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2023 Canadian Urological Association/ Pediatric Urologists of Canada guideline: Pediatric patients with neurogenic lower urinary tract dysfunction

Full-text version

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INTRODUCTION AND BACKGROUND

Neurogenic lower urinary tract dysfunction (NLUTD) refers to abnormal function of the bladder, bladder neck, and/or sphincters associated with any neurologic disorder.[1] Congenital pediatric NLUTD is mainly caused by spinal dysraphism, commonly spina bifida (SB).[2] Pediatric NLUTD is increasingly prevalent in Canada. A population-based study conducted in Canada (excluding Quebec) from 2004–2015 showed that there were 4.4 cases of neural tube defects (NTDs) per 10 000 total births; however, the prevalence of NTDs increased from 3.6 in 2004 to 4.6 per 10 000 in 2015. Specifically, SB was the only NTD subtype with an increasing prevalence over time.[3,4]

Pediatric patients with NLUTD are at risk for recurrent urinary tract infections (UTI) and upper tract damage leading to chronic kidney disease, necessitating early detection and management.[2] In addition, advances in prenatal diagnosis of congenital spinal dysraphism in Canada enable early detection and prenatal intervention.[5,6] Managing the resultant pediatric NLUTD requires collaboration among various healthcare providers to ensure healthy long-term outcomes.

Purpose and scope

The Pediatric Urologists of Canada (PUC) and the Canadian Urological Association (CUA) collaborated to provide this guideline of evidence-based recommendations for the diagnosis, management, and treatment of pediatric patients with NLUTD. The target readers of this guideline include pediatric urologists, general urologists, pediatricians, and allied health professionals with the goal of optimizing care and achieving improved subpopulation health outcomes.

The definition, terminology, and classification of NLUTD are described in prior CUA clinical practice guidelines on adult patients with NLUTD,[7] which were adapted from the International Continence Society (ICS).[8] For pediatric NLUTD-specific descriptions, we refer readers to the 2016 update report from the standardization committee of the International Children's Continence Society (ICCS).[9] Specifically, for this guideline, the definition for bladder hostility encompasses bladders that are considered high risk for urologic morbidity and is summarized in Table 1, with relevant additional definitions and terminology for pediatric NLUTD.

METHODOLOGY

The CUA Guidelines Committee pre-approved the pediatric NLUTD guideline methodology, which uses the ADAPTE approach. The process included a critical appraisal of recent pediatric neurogenic bladder guidelines using AGREE II.[10,11] For the purpose of this guideline formulation, two licensed reference special-

ist librarians performed the initial search on relevant pediatric NLUTD guidelines up to March 2022, then an updated search on September 2022. The search included both 'Medical Subject Heading (MeSH)' and 'free text' protocols, focusing on four broad concepts: 1) neurogenic bladder; 2) pediatrics; 3) diagnosis and treatment; and (4) guidelines. References were selected if they contained at least one term from each concept.

Electronic databases searched included EMBASE, Google Scholar, MEDLINE, AAP, CPS, and NICE. Five reviewers conducted an initial screening of search records, followed by a full-text assessment by three reviewers to determine eligibility. The selected guidelines were then appraised by a team of six reviewers using the AGREE II instrument, which consists of 23 items covering six domains. Ratings were given on a scale of 1–7, with 1 representing "strongly disagree" and 7 representing "strongly agree." Quality scores were calculated for each domain, and scores below 70 were considered low, while an average total score of 80 or higher was considered satisfactory.

The AGREE II appraisal results were published for the available guidelines specific to pediatric patients with NLUTD, which included: the National Institute for Health and Care Excellence (NICE), European Society for Pediatric Urology (ESPU), ICCS, Irish, Spina Bifida Association (SBA), and *International Brazilian Journal of Urology* guidelines. The top three guidelines identified based on domain scores were NICE, SBA, and Irish guidelines. The appraisal of the guidelines and consolidation of the key recommendation statements involved considering the expertise and perspective of all relevant stakeholders. In the process of evaluating the recommendation statements from the top three guidelines identified, evaluators included a general urologist, pediatrician, pediatric surgeon, pediatric urologists, adult reconstructive urologist, functional urologist, transitional care/adolescence specialist, pediatric nephrologist/medical urologist, and an advanced specialty nurse practitioner, as well a patient with NLUTD and their parents.[12]

The key recommendation statements were direct quotations and/or adaptations, with some modification from the referred guidelines. Additional modifications to key recommendation statements were congregated from a de novo literature search on Medline-indexed peer-reviewed publications up to April 2023. The key recommendation statements were also linked to the most recent evidence relevant to the topic. A consensus on the recommendations was formed using a two-round modified Delphi process. In the first round, the author group drafted recommendation statements based on key recommendations from the evaluated guidelines and specific recommendations tailored to the Canadian context. In the second round, the draft was shared with PUC members to obtain their agreement on the statements. A response rate of at least 60% among PUC members was achieved to ascertain the majority perspective.[13]

Table 1. Indicators of NLUTD patient characteristics potentially at higher risk of urological morbidity

Basis of high-risk diagnoses	Features of bladder hostility
Etiology of neurogenic bladder	SCI, SB, advanced MS, SCI patients with autonomic dysreflexia associated with bladder function
Bladder management method	Valsalva/Credé/reflexive bladder emptying, indwelling catheter
VideoUrodynamics (VUDS) or urodynamics + voiding cystourethrogram (VCUG)	DSD, NDO, impaired compliance (cystometric bladder capacity/ end filling pressure <20 mL/cmH_2O), DLPP >40 cmH_2O, VUR, trabeculated irregular bladder wall on VUDS/ VCUG
Renal-bladder imaging	New-onset/worsening hydronephrosis, stone disease, renal atrophy/ scarring, abnormal bladder morphology
Renal function	New-onset/worsening renal insufficiency

Additional definitions and terminologies
- Detrusor overactivity is the occurrence of involuntary detrusor contractions during filling cystometry.
- Detrusor underactivity denotes a voiding contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete emptying within a normal time span.
- Compliance is calculated by dividing the volume change (ΔV) by the change in detrusor pressure (ΔPdet) during that change in bladder volume (C=ΔV/ΔPdet). Compliance is expressed as ml per cmH_2O.
- High DLPP (e.g.,>40 cmH_2O) is associated with reduced bladder muscle compliance and poses a risk for upper urinary tract deterioration.
- DSD is discoordination between the detrusor and external urethral sphincter muscles during voiding (i.e., detrusor contraction synchronous with contraction of the urethral and/or periurethral striated muscles).

Adopted from Kavanagh et al, 2019, with permission.[7] Additional caveat definition from ICCS 2016.[5] DLPP: detrusor leak point pressure; DSD: detrusor sphincter dyssynergia; MS: multiple sclerosis; NDO: neurogenic detrusor overactivity; NLUTD: neurogenic lower urinary tract dysfunction; SB: spina bifida; SCI: spinal cord injury; VCUG: urodynamics + voiding cystourethrogram; VUDS: video-urodynamics; VUR: vesicoureteral reflux.

Level of evidence, grade of recommendation

The levels of evidence (LE) and grades of recommendation for this guideline employ the International Consultation on Urologic Diseases (ICUD)/WHO-modified Oxford Center for Evidence-Based Medicine grading system.[14] In addition, based on a modified GRADE methodology from prior CUA guideline formulation, the strength of each recommendation is represented by the words STRONG or WEAK.[15]

RECOMMENDATIONS

A summary table and citation of the corresponding source of guideline adaptation were generated to facilitate better adaptation and clinical application of the key recommendation statements into practice (Table 2). Table 3 presents a summary of the investigations recommended for different age ranges in pediatric NLUTD, whereas Table 4 provides a brief overview of the considerations for surgical interventions in pediatric NLUTD.

Table 2. Summary of key recommendation statements

Domains	Key recommendation statements	Level of evidence and grade of recommendation	Adaptation source with direct quote or modified
Antenatal period management	– Clinicians should convey information about the medical care and lifelong functional impact of SB in an evidence-based, collaborative manner while seeking from families an understanding of their needs, values, and beliefs. – Clinicians should review evidence-based treatment options with the family, including fetal surgery. – Clinicians should offer families the opportunity to meet with key members of the SB team.	Level of evidence III– IV, strong recommendation based on available evidence and best practice	SBA/Irish
Postnatal period initial approach	– Clinicians should obtain a postnatal baseline renal and bladder ultrasound after 48 hours and within the first 1–4 week of birth. – Clinical should obtain a postnatal baseline renal function test-serum creatinine after 48 hours and within the first 1–4 weeks of birth. – Clinicians should educate parents about the possible need for CIC. CIC should be initiated if there is concern for high risk of urologic morbidity based on urinary tract imaging (i.e., dilated upper tract/high-grade hydronephrosis/megacystis). – Clinicians should refer a newborn with spinal dysraphism to the MDT for initial evaluation.	Level of evidence III–IV, strong recommendation based on evidence reports	SBA/EAU-ESPU
MDT SB service/ clinic	– Children with NLUTD should be reviewed at least annually at the MDT SB clinic. – The specialist SB team is responsible for the education and support of local teams. – A fully staffed MDT SB clinic ideally consists of the following key professionals: neurosurgeon, urologist, orthopedic surgeon, SB nurse specialist, advanced nurse practitioner, pediatrician, social worker, physiotherapist, and occupational therapist. Other healthcare professionals of benefit may include a dietitian.	Level of evidence III–IV, strong recommendation based on evidence reports	Irish/SBA/ NICE
History and physical examination	– When assessing lower urinary tract dysfunction in patients with pediatric NLUTD, take a clinical history and physical examination, including information on: a. urinary tract symptoms, such as symptomatic UTIs, bladder management and condition (including bladder diary or frequency/volume chart); b. neurological symptoms and diagnosis (if known); c. clinical course of the neurologic disease; d. bowel symptoms and management; e. sexual function in adolescent patients; f. comorbidities; g. use of prescription and other medication and therapies; h. mobility hand function; i. cognitive function; j. social support; k. lifestyle; l. measuring blood pressure; m. abdominal examination; n. external genitalia examination; o. vaginal or rectal examination if clinically indicated (e.g., to look for evidence of fecal loading or alterations in anal tone).		NICE/SBA
Diagnostics & workup	*Renal and bladder ultrasound* – For children with NLUTD or at high-risk of developing NLUTD, clinicians should obtain a baseline renal/bladder ultrasound, within 3 months of birth and repeat in 6 months. – For children with NLUTD, clinicians should obtain renal/bladder ultrasound every 6 months when the child is under the age of 2. – After a child with pediatric NLUTD is above 2 years of age, clinicians should obtain an US yearly if the child is stable, without UTIs or imaging changes. – Obtain a renal/bladder US, as needed, if the child has recurring symptomatic UTIs or if urodynamic testing identifies bladder hostility.	Level of evidence II–III, strong recommendation based on evidence report and current best practice	SBA/NICE/ Irish

Antenatal period management

■ RECOMMENDATION 1 *(STRONG RECOMMENDATION, LEVEL OF EVIDENCE [LE] III–IV)*

– Clinicians should convey information about the medical care and lifelong functional impact of SB in an evidence-based, collaborative manner while seeking from families an understanding of their needs, values, and beliefs.
– Clinicians should review evidence-based treatment options with the family, including fetal surgery.
– Clinicians should offer families the opportunity to meet with key members of the SB team.

Table 2 (cont'd). Summary of key recommendation statements

Domains	Key recommendation statements	Level of evidence and grade of recommendation	Adaptation source with direct quote or modified
Diagnostics & workup (cont'd)	*Assessment of renal function* – Clinicians should obtain a baseline serum creatinine within 3 months of birth and repeat as clinically indicated (i.e., needed for monitoring due to baseline elevated or diagnostic imaging suggestive of high-risk for upper tract damage). – Clinicians should obtain a serum Cr test when a child with NLUTD is 1–5 years old, if there is a change in the upper urinary tract findings on US; however, serum Cr can also be ordered based on clinical suspicion and ultrasonography is not a prerequisite because renal US can have poor sensitivity for early decline in eGFR. – Clinicians should obtain serum chemistry (including serum Cr) for children with NLUTD when they are 5 years old. Thereafter, clinicians should consider obtaining a serum Cr test yearly as monitoring if concern for CKD or monitoring for kidney function due to change in the upper urinary tract findings on US. If the child has low muscle mass, consider an alternative measure of renal function, such as cystatin-C or nuclear studies. – Clinicians should only order DMSA scans in infants with SB who either had a febrile UTI or are found to have VUR on a voiding cystourethrogram.	Level of evidence II–III, strong recommendation based on evidence and current best practice	SBA/NICE
	Urodynamic studies – Clinicians should obtain a baseline video urodynamic (or urodynamic + VCUG) testing for all patients born with SB within 3–12 months. – Clinicians should consider obtaining urodynamic testing for patients with pediatric NLUTD annually until the child is 3 years old, especially if the following are noted: bladder hostility, upper urinary tract changes, recurrent symptomatic UTIs – Clinicians should obtain urodynamic testing for patients with pediatric NLUTD between the ages of 3–5 years old, only if the following are present: upper tract changes, recurring UTIs, patient and family's interest in beginning a urinary continence program (i.e., familial/patient readiness for initiation of a urinary continence program) – Clinicians should obtain urodynamic testing for patients with pediatric NLUTD over the age of 5 years old, when initiating a urinary continence program, or if the following are present: hydronephrosis or renal scarring, recurring symptomatic UTIs, changes in urinary continence status	Level of evidence II-III, Strong recommendation based on evidence and current best practice	SBA/ ICCS/ Irish/ NICE
Treatment recommendations	*Clean intermittent catheterization (CIC)* – Clinicians should initiate CIC and antimuscarinic therapy to infants with NLUTD for the treatment of bladder hostility when indicated based on renal/bladder ultrasound, urodynamic studies, and/or serum Cr. – When children with NLUTD reach the age of 3 or older, clinicians should initiate CIC and antimuscarinic therapy when indicated by upper urinary tract changes, recurring symptomatic UTIs, or bladder hostility noted on urodynamic testing, or when there is a family's interest in starting a urinary continence program, indicating familial or patient readiness for such an intervention.	Level of evidence II–III, strong recommendation based on evidence	SBA/Irish/ NICE
	Antibiotic prophylaxis – Clinicians should not routinely use antibiotic prophylaxis against UTIs in pediatric patients with NLUTD. – Clinicians should consider using antibiotic prophylaxis for pediatric patients with NLUTD if they have a recurrent or severe UTIs within the last 3–6 months. – Before prescribing antibiotic prophylaxis against UTIs, clinicians should: a. investigate the urinary tract for an underlying treatable cause (such as urinary tract stones or incomplete bladder emptying); b. take into account and discuss with the patient and/or their guardians, the risks and benefits of prophylaxis; c. refer to local protocols approved by a microbiologist or discuss suitable regimens for antibiotic prophylaxis with a microbiologist. – Consider antibiotic prophylaxis for NLUTD patients with a history of symptomatic UTI after catheter change or experience trauma during catheterization.	Level of evidence II, strong recommendations based on evidence	SBA/ NICE

Since spinal dysraphism, specifically, SB, is frequently diagnosed before birth, it is crucial to provide expectant parents with SB-specific prenatal counselling.[16] SBA recommends that all evidence-based treatment options be offered, including antenatal or fetal closure, closure after birth, termination of the pregnancy, and adoption.[17] Timely consultation is crucial to ensure all options are available to the family, especially immediately following antenatal identification, between 18–20 weeks.[16,18] Based on the literature, fetal closure is a viable option until the 25th week of gestation, and should be offered at treatment centers with expertise in the surgical and

Table 2 (cont'd). Summary of key recommendation statements

Domains	Key recommendation statements	Level of evidence and grade of recommendation	Adaptation source with direct quote or modified
Treatment recommendations (cont'd)	*Antibiotic prophylaxis* – Clinicians should not routinely use antibiotic prophylaxis against UTIs in pediatric patients with NLUTD. – Clinicians should consider using antibiotic prophylaxis for pediatric patients with NLUTD if they have a recurrent or severe UTIs within the last 3–6 months. – Before prescribing antibiotic prophylaxis against UTIs, clinicians should: a. investigate the urinary tract for an underlying treatable cause (such as urinary tract stones or incomplete bladder emptying); b. take into account and discuss with the patient and/or their guardians, the risks and benefits of prophylaxis; c. refer to local protocols approved by a microbiologist or discuss suitable regimens for antibiotic prophylaxis with a microbiologist. – Consider antibiotic prophylaxis for NLUTD patients with a history of symptomatic UTI after catheter change or experience trauma during catheterization.	Level of evidence II, strong recommendations based on evidence	SBA/ NICE
	Anticholinergics – Clinicians should offer antimuscarinic drugs to pediatric patients with NLUTD with symptoms of an OAB, such as increased frequency, urgency, and incontinence. The most common antimuscarinic used is oxybutynin syrup (dosage 0.2–0.4 mg/kg weight per day). – Clinicians should consider antimuscarinic drug treatment in pediatric patients with NLUTD, and conditions affecting the brain (i.e., cerebral palsy) and symptoms of an OAB. – Clinicians should consider antimuscarinic drug treatment in pediatric patients with NLUTD with urodynamic investigations showing impaired bladder storage (NDO and poor compliance). – Clinicians should monitor residual urine volume in pediatric patients with NLUTD who are not using intermittent or indwelling catheterization after starting antimuscarinic treatment.	Level of evidence II–III, strong recommendation on evidence and current best practice	SBA/ ICCS/ Irish
	Botulinum toxin injection – Clinicians should consider bladder wall injection with botulinum toxin type A (6–10 units per kg per dose up to maximum 300 units per dose) for children and adolescents with spinal cord disease and symptoms of an OAB and/or with urodynamic investigations showing impaired bladder storage and in whom antimuscarinic drugs have proved ineffective or poorly tolerated	Level of evidence II–III, strong recommendation based on evidence	NICE/ EAU-ESPU/ ICCS
Surgical management	*Vesicostomy* – In patients with high-grade reflux and recurrent febrile UTI, a temporary incontinent diversion (e.g., ureterocutaneostomy) can be considered to protect the upper tract. – An incontinent vesicostomy — preferably a Blocksom stoma — is an option to reduce bladder pressure in children/newborns if the parents are noncompliant with CIC and/or CIC through the urethra is extremely difficult or impossible due to anatomical or social circumstances.	Level of evidence III–IV, weak recommendation on evidence and current best practice	EAU-ESPU/ ICCS/NICE
	Continent catheterizable channel – Creation of a continent cutaneous catheterizable channel may be offered to select school-aged or all adolescent pediatric NLUTD who have difficulties performing CICs via the urethra.	Level of evidence III–IV weak recommendation on evidence and current best practice	EAU-ESPU
	Augmentation cystoplasty – Clinicians should consider augmentation cystoplasty using an intestinal segment for pediatric patients with NLUTD: a. with non-progressive neurological disorders and complications of impaired bladder storage (e.g., hydronephrosis or incontinence); and b. only after a thorough clinical and urodynamic assessment and discussion with the patient and/or their family members and carers about complications, risks, and alternative treatments. – Clinicians should obtain serum chemistries, including B12 yearly on patients who have had augmentation cystoplasty and offer patients life-long followup because of the risk of long-term complications.	Level of evidence III, weak recommendation on evidence and current best practice	NICE/ SBA/ Irish/ EAU-ESPU

obstetrical management of NTDs.[5,6,17,18] The impact of fetal spine closure on urinary incontinence remains uncertain, with conflicting findings regarding its effect on neurogenic bladder dysfunction, bladder wall thickening, and febrile urinary tract infections (UTIs) compared to postnatal closure.19,20 When postnatal closure is

Table 2 (cont'd). Summary of key recommendation statements

Domains	Key recommendation statements	Level of evidence and grade of recommendation	Adaptation source with direct quote or modified
Surgical management (cont'd)	*Slings, bulking agents, and AUS for neurogenic stress incontinence* – Clinicians should consider autologous fascial sling surgery for pediatric patients with NLUTD and neurogenic stress incontinence. – Clinicians should not routinely use synthetic tapes and slings in pediatric patients with NLUTD and neurogenic stress incontinence because of the risk of urethral erosion. – In selected pediatric patients with NLUTD, clinicians may consider endoscopic injection of bulking agent for the treatment of urinary incontinence in children with neurogenic bladder. – Clinician should consider inserting an artificial urinary sphincter for pediatric patients with NLUTD and neurogenic stress urinary incontinence only if an alternative procedure (e.g., autologous fascial sling) is likely unsuccessful based on 24hr pad weight (>400 g/day) or pad per day (>5 per day). When considering inserting an AUS: a. discuss with the person and/or their family members and carers the risks associated with the device, the possible need for repeat operations, and alternative procedures; b. ensure that the bladder has adequate low-pressure storage capacity.	Level of evidence III–IV, weak recommendation on evidence and current best practice	NICE/EAU-ESPU
	Antegrade continence enema (ACE) or cecostomy tube for bowel management – Clinicians should discuss cecostomy or ACE for children with severe constipation who have failed dietary changes, oral laxatives, rectal therapy, and transanal irrigations.	Level of evidence III–IV, weak recommendations on evidence and current best practice	SBA/ICCS/ EAU-ESPU/ Irish
Lifelong followup and transitional care	*Followup monitoring and surveillance protocols* – Clinicians should not rely solely on serum creatinine and eGFR in isolation to monitor renal function in people with NLUTD. – Clinicians should consider using isotopic GFR when an accurate measurement is required (e.g., if imaging of the kidneys suggests that renal function might be compromised) – Clinicians should offer lifelong ultrasound surveillance of the kidneys to people at high risk of renal complications (e.g., consider surveillance ultrasound scanning at annual or 2-year intervals). Those at high risk include those with SB and those with adverse features on urodynamic investigations, such as poor bladder compliance, DSD, or VUR. – Clinicians should consider urodynamic investigations as part of a surveillance regimen for people at high risk of urinary tract complications (e.g., people with SB, spinal cord injury, or anorectal abnormalities) – Clinicians should not use renal scintigraphy for routine surveillance in people with NLUTD. – Clinicians should not use cystoscopy for routine surveillance in people with NLUTD. – Clinicians should undertake cystoscopy and appropriate upper tract imaging in adolescent and young adults who have had a bladder augmentation when the following are present: a. clinically noted change in upper or lower urinary tract status; b. gross hematuria; c. recurrent symptomatic UTIs; d. increasing incontinence; e. pelvic pain; f. had a renal transplant with the presence of BK/polyomavirus.	Level of evidence III–IV, strong recommendation based on evidence and best practice	NICE/SBA
	Transitional care – Transitional care should be offered to promote access to uninterrupted, developmentally appropriate SB condition management and preventative care throughout transition — around ages 14–21 years.	Level of evidence III–IV, strong recommendation based on evidence and current best practice	SBA/NICE/ Irish/EAU-ESPU

AUS: artificial urinary sphincter; CIC: clean intermittent catheterization; CKD: chronic kidney disease; Cr: creatinine; eGFR: estimated glomerular filtration rate; DMSA: dimercapto succinic acid; DSD: detrusor sphincter dyssynergia; EAU: European Association of Urology; ESPU: European Society for Pediatric Urology; ICCS: International Children's Continence Society; MDT: multidisciplinary team; NDO: neurogenic detrusor overactivity; NICE: National Institute for Health and Care Excellence; NLUTD: neurogenic lower urinary tract dysfunction; OAB: overactive bladder; SB: spina bifida; SBA: Spina Bifida Association; US: ultrasound; UTI: urinary tract infection VCUG: urodynamics + voiding cystourethrogram; VUR: vesicoureteral reflux.

chosen, performing a cesarean delivery at 37 weeks and closing the opening within 24 hours of birth is generally recommended. It is essential to provide parents and caregivers with clear explanations of the expected procedures and post-surgical care.[17,21] After the initial consultation with fetal medicine/obstetrics specialists for

Table 3. Summary of recommended investigations in a pediatric patient with NLUTD

Age (years)	Recommended studies
0–3 months	• Baseline renal/bladder ultrasound • Baseline serum creatinine • DMSA scans if febrile UTI or vesicoureteral reflux
3–12 months	• Repeat renal/bladder ultrasound (every 3–6 months) • Baseline video urodynamic (or urodynamic + VCUG) testing • Serum creatinine if a change in upper urinary tract findings
1–2 years	• Renal/bladder ultrasound every six months • Annual urodynamic testing • Serum creatinine if a change in upper urinary tract findings
2–5 years	• Annual renal/bladder ultrasound if stable without UTIs or imaging changes • Additional ultrasound as needed for recurring symptomatic UTIs or bladder hostility identified by urodynamic testing • Serum creatinine if a change in the upper urinary tract findings or clinical suspicion of renal function deterioration • Annual urodynamic testing till three years • Urodynamic testing between 3–5 years only if upper tract changes, recurring UTIs, patient and family's interest in beginning a urinary continence program
Five years and above	• Serum creatinine yearly if concern for CKD or changes in upper urinary tract findings • Urodynamic testing if initiating a urinary continence program; or if hydronephrosis or renal scarring, recurring symptomatic UTIs, or changes in urinary continence status

CKD: chronic kidney disease; DSMA: dimercapto succinic acid; NLUTD: neurogenic lower urinary tract dysfunction; UTI: urinary tract infection; VCUG: urodynamics + voiding cystourethrogram.

the management of a pregnancy with a prenatal NTD diagnosis, the family should be offered the opportunity to meet a multidisciplinary team (MDT) of experts (see below) to review available management options and to initiate referrals for further evaluation, as well as long-term management.[17,18]

Postnatal period initial approach

■ RECOMMENDATION 2 *(STRONG RECOMMENDATION, LE III–IV)*

- Clinicians should obtain a postnatal baseline renal and bladder ultrasound after 48 hours and within the first 1–4 week of birth.
- Clinicians should obtain a postnatal baseline renal function test-serum creatinine after 48 hours and within the first 1–4 weeks of birth.
- Clinicians should educate parents about the possible need for clean intermittent catheterization (CIC). CIC should be initiated if there is concern for high risk of urologic morbidity based on urinary tract imaging (i.e., dilated upper tract/high-grade hydronephrosis/megacystis).
- Clinicians should refer a newborn with spinal dysraphism to the MDT for initial evaluation.

The optimal timing for the first postnatal ultrasound (US) examination has been studied to a limited extent;[22,23] however, it has become common practice to avoid performing an US within the first two days after birth on account of concerns about underestimating the degree of hydronephrosis due to physiologic dehydration of the newborn.[24] The ESPU-EAU, CUA-PUC guidelines on antenatal hydronephrosis evaluation and the Society for Fetal Urology (SFU) suggest obtaining an US within 1–4 weeks postnatally.[24,25] It is reasonable to assume that high-grade antenatal hydronephrosis (SFU grades 3–4) should be imaged promptly in order to establish a baseline for future comparisons, while low-grade hydronephrosis (SFU grades 1–2) can be imaged at a later time interval.[24,26] It is commonly advised to schedule a followup US examination at 4–6 weeks of age to reassess for the presence of hydronephrosis.[26]

During the first few days of life, the neonate's serum creatinine level is primarily reflective of placental clearance and the mother's kidney function. Baseline creatinine levels can commence on day 2 of life.[27] Healthy, full-term infants usually reach baseline serum creatinine levels within two weeks of age, while relatively healthy premature infants may take anywhere from 3–8 weeks before their levels stabilize.[28]

According to the SBA-UMPIRE (Urologic Management to Preserve Initial Renal Function Protocol for Young Children with Spina Bifida) protocol and the ESPU-EAU guideline, an indwelling catheter is placed for postnatally repaired meningomyelocele until the patient is safe to be positioned supine. Then, CIC is initiated every six hours.[23,29] The concept of early initiation of CIC may be challenging to accept for families, especially with young parents. Clinicians must understand the facilitators and barriers to implementation of CIC.[26,30] Caregivers benefit from an adjustment period to learn about their child's need for CIC; prenatal or early postnatal information helps them process CIC. Clinicians should provide information about the low morbidity of CIC, which could enhance acceptance and adherence.[31] The healthcare team's teaching and reassurance builds caregiver confidence. Furthermore, several studies have shown that early initiation of CIC addressing the hostile bladder enables preservation of renal function.[32,33] Furthermore, an initial referral and continuous evaluation by the MDT enable better informed decisions.[34] It is imperative to note that the prevalence of latex allergy is higher in patients with SB; therefore, it is of utmost importance to ensure a latex-free environment and exercise caution regarding the use of natural rubber latex materials around SB patients.[35]

Table 4. Overview of the considerations for different surgical interventions in pediatric NLUTD

Surgical option	Purpose	Benefits	Considerations	Patient characteristics
Vesicostomy	Diversion of urine through an abdominal stoma	Prevention of upper urinary tract damage	Incontinent form of urinary diversion	Suitable for infant/ young toddlers with poor bladder emptying, recurrent UTIs, or inability to perform CIC
Mitrofanoff continent catheterizable channel (appendicovesicostomy)	Continent urinary diversion	Improved bladder management Preservation of upper tract function Improved independence without indwelling catheters	Potential for stomal complications (i.e., stricture, leak, infection, or mucosal prolapse)	Suitable for patients with intact appendix or alternative suitable structures (i.e., ileum- Monti tube) for catheterizable conduit
Augmentation cystoplasty	Increase the bladder storage capacity and compliance	Improved bladder function Reduction in intravesical pressures Enhanced urinary continence Prevention of upper urinary tract damage	Risk of persistent urinary incontinence Dependence on catheterization The potential need for metabolic evaluation, treatment of electrolytes imbalance Assess for compliance	Suitable for patients with low bladder capacity and poor compliance, without contraindications (e.g., inflammatory bowel disease, significant prior small bowel resection). Able to perform CIC and compliant with regular irrigation to prevent complications (mucus plug, stone, recurrent infection, or rupture)
Slings	Restoration of urinary continence	Effective treatment for sphincteric incompetence	Consideration of autologous material choice and potential complications of the donor site.	Suitable for patients with moderate stress incontinence due to sphincteric incompetence and adequate abdomino-detrusor pressure to overcome outlet resistance
Bulking agents	Restoration of urinary continence	Less invasive treatment option and lower complication rate than other surgical options	Limited long-term results	Suitable for patients with mild SUI and poor response to conservative treatments
Artificial urinary sphincter	Restoration of urinary continence	High success rates for stress incontinence Improved quality of life	Risk of mechanical failure and revision surgery A potential complication of urethral erosion and infection	Suitable for patients with moderate to severe incontinence due to sphincteric incompetence, normal cognitive abilities, and manual dexterity to manipulate the device
Malone antegrade continence enema (MACE) or cecostomy	Facilitation of bowel management Creation of continent catheterizable conduit for bowel cleanout	Improved bowel continence Enhanced quality of life	Risk of stomal complications (i.e., stenosis, leakage, and mucosal prolapse)	Suitable for patients with neurogenic bowel dysfunction and poor response to conservative treatments, with an intact appendix for catheterizable conduit for MACE; cecostomy for preference of device or when appendix is not available

CIC: clean intermittent catheterization; NLUTD: neurogenic lower urinary tract dysfunction; SUI: stress urinary incontinence; UTI: urinary tract infection.

Multidisciplinary spina bifida service/ clinic

■ RECOMMENDATION 3 *(STRONG RECOMMENDATION, LE III-IV)*

- Children with NLUTD should be reviewed at least annually at the MDT SB clinic.
- The specialist SB team is responsible for the education and support of local teams.
- A fully staffed MDT SB clinic ideally consists of the following key professionals: neurosurgeon, urologist, orthopedic surgeon, SB nurse specialist, advanced nurse practitioner, pediatrician, social worker, physiotherapist, and occupational therapist. Other healthcare professionals of benefit may include a dietitian.

Table 5. Components of clinical history and physical examinations

- Urinary tract symptoms, such as symptomatic urinary tract infections, bladder management and condition (including bladder diary or frequency/volume chart)
- Neurological symptoms and diagnosis (if known)
- Clinical course of the neurologic disease
- Bowel symptoms and management
- Sexual function in adolescent patients
- Comorbidities
- Use of prescription and other medications and therapies
- Mobility, hand function
- Cognitive function
- Social support
- Lifestyle
- Measuring blood pressure
- Abdominal examination
- External genitalia examination
- Vaginal or rectal examination if clinically indicated (for example, to look for evidence of fecal loading or alterations in anal tone)

Table 6. Defining a symptomatic UTI in the SB population

UTI according to clinical symptoms, positive UA, and UC: – Positive UA – Positive UC on a catheterized specimen – Leakage between CIC – Onset of pelvic or back pain – Fever (100.4 F/38.0 C)
Positive UA (+UA): – > trace nitrite or leukocyte esterase on dip UA – >10 white blood cells/high power field, uncentrifuged specimen, or >5 white blood cells/high power field, centrifuged specimen
Positive UC (+UC): – >50 000 colony-forming units/mL (sterile specimen obtained by catheter or suprapubic catheter aspirate) – >100 000 colony-forming units/mL in a clean voided specimen

CIC: clean intermittent catheterization; UA: urinalysis; UC: urine culture; UTI: urinary tract infection.

Both SBA and Irish guidelines recommend that pediatric patients with NLUTD should be reviewed at least annually to ensure routine followup and evaluation by a MDT specialized in the care of NLUTD.[36,37] The literature has shown that a MDT clinic is essential to ensure coordinated care and maintaining health among patients with NLUTD.[34,37-39] Both SBA and Irish guidelines stated that the crucial members of the MDT include neurosurgeons, who can offer comprehensive information on antenatal and postnatal surgical approaches and provide realistic long-term management.[36,37] Urologists address renal health, urinary and social continence, bladder-bowel intervention (usually along with a team of gastroenterology specialized nurses or nurse practitioners), while orthopedic surgeons manage skeletal growth, mobility, and function. Developmental pediatricians, physiotherapists, occupational therapists, and advanced practice nurses focus on optimizing overall function, bladder and bowel management, medical needs, caregiver support, resource identification, access to care, and mental health support. Social workers provide emotional support and mental health screening and facilitate access to financial and emotional resources. Occasionally, a dietitian could assist in weight management and nutritional evaluation.[37]

History and physical examination

■ RECOMMENDATION 4 *(STRONG RECOMMENDATION, LE IV)*

When assessing lower urinary tract dysfunction in patients with pediatric NLUTD, clinicians should take a clinical history and physical examination, including the information detailed in Table 5.

The NICE and SBA guidelines recommend that the evaluation of pediatric NLUTD should include a comprehensive clinical assessment with history and physical examination.[36,40] Information elicited from the clinical history and physical examination aid in the discussions with patients, caregivers, and clinical teams, leading to informed decisions on appropriate management approaches.[40] Specifically, the assessment of NLUTD requires consideration of both urinary tract dysfunction and underlying neurologic conditions that can affect patients in different ways, and every patient must be managed in an individualized regimen.

Diagnostics and workup

■ RECOMMENDATION 5: RENAL AND BLADDER ULTRASOUND *(STRONG RECOMMENDATION, LE II–III)*

- For children with NLUTD or at high risk of developing NLUTD, clinicians should obtain a baseline renal/bladder US within three months of birth and repeat in six months.
- For children with NLUTD, clinicians should obtain renal/bladder US every six months when the child is under the age of two.
- After a child with pediatric NLUTD is above two years of age, clinicians should obtain an US yearly if the child is stable, without UTIs or imaging changes.
- Obtain a renal/bladder US, as needed, if the child has recurring symptomatic UTIs or if urodynamic testing identifies bladder hostility.

Non-invasive US monitoring is suitable as the initial screening for children with NLUTD to guide further management. Most newborns with SB have normal upper urinary tract. A study by Tanaka et al found

that of 188 infants with SB with two kidneys, only 3.7% had high-grade hydronephrosis in one or both kidneys, 40.4% had low-grade hydronephrosis in one or both kidneys, and 55.9% had two normal kidneys. Additionally, 84.6% of infants with SB had no reflux;[22] however, initial findings of changes in the kidney/bladder US indicate risk for upper tract changes, such as bladder wall thickness seen on an US that can predict renal damage. If increasing bladder wall thickness on US is left unattended, without proper preventive measures or even with early proactive management, approximately 50% of children will suffer upper urinary tract damage within five years due to bladder hostility.[29,41-43] Thus, adapting the SBA guideline, the consensus of the CUA guideline authorship group was that during the first few years of life, it is important to focus on surveillance of urinary tract imaging to prevent renal damage while ensuring a low-pressure bladder and infection-free urinary system.[29,44]

■ RECOMMENDATION 6: ASSESSMENT OF RENAL FUNCTION *(STRONG RECOMMENDATION, LE II–III)*

- Clinicians should obtain a baseline serum creatinine within three months of birth and repeat as clinically indicated (i.e., needed for monitoring due to baseline elevated or diagnostic imaging suggestive of high risk for upper tract damage).
- Clinicians should obtain a serum creatinine test when a child with NLUTD is 1–5 years old if there is a change in the upper urinary tract findings on US; however, serum creatinine can also be ordered based on clinical suspicion and US is not a prerequisite, as renal US can have poor sensitivity for early decline in estimated glomerular filtration (eGFR).
- Clinicians should obtain serum chemistry (including serum creatinine) for children with NLUTD when they are five years old. Thereafter, clinicians should consider obtaining a serum creatinine test yearly if there is concern for chronic kidney disease (CKD) or to monitor for kidney function due to change in the upper urinary tract findings on US. If the child has low muscle mass, consider an alternative measure of renal function, such as cystatin C or nuclear studies.
- Clinicians should only order dimercapto succinic acid (DMSA) scans in infants with SB who either had a febrile UTI or are found to have vesicoureteral reflux (VUR) on a voiding cystourethrogram (VCUG).

The underlying goal of urologic management for pediatric patients at risk of developing NLUTD is to maintain normal renal function starting from birth.[22,23,29] Therefore, it is important to establish objective renal function assessment while monitoring. The Canadian Society of Nephrology concurred with Kidney Disease Improving Global Outcomes 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (KDIGO), which suggests routinely assessing renal function in all patients with CKD or at risk of progression.[45] While using serum creatinine and an eGFR equation for initial renal function assessment is acceptable, creatinine is a poor marker of eGFR due to low muscle mass among SB patients, with overestimation of kidney function, particularly in patients who are non-ambulatory.[46,47] Thus, if the patient is determined to have low muscle mass, clinicians should consider cystatin-C or nuclear studies as an alternative measure of renal function with better accuracy.[47,48] DMSA scan should only be selectively used for renal function assessment of a newborn with spinal dysraphism after an initial US evaluation. Based on the recent study by Cascio et al, it is recommended that nuclear scans be limited to infants with SB who have a febrile UTI or VUR to avoid unnecessary nuclear scan testing.[44]

■ RECOMMENDATION 7: URODYNAMIC STUDIES *(WEAK RECOMMENDATION, LE II–III)*

- Clinicians should obtain a baseline video urodynamic (or urodynamic + VCUG) testing for all patients born with SB within 3–12 months.
- Clinicians should consider obtaining urodynamic testing for patients with pediatric NLUTD annually until the child is three years old, especially if the following are noted: bladder hostility, upper urinary tract changes, recurrent symptomatic UTIs.
- Clinicians should obtain urodynamic testing for patients with pediatric NLUTD between the ages of 3–5 years old, only if the following are present: upper tract changes, recurring UTIs, patient and family's interest in beginning a urinary continence program (i.e., familial/patient readiness for initiation of a urinary continence program).
- Clinicians should obtain urodynamic testing for patients with pediatric NLUTD over the age of five years old when initiating a urinary continence program or if the following are present: hydronephrosis or renal scarring, recurring symptomatic UTIs, changes in urinary continence status.

Baseline and followup urodynamic evaluation are critical in assessing bladder function, including capacity, compliance, and pressure.[7,9,49] Urodynamics can identify and monitor pediatric patients with NLUTD who are at risk of bladder dysfunction progression that requires prompt management of the hostile bladder parame-

ters to prevent adverse upper urinary tract development.[23,49] The proactive and reactive approaches for pediatric patients with NLUTD are both considered in the setting of the Canadian health system, with variable resource availability;[50] however, voiding urodynamic studies (UDS) or urodynamic + VCUG is preferred for detecting reflux and bladder abnormalities and indicating intervention for detrusor leak-point pressures DLPP) ≥40 cmH_2O or neurogenic detrusor overactivity (NDO) and detrusor sphincter dyssynergia (DSD).[22,23,25,29,42,49]

Several research studies have indicated that children above the age of three who possess an occult neural tube defect but have not undergone surgery or received a delayed diagnosis of occult dysraphism commonly exhibit either an upper or lower motor neuron lesion, or a combination of both.[51-53] Following a growth spurt, these children may develop new urologic symptoms due to the tethering of the spinal cord; such cases often manifest as incontinence or constipation when the child reaches the age of three or older.[53] Urodynamic testing serves as a vital means to objectively establish the impact of an occult spinal dysraphism on lower spinal cord function.[53] Hence, it is recommended that urodynamic testing be considered annually for pediatric patients with NLUTD until they reach the age of three.[40]

Treatment recommendations

■ RECOMMENDATION 8: CLEAN INTERMITTENT CATHETERIZATION *(STRONG RECOMMENDATION, LE II–III)*

- Clinicians should initiate clean intermittent catheterization (CIC) and antimuscarinic therapy to infants with NLUTD for the treatment of bladder hostility when indicated based on renal/bladder US, UDS, and/or serum creatinine.
- When children with NLUTD reach the age of three or older, clinicians should initiate CIC and antimuscarinic therapy when indicated by upper urinary tract changes, recurring symptomatic UTIs, or bladder hostility noted on urodynamic testing, or when there is a family interest in starting a urinary continence program, indicating familial or patient readiness for such an intervention.

After achieving stability following neurosurgical closure or in the presence of radiographic or clinical indications of significant changes, baseline, and annual UDS are conducted until age three.[29] The primary objective of early UDS and CIC is to detect patients with hazardous bladder parameters to intervene before upper urinary tract injury develops. Therefore, implementing the strategy of early CIC with anticholinergic therapy is recommended during the neonatal period, guided by the renal bladder US, UDS findings, and/or renal function workup.[29,54]

Several studies have shown that early initiation of CIC addressing the hostile bladder enables preservation of renal function. Studies have shown that reactive and delayed bladder management of pediatric patients with NLUTD risks up to 50% of patients experiencing renal function deterioration, while the proactive approach has shown that only 2–19% progressed to renal function deterioration.[32,33,43,50,54,55] Furthermore, when comparing indwelling urethral catheter vs. CIC, a recent systematic review and meta-analysis found that among patients with neurogenic bladder requiring catheter-based drainage, the use of CIC is associated with lower rates of UTI than indwelling catheters.[56] Adapting the SBA guideline recommendation, the panel also recommends initiating the child's involvement in self-catheterization when cognitively capable and physically able. The rationale for early patient engagement in CIC is to promote social continence at an early age.

■ RECOMMENDATION 9: ANTIBIOTIC PROPHYLAXIS *(STRONG RECOMMENDATION, LE II)*

- Clinicians should not routinely use antibiotic prophylaxis against UTIs in pediatric patients with NLUTD.
- Clinicians should consider using antibiotic prophylaxis for pediatric patients with NLUTD if they have a recurrent or severe UTS within the last 3–6 months.
- Before prescribing antibiotic prophylaxis against UTIs, clinicians should:
  a. Investigate the urinary tract for an underlying treatable cause (such as urinary tract stones or incomplete bladder emptying);
  b. Take into account and discuss with the patient and/or their guardians, the risks and benefits of prophylaxis;
  c. Refer to local protocols approved by a microbiologist or discuss suitable regimens for antibiotic prophylaxis with a microbiologist.
- Consider antibiotic prophylaxis for NLUTD patients with a history of symptomatic UTI after catheter change or experience trauma during catheterization.

According to a recent study by Wallis et al, during the initial four months of life, symptomatic UTI with a positive culture was infrequent (~4-7%) in newborns

with SB. Therefore, the study suggests that routine antibiotic prophylaxis may not be necessary for most newborns with SB.[57] Furthermore, a study by Zegers et al also described that antibiotic prophylaxis for UTI in SB children on CIC is not indicated.[58] Not initiating antibiotic prophylaxis has been shown to increase asymptomatic bacteria but not increase symptomatic UTI events, particularly in boys, patients with low UTI rates, and those without VUR.[58] Similarly, congregated evidence by NICE guidelines found that the incidence of symptomatic UTI for SB children with and without antibiotic prophylaxis is not significantly different (relative risk 0.92, 95% confidence intervals 0.52–1.62).[40]

Nonetheless, considering recurrent UTI in pediatric patients with NLUTD could cause considerable morbidity, including renal functional impairment, the guideline panel has adopted the NICE guideline recommendation of considering antibiotic prophylaxis in pediatric patients with NLUTD with recurrent or severe symptomatic UTI. Clinicians should investigate for underlying UTI etiology and consult the local antibiogram protocol while practicing shared decision-making with the family.[40] The panel also recommends adapting the antibiotic stewardship principle and the American Urological Association (AUA) recommendation for prophylactic antibiotic usage relevant to catheter exchange or traumatic catheterization, particularly among NLUTD patients at high risk for recurrent UTIs.[59]

In defining a symptomatic UTI in the SB population, we recommend adapting the definition by Madden-Fuentes et al (Table 6).[60]

■ RECOMMENDATION 10: ANTICHOLINERGICS *(STRONG RECOMMENDATION, LE II–III)*

- Clinicians should offer antimuscarinic drugs to pediatric patients with NLUTD with symptoms of an overactive bladder (OAB), such as increased frequency, urgency, and incontinence. (Note: The most common antimuscarinic used is oxybutynin syrup, dosage 0.2–0.4 mg/kg weight per day).
- Clinicians should consider antimuscarinic drug treatment in pediatric patients with NLUTD and conditions affecting the brain (i.e., cerebral palsy), and symptoms of an OAB.
- Clinicians should consider antimuscarinic drug treatment in pediatric patients with NLUTD with UDS showing impaired bladder storage (NDO and poor compliance).
- Clinicians should monitor residual urine volume in pediatric patients with NLUTD who are not using intermittent or indwelling catheterization after starting antimuscarinic treatment.

Anticholinergic drugs, such as oxybutynin, propiverine, solifenacin, and tolterodine, are commonly used to manage detrusor overactivity (DO) symptoms in individuals with neurogenic bladder dysfunction, specifically addressing urgency, frequency, and urinary incontinence.[40,61] A recent study by Franco et al evaluated the efficacy and safety of solifenacin oral suspension in pediatric patients with NDO.[62] The study involved sequential doses of solifenacin for 12 weeks to determine the optimal dose, followed by a fixed-dose treatment period of at least 40 weeks. The study demonstrated that solifenacin effectively increased maximum cystometric capacity, indicating that the bladder can accommodate increased fluid volume before reaching pressures that could cause kidney damage or leakage.[62]

Current evidence for the management of pediatric patients with NLUTD does not provide specific criteria or timing for initiating anticholinergics, which is left to the discretion of healthcare providers or institutional protocols.[50] Furthermore, except for oxybutynin (dosage 0.2–0.4 mg/kg weight per day) and propiverine hydrochloride (0.8–1.1 mg/kg per day), which were approved by Health Canada for the pediatric population, the use of other anticholinergic medications in pediatric patients with NDO is considered off-label and associated with several adverse effects, such as behavioral changes, urinary retention, and constipation.[40,50,61,63] Antimuscarinic treatment can reduce bladder emptying, possibly increasing the risk of UTIs.

When prescribing antimuscarinics, clinicians should consider that antimuscarinics are known to cross the blood-brain barrier (e.g., oxybutynin) and potentially cause central nervous system-related side effects (such as confusion). Some studies suggest that the use of high-dose anticholinergic medications is linked to a higher likelihood of cognitive decline and dementia in adulthood, particularly among individuals who already have cognitive impairment or existing neurodegenerative conditions;[64,65] however, the use of anticholinergic medications does not seem to be linked to negative cognitive outcomes in children, unlike their impact on cognitive function in older adults.[66] It is crucial to emphasize this to patients and their caregivers and to provide comprehensive counselling regarding the potential risks associated with these medications. An alternative option is intravesical oxybutynin instillation, which in a systematic review showed a mean percentage of 74.6% of children with NLUTD describing "dry or improved" conditions after treatment, suggesting a good efficacy and fewer side effects.[67]

■ RECOMMENDATION 11: BOTULINUM TOXIN INJECTION *(STRONG RECOMMENDATION, LE II–III)*

Clinicians should consider bladder wall injection with botulinum toxin type A (6–10 units per kg per dose up to maximum 300 units per dose) for children and adolescents with spinal cord disease and symptoms of an OAB and/or with UDS showing impaired bladder storage and in whom antimuscarinic drugs have proved ineffective or poorly tolerated.

Most recent trials and systematic review suggested that botulinum toxin type A (BTX-A) injection (6–10 unit/kg; maximum of 300 units) is a safe and effective treatment for neurogenic bladder in children who have not responded to other therapies.[68,69] It is well-tolerated, with minimal adverse effects, and improvements in incontinence and VUR are commonly reported outcomes;[68,69] however, no evidence supports its use as a first-line therapy. Further, regarding the mode of injection, intradetrusor injection is as effective as submucosal injection.[70] The most commonly reported urodynamic parameters are improvements in detrusor pressure, bladder capacity, and compliance, while patient satisfaction remains controversial.[69,71,72]

According to the NICE guideline, BTX-A injection into the detrusor is an effective way to manage incontinence and improve urodynamic measures of bladder storage, potentially protecting the kidneys from high intravesical pressures.[40] This treatment is well-tolerated across different age groups and conditions. Although the evidence quality is variable, the effect is maintained over multiple injections.[72-74] It is crucial to ensure that pediatric patients with NLUTD who have been offered continuing treatment with repeated BTX-A injections have prompt access to repeat injections when symptoms return or every 3–6 months.[72,74] It is also important to explain to the patient and/or their family members and carers that a catheterization may be needed in most people with NLUTD after bladder BTX-A injection treatment; clinicians need to ensure they are able and willing to start catheterization should urinary retention develops after the treatment. In addition, it is essential to monitor the upper urinary tract in pediatric NLUTD patients who are at risk of renal complications (i.e., those with high intravesical pressures on filling cystometry), since the efficacy could decrease over time, and alternative management options (such as enterocystoplasty) should be offered.[73-76]

SURGICAL MANAGEMENT

Surgical interventions can bring about improvements in urinary function by augmenting bladder capacity, decreasing intravesical pressures, and enhancing voiding capabilities. Consequently, there is a reduction in urinary incontinence, diminished susceptibility to UTIs, and preservation of upper urinary tract health. By effectively addressing urinary and bowel dysfunction, these interventions contribute to enhanced functional autonomy and an improved quality of life. Patients experience heightened self-assurance, increased engagement in social activities, and an overall sense of well-being. The regained control over these physiological functions also enhances self-esteem and promotes better mental health. Nonetheless, it is essential to acknowledge the potential for long-term complications, such as persistent urinary incontinence, reliance on catheterization, and issues related to the surgical procedure itself. Consistent monitoring and comprehensive interdisciplinary care are imperative to address and manage any complications that may arise. Furthermore, individual responses to treatment and the presence of concurrent comorbidities can impact the long-term outcomes of surgical interventions.

■ RECOMMENDATION 12: VESICOSTOMY *(WEAK RECOMMENDATION, LE III–IV)*

In patients with high-grade reflux and recurrent febrile UTI, a temporary incontinent diversion (e.g., ureterocutaneostomy) can be considered to protect the upper tract; An incontinent vesicostomy — preferably a Blocksom stoma — is an option to reduce bladder pressure in children/newborns if the parents are non-compliant with CIC and/or CIC through the urethra is extremely difficult or impossible due to anatomical or social circumstances.

In order to protect the upper tract from high-grade reflux, non-compliant bladder, and recurrent febrile UTI, a temporary incontinent diversion has been reported to be a viable option to address hostile bladder in children with NLUTD at high risk for chronic kidney disease.[77,78] In addition, vesicostomy can be offered, especially among patients and parents who have difficulty performing CIC via the urethra.[79] A cystostomy button may be an alternative; however, the complication rate (mostly UTI) can be up to 34% within a mean followup of 37 months.[80,81]

At an appropriate age, the patient can undergo reconstruction or closure of vesicostomy with a high likelihood of continence.[82] Otherwise, there have been reports of long-term vesicostomy into adulthood with high contentment and low complication; thus, in some well-selected patients, it may be a good long-term approach to prevent infection and upper tract deterioration, with no need for planned re-operation.[83]

RECOMMENDATION 13: CONTINENT CATHETERIZABLE CHANNEL *(WEAK RECOMMENDATION, LE III–IV)*

Creation of a continent cutaneous catheterizable channel may be offered to select school-aged or all adolescent pediatric NLUTD who have difficulties performing CICs via the urethra.

Continent urinary diversion as an effective and durable treatment can be offered to well-selected older pediatric NLUTD for whom transurethral CIC is not feasible.[84] Recent reports and reviews described that patients on continent catheterizable channels have a good overall quality of life and associated patient satisfaction;[85-87] However, relatively common long-term reintervention rates and comorbidities may need to be discussed preoperatively with the patient and family to ensure an informed decision.[88,89]

■ RECOMMENDATION 14: AUGMENTATION CYSTOPLASTY *(WEAK RECOMMENDATION, LE III)*

- Clinicians should consider augmentation cystoplasty using an intestinal segment for pediatric patients with NLUTD:
  a. with non-progressive neurological disorders and complications of impaired bladder storage (for example, hydronephrosis or incontinence); and
  b. only after a thorough clinical and urodynamic assessment and discussion with the patient and/or their family members and carers about complications, risks, and alternative treatments;
- Clinicians should obtain serum chemistries, including B12, yearly on patients who have had augmentation cystoplasty and offer patients lifelong followup because of the risk of long-term complications.

Congregated evidence generated by the NICE and SBA guidelines, as well as recent reports, has shown that augmentation cystoplasty improves bladder capacity and reduced detrusor pressure, decreasing the likelihood of incontinence, specifically in older pediatric patients with NLUTD.[29,40,90,91] Augmentation cystoplasty increases the need for intermittent catheterization; however, it may also improve patient satisfaction and quality of life.[40,91,92] In patients where both augmentation cystoplasty and BTX-A therapy are viable options, analysis shows that augmentation cystoplasty is cost-effective for patients likely to benefit from incontinence treatment for more than 10 years.[40,93]

It is vital to inform the patient and families regarding the associated severe adverse events with augmentation cystoplasty.[40,94] The most commonly reported adverse events were symptomatic UTIs, bladder stones, and bowel obstruction. The augmented bladder is not a typical sensate bladder and thus there is a risk of overdistension and rupture, a life-threatening complication, if it is not emptied regularly. Long-term morbidity includes some micronutrient malabsorption; hence, obtaining serum chemistries, including B12, yearly is recommended in a patient who has had augmentation cystoplasty, and patients require lifelong followup because of the risk of long-term complications.[40,95]

■ RECOMMENDATION 15: SLINGS, BULKING AGENTS, AND ARTIFICIAL URINARY SPHINCTERS FOR NEUROGENIC STRESS INCONTINENCE *(WEAK RECOMMENDATION, LE III–IV)*

- Clinicians should consider autologous fascial sling surgery for pediatric patients with NLUTD and neurogenic stress incontinence.
- Clinicians should not routinely use synthetic tapes and slings in pediatric patients with NLUTD and neurogenic stress incontinence because of the risk of urethral erosion.
- In selected pediatric patients with NLUTD, clinicians may consider endoscopic injection of bulking agent for the treatment of urinary incontinence in children with neurogenic bladder.
- Clinician should consider inserting an artificial urinary sphincter (AUS) for pediatric patients with NLUTD and neurogenic stress urinary incontinence only if an alternative procedure (e.g., autologous fascial sling) is likely unsuccessful based on 24-hour pad weight (>400 g/day) or pads per day (≥5). When considering inserting an AUS:
  a. discuss with the person and/or their family members and carers the risks associated with the device, the possible need for repeat operations; and alternative procedures;
  b. ensure that the bladder has adequate low-pressure storage capacity.

Evidence from the NICE guideline and European Association of Urology (EAU) has shown that autologous fascial sling increases the bladder outlet resistance and improves continence by 40–100%;[40,79] however, autologous fascial slings may be associated with catheterization difficulties and risk of damage to the urethra or bladder during or after surgery.[40,79,96] In contrast to autologous slings, synthetic slings have a high complication rate in girls who perform transurethral

CIC.[40,79,97] Currently, there is no accepted cutoff for stress urinary incontinence procedure selection; some adult studies have shown that slings have significantly lower efficacy above 400 g on 24-hour pad test or ≥5 pads per day.[98,99]

Bulking agents have demonstrated some success (10–40%) in addressing urinary incontinence in pediatric patients with NLUTD, yet the effect could be temporary. While definitive surgical procedures may be required in the future, the use of bulking agents at the level of the bladder outlet has been demonstrated not to have a negative impact on the overall outcome.[100-103]

The AUS is currently the standard treatment for adult male stress urinary incontinence with NLUTD; however, the NICE guideline and recent reports have suggested that AUS might improve incontinence in pediatric patients with NLUTD as well.[40,104-106] Its application in children is less well-established, thus, should only be offered if an alternative procedure (e.g., autologous fascial sling) is likely to be unsuccessful. The main adverse effects and most prominent risks associated with AUS were device failure (26%), bladder neck erosion or device infection (11%), the need for revision (34%), the need for complete removal (22%), UTIs (9%), and upper tract complications (8%).[40]

It is important to recognize that treating stress incontinence in patients with NLUTD can be associated with upper tract deterioration, particularly if bladder pressures are high. Therefore, bladder pressure flow evaluation is required as part of the preoperative assessment; likewise, postoperative surveillance of the upper urinary tract should be maintained. Subsequent augmentation cystoplasty may be required if the bladder condition is hostile and the upper tract is at risk.[29,40,79,105]

RECOMMENDATION 16: ANTEGRADE CONTINENCE ENEMA OR CECOSTOMY TUBE FOR BOWEL MANAGEMENT *(WEAK RECOMMENDATIONS, LE III–IV)*

Clinicians should discuss cecostomy or antegrade continence enema (ACE) for children with severe constipation who have failed dietary changes, oral laxatives, rectal therapy, and transanal irrigations.

Addressing neurogenic bowel dysfunction (NBD) can potentially yield additional advantages in the management of pediatric patients with NLUTD, such as enhancing functional bladder capacity by alleviating compression caused by the rectum and mitigating reflex DO induced by rectal distension.[79,107] Furthermore, NBD may decrease UTIs by improving bladder dynamics and reducing perineal soiling.[107] According to a recent ICCS review on NBD, the initial approach for the treatment of NBD should always be via non-surgical management. Bowel management proceeds stepwise from least invasive to most invasive mode of treatment, which includes oral medications, digital rectal stimulation, suppositories, enemas, cone/balloon large volume enema, transanal irrigation system, antegrade enemas (MACE, cecostomy), and finally pouched fecal diversion (colostomy/ileostomy).[108]

Both cecostomy tube and ACE are surgical options available to pediatric NLUTD with NBD who failed conservative, medical, or transanal irrigation management.[79,109] Recent systematic reviews and clinic reports on long-term outcomes of ACE and cecostomy tubes have shown that cecostomy is associated with fewer post-procedural complications, while stomal complication is common in ACE procedures; however, patient satisfaction and impact on quality of life were similar following both procedures.[110,111]

LIFELONG FOLLOWUP AND TRANSITIONAL CARE

■ RECOMMENDATION 17: FOLLOWUP MONITORING AND SURVEILLANCE PROTOCOLS *(STRONG RECOMMENDATION, LE III–IV)*

- Clinicians should not rely solely on serum creatinine and eGFR in isolation to monitor renal function in people with NLUTD.
- Clinicians should consider using isotopic GFR when an accurate measurement is required (e.g., if imaging of the kidneys suggests that renal function might be compromised).
- Clinicians should offer lifelong US surveillance of the kidneys to people at high risk of renal complications (e.g., consider surveillance US scanning at annual or two-yearly intervals). Those at high risk include SB and those with adverse features on UDS, such as poor bladder compliance, DSD, or VUR.
- Clinicians should consider UDS as part of a surveillance regimen for people at high risk of urinary tract complications (e.g., people with SB, spinal cord injury, or anorectal abnormalities).
- Clinicians should not use renal scintigraphy for routine surveillance in people with NLUTD.
- Clinicians should not use cystoscopy for routine surveillance in people with NLUTD.
- Clinicians should undertake cystoscopy and appropriate upper tract imaging in adolescent and young adults who have had a bladder augmentation when the following are present:
  a. Clinically noted change in upper or lower urinary tract status

b. Gross hematuria
c. Recurrent symptomatic UTIs
d. Increasing incontinence
e. Pelvic pain
f. Had a renal transplant with the presence of BK/polyomavirus.

Currently, research is lacking on the most effective and economic surveillance methods for patients with NLUTD;[112] however, NICE, SBA, and EAU guidelines outlined the lifelong followup regimen to achieve surveillance of the bladder, upper tract, and renal condition.[29,40] Due to low muscle mass among pediatric patients with NLUTD, serum creatinine often overestimates renal function. Thus, it is recommended not to rely solely on serum creatinine for renal function surveillance or monitoring. Instead, a nuclear scan should be considered if an accurate renal function assessment is required.[40]

There is evidence that supports the routine use of US as surveillance among NLUTD for the detection of renal function conditions, such as hydronephrosis, while some available evidence also suggests that surveillance UDS is likely to modify patient treatment and often demonstrates findings that modify treatment in the presence of symptoms of progression or upper tract imaging changes.[29,40,79,113] No clear evidence is available to support routine cystoscopy surveillance in pediatric NLUTD, except for patients who had bladder augmentation that are at risk for malignancy development and usually present with changes in upper tract status, gross hematuria, recurrent UTI, worsening lower urinary tract symptoms, persistent pain, and/or are immunocompromised.[40,79,114]

■ RECOMMENDATION 18: TRANSITIONAL CARE *(STRONG RECOMMENDATION, LE III–IV)*

Transitional care should be offered to promote access to uninterrupted, developmentally appropriate SB condition management and preventative care throughout transition — around the ages 14–21 years old.

All pediatric patients with NLUTD will need lifelong urologic care; a transitional care process to advocate self-care/management can improve their long-term health outcome.[90,115,116] The guiding principle in managing adolescents and young adults with NLUTD involves maximizing their health and participating in emerging adult milestones throughout the transition process.[116] The SBA guideline and recent reviews recommend assessing the patient transition readiness annually to determine cognitive maturity and preparedness using an objective tool.[29,116,117] The transition process needs to involve a MDT (medical and surgical team, pediatric and adult urologist) to provide patient-centered, comprehensive transition care that includes: transition planning and care coordination beginning at least a few years prior to transition; self-management coaching; decision-making support; education and employment resources; and independent-living support.[118] During the transition planning, the care should be supported with a designated clinic or care coordinator, considering the patient's preferences and providing patient-centered care. In the age range of 6–11 years, neurocognitive assessments can be considered to identify any support needs, and chronic condition management should be evaluated. Specifically, around age of 14–17 years old, the transition plan should encompass medical history, self-management skills, financial planning, education, employment resources, goal-setting, decision-making supports, and should be adjusted to promote self-management and independence. At age 18 and above, individuals should establish care with adult providers while continuing to be counselled on long-term financial and supportive living plans. Discussions of sexuality and fertility should also be part of transition counselling in an older patient.[117,119]

FUTURE CONSIDERATIONS

Beta-3 agonist

ß3-adrenergic receptor agonists (ß3 agonists) have been used to treat OAB and NDO in adults and children.[25,120] The U.S. Food and Drug Administration has recently approved their use in children with NDO.[121] A recent meta-analysis by Kim et al indicated that ß3 agonists could be considered an effective and safe alternative or adjunctive therapy for pediatric NDO or OAB, improving both objective urodynamic parameters and subjective patient-reported outcomes.[122] ß3 agonists appear to be a promising, effective, and safe alternative/adjunctive therapy in managing pediatric NDO or OAB. They may also be an alternative agent and effective in patients with neurogenic bladders.

Alpha-adrenergic antagonists

According to the NICE guideline, insufficient evidence supports using alpha-blockers in pediatric patients with NLUTD.[40,123,124] Nonetheless, some prior studies have indicated that alfuzosin and tamsulosin could potentially aid bladder emptying in children with neurogenic bladder, resulting in reduced bladder pressure and a safer environment for the kidneys;[25,125,126] however, there is no clear evidence for the use of alpha-blockers as a treatment in NLUTD children with bladder emptying problems caused by neurological disease. Some may

consider its use in select cases to facilitate bladder-emptying causing lower pressure in the bladder.

Neurostimulation

Neurostimulation has been reported to improve pediatric OAB and nocturnal enuresis.[127,128] While there are trials and reports on the use of neuromodulator therapy in neurogenic bladder patients, to date, insufficient evidence to support the use of electrical stimulation of the bladder, sacral nerve stimulation, and transcutaneous neuromodulation for pediatric NLUTD.[79,129] These modalities remain experimental in children with neurogenic bladder dysfunction and, therefore, cannot be recommended outside the confines of clinical trials.

Intrasphincteric botulinum toxin injection

Some studies have indicated that administering BTX-A through injection into the urethral sphincter can successfully reduce urethral resistance in patients with DSD or underactive bladder;[79,130,131] however, the available evidence is inadequate to endorse its routine usage for reducing bladder outlet resistance. It may be considered as an option for certain patients who cannot or choose not to undertake periodic CIC.[79] Nevertheless, cautioning patients about the potential risk for urinary incontinence is necessary.

DISCUSSION

The impact of the NLUTD on children's health outcomes can be significant, leading to frequent UTIs, long-term kidney damage, and decreased quality of life. Pediatric patients with NLUTD significantly burden the healthcare system, with high direct and indirect costs, including lost productivity and decreased workforce participation. Guidelines aim to optimize care by implementing evidence-based practices to improve subpopulation health outcomes, reduce the risk of complications, and increase quality of life. The development of this clinical practice guideline for pediatric patients with NLUTD was tailored to the unique features of the Canadian healthcare system and accounted for variations in resources across different institutions.

Limitations

Despite its strengths, the development of this guideline has some limitations that must be acknowledged.

First, the guideline development process relied heavily on existing evidence, which may have been limited in quantity or quality, and there may be gaps in the available evidence base. As a result, the recommendations made in the guideline may not be applicable to all patients or may require modification depending on individual patient characteristics or circumstances. For instance, it was difficult to make recommendations on patients who have undergone fetal surgery for spinal dysraphism, as the literature is scant and conflicting; moreover, none of the existing guidelines provide concrete recommendations on the same.[20]

Second, although the guideline development process involved stakeholder input and accounted for variations in resources across different institutions, it is possible that some stakeholders may not have been adequately represented or their perspectives may have been overlooked. This could potentially result in recommendations that are not feasible or acceptable for some healthcare providers or patients.

Third, the guideline was developed specifically for the Canadian healthcare system and may not be directly applicable to other healthcare systems or countries. The recommendations made in the guideline may need to be adapted or modified to account for differences in available resources, healthcare infrastructure, or patient populations.

Finally, due to the rapidly evolving nature of the field of NLUTD management, new evidence may emerge that could impact the recommendations made in the guideline. As such, the guideline will be reviewed and updated in 3–5 years to ensure that it reflects the latest evidence and best practices.

CONCLUSIONS

The development of guidelines for pediatric patients with NLUTD is an essential step in improving the management and outcomes of this condition. Although the guidelines represent a contemporary approach to the appropriate management of pediatric NLUTD, further well-designed clinical trials are necessary to provide high-quality evidence and refine the recommendations, ensuring that they remain relevant and effective over time. Furthermore, the guidelines' successful implementation will require careful consideration of local concerns, stakeholder perspectives, patient preferences, and individual clinical circumstances. Ultimately, the successful implementation of the guidelines will reduce the burden on the healthcare system, improve the quality of life of affected children, and promote the standardization of the management of pediatric patients with NLUTD.

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