible to find standard mortality data for the UK [4] and determine life expectancy, thus allowing a lifetime horizon to be considered in the model. The model uses a standardised mortality ratio from a group of patients with spinal cord injury[5]. Standard mortally for the UK will be considered in a sensitivity analysis. Subgroup analysis will be carried out on different patients to determine cost effectiveness in a paediatric population.

However, not all of the comparators are relevant in every situation. For some patients, such as multiple sclerosis patients, the AC comparator is not relevant as they are not suitable for this surgical option. There are therefore two base case comparisons. Base case 1 is all the comparators compared together. The second base case analysis is simply BTX compared with No-Rx.

I.2.1.13 Time horizon, perspective, discount rates used

The time horizon is defined as a lifetime using a 3.5% discount rate per year on both outcomes and costs but this was varied between 0 and 6% for outcomes and costs in a sensitivity analysis as per the NICE reference case[6]. A specific analysis will be done on a discount factor of 1.5% for Quality Adjusted Life Years (QALYs) and 3.5% for costs. The analysis is conducted from the National Health Service and Personal Social Service perspective.

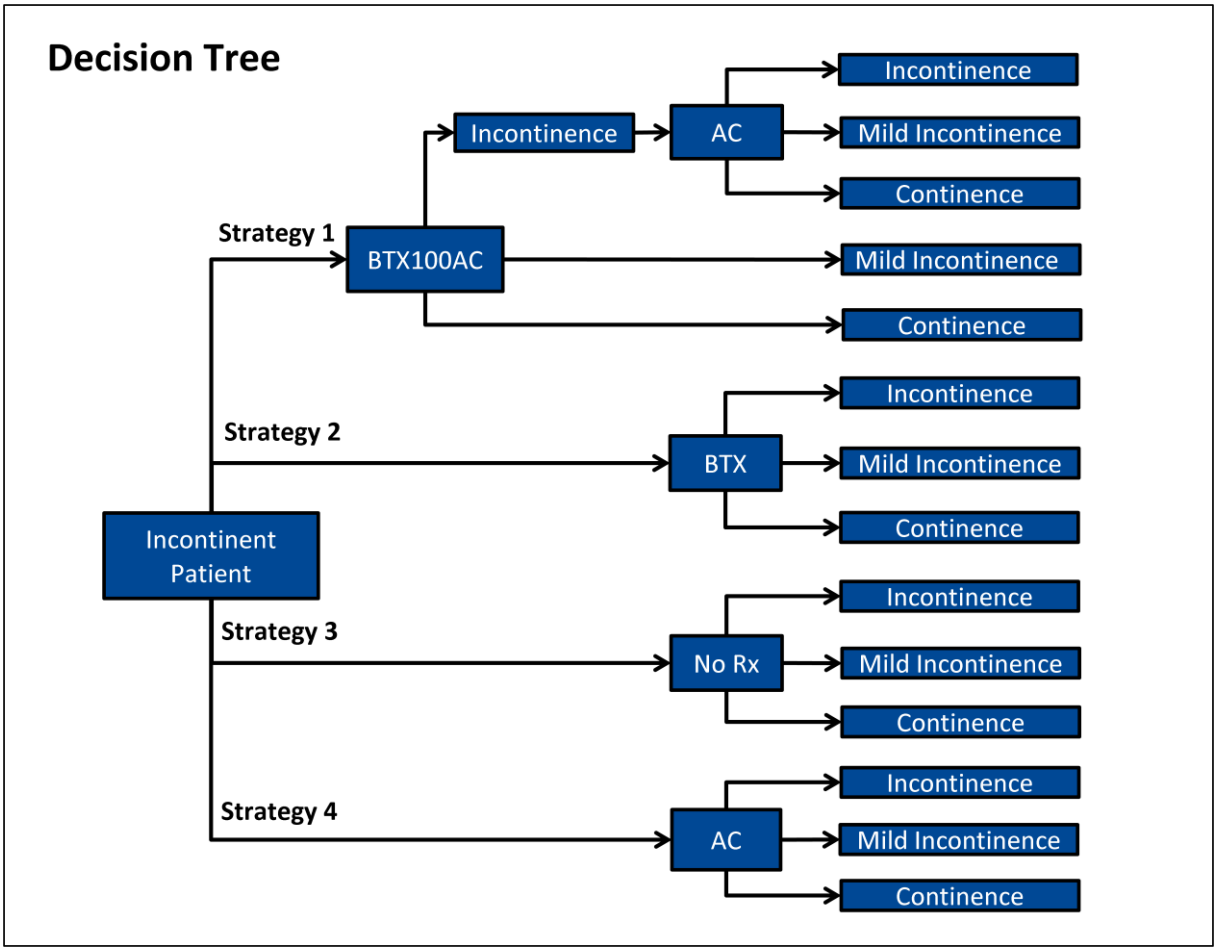
1.2.2 Approach to modelling

A decision tree was constructed in Windows Excel® to model the comparison of cost and effectiveness of the interventions. Life tables were then attached to each of the final health states in the tree and a hypothetical cohort of a thousand patients was run through the model. The trials that were used to inform the model used frequency of incontinence episodes as the main outcome. Quality of Life weights were attached to being either incontinent, continent or having mild incontinence on the basis of the frequency of episodes. As adverse events and the presence or absence of urinary tract infections have important quality of life and cost implications, these were also included. The cost components included costs of the treatment itself, the ongoing costs associated with adverse events and any monitoring or follow up treatments.

1.2.2.1 Model structure

The decision tree compared the three management strategies (AC, BTX and BTX with AC in non-responders) and one no treatment strategy emanating from the initial choice node. Then at each of the chance nodes, a probability is attached that is determined by the effectiveness of the given treatments. At the end of each branch there is a Markov model for each of the outcome states that enable calculation of costs and QALYs over the time horizon. This allows the consideration of mortality data and life expectancy. The structure of the decision tree can be seen in Figure 56.

Figure 56: Decision Tree



BTX100AC : BTX for two attempts then transfer to Augmentation if BTX is unsuccessful. BTX: Botulinum Toxin. NoRx: No Treatment. AC: Augmentation Cystoplasty.

Note: At every health state, a patient may progress to the "absorptive" state, the death state using standard life tables adjusted with condition specific data.

With each of the four options, an incontinent patient upon receiving treatment will either become continent meaning that the treatment was effective, they will have improved continence but will not be fully continent, mild incontinence, or they will remain incontinent. Each of these options is determined by the effectiveness of each treatment. This is true of all the arms but there is a slight difference in the BTX100AC arm. In this arm, the patient will receive two cycles of BTX treatment, however those patients who remain incontinent, rather than remaining in the incontinent state for the rest of the model, they will opt to undergo an AC, incurring all the benefits and harms of that treatment arm. In the BTX only arm, the patients that do not respond will receive BTX for two cycles then will no longer receive BTX and will manage their incontinence using appliances such as pads and catheters.

The frequency of incontinence episodes is used as the main outcome. Due to the inconsistent reporting of the effectiveness of treatments between studies, assumptions had to be made about the frequency of incontinence episodes that constituted each outcome. This was done so that costs and effects could be calculated. It was assumed that in the continent group a patient would suffer from one incontinence episode per week, in the mild incontinent group, they would suffer from two episodes per day and in the incontinent group, they would suffer from five episodes per day. All these options were given an assumed standard error 20% of the mean and normally distributed for the probabilistic analysis.

Table 1: Frequency of incontinence episodes as defined by continence status

	Incontinent	Mild Incontinent	Continent
Number of episodes per day	5	2	0.14

Once a patient is in one of the outcome groups; continent, mild incontinent or incontinent, it is assumed that they will remain within this group for the duration of the lifetime horizon. In order to model this, life tables are attached to each of the outcome groups. Life tables are mortality rates for a given population, in this case England and Wales[4]. In the base case analysis a standardised mortality ratio (SMR) is used that fits the mortality to a more appropriate population. The SMR used was from a retrospective 50 year study in spinal cord injury patients[5]. This SMR increased the mortality rate in patients by a factor of between two and four, depending on age.

The use of a life table allows costs and outcomes to be calculated over a lifetime. It allows the cycle length, the period over which these costs and outcomes are borne, to be varied in a sensitivity analysis. The model uses the mean time that patients requested retreatment with BTX as the cycle length, enabling the costs and outcomes of each intervention to be calculated over the same period. The trial[3] used as the basis of the BTX data reported 8 months mean time to request retreatment and 10 months as the median. Therefore the mean is used as the base case but the median is tested in a sensitivity analysis. This cycle length determined the frequency of reinjection with BTX. Changing the cycle length will not impact on the effectiveness of BTX. BTX is assumed to retain the same effectiveness no matter how long or short the reinjection time is. This is a substantial simplification that reduces the precision of the result, due to the uncertainty about how long the patient will remain continent for. The effectiveness data is only for 12 weeks, however the 8 month reinjection period is based on the same study so there is internal consistency

I.2.3.2 Uncertainty

The model is built probabilistically to take account of the uncertainty around parameter point estimates. In order to do this a probability distribution is defined for each model input. So that when the model is run, a value for each input gets randomly selected from its respective probability distribution simultaneously. This is done repeatedly – 1000 times – and results are summarised. Probability distributions are based on error estimates from data sources, for example: the standard error around a point estimate. The number of simulations used was chosen considering the Monte

Carlo error of the incremental costs, QALYs and net monetary benefit using the methods as described by Koehler and colleagues {Koehler, 2009 20261 /id}. It is set to ensure that the Monte Carlo error is not more than 5% of the standard error for these parameters.

In addition, various deterministic (one-way) sensitivity analyses were undertaken to test the robustness of model assumptions and data sources. In these, one or more inputs are changed and the analysis is rerun to see the impact on results. This was done using the deterministic (non-probabilistic) data.

8.2.3 Model inputs

Model inputs were based on clinical evidence identified in the systematic review undertaken for the guideline, supplemented by additional data from standard national sources. Model inputs were agreed by clinical members of the GDG.

I.2.3.1 Initial cohort settings

The Model is based on a hypothetical cohort of patients. Baseline patients are defined as patients suffering from incontinence from NLUTD. The patient has undergone treatment with antimuscarinics and is either intolerant or is unresponsive to them. Therefore the baseline patient currently manages their incontinence with catheters in order to void and absorptive pads or incontinence sheaths in order to counteract incontinence episodes. The base case patient is 49 years old, 53% female and 47% male. There was no acceptable data in children for either BTX or AC, therefore the same data is used in the paediatric sensitivity analysis although there are differences in the rate of adverse events.

I.2.3.2 Treatment effects

No studies were identified in the clinical review that compared botulinum toxin (BTX) with augmentation cystoplasty (AC) directly. Therefore studies that compared BTX and AC to “usual care” were used. However considering BTX and AC are both interventions in those where first line treatment had failed, usual care consisted of no treatment (No-RX).

The data for the effectiveness of BTX comes from a randomised controlled trial of 275 patients[3]. This study compared the use of 30 intradetrusor injections of 200U and 300U of “botulinum toxin type A” (BTX) with placebo over a period of 12 weeks. In the base case, this analysis will be looking at 200U of BTX. To measure the effectiveness of the treatment, the frequency of incontinence episodes is used. The study showed a decrease from baseline in the frequency of episodes at 6 and 12 weeks compared to placebo. In the study, the mean frequency of incontinence episodes was reported. However in order to be able to put the data into the model in a comparable form with the AC data, it was necessary to convert it to a categorical variable. The categorical variable was: those patients who did not respond to treatment (incontinent), those who responded but were not completely dry (mild incontinence) and those who were completely dry after treatment (continent). A request was therefore submitted to the authors of the paper for additional data[a]. The data was supplied in the form of a responder analysis. The data was consistent with that presented in the original paper but was in a more applicable form for this analysis. The study also showed the time to request re-treatment with BTX: mean 8 months median 10 months. A Dirichlet distribution was applied to take into account the uncertainty around the probability point estimates (The Dirichlet distribution is the multivariate generalisation of the beta distribution that confines all the parameters between 0 and 1 and allows order to be maintained between linked probabilities). However there was no long-term, follow-up, data of BTX for the treatment of neurological incontinence. An assumption therefore had

[a] The Request was submitted to Allergan Limited Marlow International, The Parkway, MARLOW Buckinghamshire, SL7 1YL, UK. Data was not submitted for publication in initial paper.

to be made on the basis of several studies[7-9] that the bladder wall does not lose responsiveness and that the therapeutic effect of BTX is maintained after long term usage.

There were no randomised controlled trials carried out on Augmentation Cystoplasty (AC) identified in the clinical review. However there were several observational studies conducted that inform the model on the effectiveness of AC. These studies where not meta-analysed due to heterogeneity. All of these studies had relatively low sample sizes and most were from inappropriate settings. One study by Reyblat *et al.* 2009[10] was from a US setting, was of an acceptable size and provided enough data on outcomes to incorporate into the model. This study was therefore selected to form the basis of the analysis of the AC arm of the model. The outcomes of this study were measured using a categorical variable: incontinence, mild incontinence or continence. The probabilistic parameters or the AC outcomes were given using a Dirichlet distribution, in order to maintain the order of probabilities.

It was assumed that in the No-Rx arm, patients remained incontinent throughout. A summary of the treatment effects used in model is provided in Table 2.

Table 2: Overview of treatment effects used in the model

Parameter description	Point estimate	Probability distribution	Source
Treatment Effects			
Continent after BTX (200U)	0.363	Dirichlet	Cruz 2011[3] (Personal communication with authors)
Mild incontinence after BTX (200U)	0.408	Dirichlet	
Incontinent after BTX (200U)	0.229	Dirichlet	
Continent after BTX (300U)	0.377	Dirichlet	
Mild incontinence after BTX (300U)	0.406	Dirichlet	
Incontinent after BTX (300U)	0.217	Dirichlet	
Continent after AC	0.79	Dirichlet	Reyblat 2009[10]
Mild incontinence after AC	0.17	Dirichlet	Reyblat 2009[10]
Incontinent after AC	0.04	Dirichlet	Reyblat 2009[10]

I.2.1.3.3 Adverse Events

The other impact that these interventions are evaluated for is adverse events (AEs) and urinary tract infections (UTIs). One of the suggested benefits of BTX over AC is the fact that it produces fewer side effects. This is captured in the analysis. The probability of UTIs and AEs can be seen in Table 3. The data used to inform the adverse event and UTI probabilities were from various different study lengths meaning they all had to be standardised to the same cycle length. In order to do this the following equations are used:

Probability to annual rate:

$$\frac{}{}$$

Annual rate to cycle length probability:

The GDG considered that the two most important side effects associated with BTX are haematuria and urinary retention. The probability of a patient experiencing haematuria following BTX treatment is given in a study by Schurch *et al.* 2005[1], this probability was given over one year and was incorporated using the method described above. It was recognised that urinary retention is an adverse event associated with BTX however the costs and effects associated with it are not modelled. This was due to the fact that the entire population is likely to undertake intermittent catheterisation and therefore urinary retention adds no extra burden.

The side effects associated with AC are more extensive. They include: ileus, bowel obstruction, perforation of the augmented bladder, bladder stones and re-augmentation. Some of these AEs represent serious events while the incidence of the various complications varies from the relatively common (bladder stones) to the rare (perforation). Where possible, the probability of experiencing an adverse event was taken from the same study as the clinical effectiveness, i.e. Reyblat *et al.* 2009[10]. This was possible for ileus, bladder stones and bladder obstruction as these were all measured outcomes with an average follow-up of 2.5 years. Ileus was considered in a different way from the other adverse events because it is a one off event. Whereas the probability of stones, obstruction or perforation continued throughout the length of time that a patient was in the model; ileus is a complication arising specifically around the time of the surgery and therefore the associated probability and costs are simply attached to the cost of the AC. The probability of having a perforated augmentation bladder is taken from Metcalfe *et al.* 2006[11], this study, in a young-adult and paediatric population, had an average follow-up of 3.8 years enabling conversion to a one year probability. The probability was therefore considered to be 2.4% per year. However, this figure was thought to be too high for adults and the GDG assumed that this figure was 4 times less in adults: 0.6% per annum. The final adverse event is the probability of redoing the surgery due to an issue with the augmentation bladder. This was assumed by the GDG to be at a probability of 30-40% over 10 years. This was converted to a standardised probability using the midpoint of this estimate, 35% and the range for the sensitivity analyses.

Table 3: Adverse Event Probabilities

Adverse Event	Probability	Distribution	Distributional Parameters	Source
Probability of UTIs when incontinent	0.93	Beta	SE =0.2	Gamé 2008[12]
Probability of UTIs with Mild incontinence	0.28	Beta	α = 0.53b β = 2.13	Gamé 2008[12]
Probability of UTIs with Continence	0.28	Beta	α = 0.53 β = 2.13	Gamé 2008[12]
Probability of Haematuria with BTX	0.04	Beta	α = 2 β = 36	Schurch 2005[1]
Probability of bladder stones with AC	0.019	Beta	α = 5 β = 68	Reyblat 2009[10]
Probability of bowel obstruction with AC	0.007	Beta	α = 2 β = 71	Reyblat 2009[10]
Probability of perforation of augmented	0.016	Beta	α = 43	Metcalfe

[b] α and β are the parameters used to define the beta distribution. These parameters can be derived in two ways: 1.) α refers to the number of events (or rate) and β refers to the number of people in the study minus the number of events. 2.) Derived using the method of moments, using mean and standard error.

Adverse Event	Probability	Distribution	Distributional Parameters	Source
bladder with AC (Children)			β = 457	2006[11]
Probability of perforation of augmented bladder with AC (Adults) - Children value *1/4	0.004			Assumption
Probability of Ileus with AC (one off with AC)	0.047	Beta	α = 12 β = 61	Reyblat 2009[10]
Probability of Re do surgery	0.028	Beta	α = 15 β = 30	Assumption

Urinary tract infections (UTIs) are defined as the symptomatic UTIs that require treatment. This definition was used as asymptomatic bacteriuria is universally present in this population of patients. A clear definition of what is classified as a UTI, which UTIs are treated and which UTIs are reported is not available. The baseline rate of UTIs in the population was taken from the study by Gamé *et al.* 2007[12], this study was used because the studies in the clinical review did not report the UTIs associated with continence status which was required so that the UTIs could be standardised for all the interventions. This gave a rate of 1.77 UTIs per patient in the six months running up to BTX injection. As the pre-BTX population is in the same as the pre-AC population, this baseline rate of UTI could apply to both. If this rate is converted to a probability it comes to 93% every 8 months. The Gamé study gives a reduction for patients who are continent to a 28% probability of a UTI after 8 months. The GDG considered that for patients who are continent post AC, a similar reduction is seen. Due to the paucity of data in this area, an assumption was made that the mild incontinent and continent groups experienced the same level of UTIs. This means that the rate of UTIs are associated with the level of incontinence and not with the treatment used. The probability of having UTIs is also tested in a sensitivity analysis.

I.2.3.64 Utilities

The Utility for the main outcome, incontinence, were taken from a study by Hollingworth 2010 [13] this study evaluated the quality of life associated with incontinence, using the SF-6D utility measure. The baseline utility of a patient with neurological incontinence is 0.66 according to the Hollingsworth study, see Table 4. The quality of life weights for "successful" treatment are 0.78 for continence and 0.75 for mild incontinence. The Utility loss from UTI is taken from the Infection Prevention guideline model on catheterisation. This gives a 0.05 reduction in quality of life and is based on UTI in catheterised patients with spinal cord injury. There is a potential limitation in that by counting UTI utility loss, we are double counting. The Utility data associated with incontinence potentially includes UTI quality of life loss. In order to measure the impact that this has on cost effectiveness, a sensitivity analysis was done, setting the utility loss from UTIs to zero.

The utility for haematuria resulting from BTX was not included because it is not considered to be painful nor does it not cause long term negative impacts. Haematuria is normally be followed up due to cancer risk but there is an obvious cause here, so this is considered unlikely. There is some potential for patient anxiety, but with explanation of the situation from the physician this should be relieved.

The AE utility loss comes from a combination of studies. The availability of utility data to populate this part of the model was very poor. Sullivan et al. 2011[14] provide a catalogue of EQ-5D disutilities and was used to input the disutility of a bladder stones which came to -0.02. Another AE was perforation or rupture of the augmented bladder. For this the Jansen 2007 study was used, although this study was in a different population and the event was not exactly the same, it was considered by the GDG to be a close approximation which came to -0.48. The same study was also used to provide data on bowel obstruction and diarrhoea which when combined came to a utility loss of -0.18. When

the utility losses are combined with the probabilities of given events, the utility loss from AC comes to -0.004 per augmentation.

The method used to combine the, per cycle, probabilities with utilities for AEs in AC are given below to demonstrate this type of calculation:

Disutility for bladder stones = -0.02

Probability of bladder stones per cycle = 0.019

= 0.019*-0.02

= -0.000376

Disutility for bladder perforation = 0.488

Probability of bladder perforation per cycle

(assumed 4x less in adult augments) = 0.00393

= 0.00393*-0.488

= -0.00192

Disutility for general bowel disruption

(Diarrhoea, blockage, Ileus) = - 0.184

Probability for bowel disruption per cycle = 0.0074

= 0.0074*-0.184

= -0.0014

Combined disutility = -0.000376 + -0.00192 +-0.0014

= - 0.0037

This same method is used to generate the other disutilities occurring in the model.

Table 4: Utilities

Utilities	Point estimate	Probability distribution	Distribution parameters	Source
Utility with incontinence	0.66	Gamma	κ = 30.25 θ = 0.02	Hollingworth 2010[13]
Utility with mild incontinence	0.75	Gamma	κ = 6.35 θ = 0.014	Hollingworth 2010[13]
Utility with continence	0.78	Gamma	κ = 8.64 θ = 0.014	Hollingworth 2010[13]
Utility loss from AE per AC	0.004	Gamma	κ = 25 θ = 0.004	Sullivan 2009 Ref Needed
Utility loss from UTI	0.05	Gamma	κ = 2.74 θ = 0.18	IPC Model

The utilities in Table 4 that need to be are converted into disutilities using the simple conversion of 1-utility. The reason this is done is to limit the utilities by 0 and 1 when the probabilistic analysis is

done. The utilities are then combined with the life years to provide a weighting to produce Quality Adjusted Life Years (QALYs). The QALYs are calculated for each cycle and the sum total over a lifetime is divided by the cohort size to provide the number of QALYs per person. Patients who move into the death state accrue zero QALYs.

I.2.3.5 Resource use and cost

It was possible to cost the resource use using official UK sources: NHS reference costs 2009/10, NHS supply Chain Catalogue 2011, the NHS drug tariff and the British National Formulary (BNF) 60. Where an appropriate cost could be found that fully covered the aspect of resource use required, this was attached. However, assumptions had to be made when the cost was not so clear. All the costs that were incorporated into the model can be found in Table 5.

The cost of BTX was constructed using a combination of the NHS reference cost for "injection of substance into bladder wall" and the price of either 200U or 300U of BTX from the BNF-60. However because BTX is not yet licensed for this use, this cost is fairly speculative and was tested in a sensitivity analysis. The adverse events associated with the injection of BTX were haematuria and urinary retention. The cost of haematuria is assumed as the cost of a consultation with a GP.

The cost of AC was simply the cost of a "major open procedure/reconstruction" in the NHS Reference costs 2009/10. This cost could also form the basis of re-augmentation and the cost of repairing a bladder perforation. The cost of bladder stone removal is a combination of endoscopic and open removal. Costing bowel obstruction required the assumption that 70% would simply require an extra week in hospital whereas 30% would require a major surgical procedure to remove the obstruction. The treatment for ileus simply consisted of an extra period in hospital; the Reyblat[10] study put the mean at 4.9 days.

The costs outlined above were the costs of treatment. The long term costs besides continued BTX treatment and the AEs associated with BTX and AC were the costs of each continence state. These included the costs of UTIs and the costs of incontinence appliances. The Cost of a UTI was calculated as the cost of a Healthcare consultation (£32), a dipstick analysis (£0.07), first-line antibiotic treatment (£2) and the dispensing fee (£1.96). In total this came to £36.

The costs of incontinence appliances were costed based on GDG assumptions about the average usage by patients. Pads were costed at £0.25, intermittent catheters costed £0.75, Indwelling catheters costed £5.31 with 30 minutes of district nurse time coming to £32 every 6 weeks and sheaths cost £0.79. All these appliances were used at different rates depending on the health state that the patient was in.

In the Incontinent group it was assumed:

- 25% of men and 50% of women would manage on pads and intermittent catheters.
- 40% of men and 50% of women would manage on indwelling catheters.
- 35% of men would manage with sheaths.

In the Mild Incontinent and Continent groups it was assumed:

- 100% of men and women would use intermittent catheters.
- All of these would wear a pad and manage episodes with pads based on the frequency defined by the treatment effectiveness.

It was also recognised that children use different levels of incontinence appliances. It was assumed, for simplicity, that patients under the age of 10 use pads only if incontinent to manage episodes. The costs of all appliances combined and multiplied by cycle length can be found in Table 5.

Table 5: Unit Costs

Costs	Point estimate	Probability distribution	Distribution parameters	Source
Intervention costs				
Cost of AC operation (also cost of bladder perforation or re-augmentation)	£5929	Gamma	κ = 3.77[c] θ = 1571.25	NHS Reference Costs 2009-2010[15]
Cost of 100U BTX	£138	Assumed fixed		BNF 60[16]
Cost of Injection of substance into bladder wall	£293	Gamma	SE = 145.14	NHS Reference Costs 2009-2010[15]
Cost of Pads	£0.25	Gamma	κ = 2.55 θ = 0.98	NHS Supply Chain Catalogue 2011[17]
Cost of Intermittent Catheter	£0.75	Gamma	κ = 2.5 θ = 0.3	NHS Supply Chain Catalogue 2011
Adverse event costs				
Cost of treating a UTIs	£36	Gamma	κ = 2.5 θ = 0.3	NHS Reference Costs 2009-2010[15]
Bladder stone removal	£522	Gamma	κ = 7.49 θ = 69.69	NHS Reference Costs 2009-2010[15]
Bowel obstruction (70% 1 extra week in hospital 30% major surgical procedure)	£1,251	Gamma	Work out how to present this	NHS Reference Costs 2009-2010[15]
Ileus	£1,381	Gamma	κ = 24.39 θ = 13.61	NHS Reference Costs 2009-2010[15]
Haematuria (GP surgery consultation lasting 11.7 min)	£32	Assumed fixed		PSSRU 2010[18]
Appliance Costs				
Pads	£0.25	Gamma	κ = 2.55 θ = 0.10	NHS supply chain Catalogue 2011[17]
Sheaths	£0.79	Gamma	κ = 3.9 θ = 0.2	NHS Drug tariff
Bags	£6.85	Gamma	κ = 4 θ = 1.71	NHS supply chain Catalogue 2011
Indwelling catheter	£5.31	Gamma	κ = 6.9 θ = 0.77	NHS supply chain Catalogue 2011
District nurse time 30 min	£32	Assumed Fixed		PSSRU 2010[18]
Average costs of intermittent catheters	£0.75	Gamma	κ = 2.47 θ = 0.30	NHS supply chain Catalogue 2011
Appliance cost Incontinent (1 cycle)	£759			
Appliance cost Mild incontinent (1 cycle)	£1,078			
Appliance cost Continent (1 cycle)	£966			

[c] κ and θ are the parameters that describe the Gamma distribution. κ describes the shape of the distribution and θ describes the scale.

Costs	Point estimate	Probability distribution	Distribution parameters	Source

These costs are then added to the number of patients in each health state while they remain within the model at each cycle. For AC, the main cost is that of the operation at the beginning, the follow on costs are then the cost multiplied by the probability of any adverse events they may incur at any given time. For BTX, the cost of the injection of BTX is incurred at every cycle as is the cost of any side effects.

6.2.4 Computations

Some methods of eliciting distributional parameters simply require the number of events and the total number in the study. The beta distribution for, example, is defined by α and β, α being the number of events and β being the total study size minus α. However often this data is not available and more complex computations have to be made in order to make the data probabilistic. This usually entails using the mean of a sample as the point estimate and some an error estimate such as a confidence interval or a standard error, is used to determine the shape of a distribution: the slope of the line and the intercept.

To elicit distribution parameters for the beta distribution (α,β) the method of moments was used (μ = mean, s = variance):

In order to elicit the distribution parameters for the gamma distribution, the method of moments was also used:

The distributional parameters for the lognormal distribution were elicited from the mean and standard error using the method of moments:

6.2.5 Sensitivity analyses

Sensitivity analyses are done on certain key parameters to test the impact that they have on the overall result. The parameters to be tested and the ranges that will be altered in are found in Table 6.

Table 6: Sensitivity Analyses

Parameter	Analysis	Reason

Parameter	Analysis	Reason
Cycle length	10 months	The Cruz study reported the median at 10 months
UTI probability	Varied from 0 to 100% across all outcomes	There is uncertainty about the proportion of UTI depending on treatment and continence status
UTI QoL	Zero change in QoL due to UTI	Possibility of double counting when using incontinence utility data
300U dose of BTX	Change in effectiveness (Cruz 2011) and cost (£414)	Lack of certainty about most appropriate dose
Reduced and increased cost of BTX	Threshold analysis	BTX is not licensed for this indication and the cost is therefore uncertain
Paediatric data	X4 prevalence of stones, Age 13, change in pad and catheter usage	Paediatric data is lacking, assumptions about treatment effectiveness and adverse event rates need testing
Stone prevalence	Changed to 60 % over 10 years	This is the assumption used in the Urinary Incontinence guideline.
Standardised Mortality Ratio (SMR)	No SMR applied	In order to test the impact that the spinal cord injury SMR has on the results
Discount factor	0-6% on both costs and outcomes	NICE Reference case to measure the impact of discounting

(a) The above SAs are all testing assumptions that were made in constructing the model. They are tested to reduce the uncertainty about the results that are seen.

13.2.6 Interpreting results

There is very little comparative data available that compares AC to BTX in any real sense. This model will aid the GDG in making decisions on which treatment or treatments to recommend on the basis of comparative cost effectiveness. The model looks at two scenarios, one, where AC and BTX are both valid options and it will give the GDG some evidence about which intervention to recommend in this case, the second scenario is where AC is not a valid comparator and the model will guide the GDG towards making a well informed and strong recommendation on BTX versus no treatment. There are clear limitations to this model including the fact that comparative data is not available and the limited data on UTI rates, paediatric data and costs of BTX. The model deals with these limitations explicitly and provides evidence is of value in estimating the costs and benefits attached to the different management approaches that are analysed.

13.3 Results

13.3.1 Base case 1 results – All interventions compared

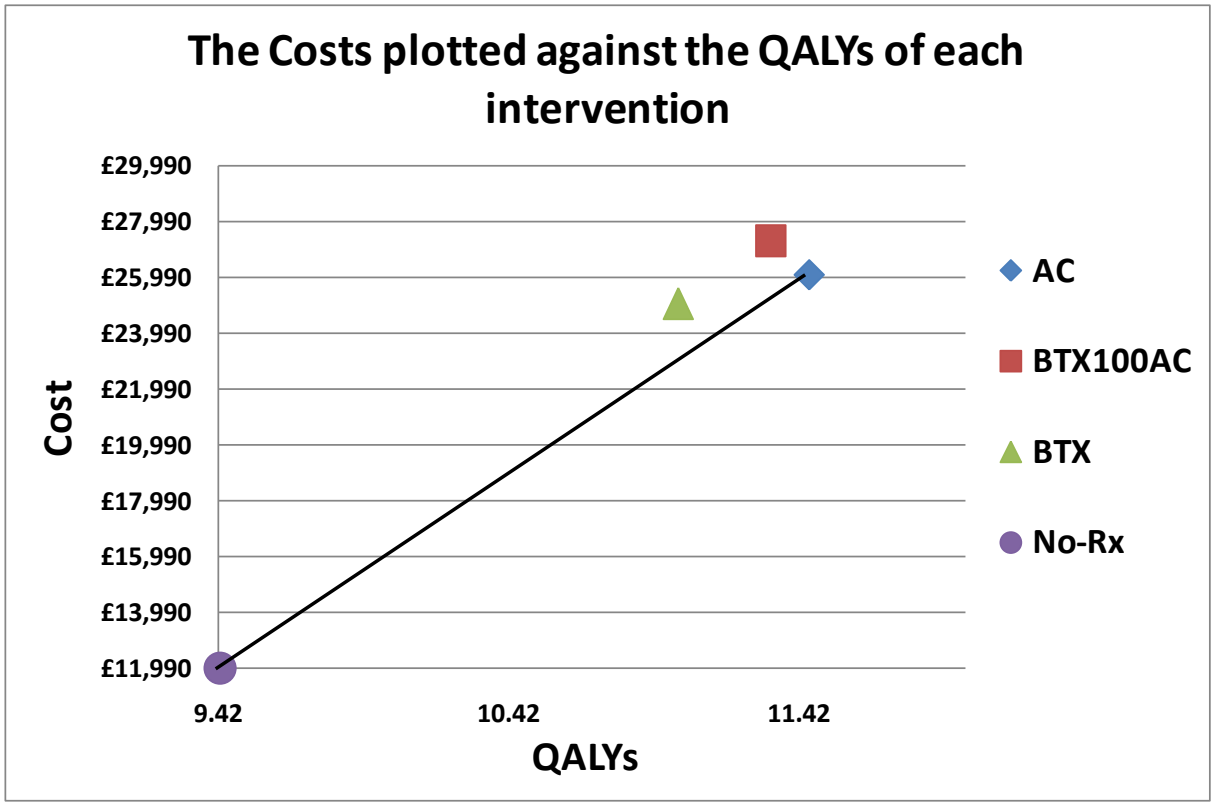
The first base case analysis compared the cost effectiveness of all the interventions outlined in the methods. The analysis revealed that Augmentation Cystoplasty (AC) is the cost effective option when compared to *botulinum toxin* (BTX) and no treatment (No-Rx) for the treatment of incontinence due to NLUTD using a lifetime horizon. The results of the analysis can be seen in Table 7, below. There is a measure of confidence in this result because, at a threshold of £20,000 per QALY, AC is cost effective with a probability of 78%.

Table 7: Base case results

Intervention	Mean Costs	Mean QALYs	NMB[d] at £20,000 per QALY gained	Rank at £20,000 per QALY gained
AC	£26,084	11.46	£1,119,752	1
BTX100AC	£27,315	11.33	£1,105,610	2
BTX	£25,059	11.01	£1,075,757	3
No-Rx	£11,991	9.43	£930,946	4

The cost effectiveness graph below demonstrates these results graphically. We can see that while BTX and AC are similar in cost-effectiveness, AC is more effective but marginally more expensive than BTX alone. The BTX100AC strategy[e] is more effective than the BTX alone strategy but also more expensive; it is more expensive and less effective than AC. No-Rx is the cheapest strategy but it is also the least effective therefore it will only be cost effective at a very low threshold.

Figure 57: Cost effectiveness graph



When the costs are broken down into the constituent parts, it is possible to pick out the elements that drive the results. This breakdown can be found in Table 8. The increased effectiveness of AC compared with all other interventions is what makes it the most cost effective option. It is cheaper than BTX100AC over a lifetime and is more effective; it is not, however, cheaper than BTX alone over a lifetime.

[d] Net Monetary Benefit (NMB) is a simple rearrangement of the Incremental cost effectiveness ratio calculation. The equation is as follows: Threshold*Effectiveness-cost>0. The resulting figure gives you the QALY gain expressed in monetary form, with each QALY costed at the threshold, net of cost. Meaning that after taking away cost, the intervention with the highest NMB is the most cost effective.

[e] Strategy where if BTX is ineffective after 2 cycles, augmentation is attempted in 100% of patients

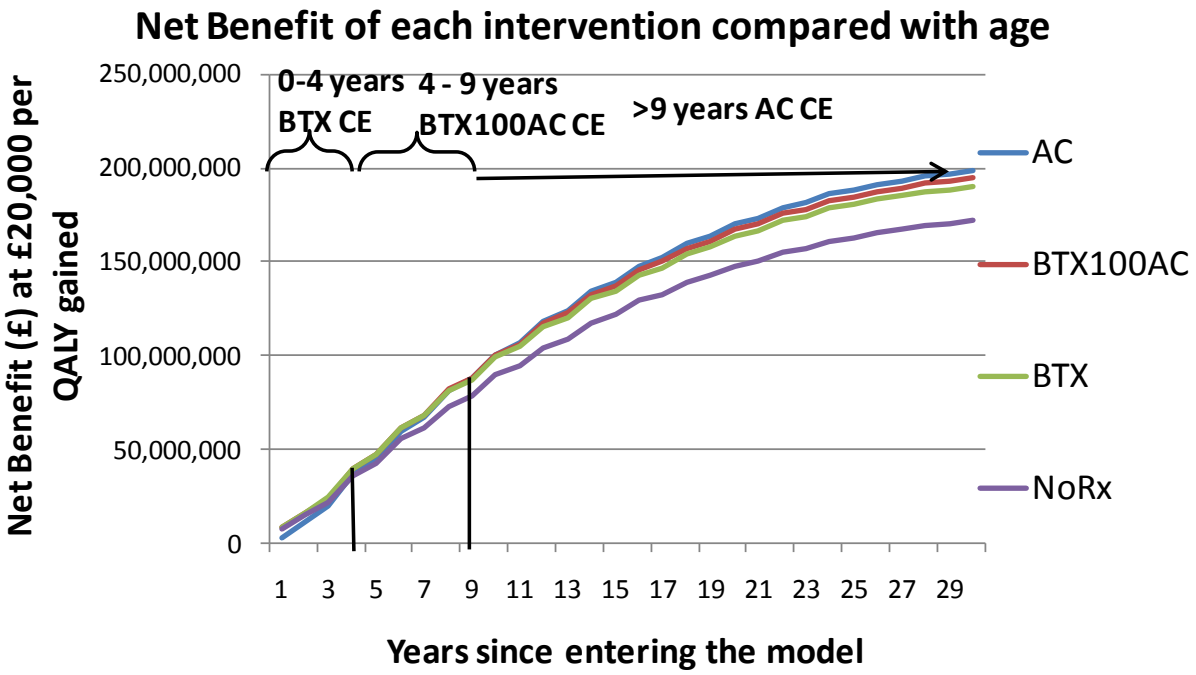
Table 8: Breakdown of costs and outcomes

	Input	BTX100AC	BTX	AC arm	NoRx
Mean Costs (Discounted)	BTX costs	£10,328	£10,328	£0	£0
	AC costs	£1,053	£0	£6,433	£0
	AE costs	£600	£15	£3,705	£0
	UTI costs	£181	£233	£169	£497
	Appliance costs	£15,152	£14,483	£15,776	£11,494
	Total costs	£27,315	£25,059	£26,084	£11,991
Mean Outcomes	Years continent	11	8	18	0
	Years mild incontinent	10	9	4	0
	Years incontinent	2	5	1	23
	Life years	22.71	22.71	22.71	22.71
	QALYs (discounted)	11.33	11.01	11.46	9.43

AC however is higher cost than the BTX alone strategy, this is a function of the discount rate[f]. Using the sensitivity analyses on discount rate [table where these are] we can see that at lower discount rates, BTX is more expensive. This shows that there are higher costs borne later on compared with AC, where the costs are borne earlier. However, AC is more effective and only marginally more expensive than BTX, meaning it is cost effective over a lifetime compared with BTX. A time horizon analysis was also carried out on this comparison in Figure 58; this revealed that for the first 5 cycles, about 3 years, BTX alone is cost effective. Between 5 and 16 cycles, about 10 years, BTX with 100% AC after failed BTX is the cost effective strategy. Beyond 16 cycles, AC is cost effective. This shows that for patients with a poor prognosis and for older patients, BTX is a more cost effective option.

[f] The discount rate is applied to all costs and outcomes. The discount rate is applied to future costs and outcomes to establish their present value. The rate of 3.5% reduction in value per year is based on the interest rate. If we invested now for a future expenditure, how much it would cost in present value.

Figure 58: Net benefit compared with age



Note: CE = Cost Effective

If this is then broken down further into the main comparison, AC-BTX100AC we can see the key drivers behind AC's cost effectiveness in Table 9. The BTX100AC strategy is analysed against AC because it is more cost effective and is the most relevant comparison for sub analysis. A patient with AC only will spend more time in the continent group than those in the BTX100AC arm will, their cost of treatment will be lower in spite of higher adverse event rates. The 18 years compared to 11 spent in the continent arm counts towards an increased QALY gain compared with BTX100AC.

Table 9: Cost Breakdown AC-BTX100AC

	Input	AC arm	BTX100AC	Difference
Mean Costs	BTX costs	£0	£10,328	-£10,328
	AC costs	£6,433	£1,053	£5,380
	AE costs	£3,705	£600	£3,105
	UTI costs	£169	£181	-£12
	Appliance costs	£15,776	£15,152	£624
	Total costs	£26,084	£27,315	-£1,231
Mean Outcomes	Years continent	18	11	7
	Years mild incontinent	4	10	-6
	Years incontinent	1	2	-1
	Life years	22.71	22.71	0.00
	QALYS undiscounted	17.02	16.84	0.18
	QALYs discounted	11.46	11.33	0.13

1.3.2 Base case 2 results – Botulinum Toxin versus No Treatment

As a second analysis we looked at a comparison of BTX with a no treatment comparator. This was to ensure that we captured the full range of potential patients in the analysis. For some patients, such as multiple sclerosis patients, the AC comparator is not relevant as neurological deterioration is likely to occur and render the management of the augmented bladder problematic. In the table below, it is possible to see that BTX is cost effective when compared to no treatment with a cost per QALY of under £9,000. This is well below the usual cost effectiveness threshold of £20,000 per QALY gained.

Table 10: BTX – No Treatment base case results

	Mean Cost	Mean QALY	Incremental Cost Effectiveness Ratio
BTX	£25,059	11.01	
No Rx	£11,990	9.43	
Diff (BTX - No Rx)	£13,068	1.58	£8,277

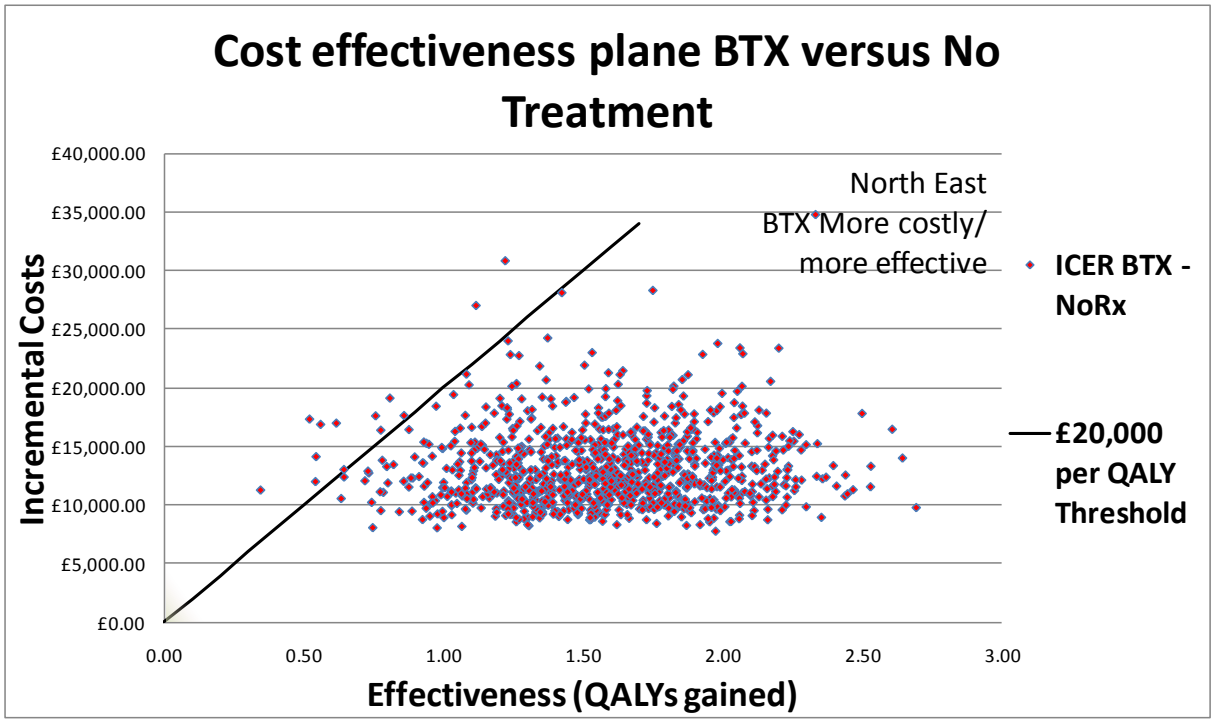
Table 11 shows where the cost and outcome differences lie. The cost of no treatment is lower than BTX but it is not zero. This is due to the cost of incontinence appliances such as pads and catheters. BTX is also more effective with increased time spent in the continence and mild incontinence groups. BTX has higher QALYs but also higher costs so it is cost effective but not dominant.

Table 11: Breakdown of costs and outcomes (BTX – No Rx)

	Input	BTX	NoRx	Difference
Mean Costs	BTX costs	£10,328	£0	£10,328
	AC costs	£0	£0	£0
	AE costs	£15	£0	£15
	UTI costs	£233	£497	-£263
	Appliance costs	£14,483	£11,494	£2,989
	Total costs	£25,059	£11,991	£13,068
Mean Outcomes	Years continent	8	0	8
	Years mild incontinent	9	0	9
	Years incontinent	5	23	-18
	Life years	22.71	22.71	0.00
	QALYS undiscounted	16.35	14.01	2.35
	QALYs discounted	11.01	9.43	1.58

As a result of these costs and of the increased effectiveness of BTX, BTX is more expensive but also more effective with a high degree of certainty. This is displayed on the cost effectiveness plane in Figure 59. This shows that using the probabilistic analysis, all of the cost effectiveness ratios for BTX versus no treatment are to the North East of zero meaning that for all 1000 iterations of the model, BTX is more costly and more effective. And the vast majority, 991, of these ratios fall under the £20,000 per QALY threshold.

Figure 59: Cost effectiveness plane



3.3.3 Sensitivity analysis

Various sensitivity analyses were carried out that explored the uncertainty present in the assumptions that were made in order to construct the model. The Sensitivity analyses are presented in Table 12.

Table 12: Sensitivity analyses results

Intervention	Mean Costs	Mean QALYs	NMB at £20,000 per QALY	Rank at £20,000 per QALY (a)	Change? (b)
Cycle length – 10 months to request retreatment (median – Cruz 2011)					
AC	£31,078	11.57	£200,266	1	No
BTX100AC	£29,551	11.42	£198,792	2	
BTX	£27,053	11.10	£194,875	3	
No-Rx	£15,084	9.49	£174,638	4	
Excluding UTI QoL					
AC	£26,088.58	11.71	£208,105.63	1	No
BTX100AC	£27,498.10	11.57	£203,951.61	2	
BTX	£25,271.63	11.32	£201,075.30	3	
No-Rx	£12,121.38	10.09	£189,670.02	4	
Using 300U BTX instead of 200U					
AC	£26,088.58	11.48	£203,429.74	1	No
BTX100AC	£30,116.97	11.33	£196,538.12	2	
BTX	£28,003.67	11.02	£192,415.95	3	
No-Rx	£12,121.38	9.39	£175,741.72	4	
Paediatric data					
AC	£39,678.25	17.88	£318,013.32	1	No
BTX100AC	£43,694.78	17.78	£311,870.34	2	

Intervention	Mean Costs	Mean QALYs	NMB at £20,000 per QALY	Rank at £20,000 per QALY (a)	Change? (b)
BTX	£42,290.96	17.27	£303,129.24	3	
No-Rx	£31,024.65	14.76	£264,105.93	4	
Stone prevalence					
AC	£26,637.32	11.45	£202,460.43	1	No
BTX100AC	£27,584.51	11.32	£198,783.65	2	
BTX	£25,271.63	10.99	£194,602.92	3	
No-Rx	£12,121.38	9.39	£175,741.72	4	
No standardized mortality ratio applied					
AC	£26,088.58	11.48	£203,429.74	1	No
BTX100AC	£27,498.10	11.32	£198,936.30	2	
BTX	£25,271.63	10.99	£194,602.92	3	
No-Rx	£12,121.38	9.39	£175,741.72	4	
Discount factor analysis					
No Impact on Cost effectiveness but had an impact on the costs and QALYs gained, discussed below.					

(a) Rank denotes the order of cost effectiveness at a £20,000 per QALY threshold.
(b) Change? Refers to whether the result of the sensitivity analysis results in a change in the base case results

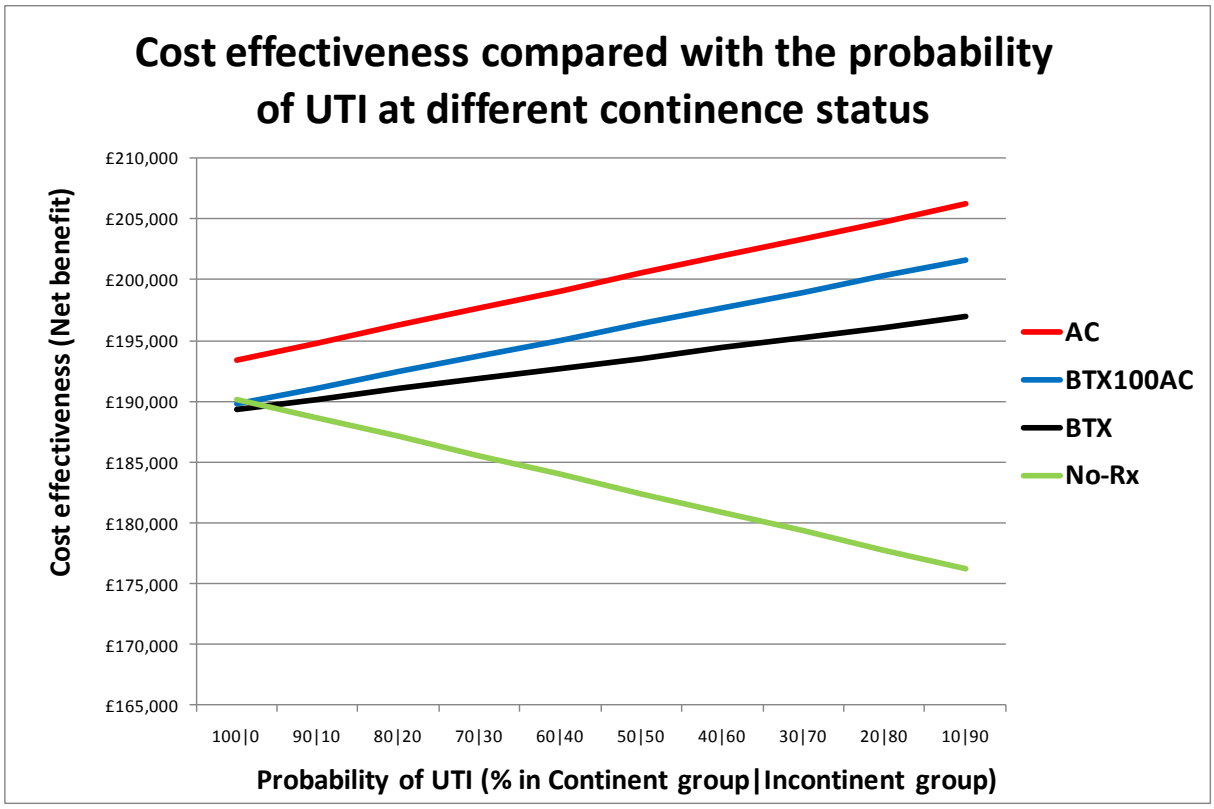
Table 12 shows the impact of various assumptions on the model. The table shows that, varying all of these parameters one by one has no impact on the overall model result at a threshold of £20,000 per QALY. This shows that the model is robust to the error in the assumptions made when constructing the model. There are however two situations where the base case result changes. These are when the cost of 200U of BTX are reduced or increased. One analysis reduced the cost from £276 to £28; at this point BTX100AC becomes more cost effective than AC over a lifetime. This was carried out as a threshold analysis, where the cost is reduced until another strategy becomes cost effective. However, given the cost of BTX currently, this £28 figure is very unlikely to be seen in the future, meaning that this analysis does not represent a realistic situation. The threshold analysis was also taken the other way with the BTX vs No treatment comparison. The cost of BTX was increased to £1,315 per 200U. At this cost, the cost effectiveness ratio of BTX reached the threshold of £20,000 making it no longer cost effective compared to no treatment. Again, this cost is very high and unlikely to be seen, given the current cost of BTX.

The sensitivity analyses set out in table 12 also allow a look at the second base case analysis, BTX vs No-Rx. It is possible to see that BTX alone, is always cost effective when compared to No-Rx, however the variables are altered.

A further factor to consider was the impact of the frequency of UTIs on the cost effectiveness of each intervention at a threshold of £20,000 per QALY. In the base case the probability of UTIs when continent is around 30% per cycle, whereas in incontinent patients the probability is 93% over the same period. However, the GDG felt that this was based on fairly weak evidence and that a sensitivity analysis was required. In order to measure the impact of UTIs, the proportion of UTIs in the incontinent group was reduced from 100% to 0% as the proportion of UTIs in the mild incontinent and continent was increased from 0 to 100%. This gave an idea of how UTIs influence cost effectiveness. In Figure 60 it is possible to see that as the proportion of incontinent UTIs increases so does the cost effectiveness of all the interventions compared to no treatment. The order is also maintained throughout: AC from BTX100AC from BTX from No-Rx. This is true except for one very extreme situation. If incontinent patients have 0% probability of UTIs and continent and mild incontinent patients have 100% probability of UTIs then No-Rx is cost effective compared to both BTX arms. This situation is extreme, however, and unrealistic. It is much more likely that the true

incidence of UTIs in the different groups lies in the range between 80/20 and 20/80, and within this range there is no change to the base case result.

Figure 60: Analysis on the frequency of UTIs by intervention.



I.3.3.51 Impact of discount factor

The discount factor is varied from 0% to 6% per year, in accordance with the NICE reference case. Varying the discount factor makes no difference to the base case result with the same order of Cost effectiveness maintained throughout. However as the discount factor is decreased on costs, BTX alone becomes more costly than AC over a lifetime, with the opposite being true as it is increased. This is in keeping with the fact that with BTX, there are continually high costs throughout, therefore with a high discount rate, costs borne further from the present will decrease in present value. The same, however, is not true of outcomes, as the discount rate is increased or decreased, the QALYs increase or decrease at the same rate as each other, meaning that even though the costs may be changing, the incremental QALYs remain the same so that the order of cost effectiveness is maintained throughout. The specific situation required by the NICE reference case of 3.5% on costs and 1.5% on outcomes results in no change to the results.

I.4 Discussion

18.4.1 Summary of results

The results show that AC is the cost effective intervention at a threshold of £20,000 per QALY over a lifetime horizon. The results also show that BTX is cost effective when compared to no intervention, where AC is not a relevant comparator. BTX100AC is a more cost effective intervention than BTX alone in populations where AC is a relevant comparator. BTX is cost effective for use in patients who have a poorer prognosis or who are likely to deteriorate at such a rate that they will not benefit from being continent beyond ten years. The results are generally robust to the uncertainty around the assumptions made as shown by the deterministic sensitivity analyses. The probabilistic data shows

that at a threshold of £20,000 per QALY gained AC is cost effective with a probability of 78%, again demonstrating the robustness of the model to uncertainty.

3.4.2 limitations & interpretation

The many limitations are almost entirely due to the lack of good quality data to populate the model. Perhaps the most important limitation is the fact that there is no comparative data on AC and BTX. Therefore the comparison between these two interventions is made on the basis of two fairly heterogeneous studies. The BTX vs placebo study was a randomized control trial [3] whereas the study used to provide AC data was based on observational data [10]. This disparity means that the outcomes: continence, mild incontinence and incontinence, are not measured in the same way. It was necessary for the GDG to make assumptions about the definition of what constituted these outcomes, which was not ideal but given the available data was the only solution. The result of this is that it makes the comparison of BTX with no treatment more reliable than the comparison of AC with BTX or no treatment. However, the probabilistic analysis allows us to take this uncertainty into account and deal with it explicitly.

Another issue with the model is the lack of long term data for both AC and BTX. The BTX study followed patients up for less than a year and the AC study was based on follow up of 2.5 years. This meant that we had to assume that the long term efficacy of BTX did not reduce and that people would not change from one outcome group to another later on in the model. This may limit the reliability of the longer term conclusions.

There was a lack of data on children from the clinical review and in the literature more generally. This is probably due to the fact that there is no licence for BTX and therefore clinicians are reluctant to look at BTX in children. However, there was some data for the side effects in AC in children. Using this in a sensitivity analysis allowed some consideration of this limitation even if the effectiveness data had to be extrapolated from the adult data.

The data on UTI was another limitation that restricted the model. Firstly there was an assumption that both mild incontinent and continent had the same frequency of episodes. Secondly, the Game 2008[12] study was used to determine the rates. However, this was a study based on 30 patients and did not provide as much information as would be desirable. The sensitivity analysis looked at this limitation in some detail and found that there is no meaningful difference in cost effectiveness as a result of UTI incidence.

A further limitation was around the cost of BTX. BTX has no licence for this indication and is therefore not costed appropriately in the BNF or NHS drug tariff. The cost used therefore is likely to change if BTX has a licensed approved. However using the sensitivity analyses it is possible to see that only if the cost of BTX becomes extremely cheap or extremely expensive will it change the base case results of this model. This means that the results insensitive to changes in the cost of BTX. The assumptions made about appliance use were kept as simple as possible so as not to over complicate the model. The costs of catheters and appliances that are calculated following the assumptions that have been made about their usage produced a fairly conservative estimation of the differences in appliance use between the comparator groups.

The final limitation to discuss was the problem with the utility data that informed the adverse event rates, these rates were informed by utilities that came from fairly disconnected sources that describe GI and Urinary tract symptoms and perforations more generally rather than the specifics of the AEs that we were looking at. However if the AE utilities are removed or given a value of 0.5, a very high disutility, there is no difference in the overall result although BTX becomes cost effective for more of the time horizon. The model is therefore fairly robust to changes in the utility of AC adverse events.

1.4.3 Generalisability to other populations / settings

The analysis took place in two parts. The first part being the comparison of all interventions in a population where all comparators were relevant, such as a spinal cord injured population. The second part was a comparison of just BTX with no treatment. This was therefore in a population where AC was not a relevant comparator such as patients with multiple sclerosis. This analysis is therefore generalisable to any patient that suffers from incontinence due to NLUTD in the UK. The model is also of potential relevance to populations outside of the UK as the model is fairly robust to changes in costs and impact of adverse events.

Comparisons with published studies

Only one other cost effectiveness study has been done that analyses AC vs BTX. The study by Padmanabhan et al. 2011[19] showed that BTX would cost about $5,000 less than AC per successful intervention. However this analysis only uses adverse events as outcomes and is a five year study from a US payer perspective. This is in keeping with what our model shows as BTX only is shown to be cost effective when compared with AC for the first six years of the model. However as the Padmanabhan study is from a US payer perspective and does not consider outcomes beyond adverse events, its relevance to the UK perspective is limited.

1.4.4 Conclusion = evidence statement

The results of the model allow four main conclusions to be drawn:

1. AC is the cost effective intervention over a lifetime horizon in the populations where it is a relevant comparator.
2. BTX is cost effective compared to AC in patients where the full benefits of surgery are unlikely to be accrued (patients with shorter life expectancy or patients with a rapidly degenerating condition).
3. A BTX strategy where AC is used (and relevant) in 100% of patients after failed BTX is cost effective compared to a 0% progression to AC strategy but is higher cost.
4. BTX is cost effective when compared to no treatment.

1.4.5 Implications for future research

The limitations of this study were fundamentally due to a lack of data in fairly key areas. Lack of comparative data between BTX and AC and AC and no treatment hindered the development of the model. Another area that was lacking in data was longer term outcomes associated with BTX and AC. An area for research that would provide this model with more precise data would be better data on the utilities associated with adverse events stemming from AC.

Appendix J: Research recommendations

J.1 Safety and efficacy of antimuscarinics 492

J.1.1 What is the safety and efficacy of more recently developed antimuscarinics compared with a) placebo/usual care b) other antimuscarinics in the treatment of neurogenic lower urinary tract dysfunction? 492

J.2 Safety and efficacy of botulinum toxin 492

J.2.1 What is the safety and efficacy of Botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in people with incontinence in neurological disease? 492

J.2.2 What is the safety and efficacy of Botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in people with primary cerebral conditions with lower urinary tract dysfunction? 492

J.3 Management strategies to reduce the risk of symptomatic UTIs 493

J.3.1 In patients with neurogenic lower urinary tract dysfunction, which management strategies (including the use of prophylactic antibiotics and various invasive and non-invasive techniques to aid bladder drainage) reduce the risk of symptomatic urinary tract infections? 493

J.4 Bladder management strategies 493

J.4.1 What are the long-term risks and effects on quality of life of different bladder management strategies for lower urinary tract dysfunction in people with neurological disease? 493

J.1 Safety and efficacy of antimuscarinics

J.1.1 What is the safety and efficacy of more recently developed antimuscarinics compared with a) placebo/usual care b) other antimuscarinics in the treatment of neurogenic lower urinary tract dysfunction?

Why this is important: No high quality clinical trials, looking at the use of the newer antimuscarinic drugs in the population with neurogenic LUT dysfunction, have been carried out. Both placebo-controlled and comparative studies are lacking. This is important because the more recently developed medications are inevitably more expensive whilst claiming (in the non-neurogenic population) to be freer of adverse side effects. The adverse effects of antimuscarinics are mostly due to that same action at sites other than the bladder (e.g. a dry mouth) but there is now increasing concern that central antimuscarinic effects may adversely impact on cognitive function in both children with brain damage (cerebral palsy or hydrocephalus) and adults with impaired cognition (due to cerebral involvement by Multiple Sclerosis or neurodegenerative diseases).

J.2 Safety and efficacy of botulinum toxin

J.2.1 What is the safety and efficacy of Botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in people with incontinence in neurological disease?

Why this is important: Further research is required to determine whether repeated intradetrusor injections of Botulinum toxin type A (BTX) have long term efficacy. The efficacy in terms of continence and upper urinary tract preservation should be studied.

BTX injection into the detrusor is an effective means of managing continence, and improves urodynamic measures of bladder storage with the potential to protect the kidneys from the effects of high intravesical pressures. It is well tolerated in a spectrum of conditions and ages. However, the longer term efficacy over many injections has not been established.

A clinical trial is required to study the outcome in terms of continence and renal preservation over many cycles of repeated injection. Quality of life is an important outcome. This should enrol children and adults. The indications for BTX need not be modified for inclusion, but entrants into a trial must have anatomically normal kidneys (on imaging) and have normal renal function.

J.2.2 What is the safety and efficacy of Botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in people with primary cerebral conditions with lower urinary tract dysfunction?

Why this is important: The effects of intradetrusor Botulinum toxin type A injection (BTX) should be investigated in groups of patients with underlying cerebral conditions that are associated with lower urinary tract dysfunction, as well as those with spinal cord injury, spinal dysraphism and multiple sclerosis. Reports of its use in other conditions are limited to small numbers of patients within case series studies that include heterogeneous groups of patients. Potential benefits of successful treatment in cerebral disease may include the avoidance of cognitive impairment which can be seen as a side effect of antimuscarinic medication.

A trial should include patients with primary cerebral conditions including (but not restricted to) stroke, head injury and cerebral palsy, but excluding multiple sclerosis. Children and adults should be recruited. Tolerability and acceptability are important outcomes, as well as the primary outcomes of continence, preservation of the upper urinary tracts and quality of life. Measurement of carer burden and quality of life is also important.

J.3 Management strategies to reduce the risk of symptomatic UTIs

J.3.1 In patients with neurogenic lower urinary tract dysfunction, which management strategies (including the use of prophylactic antibiotics and various invasive and non-invasive techniques to aid bladder drainage) reduce the risk of symptomatic urinary tract infections?

Why this is important: Recurrent UTIs in patients with neurogenic bladder dysfunction are a cause of considerable morbidity. UTIs may exacerbate incontinence, cause symptoms of malaise and may progress to involve the upper urinary tract with possible loss of renal function. In the population with neurological diseases such as Multiple Sclerosis (MS), Parkinson's Disease and Dementia, the rise in temperature with UTI can cause deterioration in neurological function and even a relapse of MS. There are therefore numerous reasons why patients with neurogenic LUT dysfunction should avoid UTIs.

The causes for the high prevalence of UTIs in such patients include loss of physiological bladder function and high intravesical pressures. Intermittent or permanent catheterisation inevitably exacerbate the problem but incomplete bladder emptying is also a predisposing factor for UTI.

Research in this area is faced by methodological difficulties, not least because it may be difficult to distinguish between bladder colonisation (asymptomatic bacteriuria) and true infection.

In the face of the considerable clinical burden of UTI and the global problem of antibiotic resistance, it is important to establish whether or not any infection prevention strategies, including patient training or the provision of information relating to prophylactic antibiotics are effective in reducing symptomatic UTIs.

J.4 Bladder management strategies

J.4.1 What are the long-term risks and effects on quality of life of different bladder management strategies for lower urinary tract dysfunction in people with neurological disease?

Why this is important: The range of bladder management strategies available to manage LUTD in neurological disease include, permanent urethral catheterisation and suprapubic catheterisation, intermittent self-catheterisation, penile sheath collection systems and pads. However, there is very sparse evidence about which strategies are most acceptable to patients and their carers. The current research base relates mainly to the spinal injury population but may be relevant to people with other neurological diseases.

Bladder management strategies are a long term treatment with implications for maintaining health and quality of life. In order to make informed choices about the most appropriate method of bladder management, patients and their carers require information about the risks and benefits of the available options. There is currently little evidence about which methods are most likely to produce long-term complications (renal impairment, urinary stones and infections, hydronephrosis, bladder malignancy). The effect on quality of life for patients and their carers of different bladder management strategies is not known. There are methodological difficulties due

to the heterogeneity of the population with neurological disease, the long time course of treatments and the presence of cognitive impairment in some sub-populations.

Proposed studies could include prospective cohort studies of disease-specific populations examining the effect of each method on quality of life using both generic and disease-specific assessment methods. In addition prospective screening for complications including renal impairment, stone formation and infection should be carried out and comparisons made for each bladder management method. Particular emphasis should be placed on quality of life outcomes for carers, especially for those looking after patients with cognitive impairment.

Appendix K: Excluded studies

K.1 What is the safety and efficacy of antimuscarincs compared with a) placebo/usual care b) other antimuscarinics 497

K.1.1 Clinical studies excluded 497

K.1.2 Economic Studies excluded 499

K.2 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care in neurological disease? 500

K.2.1 Clinical studies excluded 500

K.2.2 Economic studies excluded 501

K.3 Does the use of the following direct treatment: Clinical assessment, urine culture, residual urine estimate, bladder diary/frequency volume chart 501

K.3.1 Clinical Studies excluded 501

K.3.2 Economic Studies excluded 502

K.4 Does the use of the following direct treatment or stratify risk (of renal complications such as hydronephrosis): Filling cystometry, leak point pressure measurements, pressure flow studies of voiding, video urodynamics. 502

K.4.1 Clinical studies excluded 502

K.4.2 Economic studies excluded 504

K.5 What criteria or signs/symptoms should be used to refer patients for specialist assessment? 504

K.6 What is the safety and efficacy of intravesical botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in neurological disease? 504

K.6.1 Clinical studies excluded 504

K.6.2 Economic studies excluded 505

K.7 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? What is the quality of life associated with the above? 505

K.7.1 Clinical studies excluded 506

K.7.2 Economic studies excluded 507

K.8 Does monitoring or do surveillance protocols improve patient outcomes? 507

K.8.1 Clinical studies included 507

K.8.2 Economic studies excluded 508

K.9 What is the safety and efficacy of augmentation cystoplasty compared with usual care in neurological disease? 508

K.9.1 Clinical studies excluded 508

K.9.2 Economic studies excluded 509

K.10 Do behavioural management programmes (timed voiding, voiding on request, bladder retraining, habit retraining,) compared with a) each other b) usual care, improve outcomes? 509

K.10.1 Clinical studies excluded 509

K.10.2 Economic studies excluded 510

K.11 Does pelvic floor muscle training with or without electrical stimulation or biofeedback compared with treatment as usual, improve outcomes? 510

K.11.1 Clinical studies excluded 510

K.11.2 Economic studies excluded 511

K.12 What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease? 511

K.13 What is the safety and efficacy of urethral tape and sling surgery compared with usual care in neurological disease? 512

K.13.1 Clinical studies excluded 512

K.13.2 Economic studies excluded 512

K.14 What is the safety and efficacy of artificial urinary sphincter compared with other treatments in neurological disease? 512

K.14.1 Clinical studies excluded 512

K.14.2 Economic studies excluded 513

K.15 What is the efficacy of the ileal conduit diversion compared with usual care in neurological disease? 513

K.15.1 Clinical studies excluded 513

K.15.2 Economic studies excluded 514

K.16 Do prophylactic antibiotics reduce the risk of symptomatic urinary tract infections? 514

K.16.1 Clinical evidence excluded 514

K.16.2 Economic evidence excluded 515

K.17 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services? 515

K.17.1 Clinical studies excluded 515

K.17.2 Economic studies excluded 516

K.18 Does provision of information about the management of neurological lower urinary tract dysfunction improve patient outcomes? 516

K.18.1 Clinical studies excluded 516

K.18.2 Economic studies excluded 517

K.19 For patients and their carers with lower urinary tract dysfunction associated with neurological disorders, what are the experiences of access to and interaction with services, that address these issues? 517

K.19.1 Clinical studies excluded 517

K.1 What is the safety and efficacy of antimuscarincs compared with a) placebo/usual care b) other antimuscarinics

K.1.1 Clinical studies excluded

Author/title	Reason for exclusion
Ab E, Dik P, Klijn AJ et al. Detrusor overactivity in spina bifida: how long does it need to be treated? Neurourology & Urodynamics. 2004; 23(7):685-688. Ref ID: 664	Sample size < 20
Amark P, Eksborg S, Juneskans O et al. Pharmacokinetics and effects of intravesical oxybutynin on the paediatric neurogenic bladder. British Journal of Urology. 1998; 82(6):859-864. Ref ID: 582	Sample size < 20
Amend B, Hennenlotter J, Schafer T et al. Effective treatment of neurogenic detrusor dysfunction by combined high-dosed antimuscarinics without increased side-effects. European Urology. 2008; 53(5):1021-1028. Ref ID: 676	Quasi RCT
Bennett N, O'Leary M, Patel AS et al. Can higher doses of oxybutynin improve efficacy in neurogenic bladder? Journal of Urology. 2004; 171(2:Pt 1):749-751. Ref ID: 697	Wrong comparison. Dose escalation study
Buyse G, Verpoorten C, Vereecken R et al. Intravesical application of a stable oxybutynin solution improves therapeutic compliance and acceptance in children with neurogenic bladder dysfunction. Journal of Urology. 1998; 160(3:Pt 2):1084-1087. Ref ID: 706	Sample size < 20
Buyse G, Verpoorten C, Vereecken R et al. Treatment of neurogenic bladder dysfunction in infants and children with neurospinal dysraphism with clean intermittent (self)catheterisation and optimized intravesical oxybutynin hydrochloride therapy. European Journal of Pediatric Surgery. 1995; 5(SUPPL. 1):31-34. Ref ID: 614	Sample size < 20
Cameron AP, Clemens JQ, Latini JM et al. Combination Drug Therapy Improves Compliance of the Neurogenic Bladder. Journal of Urology. 2009; 182(3):1062-1067. Ref ID: 46	Wrong comparison. No drug vs two or three drug combinations (drugs not all antimuscarinics)
Cartwright PC, Coplen DE, Kogan BA et al. Efficacy and safety of transdermal and oral oxybutynin in children with neurogenic detrusor overactivity. Journal of Urology. 2009; 182(4):1548-1554. Ref ID: 714	Wrong comparison. Transdermal vs oral
Chapple CR, Khullar V, Gabriel Z et al. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. [Review] [52 refs]. European Urology. 2008; 54(3):543-562. Ref ID: 739	Population not neurological disease
Ellsworth PI, Borgstein NG, Nijman RJ et al. Use of tolterodine in children with neurogenic detrusor overactivity: relationship between dose and urodynamic response. Journal of Urology. 2005; 174(4:Pt 2):1647-1651. Ref ID: 776	Wrong comparison. Dose escalation study
Ersoz M, Yildiz N, Akyuz M et al. Efficacy of combined oral-intravesical oxybutynin hydrochloride treatment for patients with overactive detrusors and indwelling urethral catheters. Rehabilitation nursing : the official journal of the Association of Rehabilitation Nurses. 2010; 35(2):80-86. Ref ID: 94	Sample size < 20
Ethans KD, Nance PW, Bard RJ et al. Efficacy and safety of tolterodine in people with neurogenic detrusor overactivity. Journal of Spinal Cord Medicine. 2004; 27(3):214-218. Ref ID: 778	Sample size < 20
Franco I, Horowitz M, Grady R et al. Efficacy and safety of oxybutynin in children with detrusor hyperreflexia secondary to neurogenic bladder dysfunction. Journal of Urology. 2005; 173(1):221-225. Ref ID: 398	Results of study 2 excluded due to sample size < 20
George J, Tharion G, Richard J et al. The effectiveness of intravesical oxybutynin, propantheline, and capsaicin in the management of neuropathic bladder following spinal cord injury. TheScientificWorldJournal. 2007; 7(pp 1683-1690):-	Sample size < 20

Author/title	Reason for exclusion
1690. Ref ID: 191	
Greenfield SP, Fera M. The use of intravesical oxybutynin chloride in children with neurogenic bladder. Journal of Urology. 1991; 146(2 (Pt 2)):532-534. Ref ID: 1131	Sample size < 20
Grigoleit U, Murtz G, Laschke S et al. Efficacy, Tolerability and Safety of Propiverine Hydrochloride in Children and Adolescents with Congenital or Traumatic Neurogenic Detrusor Overactivity-A Retrospective Study. European Urology. 2006; 49(6):1114-1121. Ref ID: 297	The conditions under which reference standards as well as the time intervals between reference and during-treatment assessment, varied widely between patients
Guerra LA, Moher D, Sampson M et al. Intravesical oxybutynin for children with poorly compliant neurogenic bladder: a systematic review. Journal of Urology. 2008; 180(3):1091-1097. Ref ID: 70	Included a master's thesis in the review. Other relevant studies included
Haferkamp A, Staehler G, Gerner HJ et al. Dosage escalation of intravesical oxybutynin in the treatment of neurogenic bladder patients. Spinal Cord. 2000; 38(4):250-254. Ref ID: 803	Wrong comparison. Dose escalation study
Hebjorn S. Treatment of detrusor hyperreflexia in multiple sclerosis: a double-blind, crossover clinical trial comparing methantheline bromide (Banthine), flavoxate chloride (Urispas) and meladrazine tartrate (Lisidonil). Urologia Internationalis. 1977; 32(2-3):209-217. Ref ID: 259	Wrong drug intervention (two drugs not in BNF)
Holland AJA, King PA, Chauvel PJ et al. Intravesical therapy for the treatment of neurogenic bladder in children. Australian and New Zealand Journal of Surgery. 1997; 67(10):731-733. Ref ID: 602	Sample size < 20
Horstmann M, Schaefer T, Aguilar Y et al. Neurogenic bladder treatment by doubling the recommended antimuscarinic dosage. Neurourology & Urodynamics. 2006; 25(5):441-445. Ref ID: 834	Wrong comparison. Non RCT of low vs high dose
Isik AT, Celik T, Bozoglu E et al. Trospium and cognition in patients with late onset Alzheimer disease. Journal of Nutrition, Health & Aging. 2009; 13(8):672-676. Ref ID: 838	Wrong intervention. Trospium vs tropsium and/or galantamine
Jewart RD, Green J, Lu CJ et al. Cognitive, behavioral, and physiological changes in Alzheimer disease patients as a function of incontinence medications. American Journal of Geriatric Psychiatry. 2005; 13(4):324-328. Ref ID: 840	Sample size < 20
Kaefer M, Pabby A, Kelly M et al. Improved bladder function after prophylactic treatment of the high risk neurogenic bladder in newborns with myelomentingocele. Journal of Urology. 1999; 162(3:Pt 2):1068-1071. Ref ID: 844	Wrong comparison. Early vs later initiation of therapy
Kasabian NG, Vlachiotis JD, Lais A et al. The use of intravesical oxybutynin chloride in patients with detrusor hypertonicity and detrusor hyperreflexia. Journal of Urology. 1994; 151(4):944-945. Ref ID: 633	Sample size < 20
Kennelly MJ, Lemack GE, Foote JE et al. Efficacy and safety of oxybutynin transdermal system in spinal cord injury patients with neurogenic detrusor overactivity and incontinence: an open-label, dose-titration study. Urology. 2009; 74(4):741-745. Ref ID: 864	Wrong comparison. Dose escalation study
Kim YH, Bird ET, Priebe M et al. The role of oxybutynin in spinal cord injured patients with indwelling catheters. Journal of Urology. 1997; 158(6):2083-2086. Ref ID: 869	Non-RCT
Lobo ED, Quinlan T, O'Brien L et al. Population pharmacokinetics of Orally administered duloxetine in patients: Implications for dosing recommendation. Clinical Pharmacokinetics. 2009; 48(3):189-197. Ref ID: 7	Wrong pharmacological intervention

Author/title	Reason for exclusion
Mahanta K, Medhi B, Kaur B et al. Comparative efficacy and safety of extended-release and instant-release tolterodine in children with neural tube defects having cystometric abnormalities. Journal of Pediatric Urology. 2008; 4(2):118-123. Ref ID: 907	Wrong comparison. Extended vs instant-release tolterodine
Mizunaga M, Miyata M, Kaneko S et al. Intravesical instillation of oxybutynin hydrochloride therapy for patients with a neuropathic bladder. Paraplegia. 1994; 32(1):25-29. Ref ID: 634	Sample size < 20
O'Leary M, Erickson JR, Smith CP et al. Effect of controlled-release oxybutynin on neurogenic bladder function in spinal cord injury. Journal of Spinal Cord Medicine. 2003; 26(2):159-162. Ref ID: 491	Sample size < 20
Pannek J, Sommerfeld HJ, Botel U et al. Combined intravesical and oral oxybutynin chloride in adult patients with spinal cord injury. Urology. 2000; 55(3):358-362. Ref ID: 961	Wrong comparison. Oral vs oral plus intravesical oxybutynin therapy
Pannek J, Diederichs W, Botel U. Urodynamically controlled management of spinal cord injury in children. Neurourology and Urodynamics. 1997; 16(4):285-292. Ref ID: 604	Sample size < 20
Prasad KVR, Vaidyanathan S. Intravesical oxybutynin chloride and clean intermittent catheterisation in patients with neurogenic vesical dysfunction and decreased bladder capacity. British Journal of Urology. 1993; 72(5 II):719-722. Ref ID: 635	Sample size < 20
Saito M, Watanabe T, Tabuchi F et al. Urodynamic effects and safety of modified intravesical oxybutynin chloride in patients with neurogenic detrusor overactivity: 3 Years experience. International Journal of Urology. 2004; 11(8):592-596. Ref ID: 432	Sample size < 20
Singh G, Thomas DG. Intravesical oxybutynin in patients with posterior rhizotomies and sacral anterior root stimulators. Neurourology and Urodynamics. 1995; 14(1):65-71. Ref ID: 625	Sample size < 20
Stohrer M, Murtz G, Kramer G et al. Efficacy and tolerability of propiverine hydrochloride extended release compared to immediate release in patients with neurogenic detrusor overactivity (Abstract number 448). Proceedings of the 39th Annual Meeting of the International Continence Society (ICS), 2009 Sep 29 - Oct 3, San Francisco, CA. 2009; Ref ID: 1130	Wrong comparison. Extended versus immediate release
Szollar SM, Lee SM. Intravesical oxybutynin for spinal cord injury patients. Spinal Cord. 1996; 34(5):284-287. Ref ID: 1055	Sample size < 20
Vaidyananthan S, Soni BM, Brown E et al. Effect of intermittent urethral catheterization and oxybutynin bladder instillation on urinary continence status and quality of life in a selected group of spinal cord injury patients with neuropathic bladder dysfunction. Spinal Cord. 1998; 36(6):409-414. Ref ID: 589	Sample size < 20
Youdim K, Kogan BA. Preliminary study of the safety and efficacy of extended-release oxybutynin in children. Urology. 2002; 59(3):428-432. Ref ID: 520	Included non-neurogenic patients

K.1.2 Economic Studies excluded

Author/title	Notes
Cardozo L, Thorpe A, Warner J, and Sidhu M. The cost-effectiveness of solifenacin vs fesoterodine, oxybutynin immediate-release, propiverine, tolterodine extended-release and tolterodine immediate-release in the treatment of patients with overactive bladder in the UK National Health Service. British Journal of Urology International, 2010.	Non-neurogenic population of patients; UK perspective
Pradelli L and Iannazzo S. Solifenacin in the treatment of overactive bladder syndrome in Italian patients: pharmacoeconomic evaluation. Journal of Medical	Non-neurogenic population of patients;

Author/title	Notes
Economics, 2009.	Italian perspective
Milsom I, Axelsen S, Kulseng-Hansen S, Mattiasson A, Nilsson C G, and Wickstrom J. Cost-effectiveness analysis of solifenacin flexible dosing in patients with overactive bladder symptoms in four Nordic countries. Acta Obstetricia et Gynecologica Scandinavica, 2009.	Non-neurogenic population of patients; perspective of four Nordic countries
Hakkaart L, Verboom P, Phillips R, and Al M J. The cost utility of solifenacin in the treatment of overactive bladder. International Urology & Nephrology, 2009.	Non-neurogenic population of patients; UK perspective
Speakman M, Khullar V, Mundy A, Odeyemi I, and Bolodeoku J. A cost-utility analysis of once daily solifenacin compared to tolterodine in the treatment of overactive bladder syndrome. Current Medical Research and Opinion, 2008.	Non-neurogenic population of patients; UK perspective
Ko Y, Malone D C, and Armstrong E P. Pharmacoeconomic evaluation of antimuscarinic agents for the treatment of overactive bladder. Pharmacotherapy, 2006.	Non-neurogenic population of patients; US perspective
Hughes D A and Dubois D. Cost-effectiveness analysis of extended-release formulations of oxybutynin and tolterodine for the management of urge incontinence. Pharmacoeconomics, 2004.	Non-neurogenic population of patients; UK perspective
Jumadilova Z, Varadharajan S, Girase P, and Ollendorf D A. Retrospective evaluation of outcomes in patients with overactive bladder receiving tolterodine versus Oxybutynin. American Journal of Health-System Pharmacy, 2006.	Non-neurogenic population of patients (95% of patients); US perspective
Getsios D, Caro J J, Ishak K J, El-Hadi W, Payne K, O'Connel M, Albrecht D, Feng D, and Dubois D. Oxybutynin extended release and tolterodine immediate release: a health economic comparison. Clinical Drug Investigation, 2004.	Non-neurogenic population of patients; UK perspective
Getsios D, Caro J J, Ishak K J, Hadi El W, and Payne K. Canadian economic comparison of extended-release oxybutynin and immediate-release tolterodine in the treatment of overactive bladder. Clinical Therapeutics, 2004.	Non-neurogenic population of patients; Canadian perspective
Guest J F, Abegunde D, and Ruiz F J. Cost effectiveness of controlled-release oxybutynin compared with immediate-release oxybutynin and tolterodine in the treatment of overactive bladder in the UK, France and Austria. Clinical Drug Investigation, 2004.	Non-neurogenic population of patients; UK, French, and Austrian perspectives
Kobelt G, Jonsson L, and Mattiasson A. Cost-effectiveness of new treatments for overactive bladder: the example of tolterodine, a new muscarinic agent. A Markov model. Neurourology and Urodynamics, 1998.	Non-neurogenic population of patients; Swedish perspective

K.2 What is the safety and efficacy of alpha adrenergic antagonists compared with a) other adrenergic antagonists b) placebo/usual care in neurological disease?

K.2.1 Clinical studies excluded

Study	Rationale for exclusion
Amark P, Beck O. Effect of phenylpropanolamine on incontinence in children with neurogenic bladders. A double-blind crossover study. Acta Paediatrica. 1992; 81(4):345-350. Ref ID: AMARK1992	Drug not in BNF
Bennett JK, Foote J, El-Leithy TR et al. Terazosin for vesicosphincter dyssynergia in spinal cord-injured male patients. Molecular Urology. 2000; 4(4):415-420. Ref ID: BENNETT2000	Observational study
Delauche-Cavallier MC, Richard JM, Buzelin M et al. Alpha-blocker therapy with alfuzosin in neurogenic bladder disease. Neurourology & Urodynamics. 1993;	Abstract

Study	Rationale for exclusion
12(4):343-344. Ref ID: DELAUCHECAVALLIER1993	
Delauche-Cavallier MC, Costa P, Robain R et al. Efficacy and tolerability of 3 doses of intravenous alfuzosin in neurogenic bladder disease. Neurourology & Urodynamics. 1993; 12(4):344-345. Ref ID: DELAUCHECAVALLIER1993A	Abstract
Hachen HJ. Clinical and urodynamic assessment of alpha-adrenolytic therapy in patients with neurogenic bladder function. Paraplegia. 1980; 18(4):229-240. Ref ID: HACHEN1980	Observational study
Husmann DA. Use of sympathetic alpha antagonists in the management of pediatric urologic disorders. [Review] [49 refs]. Current Opinion in Urology. 2006; 16(4):277-282. Ref ID: HUSMANN2006	Review
Kakizaki H, Ameda K, Kobayashi S et al. Urodynamic effects of alpha1-blocker tamsulosin on voiding dysfunction in patients with neurogenic bladder. International Journal of Urology. 2003; 10(11):576-581. Ref ID: KAKIZAKI2003	Observational study
Sakakibara R, Hattori T, Uchiyama T et al. Are alpha-blockers involved in lower urinary tract dysfunction in multiple system atrophy? A comparison of prazosin and moxisylyte. Journal of the Autonomic Nervous System. 2000; 79(2-3):191-195. Ref ID: SAKAKIBARA2000	Wrong drug comparison
Swierzewski SJ, III, Gormley EA, Belville WD et al. The effect of terazosin on bladder function in the spinal cord injured patient. Journal of Urology. 1994; 151(4):951-954. Ref ID: SWIERZEWSKI1994	Observational study
Vaidyanathan S.Rao. Possible use of indoramin in patients with chronic neurogenic bladder dysfunction. Journal of Urology 129 (1):96-101, 1983.	Observational study
Yamanishi T, Yasuda K, Homma Y et al. A multicenter placebo-controlled, double-blind trial of urapidil, an alpha-blocker, on neurogenic bladder dysfunction. European Urology. 1999; 35(1):45-51. Ref ID: YAMANISHI1999	Drug not in BNF
Yasuda K, Yamanishi T, Kawabe K et al. The effect of urapidil on neurogenic bladder: a placebo controlled double-blind study. Journal of Urology. 1996; 156(3):1125-1130. Ref ID: YASUDA1996	Drug not in BNF

K.2.2 Economic studies excluded

No relevant economic evaluations comparing alpha adrenergic antagonists with usual care were identified.

K.3 Does the use of the following direct treatment: Clinical assessment, urine culture, residual urine estimate, bladder diary/frequency volume chart

K.3.1 Clinical Studies excluded

Author/title	Reason for exclusion
Borg H, Holmdahl G, Olsson I et al. Impact of spinal cord malformation on bladder function in children with anorectal malformations. Journal of Pediatric Surgery. 2009; 44(9):1778-1785. Ref ID: BORG2009	No relevant outcomes
Chandiramani VA, Palace J, Fowler CJ. How to recognize patients with parkinsonism who should not have urological surgery. British Journal of Urology. 1997; 80(1):100-104. Ref ID: CHANDIRAMANI1997	No relevant outcomes
Jensen AE, Hjeltnes N, Berstad J et al. Residual urine following intermittent catheterisation in patients with spinal cord injuries. Paraplegia. 1995; 33(12):693-696. Ref ID: JENSEN1995	No relevant outcomes
Persun ML, Ginsberg PC, Harmon JD et al. Role of urologic evaluation in the adult spina bifida patient. Urologia Internationalis. 1999; 62(4):205-208. Ref ID:	No relevant outcomes

Author/title	Reason for exclusion
PERSUN1999	
Sammour ZM, Gomes CM, Barbosa ER et al. Voiding dysfunction in patients with Parkinson's disease: impact of neurological impairment and clinical parameters. Neurourology & Urodynamics. 2009; 28(6):510-515. Ref ID: SAMMOUR2009	No relevant outcomes
Sasani M, Asghari B, Asghari Y et al. Correlation of cutaneous lesions with clinical radiological and urodynamic findings in the prognosis of underlying spinal dysraphism disorders. Pediatric Neurosurgery. 2008; 44(5):360-370. Ref ID: SASANI2008	No relevant outcomes
Tins B, Teo HG, Popuri R et al. Follow-up imaging of the urinary tract in spinal injury patients: is a KUB necessary with every ultrasound? Spinal Cord. 2005; 43(4):219-222. Ref ID: TINS2005	No relevant outcomes
Vaidyanathan S, Hughes PL, Soni BM. A comparative study of ultrasound examination of urinary tract performed on spinal cord injury patients with no urinary symptoms and spinal cord injury patients with symptoms related to urinary tract: do findings of ultrasound examination lead to changes in clinical management? TheScientificWorldJournal. 2006; 6:2450-2459. Ref ID: VAIDYANATHAN2006	No relevant outcomes

K.3.2 Economic Studies excluded

Author/title	Notes
Weber A M, Taylor R J, Wei J T, Lemack G, Piedmonte M R, and Walter M D. The cost-effectiveness of preoperative testing (basic office assessment vs urodynamics) for stress urinary incontinence in women. British Journal of Urology International, 2002.	Non-neurogenic population of patients; US perspective
Weber A M and Walters M D. Cost-effectiveness of urodynamic testing before surgery for women with pelvic organ prolapse and stress urinary incontinence. American Journal of Obstetrics and Gynecology, 2000	Non-neurogenic population of patients; US perspective

K.4 Does the use of the following direct treatment or stratify risk (of renal complications such as hydronephrosis): Filling cystometry, leak point pressure measurements, pressure flow studies of voiding, video urodynamics.

K.4.1 Clinical studies excluded

Author/title	Reason for exclusion
Decter RM, Bauer SB, Khoshbin S et al. Urodynamic assessment of children with cerebral palsy. Journal of Urology. 1987; 138(4 Pt 2):1110-1112. Ref ID: DECTER1987	No relevant outcome data
Gomelsky AL. Urodynamic patterns following ischemic spinal cord events. Journal of Urology. 2003; 170(1):122-125. Ref ID: GOMELSKY2003	No relevant outcome data
Groenendijk PM, Nyeholt AA, Heesakkers JP et al. Urodynamic evaluation of sacral neuromodulation for urge urinary incontinence. BJU International. 2008; 101(3):325-329. Ref ID: GROENENDIJK2008	Non-neurogenic population
Gunasekera WS, Richardson AE, Seneviratne KN et al. Detrusor hyperreflexia in neurogenic bladder disorders caused by localized partial lesions of the spinal cord and cauda equina. Surgical Neurology. 1983; 20(1):63-66. Ref ID: GUNASEKERA1983	No relevant outcome data
Gupta AT. Urodynamic profile in myelopathies: A follow-up study. Annals of Indian Academy of Neurology. 2009; 12(1):35-39. Ref ID: GUPTA2009	Relationship between urodynamics and

Author/title	Reason for exclusion
	neurological recovery
Houser EE, Bartholomew TH, Cookson MS et al. A prospective evaluation of leak point pressure, bladder compliance and clinical status in myelodysplasia patients with tethered spinal cords. Journal of Urology. 1994; 151(1):177-180. Ref ID: HOUSER1994	No relevant outcome data
Kang HS, Wang KC, Kim KM et al. Prognostic factors affecting urologic outcome after untethering surgery for lumbosacral lipoma. Childs Nervous System. 2006; 22(9):1111-1121. Ref ID: KANG2006	No post-operative urodynamic data
Kumar R, Singhal N, Gupta M et al. Evaluation of clinico-urodynamic outcome of bladder dysfunction after surgery in children with spinal dysraphism - a prospective study. Acta Neurochirurgica. 2008; 150(2):129-137. Ref ID: KUMAR2008	No relevant outcome data
Macejko AM, Cheng EY, Yerkes EB et al. Clinical urological outcomes following primary tethered cord release in children younger than 3 years. Journal of Urology. 2007; 178(4 Pt 2):1738-1742. Ref ID: MACEJKO2007	No relevant outcome data
McGuire EJ, Savastano JA. Urodynamic findings and clinical status following vesical denervation procedures for control of incontinence. Journal of Urology. 1984; 132(1):87-88. Ref ID: MCGUIRE1984	No relevant outcome data
Moiyadi AV, Devi BI, Nair KP. Urinary disturbances following traumatic brain injury: clinical and urodynamic evaluation. Neurorehabilitation. 2007; 22(2):93-98. Ref ID: MOIYADI2007	Reporting on asymptomatic urodynamic abnormalities
Nitti VW, Adler H, Combs AJ. The role of urodynamics in the evaluation of voiding dysfunction in men after cerebrovascular accident. Journal of Urology. 1996; 155(1):263-266. Ref ID: NITTI1996	No relevant outcome data
Pannek J, Greving I, Tegenthoff M et al. Urodynamic and rectomanometric findings in patients with spinal cord injury. Neurourology & Urodynamics. 2001; 20(1):95-103. Ref ID: PANNEK2001	No relevant outcome data
Patki PW. Lower Urinary Tract Dysfunction in Ambulatory Patients With Incomplete Spinal Cord Injury. Journal of Urology. 2006; 175(5):1784-1787. Ref ID: PATKI2006	No relevant outcome data
Pesce F, Castellano V, Finazzi AE et al. Voiding dysfunction in patients with spinal cord lesions at the thoracolumbar vertebral junction. Spinal Cord. 1997; 35(1):37-39. Ref ID: PESCE1997	No relevant outcome data
Reitz A, Haferkamp A, Wagener N et al. Neurogenic bladder dysfunction in patients with neoplastic spinal cord compression: adaptation of the bladder management strategy to the underlying disease. Neurorehabilitation. 2006; 21(1):65-69. Ref ID: REITZ2006	Decision based on underlying disease and urodynamic testing
Rendeli C, Ausili E, Tabacco F et al. Urodynamic evaluation in children with lipomeningocele: timing for neurosurgery, spinal cord tethering and followup. Journal of Urology. 2007; 177(6):2319-2324. Ref ID: RENDELI2007	Evaluation of timing of surgery
Sidi AA, Peng W, Gonzalez R. Vesicoureteral reflux in children with myelodysplasia: natural history and results of treatment. Journal of Urology. 1986; 136(1 Pt 2):329-331. Ref ID: SIDI1986	Review of authors experience of managing vesicoureteral reflex
Smith CP, Kraus SR, Nickell KG et al. Video urodynamic findings in men with the central cord syndrome. Journal of Urology. 2000; 164(6):2014-2017. Ref ID: SMITH2000	No relevant outcome data
Tarcan T, Bauer S, Olmedo E et al. Long-term followup of newborns with myelodysplasia and normal urodynamic findings: Is followup necessary? Journal of Urology. 2001; 165(2):564-567. Ref ID: TARCAN2001	No relevant outcome data

K.4.2 Economic studies excluded

Author/title	Notes
Weber A M, Taylor R J, Wei J T, Lemack G, Piedmonte M R, and Walter M D The cost-effectiveness of preoperative testing (basic office assessment vs urodynamics) for stress urinary incontinence in women. British Journal of Urology International, 2002.	Non-neurogenic population of patients; US perspective
Weber A M and Walters M D. Cost-effectiveness of urodynamic testing before surgery for women with pelvic organ prolapse and stress urinary incontinence. American Journal of Obstetrics and Gynecology, 2000.	Non-neurogenic population of patients; US perspective

K.5 What criteria or signs/symptoms should be used to refer patients for specialist assessment?

No search conducted

K.6 What is the safety and efficacy of intravesical botulinum toxin compared with a) usual care b) antimuscarinics c) augmentation cystoplasty in neurological disease?

K.6.1 Clinical studies excluded

Author/title	Reason for exclusion
Abdel-Meguid TA. Botulinum toxin-a injections into neurogenic overactive bladder-to include or exclude the trigone? A prospective, randomized, controlled trial. Journal of Urology. 2010; 184(6):2423-2428. Ref ID: ABDELMEGUID2010	Trial comparing trigone vs non-trigone injections
Akbar M, Abel R, Seyler TM et al. Erratum: Repeated botulinum-A toxin injections in the treatment of myelodysplastic children and patients with spinal cord injuries with neurogenic bladder dysfunction (BJU International (2007) 100 (639-645)). BJU Int. 2007; 100(3):719. Ref ID: AKBAR2007A	Erratum of included study
Albavera-Hernandez C, Rodriguez JM, Idrovo AJ. Safety of botulinum toxin type A among children with spasticity secondary to cerebral palsy: A systematic review of randomized clinical trials. Clin Rehabil. 2009; 23(5):394-407. Ref ID: ALBAVERAHERNANDEZ2009	Treatment for spasticity
Chen YH, Kuo HC. Botulinum A toxin treatment of urethral sphincter pseudodyssynergia in patients with cerebrovascular accidents or intracranial lesions. Urologia Internationalis. 2004; 73(2):156-161. Ref ID: CHEN2004	Non-RCT
DasGupta R, Murphy FL. Botulinum toxin in paediatric urology: a systematic literature review. [Review] [38 refs]. Pediatr Surg Int. 2009; 25(1):19-23. Ref ID: DASGUPTA2009	Studies included
Dykstra DD, Sidi AA. Treatment of detrusor-sphincter dyssynergia with botulinum A toxin: A double-blind study. Archives of Physical Medicine and Rehabilitation. 1990; 71(1):24-26. Ref ID: DYKSTRA1990	Treatment regimen no longer used
Franco I, Landau-Dyer L, Isom-Batz G et al. The Use of Botulinum Toxin A Injection for the Management of External Sphincter Dyssynergia in Neurologically Normal Children. Journal of Urology. 2007; 178(4 SUPPLEMENT):1775-1780. Ref ID: FRANCO2007A	Non-neurological population
Gallien P, Reymann JM, Amarenco G et al. Placebo controlled, randomised, double blind study of the effects of botulinum A toxin on detrusor sphincter dyssynergia in multiple sclerosis patients. J Neurol Neurosurg Psychiatry. 2005; 76(12):1670-1676. Ref ID: GALLIEN2005	Injections into the detrusor sphincter

Author/title	Reason for exclusion
Grise P, Ruffion A, Denys P et al. Efficacy and tolerability of botulinum toxin type a in patients with neurogenic detrusor overactivity and without concomitant anticholinergic therapy: Comparison of two doses. Eur Urol. 2010; 58(5):759-766. Ref ID: GRISE2010	Dose comparison study
Herschorn S, Gajewski J, Ethans K et al. Botulinum toxin A in patients with neurogenic detrusor overactivity: preliminary results from a Canadian multicentre randomized trial (Abstract number: Poster# 50). Neurourol Urodyn. 2009; 28(2):138-139. Ref ID: HERSCHORN2009	Exclude (abstract with no details of randomisation, allocation concealment, blinding or drop-outs)
Hori S, Patki P, Attar KH et al. Patients' perspective of botulinum toxin-A as a long-term treatment option for neurogenic detrusor overactivity secondary to spinal cord injury. BJU Int. 2009; 104(2):216-220. Ref ID: HORI2009	Non-RCT (study included patients who had only one injection)
Kulaksizoglu H, Parman Y. Use of botulinim toxin-A for the treatment of overactive bladder symptoms in patients with Parkinsons's disease. Parkinsonism and Related Disorders. 2010; 16(8):531-534. Ref ID: KULAKSIZOGLU2010	Non-RCT
Kuo HC. Therapeutic Satisfaction and Dissatisfaction in Patients With Spinal Cord Lesions and Detrusor Sphincter Dyssynergia Who Received Detrusor Botulinum Toxin A Injection. Urology. 2008; 72(5):1056-1060. Ref ID: KUO2008	Non-RCT
Naidu K, Smith K, Sheedy M et al. Systemic adverse events following botulinum toxin A therapy in children with cerebral palsy. Dev Med Child Neurol. 2010; 52(2):139-144. Ref ID: NAIDU2010	Treatment for spasticity
Panicker J, Khan S, Game X et al. PAW26 Are the beneficial effects of Botulinum toxin for refractory detrusor overactivity in multiple sclerosis sustained with repeat injections? Journal of Neurology, Neurosurgery & Psychiatry. 2010; 81(11):e30-e31. Ref ID: PANICKER2010A	Abstract (insufficient detail)
Schurch B, de SM, Denys P et al. Botulinum toxin A (Botox©) in neurogenic urinary incontinence: results from a multi-centre randomised, controlled trial (Abstract). Neurourology & Urodynamics. 2004; 23(5/6):609-610. Ref ID: SCHURCH2004B	Abstract of included paper
Stoehrer M, Wolff A, Kramer G et al. Treatment of neurogenic detrusor overactivity with botulinum toxin A: The first seven years. Urologia Internationalis. 2009; 83(4):379-385. Ref ID: STOEHRER2009	Non-RCT

K.6.2 Economic studies excluded

Author/titles	Reason for exclusions
Kalsi V, Popat R, Apostolidis A, Kavia R, Odeyemi IAO, Dakin HA et al. Cost-consequence analysis evaluating the use of botulinum neurotoxin-A in patients with detrusor overactivity based on clinical outcomes observed at a single UK centre. European Urology. 2006; 49(3):519-527	Potentially serious limitations and partial applicability.
Padmanabhan P, Scarpero H, Milam D, Dmochowski R, Penson D. Five year cost analysis of intra-detrusor injection of botulinum toxin type A and augmentation cystoplasty for refractory neurogenic detrusor overactivity. Journal of Urology. (Padmanabhan, Scarpero, Milam, Dmochowski, Penson) NashvilleTNUnited States 2010; 183(4 Suppl.):e136	Potentially serious limitations and partial applicability.

K.7 What are the long term risks (renal impairment, hydronephrosis, urinary tract stones, urinary tract infection, malignancy (bladder cancer) associated with the long-term use of intermittent

catheterisation, indwelling catheters (supra pubic and urethral) and penile sheath collection/pads? What is the quality of life associated with the above?

K.7.1 Clinical studies excluded

Author/title	Reason for exclusion
Bennett CJ, Young MN, Darrington H. Differences in urinary tract infections in male and female spinal cord injury patients on intermittent catheterization. Paraplegia. 1995; 33(2):69-72. Ref ID: BENNETT1995B	Follow up < 1 year
Drake MJ, Cortina-Borja M, Savic G et al. Prospective evaluation of urological effects of aging in chronic spinal cord injury by method of bladder management. Neurourology & Urodynamics. 2005; 24(2):111-116. Ref ID: DRAKE2005	No risks reported for patients using catheters
Gallien P, Nicolas B, Robineau S et al. Influence of urinary management on urologic complications in a cohort of spinal cord injury patients. ARCH PHYS MED REHABIL. 1998; 79(10):1206-1209. Ref ID: GALLIEN1998	Type of urologic complication not specified/ no relevant outcomes
Hall MK, Hackler RH, Zampieri TA et al. Renal calculi in spinal cord-injured patient: association with reflux, bladder stones, and foley catheter drainage. Urology. 1989; 34(3):126-128. Ref ID: HALL1989	No relevant outcomes
Kalisvaart JF, Katsumi HK, Ronningen LD et al. Bladder cancer in spinal cord injury patients. Spinal Cord. 2010; 48(3):257-261. Ref ID: KALISVAART2010	No separate outcomes for patients using catheters
Kurzycki L. Intermittent self-catheterisation in people with multiple sclerosis improves urinary symptoms and quality of life. Australian and New Zealand Continence Journal. 2006; 12(1):4. Ref ID: KURZYCKI2006	Abstract
Lin-Dyken DC, Wolraich ML, Hawtrey CE et al. Follow-up of clean intermittent catheterization for children with neurogenic bladders. Urology. 1992; 40(6):525-529. Ref ID: LINDYKEN1992	No relevant outcome data
Menon EB, Tan ES. Pyuria: index of infection in patients with spinal cord injuries. British Journal of Urology 1992; 69: 144-146	Length of follow up not stated
Oh SJ, Shin HI, Paik NJ et al. Depressive symptoms of patients using clean intermittent catheterization for neurogenic bladder secondary to spinal cord injury. Spinal Cord. 2006; 44(12):757-762. Ref ID: OH2006	No relevant outcomes
Parker L. Quality of life due to bladder management in spinal cord injured patients. Disability & Rehabilitation. 2007; 29(20-21):1663. Ref ID: PARKER2007	Abstract
Pearman JW. Urological follow-up of 99 spinal cord injured patients initially managed by intermittent catheterisation. Br J Urol. 1976; 48(5):297-310. Ref ID: PEARMAN1976	No relevant outcomes
Perrouin-Verbe B, Labat JJ, Richard I et al. Clean intermittent catheterisation from the acute period in spinal cord injury patients. Long term evaluation of urethral and genital tolerance. Paraplegia. 1995; 33(11):619-624. Ref ID: PERROUINVERBE1995	Unclear allocation of subjects to bladder management groups
Sekar P, Wallace DD, Waites KB et al. Comparison of long-term renal function after spinal cord injury using different urinary management methods. ARCH PHYS MED REHABIL. 1997; 78(9):992-997. Ref ID: SEKAR1997	No relevant outcomes
Shekelle PG, Morton SC, Clark KA et al. Systematic review of risk factors for urinary tract infection in adults with spinal cord dysfunction. [Review] [33 refs]. J Spinal Cord Med. 1999; 22(4):258-272. Ref ID: SHEKELLE1999	Papers included in evidence review
Stott DJ, Falconer A, Miller H, Tilston JC, Langhorner P. Urinary tract infection after stroke. Q J med 2009; 102: 243-249.	Follow up < 1 year
Vaidyanathan S, Soni BM, Gurpreet S et al. Protocol of a prospective cohort	Study protocol

Author/title	Reason for exclusion
study of the effect of different methods of drainage of neuropathic bladder on occurrence of symptomatic urinary infection, and adverse events related to the urinary drainage system in spinal cord injury patients. BMC Urology. 2001; 1:2. Ref ID: VAIDYANATHAN2001	
Van Kerrebroeck PE, Koldewijn EL, Scherpenhuizen S et al. The morbidity due to lower urinary tract function in spinal cord injury patients. Paraplegia. 1993; 31(5):320-329. Ref ID: VANKERREBROECK1993	No relevant outcomes
Unsal-Delialioglu S, Kaya K, Sahin-Onat S, Kulakli F, Culha C, Ozel S. Fever during rehabilitation in patients with traumatic spinal cord injury: analysis of 392 cases from a national rehabilitation hospital in turkey. J Spinal Cord med. 2010; 33: 243-248.	Follow up < 1 year
West DA, Cummings JM, Longo WE et al. Role of chronic catheterization in the development of bladder cancer in patients with spinal cord injury. Urology. 1999; 53(2):292-297. Ref ID: WEST1999	No outcomes reported according to type of bladder management

K.7.2 Economic studies excluded

No relevant economic evaluations comparing the short and long term use of intermittent catheterisation, indwelling catheters and penile sheath collection/pads were identified.

K.8 Does monitoring or do surveillance protocols improve patient outcomes?

K.8.1 Clinical studies included

Author/title	Reason for exclusion
Ahmad I, Granitsiotis P. Urological follow-up of adult spina bifida patients. Neurourol Urodyn. 2007; 26(7):978-980. Ref ID: AHMAD2007	Review paper
Bauer SB, Lais A, Scott RM. Continuous urodynamic surveillance of babies with myelodysplasia: implications for further neurosurgery. Eur J Pediatr Surg. 1992; 2 Suppl 1:35-36. Ref ID: BAUER1992	No relevant outcomes
Dator DP, Hatchett L, Dyro FM et al. Urodynamic dysfunction in walking myelodysplastic children. Journal of Urology. 1992; 148(2 Pt 1):362-365. Ref ID: DATOR1992	Results of excretory urography, ultrasonography and cystourethrography not reported separately
Kaufman AM, Ritchey ML, Roberts AC et al. Decreased bladder compliance in patients with myelomeningocele treated with radiological observation. Journal of Urology. 1996; 156(6):2031-2033. Ref ID: KAUFMAN1996	No relevant outcomes
Khanna R, Sandhu AS, Doddamani D. Urodynamic management of neurogenic bladder in spinal cord injury. Medical Journal Armed Forces India. 2009; 65(4):300-304. Ref ID: KHANNA2009	No relevant outcomes
Lais A, Kasabian NG, Dyro FM et al. The neurosurgical implications of continuous neurourological surveillance of children with myelodysplasia. Journal of Urology. 1993; 150(6):1879-1883. Ref ID: LAIS1993	No relevant outcomes
Liptak GS, Campbell J, Stewart R et al. Screening for urinary tract infection in children with neurogenic bladders. American Journal of Physical Medicine and Rehabilitation. 1993; 72(3):122-126. Ref ID: LIPTAK1993	No relevant outcomes
Sipski ML, Estores IM, Alexander CJ et al. Lack of justification for routine abdominal ultrasonography in patients with chronic spinal cord injury. J Rehabil Res Dev. 2004; 41(1):101-108. Ref ID: SIPSKI2004	Abdominal ultrasound (most patients also underwent renal ultrasound but the

Author/title	Reason for exclusion
	results were not reported)
Tanaka ST, Stone AR, Kurzrock EA. Transverse myelitis in children: long-term urological outcomes. Journal of Urology. 2006; 175(5):1865-1868. Ref ID: TANAKA2006	Wrong patient population
Thomsen F, Thorup J, Johnsen A. Hippuran renography and scintigraphy in children with myelomeningocele. Eur Urol. 1986; 12(1):12-15. Ref ID: THOMSEN1986	Intervention not specified in review protocol
Weld KJ, Wall BM, Mangold TA et al. Influences on renal function in chronic spinal cord injured patients. Journal of Urology. 2000; 164(5):1490-1493. Ref ID: WELD2000	No relevant outcomes

K.8.2 Economic studies excluded

Author/title	Reason for Exclusion
Consortium for Spinal Cord Medicine (US). Bladder Management for Adults with Spinal Cord Injury: A Clinical Practice Guideline for Health-Care Providers, 2006	No recommendations made on diagnosis or follow up. Refers to the VHA Handbook 1176.1.
National Institute for Health and Clinical Excellence (UK England and Wales). Parkinson's Disease. National clinical guideline for diagnosis and management in primary and secondary care, 2006	No recommendations made on diagnosis or follow up.
Scottish Intercollegiate Guidelines Network (UK Scotland). Management of patients with stroke: Rehabilitation, prevention and management of complications, and discharge planning. A national clinical guideline, 2010	No recommendations made on follow up; recommendations made on assessment.
Fowler C J, et al. A UK consensus on the management of the bladder in multiple sclerosis, 2009	Recommendations made but not detailed enough to breakdown.
Tekgul et al. European Association of Urology. Guidelines on Paediatric Urology, 2009.	Recommendations made but not detailed enough to breakdown.
Abrams et al. 4th International Consultation on incontinence, 2010.	No recommendations made on diagnosis or follow up
Wyndaele et al. Neurologic urinary incontinence, 2010.	This paper documents the discussion in one of the working groups of the 4th international consultation. And makes no recommendations on follow up.

K.9 What is the safety and efficacy of augmentation cystoplasty compared with usual care in neurological disease?

K.9.1 Clinical studies excluded

Author/title	Reason for exclusion
Bennett CJ, Bennett JK. Augmentation cystoplasty and urinary diversion in patients with spinal cord injury. Physical medicine and rehabilitation clinics of	Narrative review

Author/title	Reason for exclusion
North America 1993; 4: 377-389	
Chartier-Kastler EJ, Ruud Bosch JLH, Perrigot M, Chancelor MB, Richard F, Denys P. Long term results of sacral nerve stimulation (S3) for the treatment of neurogenic refractory urge incontinence related to detrusor hyperreflexia. 2000; 164: 1476-1480	Incorrect intervention used – augmentation cystoplasty not included.
Ivancic V, DeFoor W, Jackson E, Alam S, Minevich E, Reddy P, Sheldon C. Progression of renal insufficiency in children and adolescents with neuropathic bladder is not accelerated by lower urinary tract reconstruction. The Journal of Urology 2010; 184: 1768-1774	Non-neurological population
Wiener JS, Antonelli J, Shea AM et al. Bladder augmentation versus urinary diversion in patients with spina bifida in the United States. Journal of Urology. 2011; 186(1):161-165. Ref ID: WIENER2011	No relevant outcomes

K.9.2 Economic studies excluded

No relevant economic evaluations comparing augmentation cystoplasty with usual care in neurological disease were identified.

K.10 Do behavioural management programmes (timed voiding, voiding on request, bladder retraining, habit retraining,) compared with a) each other b) usual care, improve outcomes?

K.10.1 Clinical studies excluded

Author/title	Reason for exclusion
Christ KF, Kornhuber HH. Treatment of neurogenic bladder dysfunction in multiple sclerosis by ultrasound-controlled bladder training. Arch Psychiatr Nervenkr. 1980; 228(3):191-195. Ref ID: CHRIST1980	Wrong intervention
Comarr AE. A more socially acceptable bladder training device. Journal of Urology. 1963; 90:337. Ref ID: COMARR1963	Wrong intervention
Comarr AE. A self-managed bladder training device for tetraplegics. Journal of Urology. 1956; 76(2):200-202. Ref ID: COMARR1956	Wrong intervention
Comarr AE, KARCHAK A, SNELSON R. An improved bladder training device. Journal of Urology. 1963; 90:335-336. Ref ID: COMARR1963A	Wrong intervention
Comarr AE. Another self-managed bladder training device for tetraplegics. Journal of Urology. 1957; 78(1):89-92. Ref ID: COMARR1957	Wrong intervention
Decter RM, Snyder P, Rosvanis TK. Transurethral electrical bladder stimulation: initial results. Journal of Urology. 1992; 148(2 Pt 2):651-653. Ref ID: DECTER1992	Wrong intervention
Dumoulin C, Korner BN, Tannenbaum C. Urinary incontinence after stroke: does rehabilitation make a difference? A systematic review of the effectiveness of behavioral therapy. Topics in Stroke Rehabilitation. 2005; 12(3):66-76. Ref ID: DUMOULIN2005	Waiting for paper
Garcia JG, Lam C. Treating urinary incontinence in a head-injured adult. Brain Injury. 1990; 4(2):203-207. Ref ID: GARCIA1990	Non-RCT
Hagglund D. A systematic literature review of incontinence care for persons with dementia: the research evidence. J Clin Nurs. 2010; 19(3-4):303-312. Ref ID: HAGGLUND2010	Studies included in Cochrane review
Herr-Wilbert IS, Imhof L, Hund-Georgiadis M et al. Assessment-guided therapy of urinary incontinence after stroke. Rehabilitation Nursing. 2010; 35(6):248-253. Ref ID: HERRWILBERT2010	Multiple interventions applied at the same time

Author/title	Reason for exclusion
Jirovec MM, Templin T. Predicting success using individualized scheduled toileting for memory-impaired elders at home. Research in Nursing and Health. 2001; 24(1):1-8. Ref ID: JIROVEC2001	Study included in Cochrane review
Kaplan WE, Richards I. Intravesical transurethral electrotherapy for the neurogenic bladder. Journal of Urology. 1986; 136(1 Pt 2):243-246. Ref ID: KAPLAN1986A	Wrong intervention
Kornhuber HH, Schutz A. Efficient treatment of neurogenic bladder disorders in multiple sclerosis with initial intermittent catheterization and ultrasound-controlled training. Eur Neurol. 1990; 30(5):260-267. Ref ID: KORNHUBER1990	Wrong intervention
Lancioni GE, Singh NN, O'Reilly MF, Sigafoos J, Bosco A, Zonno N, Badagliacca F. Persons with mild or moderate Alzheimer's disease learn to use urine alarms and prompts to avoid large urinary accidents. Research in Developmental Disabilities 2011; 32: 1998-2004	Different outcomes covered
Madersbacher H, Pauer W, Reiner E et al. Rehabilitation of micturition in patients with incomplete spinal cord lesions by transurethral electrostimulation of the bladder. Eur Urol. 1982; 8(2):111-116. Ref ID: MADERSBACHER1982	Wrong intervention
Menon EB, Tan ES. Bladder training in patients with spinal cord injury. Urology. 1992; 40(5):425-429. Ref ID: MENON1992	Non-RCT
SULLIVAN FJ, BORS E. A self-help device for bladder training of tetraplegic patients. Journal of Urology. 1960; 84:431-432. Ref ID: SULLIVAN1960	Wrong intervention
Thomas LH, Cross S, Barrett J et al. Treatment of urinary incontinence after stroke in adults. Cochrane Database of Systematic Reviews. 2008;(1):CD004462. Ref ID: THOMAS2008	Relevant studies are available as abstracts only
Tries J. The use of biofeedback in the treatment of incontinence due to head injury. J Head Trauma Rehabil. 1990; 5(4):91-100. Ref ID: TRIES1990	Discussion paper
Vaughan CP, Juncos JL, Burgio KL et al. Behavioral therapy to treat urinary incontinence in Parkinson disease. Neurology. 2011; 76(19):1631-1634. Ref ID: VAUGHAN2011	Non-RCT

K.10.2 Economic studies excluded

No relevant economic evaluations comparing behavioural management programmes with each other or with usual care were identified.

K.11 Does pelvic floor muscle training with or without electrical stimulation or biofeedback compared with treatment as usual, improve outcomes?

K.11.1 Clinical studies excluded

Author/title	Reason for exclusion
de Ridder D, Vermeulen C, De SE et al. Clinical assessment of pelvic floor dysfunction in multiple sclerosis: Urodynamic and neurological correlates. Neurourol Urodyn. 1998; 17(5):537-542. Ref ID: DERIDDER1998	No relevant outcomes
Ishigooka M, Hashimoto T, Izumiya K et al. Electrical pelvic floor stimulation in the management of urinary incontinence due to neuropathic overactive bladder. Frontiers of Medical and Biological Engineering. 1993; 5(1):1-10. Ref ID: ISHIGOOKA1993	Not MS or stroke population
Ishigooka M, Hashimoto T, Hayami S et al. Electrical pelvic floor stimulation: a possible alternative treatment for reflex urinary incontinence in patients with	Not MS or stroke population

Author/title	Reason for exclusion
spinal cord injury. Spinal Cord. 1996; 34(7):411-415. Ref ID: ISHIGOOKA1996	
Khan F, Pallant JF, Pallant JI et al. A randomised controlled trial: outcomes of bladder rehabilitation in persons with multiple sclerosis. J Neurol Neurosurg Psychiatry. 2010; 81(9):1033-1038. Ref ID: KHAN2010	Multiple interventions implemented at the same time
Killam PE, Jeffries JS, Varni JW. Urodynamic biofeedback treatment of urinary incontinence in children with myelomeningocele. Biofeedback and Self Regulation. 1985; 10(2):161-171. Ref ID: KILLAM1985	Wrong patient population
Klarskov P, Heely E, Nyholdt I et al. Biofeedback treatment of bladder dysfunction in multiple sclerosis. A randomized trial. Scandinavian Journal of Urology and Nephrology Supplementum. 1994; 157:61-65. Ref ID: KLARSKOV1994	Pelvic floor muscle training plus behavioural therapy given to all subjects
McClurg D, Lowe-Strong A, Ashe RG. The benefits of pelvic floor muscle training in people with multiple sclerosis and lower urinary tract dysfunction. Journal of the Association of Chartered Physiotherapists in Women's Health. 2008;(103):21-28. Ref ID: MCCLURG2008A	Subjects were the same as in included study
Middaugh SJ, Whitehead WE, Burgio KL, Engel BT. Biofeedback in treatment of urinary incontinence in stroke patients. Biofeedback and self-regulation 1989; 14: 3-19	Observational study
Porena M, Costantini E, Rociola W et al. Biofeedback successfully cures detrusor-sphincter dyssynergia in pediatric patients. Journal of Urology. 2000; 163(6):1927-1931. Ref ID: PORENA2000	Non neurological population
Thomas LH, Cross S, Barrett J et al. Treatment of urinary incontinence after stroke in adults. Cochrane Database of Systematic Reviews. 2008;(1):CD004462. Ref ID: THOMAS2008	Papers included in the review
Tibaek S, Gard G, Jensen R. Is there a long-lasting effect of pelvic floor muscle training in women with urinary incontinence after ischemic stroke? A 6-month follow-up study. International Urogynecology Journal. 2007; 18(3):281-287. Ref ID: TIBAEK2007	Results the same as for Tibaek S, Jensen R, Lindskov G et al. Can quality of life be improved by pelvic floor muscle training in women with urinary incontinence after ischemic stroke? A randomised, controlled and blinded study. International Urogynecology Journal. 2004; 15(2):117-123. Ref ID: TIBAEK2004

K.11.2 Economic studies excluded

No relevant economic evaluations comparing pelvic floor muscle training (with or without electrical stimulation or biofeedback) with usual care were identified.

K.12 What is the safety and efficacy of the catheter valve compared with urinary drainage bags in neurological disease?

No papers were ordered for this question

K.13 What is the safety and efficacy of urethral tape and sling surgery compared with usual care in neurological disease?

K.13.1 Clinical studies excluded

Author/title	Reason for exclusion
Ghoniem GM. Bladder neck wrap: a modified fascial sling in treatment of incontinence in myelomeningocele patients. Eur Urol. 1994; 25(4):340-342. Ref ID: GHONIEM1994	No relevant outcomes
Gosalbez R, Castellan M. Defining the role of the bladder-neck sling in the surgical treatment of urinary incontinence in children with neurogenic incontinence. World J Urol. 1998; 16(4):285-291. Ref ID: GOSALBEZ1998	Discussion paper
Snodgrass WT, Elmore J, Adams R. Bladder neck sling and appendicovesicostomy without augmentation for neurogenic incontinence in children. Journal of Urology. 2007; 177(4):1510-1514. Ref ID: SNODGRASS2007	Patients included in Snodgrass W, Barber T. Comparison of bladder outlet procedures without augmentation in children with neurogenic incontinence. Journal of Urology. 2010; 184(4 Suppl):1775-1780. Ref ID: SNODGRASS2010
Ghoniem GM. Bladder neck wrap: a modified fascial sling in treatment of incontinence in myelomeningocele patients. Eur Urol. 1994; 25(4):340-342. Ref ID: GHONIEM1994	No relevant outcomes

K.13.2 Economic studies excluded

No relevant economic evaluations comparing urethral tape and sling surgery with bladder neck closure were identified.

K.14 What is the safety and efficacy of artificial urinary sphincter compared with other treatments in neurological disease?

K.14.1 Clinical studies excluded

Author/title	Reason for exclusion
Abdill CK, Rivas DR, Chancellor MB. Transurethral placement of external sphincter wire mesh stent for neurogenic bladder. SCI Nurs 1994 Jun;11:38-41.	Involves a stent used to keep the bladder neck open for improved urine removal, not an artificial sphincter to reduce incontinence
Chancellor MB, Karusick S, Erhard MJ, et al. Placement of a wire mesh prosthesis in the external urinary sphincter of men with spinal cord injuries. Radiology 1993 May;187:551-5.	Involves a stent used to keep the bladder neck open for improved urine removal, not an artificial sphincter to reduce incontinence
Chancellor MB, Rivas DA, Abdill CK, et al. Prospective comparison of external sphincter balloon dilatation and prosthesis placement with external sphincterotomy in spinal cord injured men. Archives of Physical Medicine & Rehabilitation 1994 Mar;75:297-305.	Involves a stent used to keep the bladder neck open for improved urine removal, not an artificial sphincter to reduce

Author/title	Reason for exclusion
	incontinence
Chancellor MB, Rivas DA, Linsenmeyer T, et al. Multicenter trial in North America of UroLume urinary sphincter prosthesis. J Urol 1994 Sep;152:924-30.	Involves a stent used to keep the bladder neck open for improved urine removal, not an artificial sphincter to reduce incontinence
Chancellor MB, Rivas DA, Abdill CK, et al. Management of sphincter dyssynergia using the sphincter stent prosthesis in chronically catheterized SCI men. J Spinal Cord Med 1995 Apr;18:88-94.	Involves a stent used to keep the bladder neck open for improved urine removal, not an artificial sphincter to reduce incontinence
Dave S, Pippi Salle JL, Lorenzo AJ, et al. Is long-term bladder deterioration inevitable following successful isolated bladder outlet procedures in children with neuropathic bladder dysfunction? J Urol 2008 May;179:1991-6.	Bladder outlet procedures not described.
Juan Garcia FJ, Salvador S, Montoto A, et al. Intraurethral stent prosthesis in spinal cord injured patients with sphincter dyssynergia. Spinal Cord 1999;37:54-7.	Involves a stent used to keep the bladder neck open for improved urine removal, not an artificial sphincter to reduce incontinence
Kryger JV, Gonzalez R, Spencer Barthold J. Surgical management of urinary incontinence in children with neurogenic sphincteric incompetence. The Journal of Urology 2000; 163: 256-263	Narrative review
Rivas DA, Chancellor MB, Bagley D. Prospective comparison of external sphincter prosthesis placement and external sphincterotomy in men with spinal cord injury. J Endourol 1994 Apr;8:89-93.	Involves a stent used to keep the bladder neck open for improved urine removal, not an artificial sphincter to reduce incontinence

K.14.2 Economic studies excluded

No relevant economic evaluations comparing the use of the artificial urinary sphincter with sling surgery or usual care were identified.

K.15 What is the efficacy of the ileal conduit diversion compared with usual care in neurological disease?

K.15.1 Clinical studies excluded

Author/title	Reason for exclusion
Cass AS, Luxenberg M, Gleich P, Johnson F and Hagen S. Clean intermittent catheterisation in the management of the neurogenic bladder in children. The Journal of Urology 1984; 132: 526-528	Wrong intervention (intermittent catheterisation)
Stein R, Weisner C, Beetz R, Pfitzenmeir J, Schwarz M, Thuroff JW. Urinary diversion in children and adolescents with neurogenic bladder: the Mainz experience. Part II: Continent cutaneous diversion using the Mainz pouch I. Pediatric Nephrology 2005; 20: 926-931	Wrong intervention (continent diversion)

K.15.2 Economic studies excluded

No relevant economic evaluations comparing Urinary Diversion with sling surgery or usual care were identified.

K.16 Do prophylactic antibiotics reduce the risk of symptomatic urinary tract infections?

K.16.1 Clinical evidence excluded

Author/title	Reason for exclusion
Brumfitt W, Smith GW, Hamilton-Miller JMT, et al. A clinical comparison between Macrodantin and trimethoprim for prophylaxis in women with recurrent urinary infections. J Antimicrob Chemother 1985;16:111-20.	Not a neurological population
Carlsen NLT, Hesselbjerg U, Glenting P. Comparison of long-term, low-dose pivmecillinam and nitrofurantoin in the control of recurrent urinary tract infection in children. An open, randomized, cross-over study. J Antimicrob Chemother 1985;16:509-17.	Not a neurological population
Everaert K, Lumen N, Kerckhaert W, et al. Urinary tract infections in spinal cord injury: prevention and treatment guidelines. Acta Clin Belg 2009 Jul;64:335-40.	Systematic review
Fried GW, Goetz G, Potts-Nulty S, et al. Prospective evaluation of antibiotic prophylaxis prior to cystometrogram and/or cystogram studies: Oral versus intramuscular routes. Archives of Physical Medicine and Rehabilitation 1996;77:900-2.	Not a neurological population
Gow JG. A comparative trial of hexamine Hippurate and hexamine mandelate in prevention of recurrent infection of the urinary tract. The Practitioner 1974; 213; 97-101	Not a neurological population
Kevorkian CG, Merritt JL, Ilstrup DM. Methenemine mandelate with acidification: An effective urinary antiseptic in patients with neurogenic bladder. Mayo Clinic Proceedings 1984; 59:523-529	Not a true antibiotic
Krebs M, Halvorsen RB, Fishman IJ, Santos-Mendoza N. Prevention of urinary tract infection during intermittent catheterisation. The Journal of Urology 1984; 131: 82-85	Not a true antibiotic
Lee BB, Haran MJ, Hunt LM, Simpson JM, Marial O, Rutkowski SB, Middleton JW, Kotsiou G, Tudehope M, Cameron ID. Spinal Injured neuropathic bladder antisepsis (SINBA) trial. Spinal Cord 2007; 45: 542-550	Not a true antibiotic
Kuhlemeier KV, Stover SL, Lloyd LK. Prophylactic antibacterial therapy for preventing urinary tract infections in spinal cord injury patients. Journal of Urology 1985 Sep;134:514-7.	Did not cover correct outcomes
Morton SC, Shekelle PG, Adams JL, et al. Antimicrobial prophylaxis for urinary tract infection in persons with spinal cord dysfunction. Archives of Physical Medicine and Rehabilitation 2002 Jan;83:129-38.	Systematic review
Mountokalakis T, Skounakis M, Tselentis J. Short-term versus prolonged systemic antibiotic prophylaxis in patients treated with indwelling catheters. Journal of Urology 1985 Sep;134:506-8.	Did not cover correct outcomes
Norberg A, Norberg B, Parkhede U, et al. Randomized double-blind study of prophylactic methenamine hippurate treatment of patients with indwelling catheters. Eur J Clin Pharmacol 1980 Nov;18:497-500.	Did not cover correct outcomes
Nunez U, Solis Z. Macrocrystalline nitrofurantoin versus norfloxacin as treatment and prophylaxis in uncomplicated recurrent urinary tract infection. Current Therapeutic Research - Clinical and Experimental 1990;48:234-45.	Not a neurological population
Pearman JW, Bailey M, Harper WE. Comparison of the efficacy of "Trisdine"	Did not cover correct

Author/title	Reason for exclusion
and kanamycin-colistin bladder instillations in reducing bacteriuria during intermittent catheterisation of patients with acute spinal cord trauma. Br J Urol 1988 Aug;62:140-4.	outcomes
van Poppel H, Willemen P, Wegge M, et al. Antibiotic cover of transurethral maneuvers with ciprofloxacin and susceptibility behavior of pathogens in patients with neurogenic bladder. Urologia Internationalis 1990;45:342-5.	Did not cover correct outcomes

K.16.2 Economic evidence excluded

No relevant economic evaluations comparing prophylactic antibiotics with usual care or no prophylactic antibiotics were identified.

K.17 What interventions or configuration of services improve outcomes when a patient is transferred from child to adult services?

K.17.1 Clinical studies excluded

Author/title	Reason for exclusion
Binks JA, Barden WS, Burke TA, et al. What do we really know about the transition to adult-centered health care? A focus on cerebral palsy and spina bifida. Archives of Physical Medicine and Rehabilitation 2007 Aug;88:1064-73. Ref ID: BINKS2007A	Systematic review
Blum RW, Garell D, Hodgman CH, et al. Transition from child-centered to adult health-care systems for adolescents with chronic conditions. A position paper of the Society for Adolescent Medicine. Journal of Adolescent Health 1993 Nov;14:570-6. Ref ID: BLUM1993	Non-systematic review/opinion
Chisanga E. Applying specialist nurse skills to improve epilepsy adolescent transition services. British Journal of Neuroscience Nursing 2009 Jun;5:274-7. Ref ID: CHISANGA2009	Descriptive/opinion
Labhard S. Transitioning to adulthood with disabilities: a holistic approach. TOP SPINAL CORD INJ REHABIL 2010 Jul;16:1-16. Ref ID: LABHARD2010	Non-systematic review/opinion
Logan S. In the UK the transition from youth to adulthood of people with cerebral palsy is poorly planned and co-ordinated. Child Care Health Dev 1997;23:480-2. Ref ID: LOGAN1997 Reprint: In File	Brief review of the Stevenson 1997 paper.
Marn LM, Koch LC. The major tasks of adolescence: implications for transition planning with youths with cerebral palsy. Work 1999 Jul;13:51-8. Ref ID: MARN1999A	Non-systematic review/opinion
Mourtzinos A, Stoffel J. Management goals for the spina bifida neurogenic bladder: a review from infancy to adulthood. Urol Clin North Am 2010 Nov;37:527-35. Ref ID: MOURTZINOS2010	Non-systematic review/opinion
Peterson PM, Rauen KK, Brown J, et al. Spina bifida: the transition into adulthood begins in infancy. Rehabilitation Nursing 1994;19:229-38. Ref ID: PETERSON1994	Not about transition services
Rekate HL. The pediatric neurosurgical patient: the challenge of growing up. Semin Pediatr Neurol 2009;16:2-8. Ref ID: REKATE2009 surgeons to general or adult neurosurgical practices. 2009 Elsevier Inc. All	Non-systematic review/opinion

Author/title	Reason for exclusion
rights reserved	
Ried S. Transition of youth from pediatric to adult care: physician's perspective and recommendations. TOP SPINAL CORD INJ REHABIL 2010;16:38-47. Ref ID: RIED2010	Non-systematic review/opinion
Sawyer SM, Macnee S. Transition to adult health care for adolescents with spina bifida: research issues. Developmental Disabilities Research Reviews 2010;16:60-5.Ref ID: SAWYER2010	Non-systematic review/opinion
Simon TD, Lamb S, Murphy NA, et al. Who will care for me next? Transitioning to adulthood with hydrocephalus. Pediatrics 2009;124:1431-7. Ref ID: SIMON2009	Non-systematic review/opinion
Soanes C, Timmons S. Improving transition: a qualitative study examining the attitudes of young people with chronic illness transferring to adult care. Journal of Child health care. 2004; 8: 102-112	No neurological patients included in the cohort.
Stevenson CJ, Pharoah PO, Stevenson R. Cerebral palsy: the transition from youth to adulthood. Dev Med Child Neurol 1997 May;39:336-42. Ref ID: STEVENSON1997	Does not deal with the transition process
Tuffrey C, Pearce A. Transition from paediatric to adult medical services for young people with chronic neurological problems. J Neurol Neurosurg Psychiatry 2003 Aug;74:1011-3. Ref ID: TUFFREY2003	Non-systematic review
Vinchon M, Dhellemmes P. The transition from child to adult in neurosurgery. Advances and Technical Standards in Neurosurgery 2007;32:3-24. Ref ID: VINCHON2007A	Non-systematic review/opinion
Young NL. The transition to adulthood for children with cerebral palsy: what do we know about their health care needs? Journal of Pediatric Orthopaedics 2007;27:476-9. Ref ID: YOUNG2007A	Non-systematic review/opinion
Young NL, McCormick A, mills W, Barden W, Boydell K, Law M, Wedge J, Fehlings D, Mukherjee S, Rumney P, Williams JI. The Transition study: A look at Youth and Adults with Cerebral palsy, Spina Bifida and Acquired Brain Injury. Physical and Occupational therapy in Pediatrics 2006; 26:25-45.	Does not include transition
Zebracki K, Anderson CJ, Chlan KM, et al. Outcomes of adults with paediatric-onset spinal cord injury: longitudinal findings and implications on transition to adulthood. TOP SPINAL CORD INJ REHABIL 2010 Jul;16:17-25. Ref ID: ZEBRACKI2010	Non-systematic review/opinion

K.17.2 Economic studies excluded

No economic studies were identified that compared the cost effectiveness of different strategies for dealing with transitions.

K.18 Does provision of information about the management of neurological lower urinary tract dysfunction improve patient outcomes?

K.18.1 Clinical studies excluded

Author/title	Reason for exclusion
Martins G, Soler ZASG, Batigalia F, Moore KN. Clean intermittent catheterisation. Educational booklet directed to caregivers of children with neurogenic bladder dysfunction. J Wound Ostomy Continence Nurs 2009; 36: 545-549.	No relevant outcomes

Author/title	Reason for exclusion
O'Hara L, Cadbury H, De Souza L, Ide L. Evaluation of the effectiveness of professionally guided self-care for people with multiple sclerosis living in the community: a randomised controlled trial. Clinical rehabilitation 2002; 16: 119-128	No relevant outcomes and the intervention was not directed at urinary management.
Eames S, Hoffmann T, Worrall L, Read S. Stroke patients' and carers' perception of barriers to accessing stroke information. Top Stroke Rehabil 2010; 17: 69-78	Concerned with perceived barriers to information access rather than the effects of information on outcomes.

K.18.2 Economic studies excluded

No economic studies were identified that compared the cost effectiveness of different strategies for the provision of information about the management of neurological lower urinary tract dysfunction.

K.19 For patients and their carers with lower urinary tract dysfunction associated with neurological disorders, what are the experiences of access to and interaction with services, that address these issues?

K.19.1 Clinical studies excluded

Author/title	Reason for exclusion
Eames S, Hoffmann T, Worrall L et al. Stroke patients' and carers' perception of barriers to accessing stroke information. Topics in Stroke Rehabilitation. 2010; 17(2):69-78. Ref ID: EAMES2010	Reporting on access to information
Neal R, Linnane J. Improving access to continence services: action in Walsall. British Journal of Community Nursing. 2002; 7(11):567-3. Ref ID: NEAL2002	Population – patients with incontinence (proportion neurological not specified)

K.19.2 Economic studies excluded

No economic studies were identified that compared the cost effectiveness of different strategies for dealing with access to and interaction with services.

Appendix L: References

1 Schurch B, De S, Denys P, Chartier-Kastler E, Haab F, Everaert K et al. Botulinum toxin type a is a safe and effective treatment for neurogenic urinary incontinence: results of a single treatment, randomized, placebo controlled 6-month study. Journal of Urology. 2005; 174(1):196-200

2 Herschorn S, Gajewski J, Ethans K, Corcos J, Carlson K, Bailly G et al. Efficacy of botulinum toxin A injection for neurogenic detrusor overactivity and urinary incontinence: a randomized double-blind trial. Neurourology and Urodynamics. 2009; 28(7):608-609

3 Cruz F, Herschorn S, Aliotta P, Brin M, Thompson C, Lam W et al. Efficacy and safety of onabotulinumtoxinA in patients with urinary incontinence due to neurogenic detrusor overactivity: a randomised, double-blind, placebo-controlled trial. European Urology. 2011; 60(4):742-750

4 Office for National Statistics. Life tables. 2011. [Last accessed: 1 April 2011]

5 Frankel HL, Coll JR, Charlifue SW, Whiteneck GG, Gardner BP, Jamous MA et al. Long-term survival in spinal cord injury: a fifty year investigation. Spinal Cord. 1998; 36(4):266-274

6 National Institute for Health and Clinical Excellence. The Guidelines Manual. London: National Institute for Health and Clinical Excellence; 2009. Available from: http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp

7 Pannek J, Gocking K, Bersch U. Long-term effects of repeated intradetrusor botulinum neurotoxin a injections on detrusor function in patients with neurogenic bladder dysfunction. BJU International. 2009; 104(9):1246-1250

8 Apostolidis A, Jacques TS, Freeman A, Kalsi V, Popat R, Gonzales G et al. Histological changes in the urothelium and suburothelium of human overactive bladder following intradetrusor injections of botulinum neurotoxin type A for the treatment of neurogenic or idiopathic detrusor overactivity. European Urology. 2008; 53(6):1245-1253

9 Karsenty G, Reitz A, Lindemann G, Boy S, Schurch B. Persistence of therapeutic effect after repeated injections of botulinum toxin type A to treat incontinence due to neurogenic detrusor overactivity. Urology. 2006; 68(6):1193-1197

10 Reyblat P, Chan KG, Josephson DY, Stein JP, Freeman JA, Grossfeld GD et al. Comparison of extraperitoneal and intraperitoneal augmentation enterocystoplasty for neurogenic bladder in spinal cord injury patients. World Journal of Urology. 2009; 27(1):63-68

11 Metcalfe PD, Cain MP, Kaefer M, Gilley DA, Meldrum KK, Misseri R et al. What is the need for additional bladder surgery after bladder augmentation in childhood? Journal of Urology. 2006; 176(4 Pt 2):1801-1805

12 Game X, Castel-Lacanal E, Bentaleb Y, Thiry-Escudie I, de Boissezon X, Malavaud B et al. Botulinum toxin A detrusor injections in patients with neurogenic detrusor overactivity significantly decrease the incidence of symptomatic urinary tract infections. European Urology. 2008; 53(3):613-618

13 Hollingworth W, Campbell JD, Kowalski J, Ravelo A, Girod I, Briggs A et al. Exploring the impact of changes in neurogenic urinary incontinence frequency and condition-specific quality of life on preference-based outcomes. Quality of Life Research. Department of Social Medicine, University of Bristol, Canynge Hall, 39 Whatley Rd, Bristol, BS8 2PS, UK. william.hollingworth@bristol.ac.uk 2010; 19(3):323-331

14 Sullivan PW, Slejko JF, Sculpher MJ, Ghushchyan V. Catalogue of EQ-5D Scores for the United Kingdom. Medical Decision Making. 2011; 31(6):800-804

15 Department of Health. NHS Reference Costs 2009-2010. London: Department of Health, 2011

16 Joint Formulary Committee. British National Formulary (BNF). 60 edition. London: British Medical Association and The Royal Pharmaceutical Society of Great Britain; 2010. Available from: http://www.bnf.org.uk

17 Department of Health. NHSCat. UK: Department of Health, 2010 Available from: https://my.supplychain.nhs.uk/catalogue

18 Personal Social Services Research Unit and Curtis, L. Unit costs of health and social care. Canterbury: University of Kent, 2010

19 Padmanabhan P, Scarpero H, Milam D, Dmochowski R, Penson D. Five-year cost analysis of intra-detrusor injection of botulinum toxin type A and augmentation cystoplasty for refractory neurogenic detrusor overactivity. World Journal of Urology. 2011; 29(1):51-57