# VCUG Research Timeline

*Compiled by the **Unsilenced Movement** Research Team*

## 1989

### Reliability of Voiding Cystourethrography to Detect Reflux (Quebec, CA)

The purpose of this study was to establish the reliability of VCUG by repeating the VCUG and comparing the results of a consecutive second and/or third cyclic filling and voiding to the first.

- “Retrograde voiding cystourethrography (VCUG) with contrast medium came into widespread use around 1958, when fluoroscopes with image intensification and cine recording became generally available.”
- “22 out of 177 patients had a discrepancy in the results between two cycles.”
- “By no means do we advocate **multiple fillings** in all children.”
- “To select patients who might benefit from cyclic voidings, we suggest that in children with urinary tract infection a sonogram be obtained **before VCUG**.”

## 1990

### The Goodman Study

## 1994

### Children’s memory for a salient medical procedure: implications for testimony (United States)

- “Children’s memory for features of a VCUG experience were examined because **this invasive procedure is similar in many respects to incidents of sexual abuse**.”
- “The children remembered 88% of the component features of the VCUG experience at the initial assessment and 83% after 6 weeks. Behavioral and salivary cortisol measures indicated that the **children were distressed during the procedure**.”

- “Although **the VCUG shares many features with instances of sexual abuse**, there are differences that may affect generalization and interpretation. Unlike many cases of sexual abuse, for this sample the VCUG did not occur repeatedly overtime. Although this ensures that previous knowledge is unlikely to inflate recall performance, it also prevents the applicability of the present findings to events that occur repeatedly over long periods of time. Additionally, the assessment of recall occurs immediately after the procedure, before time has elapsed during which, forgetting, and or suggestion may occur. To address these differences, children are now being recruited who had multiple experiences with the VCUG.”

## 1997

### Remembering early experiences during childhood (United States)

- **Another instance of VCUGs being used to test the recall of traumatic memories in children.**
- “Several recent studies have explored **children’s memories of painful and even distressing medical procedures, such as… the fluoroscopic VCUG**. These procedures, although by no means perfect analogues for the kinds of events of interest in the debate concerning memory for traumatic events, include a number of important features that may enhance their ecological validity. **A number of aspects of the VCUG procedure, in particular, make it a potentially useful analogue event**.”
- “There is evidence that children remember the VCUG better than a more routine physical examination.”

### The medical management of intersexed children: an analogue for childhood sexual abuse (United States)

- “Medical procedures have often been used as analogues for childhood sexual abuse (CSA) and have been seen as opportunities to observe children’s memories of these experiences in a naturalistic context. **Medical traumas share many of the critical elements of childhood abuse, such as fear, pain, punishment, and loss of control, and often result in similar psychological sequelae**.”

- “The study which has come closest to identifying the factors likely to be involved in children’s recall of CSA is a study by **Goodman (1990)** involving children who experienced a VCUG test to identify bladder dysfunction. Goodman’s study was unique in its inclusion of direct, painful, and embarrassing genital contact, involving the child’s being genitally penetrated and voiding in the presence of the medical staff. Goodman found that several factors led to greater forgetting of the event: embarrassment, lack of discussion of the procedure with parents, and PTSD symptoms. These are precisely the dynamics likely to operate in a familial abuse situation.”
- “Children who had experienced more than one VCUG were more likely to have expressed **fear and embarrassment about the most recent test** and to have **cried about it since it occurred**. **A few even denied that they had had the VCUG**.”

### Follow-up study of urinary tract infection associated with vesicoureteral reflux (South Korea)

- “**Rates of disappearance of VUR in medical and surgical management were 66% and 97%, respectively**. The spontaneous cure rate of VUR seemed to be higher in the cases with a milder grade of reflux and before 5 years of age.”

### Management of anxious and painful manifestations in pediatric uroradiology (United States)

- “Pediatric radiologists should evaluate pain and stress in their patients as they can be **easily and safely limited**.”

## 1998

### Test or trauma? The voiding cystourethrogram experience of young children (United States)

- “Healthcare professionals often perceive invasive procedures such as surgery and needle biopsies as **more painful and threatening to the child** than ‘tests’ such as

VCUGs. However, clinical experience indicates that **the VCUG is often perceived by children as more highly distressing** than other procedures."

## 1999

### Emotion and memory: children's long-term remembering, forgetting, and suggestibility (United States)

- "We examined children's long-term memory for a documented medical procedure, VCUG, that involves **painful and stressful genital contact**."
- "In the present study, we examined children's long-term memory for VCUG, a test that **many children find frightening, distressing, and also embarrassing**."

### Children's recall of medical experiences: the impact of stress (New Zealand)

- "Ratings of stress were significantly higher for children who underwent the VCUG than those who underwent the pediatric assessment."
- "Several recent studies have investigated children's memory for VCUG which involves an X-ray of the child's kidneys. This procedure has some of the **features of an abusive experience** in that it is likely to involve discomfort and, in many cases, stress for the child, and **also involves genital touch**."

### Evaluation of timing of voiding cystourethrogram after urinary tract infection (South Korea)

- "We analyzed patients' records to evaluate whether the timing of VCUG after UTI influenced the prevalence or severity of VUR."
- *This study reviewed 213 children diagnosed with UTI between March 1997 and December 2000. The children were divided into two groups: 1.) scheduled VCUG within 1 week of UTI and 2.) scheduled VCUG after 1 week of UTI.*
- "Reflux was present in 19% of patients studied within 1 week after UTI and 18% of those studied after 1 week. **The difference was not statistically significant**."

### Reduction in voiding cystourethrographies after the introduction of contrast enhanced sonographic reflux diagnosis (Germany)

- “Voiding urosonography (VUS) using the intravesical application of an US contrast medium (Levovist) has been shown to have very high sensitivity and specificity in the diagnosis of vesicoureteral reflux (VUR) compared to voiding cystourethrography (VCUG).”
- “**The number of VCUGs was significantly reduced** as a result of the implementation of VUS as part of the routine diagnostic imaging modality for VUR. Consequently, **the number of children that would have been exposed to ionizing radiation was reduced by over half**.”

## 2002

### Predicting children’s response to an invasive medical investigation: the influence of effortful control and parent behavior (United States)

- “Children manifested relatively **high rates of distress** and **low rates of coping**. Their coping attempts were not associated with reduced rates of distress.”

## 2004

### Detecting deception in children: event familiarity affects criterion-based content analysis ratings (United States)

- “**The VCUG procedure was used as the target event in this study because it is similar in many ways to child sexual abuse**, the real world behavior that we hope to generalize these results to. However, whereas we knew exactly what had occurred in the medical procedure that each child in this study participated in (the procedures were videotaped), practitioners rarely know what transpired in alleged incidents of sex abuse.”

## 2005

### Hypnosis reduces distress and duration of an invasive medical procedure for children (United States)

- “VCUG is a **commonly performed** radiologic procedure in children that can be **both painful and frightening**. Given the distress that some children experience during the VCUG and the need for children to be alert and cooperative during the procedure, finding **a psychological intervention** that helps children to manage **anxiety, distress, and pain** is clearly desirable.”
- “Results indicate significant benefits for the hypnosis group compared with the routine care group in the following four areas: (1) parents of children in the hypnosis group compared with those in the routine care group reported that the procedure was ***significantly less traumatic*** for their children compared with their previous VCUG procedure, (2) observational ratings of typical distress levels during the procedure were ***significantly lower*** for children in the hypnosis condition compared with those in the routine care condition, (3) ***medical staff reported a significant difference*** between groups in the **overall difficulty of conducting the procedure**, with less difficulty reported for the hypnosis group, and (4) total procedural time was ***significantly shorter*** by almost 14 minutes for the hypnosis group.”

### Systematic review of age-related errors in children’s memories for Voiding Cystourethrogram (VCUG) (Europe)

- “This finding is consistent with general research on children’s ability to recount past experiences and **supports** the view that **even young children may be able to provide accurate and forensically relevant information regarding unpleasant personal events** during free recall.”

## 2006

### 2006 AUA Meeting Discussion (Q&A)

*It gives me great pleasure to introduce two experts whose specialties are outside the field of radiology.* ***Dr. David Diamond*** *specializes in pediatric urology and robotic surgery. He is an Associate Professor of Urology at the Harvard Medical School. The second honored*

*guest is **Dr. John T. Boyle**, who is Professor and Chief of Pediatric Gastroenterology at the University of Alabama at Birmingham.*

- Presentation depicts VCUG as "**traumatic**," "**distressful**," "**dehumanizing**," and "**like sexual abuse**."
- "Once [VUR] is diagnosed, it has been the tradition that most pediatric urologists reassess patients annually. The issues involved with regard to follow up of the study of reflux are **radiation exposure**, **repeated instrumentation of the child**, which is a major issue for many families, **antibiotic exposure**, [and] **cost**."

**Q:** "We as physicians interested in the urinary tract are severely criticized by many people for saying that we have really not asked the right questions...I want to know the outcome. I think we do too many cystograms and I want to know how the outcome of what you described versus not doing the cystogram [...] I think the real issue is that within 5 years, we will not be doing cystograms [or] even ultrasonic cystograms, **because I think catheterizing is invasive unless there is a real reason to do it**. What is your feeling about this?"

**Dr. Diamond:** "This is an opinion that has been in the literature. The sense that I have [...] it is exceedingly uncommon nowadays to see a patient present in renal failure due to [VUR]. My belief is that this is because we are probably doing something right. What does it cost? Is it worth it? Those are questions that I cannot answer...**Undoubtedly, more studies are being done than absolutely need to be done**.

"Our perspective is different from the radiologist's perspective in terms of what your threshold should be for doing this study. It is largely because we as the tertiary consultants do not want to miss pathology...I think our feeling is that it is still important to err on being aggressive when the clinical indications are there, but at the end of the day, there are going to be many negative studies in children who were studied who would perhaps **do just as well without it**."

**Q:** "The radiation-producing test that is not done reduces radiation 100%. I think that it is our job **when we think a test is ordered inappropriately**, and we may well be wrong, to

call the physician up and talk to him about it. How do you as referring physicians feel about that?”

**Dr. Diamond:** “I have no problems. The problem is trying to get a hold of the physicians.

“Whenever I get a call from the radiologist, **I will pull out the chart to see why I ordered that test**. Sometimes there will be a little piece that was not communicated to the radiologist and he will say, ‘Fine, that makes sense.’ Sometimes he will say, ‘**David, an ultrasound will do the job. What do you say we just send the kid over to ultrasound**?’

“I always respect that call because it shows that they are doing a very thorough job. My perspective is that the practice of pediatric urology has changed. **It has become a much busier enterprise**. We are asked to see more patients in less time and sometimes these details slip through the cracks.”

**Q:** “In ordering a procedure, do you feel that it is your obligation to discuss with the parents what the procedure involves in terms of **catheterization**, **potential pain**, **radiation exposure**, etc., or do you then relegate that responsibility to the radiology personnel? Oftentimes, parents arrive and say, ‘**What, a catheter?!**’ or ‘**What radiation?!**’ and **there has been absolutely no preparation for these families**. What do you think should be the clinician’s responsibility for preparing the family for both procedures that can involve pain?”

**Dr. Diamond:** “**I have never as a routine gone into the radiologic details** because there are limited times in the day for me to see the patients that I need to see…Given the number of studies that we order throughout the day, there is not time to go over real issues with the parents. **I think it is proper that someone do it, but it is not workable for us to do it**.”

**Dr. Boyle:** “Our nurses do tell the parents that their child may be restrained.”

### Fluoroscopy-controlled voiding cystourethrography in infants and children: are the radiation risks trivial? (Europe)

- "Mean radiation risks for **genetic anomalies and carcinogenesis** following VCUG during childhood were estimated to be **up to 15 per million and 125 per million**, respectively."
- "**Radiation risks** associated with pediatric patients undergoing VCUG **should not be disregarded** if such a procedure is to be justified adequately."

### Brief report: optimizing children's memory and management of an invasive medical procedure: the influence of procedural narration and distraction (United States)

- "Relative to the PI condition [**limited procedural information**], children in the CI + D condition [**complete procedural information**] recalled more information, appraised the VCUG as less painful, and were less distressed."
- "An inexpensive, theoretically driven intervention can enhance children's memory and **reduce distress** during an invasive procedure."

## 2007

### Study of post procedural complications associated with voiding cystourethrography (Korea)

*269 patients who underwent VCUGs between October 2005 and September 2006 were analyzed. Chart review and telephone interview with parents was completed.*

- "The procedure is relatively simple, **but it involves discomfort and some complications**. We studied **post procedural symptoms** and complications in children who underwent VCUG."
- "Our study demonstrated that **32.7% of patients showed complications**, including [urinary] bladder rupture and urinary tract infection [UTI] after VCUG. We also found that prophylactic antibiotic use **did not prevent urinary tract infection** nor **decrease the rate of complications** associated with VCUG."

- "Therefore, we suggest that **the procedure must be done carefully** and we should closely observe the children who undergo VCUG for development of possible complications."

### Infantile Bladder Rupture During Voiding Cystourethrogram (VCUG) (Brazil)

- "We report two cases of infantile bladder rupture during voiding cystourethrography (VCUG). **This report reinforces the criteria for <u>proper VCUG imaging procedure</u>**."

### Voiding urosonography as first step in the diagnosis of vesicoureteral reflux in children: a clinical experience (United States)

- "Our experience suggests that we can use ceVUS [contrast-enhanced voiding urosonography] as **the first step in the diagnosis of VUR in children**, boys and girls, with a **<u>significant reduction in radiation exposure</u>**."

## 2008

### Comparing stress levels in children aged 2-8 years and in their accompanying parents during first-time versus repeated voiding cystourethrograms (Germany)

- "Invasive procedures such as voiding cystourethrograms (VCUGs) **cause distress in both children and their accompanying parents**."
- "The stress levels of children undergoing a repeated VCUG **<u>do not differ</u>** from those of children undergoing a VCUG for the first time, but parental stress levels were significantly lower during repeated VCUGs."
- "In both VCUG groups, there was **significant positive correlation** between parental distress-promoting behavior and child distress, and between parental stress levels and child distress. **<u>Parental coping-promoting behavior showed no significant correlation with child distress or parental stress levels in either VCUG group</u>**. Parental stress levels and parental distress-promoting behavior correlated positively only for repeated VCUGs. Neither parental coping- nor distress-promoting behavior differed between first-time versus repeated VCUG groups."

- *Conclusion*: "**Repeated VCUGs and first-time VCUGs are both highly distressing procedures for children**. Even though parental stress levels are lower during repeated VCUGs, spontaneous parental behavior proves to be **ineffective or even counterproductive in reducing the child's distress**."

### Urinary tract infection following voiding cystourethrography (South Korea)

*Medical records of 284 patients who underwent VCUGs in 2007 were reviewed.*

- "It is well known that VCUG can cause UTI (**post-VCUG UTI**)."
- "7 of 284 children (2.5%) developed UTI after they underwent VCUG. High-grade VUR was the only statistically significant risk factor for post-VCUG UTI, while sex, age, and other anomalies of the urinary system were not significant."
- "**Antibiotic use did not prevent post-VCUG UTI in this study**."

### Chronological age for the spontaneous resolution of vesicoureteral reflux (Spain)

- "We analyze the chronological age of the patient at which VUR resolves spontaneously, so that we know when we should have a more precise control with VCUG, **avoiding a traumatic test and irradiation**, but also avoiding to give prophylactic antibiotics without real need."

## 2009

### Effective dose estimation for pediatric voiding cystourethrography using an anthropomorphic phantom set and metal oxide semiconductor field-effect transistor (MOSFET) technology (United States)

- "The risks associated with radiation exposure are **higher in children than in adults**."
- "Effective doses ranged from 0.10 to 0.55 mSv, increased with age, and **were higher in girls**."
- "Effective doses for VCUG examinations performed in children <or= 10 years of age are low, **but are not negligible**."

## 2010

### Development of a patient educational intervention to improve satisfaction of parents whose children are having a VCUG (United States)

- "Any individual undergoing an invasive procedure in a hospital can attest to the hospital's **inherent disruption on physical and emotional dimensions of his or her well-being**. The conditions under which the procedure is performed may be **frighteningly foreign and threatening** to a child's and his or her parents' integrity. Catheter insertion causes mechanical discomfort along with sensations of a full bladder. **Emotional distress can occur when a child's private areas are uncovered, prepped, and the catheter inserted**. In summary, a pediatric voiding cystourethrogram (VCUG) procedure **can and does cause physical and emotional distress to children and their families.**"

### Assessment of parental satisfaction in children undergoing VCUG without sedation (United States)

- "**Children in the process of toilet training had the most difficulty with the procedure**, correlating with lower levels of parental satisfaction."
- "More than 750 VCUGs were performed in the authors' diagnostic radiology unit annually, and **this number was projected to continue increasing** (Tacoma General Hospital, 2008)."
- **"Because patients came from more than 300 referral sources, education was inconsistent and sometimes nonexistent."**
- "The educational DVD produced by the project improved the satisfaction and confidence of a parent whose child was scheduled for a VCUG…. The results showed an increase in parent satisfaction and children's ability to cope with the procedure because of the educational information plus the increase in confidence of their ability to care for their child."

## Summary of the AUA Guideline on Management of Primary Vesicoureteral Reflux in Children (United States)

*These are the official guidelines specified by the American Urology Association for treating VUR, which all urologists* ***should*** *be following.*

- "Because VUR and UTI may affect renal structure and function, performing **renal ultrasound** to assess the upper urinary tract is recommended."
- "**DMSA renal imaging** can be obtained to assess the status of the kidneys for scarring and function."
  - *Note: Nowhere in the guidelines does it say that children should receive a VCUG upon initial presentation.*
- "**Involvement of the family in clinical decision making related to VUR is critical**, and **must** include **balanced and objective education** to permit informed decisions regarding imaging and therapy, particularly when one approach may have no demonstrable benefit or advantage over another."
- "If clinical evidence of BBD [bladder and bowel dysfunction] is present, treatment of BBD is indicated, **preferably before any surgical intervention for VUR** is undertaken."
  - *Note: Again, there is no mention of VCUG. Although a VCUG might be clinical evidence of BBD, renal ultrasounds and urinalysis (both previously discussed in the guidelines) are also examples of clinical evidence that can very effectively indicate BBD.*
- "For high-grade VUR, follow-up as soon as 12 months may be too early, but for low grade it may be appropriate. **Compliance with follow-up** as well as **parental anxiety** are factors in this determination. **There is little rationale for repeating a VCUG within 12 months of the previous study**, and an outer limit of 24 months appears to be a reasonable time frame to avoid loss of follow-up or prolonged use of unnecessary CAP if the VUR has resolved."
  - *It is mentioned that compliance with follow-up and parental anxiety can be issues, but they don't go as far as to offer a rationale for this assertion.*
- "Voiding cystography (radionuclide cystogram or low-dose fluoroscopy, when available) is recommended every 12 to 24 months with longer intervals between

follow-up studies in patients in whom evidence supports lower rates of spontaneous resolution (i.e. those with higher grades of VUR [**grades III–V**], BBD and older age). This is to limit the overall number of imaging studies performed."

- "For children with grade I–II VUR and more likely spontaneous resolution, follow-up imaging to identify VUR is considered an option. While follow-up VCUG is appropriate, **there are no data to support its necessity.** This is particularly true if CAP is not being used, as **the VCUG findings are not likely to alter management**."
    - *Note: If there are no data to support the necessity of VCUG in follow-up, why do many physicians incessantly push parents to conduct regular follow-up VCUGs? Perhaps this happens so urologists can confirm the resolution of VUR and thus boast higher success rates.*

## Parents compliance to perform the voiding cystourethrogram test after urinary tract infection (Israel)

*The stated purpose of this study was to examine parents' compliance to perform VCUG test after hospitalization due to UTI and factors affecting their decision.*

- "Overall, 52% of the children didn't perform the VCUG because of concern about **exposure to radiation** (55%), **fear and distress from pain during the test** (43%), **fear of irreversible damage to the urinary tract** (40%), **lack of relevant information** (35%), and **the primary pediatrician's recommendation** to postpone the test."
- "The remaining 48% conducted the test because of **the hospital doctor's recommendation** (94%), **primary pediatrician recommendation** (94%), and because of **the desire to terminate prophylactic treatment** (64%)."
- "There is **a significant correlation** between the doctors' recommendation and the extent and clarity of their explanation to the parents' understanding of the importance of the test, to the parents' satisfaction from the explanation and to the compliance to perform the test."
- "Conclusion: **There is a need to improve the doctors' explanation regarding the performance of VCUG test post UTI**."

### Difference of anxiety of parents: before & after the VCUG (South Korea)

*68 parents whose children underwent VCUG were put into 2 groups. Group 1 received a detailed explanation using pictures. Group 2 only received an oral explanation.*

- "As it is a **potentially distressing and invasive test**, most of the parents are so concerned about the child's stress."
- "It showed that a doctor's explanation on the procedure in advance may raise the perception of pain and the possibility of refusal by parents. Anxiety after VCUG were significantly decreased in Group 1, while the confusion and pain were increased in Group 2. Therefore, we suggest that **prior and sufficient explanation about invasive procedures like VCUG** can be helpful in ameliorating the anxiety of the parents."

## 2011

### Is parental anxiety and coping associated with girls' distress during a VCUG? Preliminary findings (United States)

*Purpose: "We investigated the relationship between parental anxiety/coping strategies and girls' distress during VCUGs."*

- "Trends indicated that parents who reported increased anxiety rated their children as **experiencing increased distress**."
- "Contrary to expectations, parent anxiety scores on the STAI completed prior to the VCUG were not significantly related to parent self-rated or staff-rated parent anxiety recorded after the VCUG (r Z 0.09 and 0.02), or to ratings of children's procedural distress (r Z 0.11, 0.01 and 0.11 respectively). However, parents with lower STAI scores did report using more emotion-focused and problem-focused coping strategies to manage their children's emotional distress caused by common stressors (r Z 0.37 and 0.40 respectively, $p < 0.05$)."
- "The analyses showed that the correlations between parent and medical staff ratings, and child self-report of procedural distress, **were all statistically significant**. There was a high correlation between the parent and staff ratings of the

child's distress and **a lesser correlation between the children's self-report and the parent/staff perceptions**."

- "A strong trend was found in the correlations that showed that **parents who reported experiencing greater distress** during the VCUG also reported that **their children experienced greater procedural distress** (r Z 0.27, p < 0.07). A similar trend was also found between medical staff ratings of parental anxiety and staff-rated child distress (r Z 0.28, p < 0.07)."
- "Analyses of the relationship between parent coping reactions to children's distress due to common stressors and children's distress ratings during the VCUG revealed that the children of parents who reported using more emotion-focused and problem-focused coping strategies to manage children's emotional distress were rated by medical staff as experiencing less procedural distress (r Z 0.30 and 0.33 respectively, p < 0.05)."
- "Also, increased parent use of emotion-focused and problem-focused coping was significantly related to the parents being rated by medical staff as less anxious during the procedure (r Z 0.40 and 0.31 respectively, p < 0.05) though **surprisingly the parents themselves did not report feeling less anxious** (r Z 0.6 and 0.17 respectively)."
- "Also, parents' emotion-focused and problem-focused coping **was not significantly related to children's self-rated procedural distress** (r Z 0.08 and 0.03 respectively)."
- "[S]ome children may feel very distressed but do not express that behavior overtly for the adults to observed, **hence the lack of high correlations between the child and adult-perceived distress scales**."
- "Surprising[ly] to us, **neither age nor number of prior studies was useful as a predictor of post-procedure reported distress**. This is, however, consistent with data reported by Volk Kernstock et al., who evaluated 31 children aged 2-8 years who had undergone first time and repeated studies."
- "Alternatively, **the experience of watching your child undergo a VCUG (or wondering about the results) may be so significant** that it affects even parents not prone to anxiety."

- “Further, although **the act of catheterization likely causes the most acute pain**, **voiding while supine <u>without</u> normal privacy** is also **often stressful to toilet-trained children**.”
- “Another potential benefit of teaching coping strategies is **<u>long term</u>**. Children and their parents **will likely experience many stressful, unpleasant situations**. The strategies they are taught to be able to cope during a VCUG **will likely be beneficial in other circumstances** in the future.”
- “The **failure to find significant relationships between parent coping and child self-rated distress** was unexpected…It may be that **the sense of relief that some children experience immediately after completing the VCUG** (which is when the child ratings were obtained) **is so great that it might actually cloud their recollection** of the distress they experienced during the procedure. To better address the question of perceived versus experienced distress, it would be useful in future work to **examine the relations between child self-rated distress and behavioral indicators of child distress**.”

## Sedation and the VCUG (United States)

- “A voiding cystourethrogram is **frequently a stressful procedure for pediatric patients, parents, and occasionally the radiology staff**. I believe most radiologists would agree with that statement **but if doubt exists, there is research that supports it.**”
- “I was taught during residency and fellowship that the patient needs to be conscious for voiding and that **the procedure is not painful**. I believed it. I took pride in my ability to calmly wait and offer reassurance to parents **that though their child was crying and screaming, the child was not really in pain** and that it would be over in a few minutes. **Sometimes, those minutes seemed like forever to everyone in the room**.”
- **<u>“I see fear and anxiety daily when performing VCUGs</u>**. In addition, the memory of previous painful experiences has effects on pain experience during subsequent procedures.”

- "I am offering sedation to more and more patients for VCUG and their parents seem grateful. This is because of increasing knowledge that **patient distress is real** and **can affect future medical procedures**."
- "Recent research in the area of pain medicine has revealed that **high-anxiety and low-pain procedures such as a VCUG cause true distress to patients** that can **last beyond the time of this procedure**."

## Effects of parental soothing behavior on stress levels of 2-8 year old children during voiding cystourethrograms by phase of procedure (Germany)

- "Using the example of a **voiding cystourethrogram (VCUG), a painful radiological procedure**, this study investigated whether parental soothing behavior… in one phase of the procedure influenced the child's distress in the following phase."
- "**Parental reassurance during the anticipatory phase significantly increased the child's distress of the following phase**, while parental "sh, sh" significantly reduced it. **Both parental behaviors showed no significant effect on the child's distress of the following phase when applied during the procedure itself**. Results underline the importance of differentiating between anticipatory and procedural phases of the VCUG."

## Children, Voiding Cystourethrograms, and Family Perceptions (United States)

- "The VCUG procedure may create distress in a child and the accompanying family members. A study by Zelikovsky indicated **that the procedure is painful, invasive, and frightening for children** and distressful for family members."
- "A VCUG test can lead to patient and family related to perceived pain, fear, and distress before, during, and after the procedure. Families that regard themselves with greater anxiety were more likely to perceive their child with more fear, distress, and pain. The most significant relationship was between high experienced anxiety and the family's perceptions of fear and pain in their children."
- "The study showed that most ***parents*** do not find the VCUG procedure as distressing as they had anticipated and the ***families'*** anxiety at the time of the procedure greatly influenced their perceptions of pain, fear, and distress perceived

in their child. The discovery that most of the ***families*** would consent to a repeat VCUG and would likely be present substantiates the findings of this study."

  - *Note: Like other studies, the child's perception of distress/pain during VCUG was **not** even considered prior to "concluding" these results of pain during VCUG. Again, the true patient experience is disregarded.*

### Population-based trend analysis of voiding cystourethrogram ordering practices in a single-payer healthcare system before and after the release of evaluation guidelines (United States)

- "While voiding cystourethrogram (VCUG) is a widely accepted test, **it is invasive and associated with radiation exposure**. Most cases of primary vesicoureteral reflux (VUR) are low-grade and **unlikely to be associated with acquired renal scarring**. To select patients at greatest risk, in 2011 the American Academy of Pediatrics (AAP) published guidelines for evaluation of children ages 2 - 24 months with urinary tract infections (UTIs)."
- "Trend analysis demonstrated that the total number of VCUGs ordered in the province has **decreased over a decade**, with a concurrent decrease in VUR diagnosis. On multivariate regression analysis, the decrease in VCUG ordering could not be explained by changes in population demographics or other baseline patient variables. Most VCUGs obtained per year were ordered by pediatricians or family physicians (mean 2,022+523.8), compared with urologists and nephrologists (mean 616+358.3). Interestingly, **while the rate of VCUG requests decreased, the annual number of surgeries performed for VUR (endoscopic or open) did not show a significant reduction over time**."
- "We present a large population-based analysis in a universal access to care system, reporting a decreasing trend in the number of cystograms and differences by primary care versus specialist providers. While it is reassuring to see practice patterns favorably impacted by guidelines, it is also encouraging to note that the number of surgeries has remained stable. This suggests that patients at risk continue to be detected and offered surgical correction. These data confirm previous institution-based assessments and affirm changes in VCUG ordering

independent of variables not relevant to the healthcare system, such as the insurance status."

## 2012

### VCUG and the recurring question of sedation: preparation and catheterization technique are key (United States)

- Estimated 50,000 children are diagnosed with VUR after UTI each year in the United States; thus "the number of children undergoing screening examinations (VCUGs), therefore, **is likely in the many hundreds of thousands**."
- "The vast majority of VCUG examinations are performed primarily on an outpatient basis, **unfortunately often with little or no preparation of the child or parent**. The VCUG examination can therefore be **perceived as a painful investigation associated with high levels of distress and anxiety** for the child, parents, and even the medical staff."
- "Unfortunately, many children have been **irreparably traumatized by previous catheterizations as well as other invasive medical procedures** and the mere thought of undergoing an unknown or repeat procedure is **unbearable**."
- "...any radiologist who performs VCUG examinations has on occasion walked into the fluoroscopy suite only to find a shocked, distraught, or even angry parent who **had no idea that their child was to undergo this type of examination**. The test is either canceled.... Or the examination proceeds in an uncomfortable environment, **more often than not resulting in a traumatic experience for the child and parent**."
- The article goes on to mention several ways that the VCUG can be improved including preparation of parent and child with thorough explanations of the examination, use of lidocaine before catheterization, distraction techniques, and sedation in select cases where necessary.
- The article then says, disrespectfully to former VCUG patients, "If the argument is that sedation is primarily needed to prevent the stress and anxiety associated with invasive medical procedures in children, then how can we justify not routinely sedating for immunizations, blood draws, nasoenteric tube placement, lumbar

punctures, etc. These procedures surely are equally as distressing to children." *(Note: These procedures are not equally as distressing; this is a baseless claim without any research to support it.)*

### Parent perspectives of the VCUG: A three-part prospective survey study (United States)

- "The VCUG is **an invasive procedure that is uncomfortable and distressing** for the pediatric patient."
- 32 girls and 13 boys, all underwent VCUGs.
- "Twelve parents (27%) reported having had no explanation about the VCUG by a healthcare provider. [15%] of non-white interviewees had received an explanation compared to 84.9% of white interviewees."
- "Of the 35 parents who completed the 2-week post VCUG study, 11 (31%) noticed changes in their child's behavior. **Eight of these parents were worried about those changes**."
- "We conclude that a significant number of parents are uninformed about the VCUG, which influences their expectations for the procedure."

### Urinary bladder rupture during voiding cystourethrography (Korea)

- "Bladder rupture is a rare complication of VCUG, and only a few cases were reported. Bladder rupture among healthy children during VCUG is an especially uncommon event."
- "Presented is a case of bladder rupture that occurred during a VCUG in a **healthy 9-month-old infant**, ***due to*** instilled action of dye by high pressure" (*emphasis added*).
- "Some reported complications of VCUG range from urinary discomfort, UTI to bacteremia, as well as bladder rupture."
- The 9-month-old had grade II VUR in the right ureter and grade III VUR in the left ureter. The VCUG went according to plan, but after the patient was tachypneic with a distended and tender abdomen. She was sent to the operating room for

exploration and urine, blood clots, and **contrast media had to be removed from the peritoneum**. Approximately **3-cm long bladder rupture** was found.

- "To perform a safe VCUG, **we should pay attention to some factors** such as bladder volume, the patient's underlying disease, the velocity of the contrast instilled, and catheter size."
- "The bladder volume is different among individuals, and the bladder dome which is the weakest part of bladder can easily be ruptured when excess volume is injected rapidly."
- "In this case, the main causes of bladder rupture are considered to be the use of the Foley catheter instead of a feeding tube, manual injection of contrast media, and the excess volume instilled more than expected volume."

## 2013

### Analysis of an intervention to reduce parental anxiety prior to VCUG (United States)

- "The VCUG is a common imaging test in pediatric urology that can be associated with anxiety in the child and parent."
- "Parental state anxiety was higher before the procedure than after the procedure. Younger parents had greater pre-procedure state anxiety. Contrary to our expectations, pre-procedure state anxiety did not differ between control and experimental groups. However, parents in the experimental group demonstrated less anxiety with some individual items in the questionnaire."
- "An educational brochure mailed to families prior to VCUG did not decrease pre-procedure parental state anxiety. However, the educational brochure can ensure accurate dissemination of information to help families prepare for this potentially distressing procedure."

### Efficacy of a cartoon and photograph montage storybook in preparing children for voiding cystourethrogram

- "Undergoing voiding cystourethrogram (VCUG) can be distressing for children."

- "The cartoon and photograph montage storybook format of preparing children for VCUG was effective in increasing their tolerance for the procedure. The storybook should be mailed out in advance because the **majority of families did not pursue information on preparing their children for VCUG**."

## 2014

### Subsequent cancer risk of children receiving post voiding cystourethrography; a nationwide population-based retrospective cohort study (Taiwan)

- 31,908 participants under 18 who underwent a VCUG between 1997 and 2008 and a non-VCUG group of participants.
- The **overall cancer risk of the VCUG cohort** is 1.92-fold higher than the non-VCUG cohort.
- The **genital cancer and urinary system cancer risks of the VCUG cohort** were 6.19-fold and 5.8-fold higher than the non-VCUG cohort.
- *Conclusion*: "**Pediatric VCUG is associated with increased subsequent cancer risk,** especially in the genitourinary system."

### Oral Midazolam for voiding dysfunction in children undergoing VCUG: a controlled randomized clinical trial (Iran)

- 84 children were split into 2 groups (control and midazolam group).
- "The use of midazolam 0.5 mg/kg reduced children's stress and increased their cooperation during the procedure."
- "Although the side effects of VCUG are not common, **they are important**. These complications that can occur in both sexes include UTI, hematuria, cystitis and urinary dysfunction following a catheterization, phobia of urination, nocturia, and stopping urination."
- **"In the literature, psychological trauma resulting from VCUG was considered the same as from a violent rape, especially in girls."**

### Children’s memory in “scientific case studies” of child sexual abuse: a review (United States)

- “One **painful and potentially embarrassing procedure involving genital penetration is VCUG**. Results from studies examining children’s memory for VCUG reveal that, although young children can accurately report details of the procedure, more distressed children tend to report fewer details in free recall.”

## 2016

### The voiding cystourethrogram: minimizing patient and parent distress in an invasive radiologic procedure (United States)

- “The VCUG can be considered **one of the more distressing invasive procedures that children may experience** in the outpatient setting.”
- “Due to the invasiveness of catheterization and the command to void in public, VCUGs can involve high levels of psychological and physical distress for the child”
- “While the VCUG is considered the standard of investigation for diagnosing reflux in children, **less attention has been paid to the stressful effect of this potentially painful procedure**. Many aspects of the VCUG can be experienced as **distressing to both the child and their parents**. The anticipated anxiety of the procedure, the **examination of the child’s genital area by a stranger**, the insertion of a catheter into the child’s body, the **embarrassment of lying uncovered** on an exam table, and **the command to urinate in front of those present** in the exam room are all aspects of the VCUG that create the possibility for distress in the child.”
- “...voiding on the exam table may be experienced as particularly traumatic for younger children who have recently been toilet-trained.”
- “The VCUG **renders the child dependent** on those in the room, as they may be **separated from their parents** and **their legs may be forced apart and held down**.”
- **“The overall perception in healthcare is that the VCUG is a short and painless procedure, despite evidence that it is distressing to children.** In one study, parents tended to rate their child’s distress and their own distress as higher than the staff ratings, indicating that parents see this procedure as having a significant

impact on their child's level of distress. In another study, 27% of the children were found to have high scores indicating severe distress on a scale measuring their reaction to the procedure."

- "In invasive procedures, children who experience high levels of pain and behavioral distress tend to form negatively exaggerated memories that later predict children's pain and distress in future procedures. Additionally, children with negatively exaggerated pain memories are at risk for **developing medical phobias and avoidance of medical care as adults**."
- "Children retain memories of their VCUG experience and that those who had a distressing experience **can replay precisely the aspects of the procedure they found most traumatic**, thereby **affecting their emotional well-being in the long-term**."
- "The **long-term effects of the VCUG** are perhaps **most evident in the behaviors that children display in the weeks and months after the procedure**. Gebarski (2013) found that **behavioral changes**, clinging to parents and disturbances in toilet-training and sleep routines **were common** after a child experienced a VCUG. In another study, 1/3 of parents reported behavior changes in their child after the procedure, including **difficulty passing urine, a fear of medical personnel, and general irritability**.... From this evidence, it is possible to conclude that **the level of distress experienced during a VCUG can significantly influence children's behavior in the long-term."**
- "**Restriction of a child's mobility is a common feature** of pediatric care, especially during invasive procedures. Restriction can be defined as a practice that occurs when risk-benefit favors immobilization for the purpose of delivering safe and timely care to the child. Among nursing and other clinical staff, **restriction is so commonplace during procedures that often staff do not realize that they are doing it."**
- "Research shows that **restriction can impact children in negative ways in the long-term.** Restriction has been linked to speech delays, high rates of recall of the distressing procedure, and raised cortisol levels after a procedure is finished..... Overall, causing distress to a child, even with potential clinical gain, is something that should be avoided by all healthcare professionals."

## Distress experienced during pediatric VCUGs – a granular, prospective assessment using the brief behavioral distress scale (United States)

- "In spite of **decades of experience with the procedure**, controversy persists as to the overall distress experienced by children and the **routine need for sedation** in children undergoing VCUGs."
- "At the root of these issues are some of the limitations of previous studies as **most incorporate inherently subjective parental questionnaires to determine distress levels rather than using an objective, unbiased observer."**
- "We find that despite there being **significantly increased distress during the catheter insertion and full bladder phases**, the distress levels during VCUGs are markedly less than in previous reports. Even the most distressful stage, catheterization, was less stressful than previously reported with levels closer to that of minor distress evinced by comfort-seeking behavior from a parent rather than more significant distress resulting in screaming."

## Variation in the level of detail in pediatric voiding cystourethrogram reports (United States)

*602 VCUGs were performed at 90 different institutions.*

- "VCUG provides a wealth of data on urinary tract function and anatomy, **but few standards exist for reporting VCUG findings**."
- "We analyzed original VCUG reports from children enrolled in the randomized intervention for children with vesicoureteral reflux trial (RIVUR). A 23-item checklist was created and used to evaluate reporting of technical, anatomic, and functional information."
- "76% were read by a pediatric radiologist, and 49% were performed at a FSPH (free-standing pediatric hospital). On average, less than half of the 23 items in our standardized assessment tool were included in VCUG reports. The **completeness of reports varied** by facility type: 51% complete at FSPH, 50% at PHWH (pediatric "hospital within a hospital"), 36% at NPH (non-pediatric hospital), and 43% at ORF (outpatient radiology facility)."

- "**There is a substantial underreporting of findings in VCUG reports** when assessing a widely represented sample of routine, community-generated reports using an idealized standard. Although VUR was often reported, other crucial anatomic and functional findings of the VCUG were **consistently underreported** across all facility types."

## Establishing a Standard Protocol for the Voiding Cystourethrography

- "VCUGs are ordered by **many** specialists and primary care providers, including pediatricians, family practitioners, nephrologists, hospitalists, emergency department physicians, and urologists. ***Current protocols for performing and interpreting a VCUG are based on the International Reflux Study in 1985***. However, more recent information provided by many national and international institutions suggests a need to refine those recommendations."
- "In addition, a recent survey directed to the chairpersons of pediatric radiology of 65 children's hospitals throughout the United States and Canada ***showed that VCUG protocols vary substantially***. Recent guidelines from the American Academy of Pediatrics (AAP) recommend a VCUG for children between 2 and 24 months of age with urinary tract infections **but did NOT specify how this test should be performed**. To improve patient safety and to standardize the data obtained when a VCUG is performed, the AAP Section on Radiology and the AAP Section on Urology initiated the current VCUG protocol to create a consensus on how to perform this test."

## The role of voiding cystourethrography in the investigation of children with urinary tract infections

- "Voiding cystourethrography (VCUG) is the radiographic test of choice to diagnose VUR. Due to its **invasive nature and questionable benefit** in many cases, the American Academy of Pediatrics (AAP) no longer recommends VCUG routinely after an initial febrile UTI."
- "Of children presenting with a febrile UTI, 25-40% are found to have vesicoureteral reflux (VUR)."

- "…many children underwent invasive surgical procedures to correct VUR. We now know that **many cases of VUR are low-grade** and have **a high rate of spontaneous resolution."**

## 2017

### Contemporary Practice Patterns of Voiding Cystourethrography Use at a Large Tertiary Care Center in a Single Payer Health Care System

- "Voiding cystourethrogram involves **radiation exposure** and is **invasive**. Several guidelines, including the 2011 AAP (American Academy of Pediatrics) guidelines, no longer recommend routine voiding cystourethrogram after the initial urinary tract infection in children. The recent trend in voiding cystourethrogram use remains largely unknown. We examined practice patterns of voiding cystourethrogram use and explored the impact of these guidelines in a single payer system in the past 8 years."

### Controversies regarding management of vesicoureteral reflux (India)

- "[Vesicoureteral] reflux (VUR) is diagnosed in 30-40% of children imaged after first febrile UTI."
- "The 'top-down' approach involving ultrasound and dimercaptosuccinic acid scan (DMSA) first after an appropriate interval following UTI, can help in **avoiding voiding cystourethrogram (VCUG), an invasive test with higher radiation exposure**."

### Use of sedative drugs at reducing the side effects of voiding cystourethrography in children

- "Although technological progress goes toward less invasive approaches, some of the current methods are still invasive and annoying."
- "**VCUG is a distressful procedure that gives serious anxiety and pain in a large proportion of children** and **fear for parents**; therefore, **using effective sedative drugs with the least side effects is necessary**."

## Local Trends in the Evaluation and Treatment of Urinary Tract Infections and Vesicoureteral Reflux in Children

- "The management of urinary tract infection in children has changed in the last decade due to worries about antibiotic overuse, and **the trauma and radiation of voiding cystourethrograms**."
- "There was a dramatic decrease in the number of voiding cystourethrograms performed from 907 in 2005 to 216 in 2013."

## Urinary tract Infections after voiding cystourethrogram

- "Reported rates of post-procedural urinary tract infection (ppUTI) after voiding cystourethrogram (VCUG) are highly variable (0-42%)."
- "This study demonstrated that the risk of ppUTI after a cystogram is very low (1.0% in this cohort). Having a pre-existing urologic diagnosis such as VUR or hydronephrosis was associated with ppUTI."
- "An analysis was performed of the guidelines from: American Academy of Pediatrics (AAP), National Institute for Health and Care Excellence (NICE), Italian Society of Pediatric Nephrology, Canadian Paediatric Society (CPS), Polish Society of Pediatric Nephrology, and European Association of Urology (EAU)/European Society for Pediatric Urology (ESPU)."
- "There was still a lack of sufficient data to formulate coherent, unequivocal guidelines on UTI management in children, with imaging tests remaining the main area of controversy."

## Critical appraisal of the top-down approach for vesicoureteral reflux (United States/Egypt)

- "Traditionally, it was mistakenly believed that every reflux should be identified and promptly treated to prevent UTI and minimize the risk of renal damage."
- "VCUG remains the gold standard tool to identify VUR. However, the **test is usually a traumatic experience to both patients and their families** due to the need for catheterization. Additionally, it carries a **risk of introducing infection into the urinary tract**. More importantly**, it identifies a population with clinically-**

**insignificant VUR that may never come to clinical attention leading to potential overtreatment**."

## 2018

### Pediatric voiding cystourethrography: an essential examination for urologists but a terrible experience for children (Japan)

- **"This invasive procedure imposes a significant burden on children and their parents."**
- "In some countries, including Japan, VCUG is mainly carried out by young urologists, but if they are inexperienced, **patients experience more distress and anxiety.**"
- "**VCUG is painful and unpleasant**, with urethral catheterization and voluntary voiding in public. After catheterization and filling the bladder with contrast medium, the patient must void in front of the X-ray camera, which causes anxiety for patients and families. **More than half the children undergoing VCUG remember it as worse than VUR surgery**. This is an extremely humiliating experience for toilet-trained children, because they are educated to void in the restroom."
- "Children's developing tissues and organs are approximately 10-fold more sensitive to ionizing radiation than adults, and mean risks for hereditary effects and cancer after VCUG during childhood have been estimated at 15 per million and 125 per million, respectively. Thus, **radiation risks associated with VCUGs are NOT negligible**."
- "Performance of VCUG **should be reserved** for those occasions when the results would affect VUR management to determine the requirement for surgical intervention."

### Pediatric cystogram: are we considering age-adjusted bladder capacity? (Eastern Ontario)

- "Generally, **bladders tended to be overfilled with 32% more volume** in mL than the expected age-adjusted bladder capacity."

- "Bladders are filled **above the estimated age-adjusted capacity** in mL at the following rates: 32% in the whole group and 64% in infants undergoing VCUG. It raises concern of **possible bladder rupture** in this age group. Furthermore, this may lead to **overgrading and over diagnosing of [vesicoureteral] reflux**."

## Vesicoscopic cross-trigonal ureteral reimplantation: High success rate for elimination of primary reflux (United States)

- "Vesicoscopic ureteral reimplantation is an approach that completely recreates all aspects of open cross-trigonal repair. **Complications were uncommon and success rates were very high** in the current study."

# 2019

## New trends in voiding cystourethrography and vesicoureteral reflux: who, when, and how? (United States)

- "The literature has shown **significant variability among institutions** regarding the VCUG protocol used, as well as **inconsistent reporting of the findings** from the VCUG between institutions."
- "Given the **invasive and relatively unpleasant nature of a VCUG**, it is important that as much information as possible is obtained and reported when these studies are carried out."
- "In addition to **potential patient and parental distress** associated with a VCUG, it also **exposes the child to radiation**."
- "Sedation or immobilization can be considered as long as these methods do not alter the ability of the child to void, which will impact the test outcomes. Patient and caregiver education, as well as a comfortable environment with child life specialists, have also been shown to reduce the stress associated with invasive testing."
- "Although the benefits generally outweigh the risks, it is logical to **optimize the quality and consistency of data obtained from each VCUG, as it is an invasive study.**"

## Adherence to the 2011 American Academy of Pediatrics Urinary Tract Infection Guidelines for Voiding Cystourethrogram Ordering by Clinician Specialty

- "Guideline adherence was more likely among urologists/nephrologists than pediatricians/others and was not associated with abnormal voiding cystourethrogram among children 2-24 months. **Multicenter evaluation is necessary to determine if ordering recommendations should be revised**."

## Population-based trend analysis of voiding cystourethrogram ordering practices in a single-payer healthcare system before and after the release of evaluation guidelines (Ontario, Canada)

- "While voiding cystourethrogram (VCUG) is a widely-accepted test, it is **invasive and associated with radiation exposure**. Most cases of primary vesicoureteral reflux (VUR) are low-grade and unlikely to be associated with acquired renal scarring. To select patients at greatest risk, in 2011 the American Academy of Pediatrics (AAP) published guidelines for evaluation of children ages 2 - 24 months with urinary tract infections (UTIs). Similarly, in 2010 the Society for Fetal Urology (SFU) published guidelines for patients with hydronephrosis. Herein a prospectively-collected database was queried through the Institute of Clinical Evaluative Sciences (ICES), exploring trends in VCUG ordering within the Ontario Health Insurance Program (OHIP), which guarantees universal access to care."
- "Trend analysis demonstrated that the total number of VCUGs ordered in the province has decreased over a decade (Figure 1), with a concurrent decrease in VUR diagnosis. On multivariate regression analysis, the decrease in VCUG ordering could not be explained by changes in population demographics or other baseline patient variables. Most VCUGs obtained per year were ordered by pediatricians or family physicians (mean 2,022+523.8), compared with urologists and nephrologists (mean 616+358.3). Interestingly, **while the rate of VCUG requests decreased, the annual number of surgeries performed for VUR (endoscopic or open) did not show a significant reduction over time**."
- "We present a large population-based analysis in a universal access to care system, reporting a **decreasing trend in the number of cystograms and differences by**

**primary care versus specialist providers**. While it is reassuring to see practice patterns favorably impacted by guidelines, it is also encouraging to note that the number of surgeries has remained stable. This suggests that **patients at risk continue to be detected and offered surgical correction**. These data confirm previous institution-based assessments and **affirm changes in VCUG ordering** independent of variables not relevant to the healthcare system, such as the insurance status."

## 2020

### Minimizing the risk of psychological trauma during pediatric voiding cystourethrogram

### Can virtual reality help children undergoing urologic procedures? (United States)

- "A VCUG can be **very distressing for young children** and many of them are **unable to get through the exam while awake**."

### Pediatric Imaging, Journal of the Korean Society of Radiology (South Korea)

- "Psychological preparation: Apart from physical preparation, **psychological preparation is necessary** for both, patients and parents as they may be anxious due to **fear of pain** and unknown, urethral catheterization, and radiation use."
- "Parents are recommended to stand beside their children for comforting them during the procedure. If the patient's mother is pregnant, she is advised to be with the patient only during catheter insertion."

## 2021

## Evaluation of the Diagnostic Value of Contrast-Enhanced Voiding Urosonography with Regard to the Further Therapy Regime and Patient Outcome-A Single-Center Experience in an Interdisciplinary Uroradiological Setting

- "Vesicoureteral reflux (VUR) describes a common pediatric anomaly in pediatric urology with a prevalence of 1-2%. In diagnostics, in addition to the gold standard of voiding cystourethrography (VCUG), contrast-enhanced urosonography (ceVUS) offers **a radiation-free procedure**, which, **despite its advantages, is NOT yet widely used**."
- "Between 2016 and 2020, 49 patients were retrospectively included and received a ceVUS to evaluate VUR. With a distribution of 47:2 (95.9%), a **clear female predominance** was present."
- "**Results**: Compared to intraoperative findings, ceVUS shows a sensitivity of 95.7% with a specificity of 100%. Allergic reactions to the contrast medium could not be observed."
- "**Conclusion**: With its high sensitivity and intraoperative validation, **ceVUS offers an excellent alternative to VCUG**, the gold standard in the diagnosis of VUR. In addition, ceVUS is a **radiation-free examination** method with a **low risk profile** that offers **an exceptional diagnostic tool** in the diagnostic clarification of recurrent urinary tract infections with the suspected diagnosis of VUR and **should also be included in the consideration** of a diagnosis next to the established VCUG, **especially in younger children**."

## Safety assessment and diagnostic evaluation of patients undergoing contrast-enhanced urosonography in the setting of vesicoureteral reflux confirmation

- "There are **many diagnostic options** available, including voiding cystourethrography (VCUG) and contrasted-enhanced urosonography (ceVUS). ceVUS combines a diagnostic tool with a high sensitivity and specificity which, according to previous study results, **was even shown to be superior to VCUG**."
- "Nevertheless, despite the recommendation of the EFSUMB, **ceVUS has not found a widespread use** in clinical diagnostics in Europe yet."

- "Materials and methods: Between 2016 and 2020, 49 patients **with a marked female dominance** (n = 37) were included."
- "The 49 patients included in the study showed no adverse effects. 51% of patients (n = 26) were referred with the initial diagnosis of suspected VUR, while 49% of patients (n = 23) came for follow-up examination or to rule out recurrence of VUR. The vast majority had at least one febrile urinary tract infection in their recent medical history (n = 45; 91,8%)."
- "**Conclusion**: ceVUS is an examination method with a low risk profile which represents with its high sensitivity and specificity an excellent diagnostic tool in the evaluation of vesicoureteral reflux, especially in consideration of a generally very young patient cohort."

Hi Shelby,

I spoke with our Pediatric Radiology Section Chief and he indicated that we do VCUG exams at Cook Children's Medical Center. PIC cystograms are only done by urology practices and involves a scope, anesthesia, etc. We do not currently offer ceVUS at this time.

Thank you,
David

## Parents' perceptions of the impact of information at a VCUG of their child: an example of person-centered care in radiography (Sweden)

- "The VCUG is associated with **a high level of distress for both the child and the parents**."
- "According to the United Nations Convention on the Rights of the Child (1989) and the Swedish Patient Act, **the best interest of the child must be considered**."
- "Regarding VCUG, it has been reported that a parent who is more distressed affects the stress level of the child negatively. Hence, it is important that **parents receive adequate information so that they can prepare themselves** and thus focus on their child's best interest during the examination."
- "According to the standard of care (Sweden), before the VCUG examination, an appointment letter about the examination, including a reference to a website, was sent to the parents of the child who was scheduled for the examination. The letter briefly described the examination procedure, and the website provided detailed

information.... Parents were requested to telephone the radiology department before the VCUG examination date after receiving the appointment letter. During the phone call, **the procedure information was repeated with an opportunity to ask questions**. The information was also **reviewed verbally by a radiology nurse** in the waiting room, and **the parent was encouraged to ask any questions** for further clarification."

- "Receiving written and then verbal information over the phone before arriving at the department **helped parents to understand what would be happening** and was perceived as **significant**. By reading educational materials and being given the opportunity to ask questions, **the parents could better prepare the child and themselves psychologically, emotionally, and physically for the upcoming examination**."
- **Direct quote from parent**: "I got to talk to a nurse, who describing a little how, what would be required of me as a parent, and it was rather nice because then I could **mentally prepare myself that this was going to be difficult**."

## Standardized protocol for voiding cystourethrogram: Are recommendations being followed? (United States)

- This study highly advocates for the VCUG procedure but anyone who has experience reading and analyzing research articles could see that this study is poorly designed and incredibly biased.
    - Internal Validity
        - Cohort not recruited in an acceptable way (not representative of the population of individuals who receive VCUGs): "Studies performed on patients >18 years of age and **those obtained for trauma evaluation were excluded from study**." - Authors also fail to explain why they made the choice to exclude these individuals.
        - The above quotation also indicates that the authors exhibited selection bias
    - External Validity
        - Results indicate that: "Timing of reflux [which would be revealed through VCUG] has been shown to predict likelihood of spontaneous

resolution and risk of breakthrough urinary tract infection; thus, its omission may limit the information used to counsel families and provide individualized care." **However**, as the results are not representative of the whole population of individuals who receive VCUGs, they **cannot** be applied to the whole population of individuals who receive VCUGs. Someone reading this research article may easily wrongly assume that these results are applicable to all individuals receiving VCUGs if they skip over the methodology section of the article.

- **This serves to provide supporting evidence that physicians and researchers are aware of the trauma caused by VCUGs, yet actively choose to ignore it.**

### Contrast-enhanced voiding urosonography in the assessment of vesical-ureteral reflux: the time has come

- "During the last 20 years, the diagnostic approach to this entity has passed through several, drastic changes: indeed, since its introduction in 1994 contrast-enhanced voiding urosonography (ceVUS) has gradually accompanied the voiding cystourethrography (VCUG) as alternative imaging technique for the diagnosis and staging of VUR. Despite a large number of papers has **strongly encouraged its use** in clinical practice, **due to the lack of ionizing radiations and its high sensitivity rate**, ***to date almost all the guidelines only include the VCUG for VUR diagnosis***."

### Characteristics and outcomes of patients receiving sedation for voiding cystourethrography

- "Voiding cystourethrogram (VCUG) is used to diagnose vesicoureteral reflux (VUR); however, it is an **invasive procedure** and can be **psychologically distressing.**"
- "There were **no significant differences in VCUG results between sedated and non-sedated patients**....Procedural sedation did not have a significant impact on test results, suggesting its potential utility in relieving pain and anxiety associated with VCUG."

## 2022

### Safety and parents' acceptance of ultrasound contrast agents in children and adolescents – contrast enhanced voiding urosonography and contrast enhanced ultrasound (Germany)

- "The parents would agree with the use of both ceVUS and CEUS as a diagnostic tool again in 96% (54/56) or 100% (30/30) of the cases, respectively and 92.9% (52/56) would **prefer ceVUS to voiding cystourethrography (VCUG)**."
- "The **vast majority of parents prefer ceVUS and CEUS to VCUG**, CT or MRI because of the **safety profile of the contrast agent** and **diagnostic accuracy**."

### Interdisciplinary collaboration in a pediatric urology outpatient clinic at a tertiary children's hospital: a case series (United States)

- "Access to a psychosocial support staff can improve adherence to medical treatment by **reducing barriers to care** and **promoting behavioral change**, **support patients in coping and reducing post-traumatic stress** following surgery and invasive procedures, **improve communication between patients, families, and medical staff**, and **treat psychological issues** that contribute to urinary symptoms."

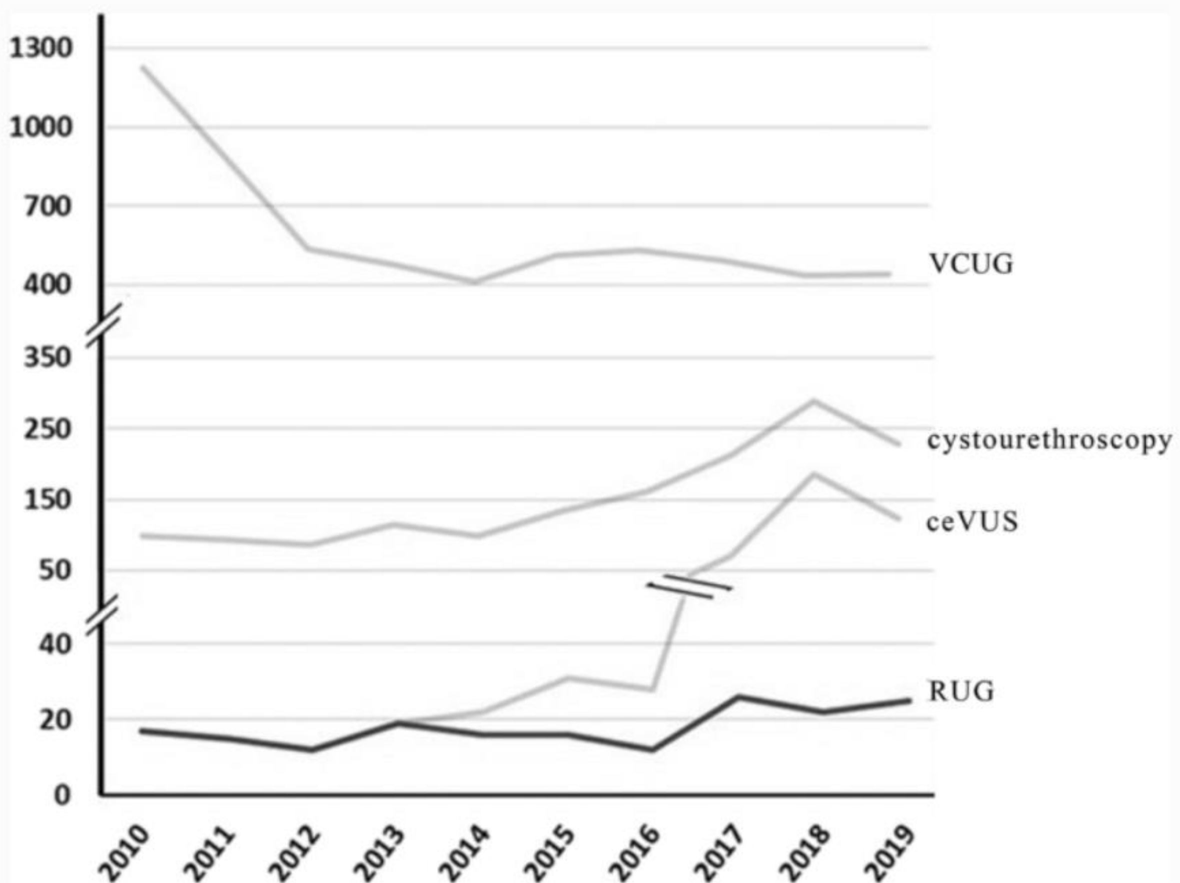
## 2023

### Pilot study from University of Pennsylvania Masters of public health graduate student (United States)

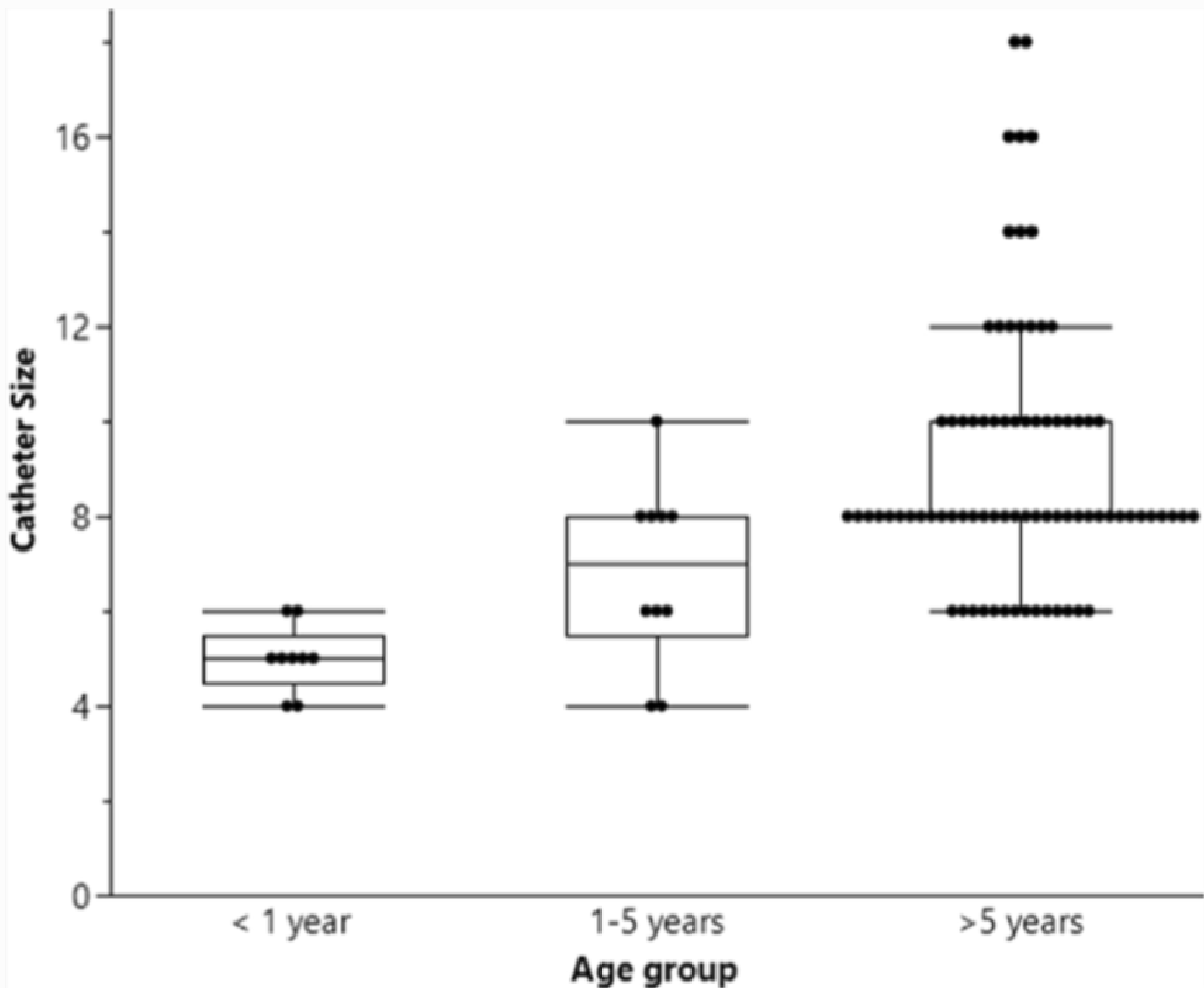
- *10 VCUG survivors and 11 non-VCUG participants.*
- The VCUG group saw themselves as **unhealthier** and had more feelings/diagnosis of **depression and PTSD.**
- Nobody in the non-VCUG group experienced **shy bladder, overactive bladder, or urinary retention**. These were prevalent in some way within the VCUG group
- The VCUG group showed **pelvic dysfunction**, while the non-VCUG group did not
- 81% of the non-VCUG group **has had a pap smear** compared to 44% of the VCUG group. 50% of the VCUG group has **never seen a gynecologist and doesn't plan to go.**

- The VCUG group felt **less comfortable receiving hugs from loved ones**, especially parents.
- Nearly all members of the VCUG group agreed they had **experienced medical trauma as a child**, agreed that **their bodies were disrespected as children**, strongly believed that **their parents and doctors did not make the right choices for their medical care**, and felt **inherently less understood**.
- The VCUG group experienced **more nightmares, restlessness, odd bodily sensations**, and intense pre-bedtime rituals.

## Retrograde urethrography in children: a decade of experience at a children's hospital (United States)



- Graph above shows frequency of retrograde urethrography (RUG, median: 17/year), contrast-enhanced voiding cystourethrography (ceVUS, median: 70/year), cystourethroscopy (median: 104/year), and voiding cystourethrography (VCUG, median: 511/year) over a ten year period (with 2020 excluded due to COVID-19)




- Graph shows **average catheter size for children** of various age groups
- "**Technical difficulties** were reported in 14 children (8%): inadequate catheter seal with suboptimal urethral distention (9) **and significant pain** (5)."

- “In 100 children… cystourethroscopy/VCUG were performed in conjunction with RUG and were used as gold standard references. Cystourethroscopy/VCUG showed pathology in 34 children and was normal in 66 children”
- “Some radiologists might rely solely on VCUG for evaluating all urethral, bladder, and reflux abnormalities without performing RUG… Radiologists should be aware that VCUG alone might not accurately demonstrate certain abnormalities of the male anterior urethra because the urethra is not fully distended to the degree seen on RUG.”

## An innovative diagnostic procedure in children: videourodynamics with contrast-enhanced voiding urosonography (Italy)

- “This technical report aims to describe a new modality of VUD in children by **replacing fluoroscopic VCUG with contrast-enhanced voiding urosonography (ceVUS)**. ceVUS using second-generation contrast media and harmonic imaging is a radiation-free and highly sensitive imaging modality used to detect VUR in children.”
- “This article describes the advantages of this method compared with a conventional technique. In addition to being radiation-free, this procedure of advanced videourodynamics method **can better detect vesicoureteral reflux and intrarenal reflux combined** with urodynamic disorders associated with VUR.”

## Urinary tract infection in children: A narrative review of clinical practice guidelines (international review)

- “Febrile infants with UTI should undergo RBUS [renal and bladder ultrasound]. VCUG should not be performed routinely after the first febrile UTI; VCUG is indicated if RBUS reveals hydronephrosis, scarring, high-grade VUR, or obstructive uropathy as well as atypical or complex circumstances.”
- “VCUG was recommended routinely for children between 2 months and 2 years **but not anymore**.”
- *This study looks at the guidelines concerning UTIs and demonstrates different places having different guidelines. For example:*
    - One place: “VCUG: not routinely recommended after first UTI”

    - Another place: “VCUG is recommended after first UTI or abnormal RBUS or if the bacterial organism other that *E. coli.”*

- “Voiding cystourethrography (VCUG)/micturating cystourethrogram is an **invasive study** that is **still considered the gold standard** for excluding or confirming VUR and for assessing the degree of VUR. It should be performed after the first febrile UTI if the ultrasound suggests either high-grade VUR or obstructive uropathy. Furthermore, it is indicated after a second episode of febrile UTI, atypical and recurrent infections in children <2 years of age and in older children, if there is abnormal voiding, which needs to be evaluated for voiding dysfunction with postvoid residual test and referral to urology before they have a VCUG. Likewise, it is indicated if hydronephrosis or thick bladder wall was found on RBUS, non-*E. coli* infection or family history of VUR were noted. The concept of limiting indications for VCUG and dimercaptosuccinic acid (DMSA) scanning is **due to significant radiation exposure, catheter risk-induced UTI, stress for young patients and their parents,** and considering **the cost** of imaging techniques.”
- “Where accessible, a nuclear cystogram (NCG) may be used instead of VCUG to evaluate VUR using radioisotopes. It offers a **lesser amount of radiation than VCUG** but provides poor anatomical detail for the male urethra, so it may miss posterior urethral valves. Using NCG as the initial test for **female VUR investigation and in follow-up studies for both genders is reasonable**.”

## Utility of Positional Instillation of Contrast Cystography for Diagnosing Occult Vesicoureteral Reflux in Children: A Report of Two Cases (Japan)

- “Positional instillation of contrast (PIC) cystography is effective for detecting occult vesicoureteral reflux (VUR), which can not be revealed by standard voiding cystourethrography (VCUG).”
- “**PIC cystography is useful for** detecting occult VUR in children with negative VUR findings on standard VCUG or **who are unable to tolerate standard VCUG**.”

## Viability of contrast-enhanced voiding urosonography as an alternative to fluoroscopy during video urodynamics (United States)

- “Contrast-enhanced voiding urosonography (**CeVUS**) has been approved in the evaluation of vesicoureteral reflux and **has been shown to have equal or superior diagnostic value to VCUG**.”

## Contrast-enhanced voiding urosonography (CEVUS) as a safe alternate means of assessing vesicoureteral reflux in pediatric kidney transplant patients (United States)

- “Although voiding cystourethrogram (VCUG) is **currently the gold standard** in VUR evaluation, there is **ionizing radiation exposure**. Contrast-enhanced voiding urosonography (CEVUS) uses ultrasound contrast agents to visualize the urinary tract and **has been reported to be safe and effective** in VUR evaluation in children.”
- “ceVUS can **provide an alternate means of safely evaluating VUR** in kidney transplant patients with **similar outcomes**, **potentially lower costs**, and **no exposure to ionizing radiation**.”

## Parental perception of contrast enhanced voiding ultrasonography urodynamics vs fluoroscopic urodynamics

- “In this study, we aimed to understand how parents perceived their child's experience of undergoing ceVUS during UDS compared to fluoroscopic (fluoro) UDS.”
- “All 53 parents (100%) were **satisfied/very satisfied with their ceVUS experience**; 48 parents (90.6%) **preferred ceVUS**, 3 parents (5.7%) preferred fluoro UDS, and 2 (3.8%) were neutral. On average, **parents perceived ceVUS to be more comfortable (72.7%) and produce better results** (67.4%) than fluoro UDS. The majority felt that both studies allowed the same contact with their child (52.3%) and took the same amount of time (50.0%). However **29.5% felt ceVUS was faster and 34.1% felt ceVUS allowed more contact with their child** (Fig. 1). 26 parents (49.1%) specifically noted **no radiation** as the reason why they preferred ceVUS over fluoro.”

- "The **majority of parents preferred ceVUS** over fluoro UDS. ceVUS was perceived to be **more comfortable and provide better results**. Many parents highlighted **no radiation** and **no fluoroscopic machinery** as factors in preference of ceVUS over fluoro. The parents who preferred ceVUS UDS had children who had both studies done at an earlier age compared to the parents who preferred fluoro UDS."

### The Utility of Noninvasive Urinary Biomarkers for the Evaluation of Vesicoureteral Reflux in Children

- "Our results encourage further studies to evaluate LL-37, IL-6, and NGAL as **noninvasive urinary markers that can improve the management of patients with VUR**. Moreover, these urinary biomarkers may become **alternative assessment tools to VCUG** and DMSA scans. According to our study, urinary NGAL and LL-37 can be **useful in differentiating severe from mild VUR**. Thus, it could be easier to identify patients who require antibiotic prophylaxis or surgical intervention."
- "All these aspects would **increase patient comfort and reduce the costs** related to hospitalizations and investigations. Also, due to the prognostic value of these markers in diagnosing RS and RN, it may be easier to identify patients at risk of developing CKD, allowing prompt therapeutic intervention that would improve clinical outcomes."
- "For the diagnosis of VUR, we used the medical records and voiding cystourethrogram (VCUG). The VCUG is the gold standard investigation for the diagnosis of VUR and consists of bladder catheterization with the inoculation of a contrast agent, followed by a radiological examination. **The VCUG allows the diagnosis of VUR, staging, and description of the anatomy of the urinary tract**, and is also indicated for **tracking the evolution of VUR**."
- "Urinary IL-6, NGAL, and LL-37 could serve as ***valuable markers for diagnosing and predicting outcomes in patients*** with VUR and RN. These biomarkers could help to **identify the severity of kidney injury in children with VUR**. Based on our results and similar ones previously published, future prospective studies will be able to establish the role of these markers in the **early detection of patients at risk** for unfavorable evolution."

- “Moreover, ***these noninvasive and easy-to-determine urinary markers*** can facilitate the monitoring of evolution, **replacing invasive and laborious examinations, such as the VCUG**. Besides the diagnostic and prognostic potential, the markers studied by us can ***influence the clinical management of patients with VUR***. They could be used to **distinguish patients who require surgical intervention from those who can be managed with prophylactic antibiotic therapy** or those who can be only followed up clinically.

## Urologic practice patterns of pediatricians: a survey from a large multisite pediatric care center

- “An anonymous 15-question survey was created and distributed to all pediatricians at our institution, a large multisite care center. This study was deemed exempt by the institutional review board.”
- “55 of the 122 (45%) providers queried responded. **93% of the participants were female**, and 7.3% were male. 55% recommended testicular self-examination at adolescence, while 39% did not recommend at any age. 78% stated that they were “Fairly confident” in the exam for undescended testicle (UTD). One-third referred patients with UDT to a subspecialist upon recognition at birth, 13% at 3 months of age, and 28% at 6 months of age. 10% reported obtaining a VCUG after the first febrile urinary tract infection (UTI), 26% after the second, and 36% only if there were abnormal findings on renal ultrasound. 28% of providers reported that they refer to pediatric urology after the initial febrile UTI. 19% provided antibiotics for UTI symptoms alone with negative urinalysis and urine culture.”
- “Despite established guidelines, *practice patterns varied* among pediatricians. Pediatricians typically followed the AAP's guidelines regarding VCUGs (62%), with *only a few adhering to urologic recommendations* (9%). Despite the consistency between AAP and AUA guidelines regarding the age at which to refer a patient for cryptorchidism, about 70% of practitioners referred patients too early or too late.”
- “Harmonized, consolidated guidelines between pediatricians and pediatric urologists would improve patient care and efficiency of the healthcare system.”
- “After initial febrile UTI, 10% of respondents reported ordering a VCUG while 28% report that they would directly refer to pediatric urology for all further work up. The

largest group of providers (36%) ordered a VCUG *only if there were abnormal findings on renal ultrasound*. 26.4% preferred to order a VCUG after a second febrile UTI.

- "75% of pediatricians adhered to AUA standards regarding the performance of GU exam. **40% of pediatricians adhered to AUA standards regarding performance of female GU exam**. 28% of pediatricians adhered to AUA guidelines regarding the timing of referral for UDT. **62% of pediatricians adhered to the AAP guidelines regarding VCUG timing**. 81% of pediatricians adhered to AAP guidelines regarding treating UTIs with a negative urine culture."

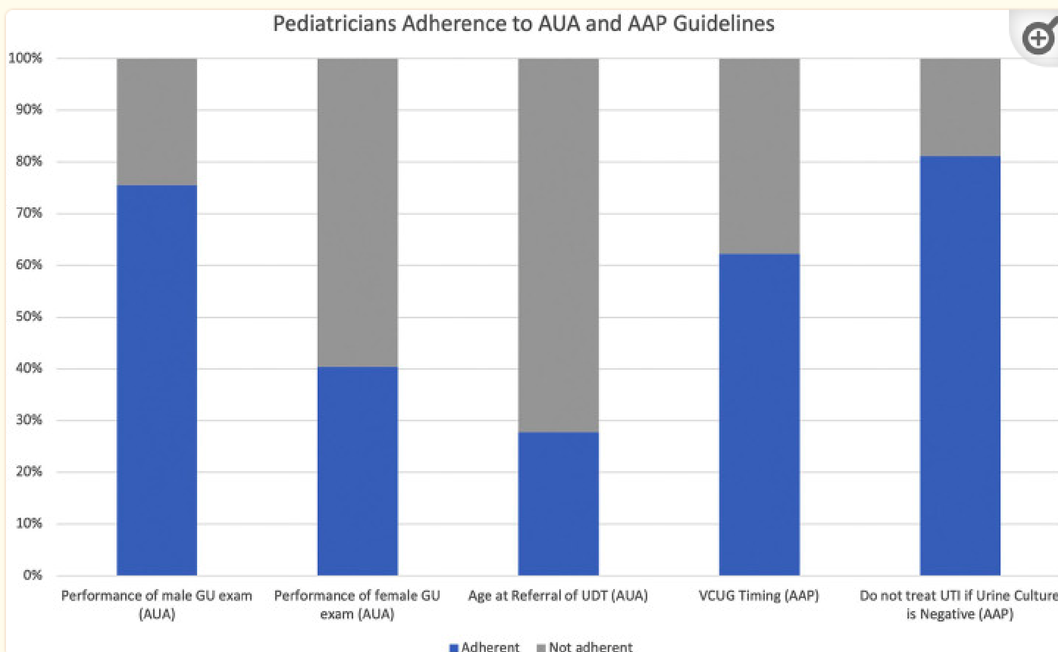



Figure 1

Pediatricians' adherence to AUA and AAP guidelines. This figure represents the percentage of pediatricians who adhere to AUA and AAP guidelines. 75% of pediatricians adhered to AUA standards regarding the performance of GU exam. 40% of pediatricians adhered to AUA standards regarding performance of female GU exam. 28% of pediatricians adhered to AUA guidelines regarding the timing of referral for UDT. 62% of pediatricians adhered to the AAP guidelines regarding VCUG timing. 81% of pediatricians adhered to AAP guidelines regarding treating UTIs with a negative urine culture.

- "***The timing of obtaining a VCUG has historically been controversial*** and our study suggests that this continues to be **an area of ongoing debate**. **62% of pediatricians** (36% obtained if abnormality seen in ultrasound and 26% obtained

after second febrile UTI) followed the most recent guidelines put forth by the AAP, which **recommends against a routine VCUG after the first febrile UTI** unless abnormalities are present on the renal bladder ultrasound or there are other clinical reasons to suspect high-grade vesicoureteral reflux or obstructive uropathy."

- "Although the majority of pediatricians are following AAP guidelines in terms of timing of obtaining a VCUG, there is growing evidence that renal scarring may be missed by not obtaining VCUGs after the first UTI: Narchi et al. showed that following AAP guidelines would have missed 56% of children with VUR ≥ grade II, and all children with renal scarring would not have been imaged."
- "While VCUGs are an **invasive imaging modality** and can cause morbidity such as **patient and parent distress**, although perhaps less with pretest preparation and child life specialist involvement (22), future studies will be necessary to delineate risk factors for developing renal scarring in order to not improperly delay the diagnosis of **symptomatic vesicoureteral reflux**."
- "A small number (9%) of pediatricians did prefer to order a VCUG after the first febrile UTI, which is **supported by the Section of Urology**."

Q4. General: How often do you perform a comprehensive genitourinary (GU) examination for female patients (well-child)?

| ANSWER CHOICES | RESPONSES | |
|---|---|---|
| GU examination is never performed at a well-child visit unless the patient or guardian(s) report a concern | 2 | 3.8% |
| GU examination is performed at every well child visit, but stopped at adolescence | 21 | 40.4% |
| GU exam is always performed at all ages and every well-child visit | 21 | 51.9% |
| GU examination is only performed at initial visit and if normal, forego future examinations | 2 | 3.8% |
| If patient sees urology, I do not continue to perform GU examinations | 0 | 0% |
| Total | 52 | |

Q5. General: How often do you perform a comprehensive genitourinary (GU) examination for male patients (well-child)?

| ANSWER CHOICES | RESPONSES | |
|---|---|---|
| GU examination is never performed at a well-child visit unless the patient or guardian(s) report a concern | 1 | 1.9% |
| GU examination is performed at every well child visit, but stopped at adolescence | 9 | 17.0% |
| GU exam is always performed at all ages and every well-child visit | 40 | 75.5% |
| GU examination is only performed at initial visit and if normal, forego future examinations | 3 | 5.7% |
| If patient sees urology, I do not continue to perform GU examinations | 0 | 0% |
| Total | 53 | |

Q9. UTI: At what time point do you order a VCUG following a febrile UTI?

| ANSWER CHOICES | RESPONSES | |
|---|---|---|
| After the first febrile UTI | 5 | 9.4% |
| After the second febrile UTI | 14 | 26.4% |
| Only if there are abnormal findings on renal ultrasound | 19 | 35.8% |
| After the first febrile UTI, referral to pediatric urology for evaluation and initiation of workup | 15 | 28.3% |
| Total | 53 | |

## Neutrophil-to-lymphocyte ratio as a predictor of primary vesicoureteral reflux evolution in children with associated acute pyelonephritis (November 2023)

- "Primary vesicoureteral reflux (VUR) is a congenital disorder, typically resulting from a short submucosal tract at the junction between ureter and bladder, ***not*** associated with other obstructive, neurological or vascular abnormalities (1). It is one of the **most common urological diseases in childhood**, with **an estimated prevalence of 0.4–1.8% in the general pediatric population** and **up to 30% in children with a history of urinary tract infection (UTI)**. In these patients, VUR plays an important role in the pathogenesis of UTIs as the relationship between acute pyelonephritis (APN), VUR and renal damage is well established…This potential morbidity makes early diagnosis essential, as well as the determination of the clinical course of VUR, **due to the high percentage of spontaneous resolution** (SR) observed during its evolution."
- "Imaging studies performed included urinary ultrasound, Tc-99m-dimercaptosuccinic acid (DMSA) renal scan scintigraphy, voiding

cystourethrography (VCUG). After APN diagnosis, urinary ultrasound and DMSA were performed during the first 5 days of admission. Subsequently, **VCUG was performed 4 weeks after APN resolution**, in order to evaluate the presence of VUR as well as the degree and laterality. Follow-up was performed by reviews in the outpatient clinic every 3 months, **with repeat VCUG to monitor the VUR clinical course at 6-monthly intervals**."

- "NLR may be considered as **a simple and cost-effective predictor of clinical outcome of VUR,** which correlates with the increased risk of developing complications of primary VUR after an episode of APN during follow-up. Therefore, it should be included in the management algorithm for these patients, although future prospective studies are still required to confirm these results."

## 2024

### Development and multi-institutional validation of a deep learning model for grading of vesicoureteral reflux on voiding cystourethrogram: a retrospective multicenter study

- "Voiding cystourethrography (VCUG) is the **gold standard** for the diagnosis and grading of vesicoureteral reflux (VUR). **However, VUR grading from voiding cystourethrograms is highly subjective with low reliability.** This study aimed to develop a deep learning model to improve reliability for VUR grading on VCUG and compare its performance to that of clinicians."

### Stratifying Antenatal Hydronephrosis: Predicting High-Grade VUR Using Ultrasound and Scintigraphy

- "Antenatal hydronephrosis (AHN), detected in approximately one percent of prenatal ultrasounds, is caused by vesicoureteral reflux (VUR) in 15–21% of cases, a condition with **significant risks** such as urinary tract infections and renal scarring. Our study addresses the diagnostic challenges of VUR in AHN. Utilizing renal ultrasonography and scintigraphy, we developed a novel scoring system that accurately predicts high-grade VUR, optimizing diagnostic precision while

**minimizing the need for more invasive methods like voiding cystourethrogram (VCUG)**;

- "Methods: This retrospective study **re-analyzed renal ultrasonography, scintigraphy, and VCUG images** from infants admitted between 2003 and 2013, excluding cases with complex urinary anomalies;
- "Results: Our analysis included 124 patients (75% male), of whom 11% had high-grade VUR. The multivariate analysis identified visible ureter, reduced renal length, and decreased differential renal function (DRF) as primary predictors. Consequently, we established a three-tier risk score, classifying patients into low, intermediate, and high-risk groups for high-grade VUR, with corresponding prevalences of 2.3%, 22.2%, and 75.0%. The scoring system demonstrated 86% sensitivity and 79% specificity;
- "Conclusions: Our scoring system, focusing on objective parameters of the visible ureter, renal length, and DRF, effectively identifies high-grade VUR in AHN patients. This method enhances diagnostics in ANH by **reducing reliance on VCUG and facilitating more tailored and less invasive patient care**."

## Risk factors for new renal scarring in children with vesicoureteral reflux receiving continuous antibiotic prophylaxis

- "This study aimed to analyze the clinical data of children receiving CAP treatment for VUR in our hospital from 2016 to 2019, with the purpose of summarizing the risk factors for new kidney scarring in children with VUR."
- "Previous studies have found that in children with VUR who use CAP intervention, high-level VUR, especially IV-V grade VUR, is an independent risk factor for NRS26. Mattoo et al.5 found in a prospective randomized controlled clinical study (RIVUR) that children with IV-V grade VUR were more likely to develop BT-UTI and renal scars, 24.2 and 1.88 times higher than those with I–III grade VUR, respectively. Sitarah Mathias et al.27 also found that patients with high-grade VUR patients were more likely than those with low-grade VUR patients to have renal scarring."

## Therapeutic Management of Children with Vesicoureteral Reflux

- "...VUR represents a risk factor for UTI development, distinguishing two different entities related to it, "reflux disease" and "reflux symptom"; the first involves predominantly **males, with a rare incidence, prenatally or under two years of age**, with severe VUR (stage IV–V), abnormal renal parenchyma and urinary tract, and **spontaneous resolution in 50% of cases**. **The second and more common form of VUR is usually assessed in females**, with low-grade I–III VUR, associated with normal kidneys and urinary tract, **with a high rate of resolution (80–90%)**.
- A voiding cystourethrogram (VCUG) is the "gold standard" for VUR detection, allowing grading of the severity from a wisp of contrast just beyond the bladder with no dilatation of the ureter or collecting system (grade I) up to dilatation and tortuosity of the ureters with calyceal clubbing (grade V). **This radiologic test is an invasive procedure requiring urethral catheterization, often painful and traumatic for the child, causing UTIs in 1 to 3% of cases**. Although a diagnostic study can be achieved with a relatively low radiation dose by using careful technique and modern equipment, in practice, **the range of doses is extremely wide**."
- "Other tests have been proposed to detect reflux, such as **contrast-enhanced voiding urosonography (ceVUS)**, an ionizing radiation-free technique using ultrasound with a contrast agent instilled into the bladder to image the urinary tract. Several studies **revealed ceVUS as a valid alternative method** for VUR assessment, with **comparable results in terms of sensitivity and specificity** with a VCUG in detecting and grading VUR."
- "However, although ceVUS has several advantages, **its limitations should be underlined**, highlighting **the lack of uniform standardization of the method**, and some issues regarding ultrasound, such as bowel gas interference. The biggest limitation of ceVUS is the ***incapability to visualize the urethra*** and, in consequence, its low diagnostic ability to ***rule out congenital urethral pathologies***, such as urethral valves. In this case, **a VCUG is reserved for the correct diagnosis**."
- "Behind radiological procedures, **several urinary biomarkers are being studied to achieve early diagnosis**, facilitating staging and therapeutic VUR management. In particular, some interleukins or neutrophil gelatinase-associated lipocalin have been associated with the innate immune reaction and proinflammatory state

***characterizing children with VUR***, with potential clinical application to **easily identify patients** who require antibiotic prophylaxis or surgical intervention."

- "However, prospective and larger studies are needed to confirm the role of these or other biomarkers as alternative, non-invasive tools to VCUG and ceVUS."
- "The choices of the patients and the radiological test to perform are not unique challenges, considering that the therapeutic approach of VUR is a matter of debate."
- There are *two distinct directions in the literature* regarding the investigation of an uncomplicated first febrile UTI in a child. In general, when presented with a first febrile UTI in a child, physicians recommend fewer investigations and less treatment, **in contrast to** surgeons who advocate extensive investigation and aggressive intervention if imaging detects an abnormality [19].
- Moreover, the child affected by VUR undergoes renal scintigraphy to complete the diagnostic process, evaluating the function of the kidneys. **The risk of a child without other congenital abnormalities of the kidney and urinary tract developing chronic kidney disease as a result of repeated febrile UTIs associated with VUR is very low**.
- Spontaneous resolution of VUR can be observed in about more than 80% of grades I and II, around 45% of grade III, and less than 10% of grades IV and V. According to the main international guidelines, VUR therapy is based on three strategies, depending on the severity of VUR ***and physicians' preferences.***
- In children without UTI symptoms and with low grades of VUR, the "wait and watch" approach could be considered due to the **high probability of spontaneous resolution.**
- If it is known that **VUR could resolve spontaneously over time**, waiting for this to occur rather than treating it should only happen in the **absence of repeated febrile UTIs**, **a risk factor for renal scarring**.
- However, regular follow-up visits are required to enable adequate monitoring of the patient's status, and this approach is recommended for patients with a relatively low risk of renal injury, such as males with low-grade VUR.
- Conversely, independently from the severity of the VUR, in children with LUTS and recurrent UTIs, continuous antibiotic prophylaxis (CAP) could be prescribed [26].

- Whether VUR contributes to the risk of chronic kidney disease (CKD) **remained unclear.**

## A Single-System Ectopic Ureter in a Child: A Challenge for Early Diagnosis

- "An ectopic ureter is an uncommon anomaly, usually associated with a duplicated urinary system. Up to 20% of ectopic ureters occur in a single system. In females, only 25% of ectopic ureters insert into the vagina and usually cause urinary incontinence, which can be confused with vaginal discharge. **The diagnostic investigation includes urinary tract ultrasound, DMSA, and urethrocystography."**