Reducing contamination rates and catheter associated urinary tract infection associated with mid stream urine collection in Pediatrics

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October 2011
Thesis declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent for a copy of my thesis to be deposited in the University Library, being made available in all forms of the media, now or thereafter.

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Date:
Acknowledgements

I thank my supervisors Professor Alan Pearson AM and Dr William Greer, for their guidance, support and comments while undertaking this Master of Clinical Science. To my colleague in Qatar – you are extremely hard working and diligent, and I wish you all the best in your PhD. To my life, my wife, thank you for your constant encouragement; your belief in me is never ending.
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Abstract

Background
Best practice recommendations for the prevention of adult catheter associated urinary tract infections are available from many international patient safety authorities such as the Cochrane Library, Joanna Briggs Institute, National Health Service, The WHO guidelines and Centre for Disease Control and Prevention. However, guidance for clinicians working with pediatric patients is, limited. Similarly, there is a lack of consensus on if periurethral cleaning is an important step in helping to reducing the contamination rates of midstream urine collection, and if a solution other than potable water is needed to undertake this cleansing. In order to ensure our pediatric population is receiving evidence based health care, as healthcare professionals it is our responsibility to ensure that guidelines and or practice recommendations are as readily available, as this not only impacts economic benefits but more importantly patients quality of life.

Objectives
The objective for this review was to synthesize the best available evidence related to the type of solution used for periurethral cleansing in reducing the rate of contamination of mid stream urine collection and catheter associated urinary tract infection in pediatric patients.

Inclusion criteria

Types of participants
This review considered studies involving children from the age of 1 month to 18 years with a short-term indwelling urethral catheter and / or children who required midstream urine sampling.

Types of intervention(s)/phenomena of interest
Any cleansing solution e.g. Soap, 10% Providone-Iodine, Sterile Water, Chlorhexidine Gluconate or Saline.

Comparison
Any alternate method (solution or no solution) to the intervention.

Types of studies
Randomized, quasi-randomized and non-randomized studies.

Types of outcomes
The primary outcome of interest was:
• The presence of urinary tract infection, as determined by the patient's urine culture growing at least one organism with a colony count of >10^4 Colony Forming Units / ml of urine.

Secondary Outcome:

• The presence of urethral meatus trauma i.e. burns, redness.

**Search strategy**
The search included both published and unpublished studies with an initial limited search of MEDLINE and CINAHL databases undertaken to identify key words contained in the title or abstract, and index terms used to describe relevant interventions. A second extensive search used all identified key words and index terms. The third step included a search of the reference lists and bibliographies of relevant articles. The databases searched included: CINAHL, MEDLINE, and Embase. The Dissertation Abstracts International and Mednar database was used to search for unpublished studies.

**Methodological quality**
Methodological quality was assessed using a standardised checklist. Critical appraisal and data extraction were conducted by two independent reviewers; discrepancies were addressed through discussion with a third reviewer as required.

**Data collection**
Data was extracted from clinical studies that fulfilled the protocol inclusion criteria. The JBI Mastari standardized data extraction tool was used to assess the quality of included studies and extract data for analysis.

**Data synthesis**
Pooling of data for bacterial contamination and midstream urine collection was undertaken using the JBI MASTARI Meta-Analysis program. Secondary outcomes were reported in a descriptive way.

**Results and Discussion**
A total of three studies met the inclusion criteria for this review: one randomised control trial (RCT) and two descriptive studies. The RCT compared periurethral cleansing with sterile water versus 10% povidone-iodine prior to the insertion of an indwelling urinary catheter whilst the descriptive studies measured the effect of meatal cleansing with 2% Castile soap on the rate of bacterial contamination during midstream urine collection. Meta-analysis of the data was
undertaken with the two descriptive studies. All three studies concluded that using a solution other that sterile water does not significantly decrease the rate of bacterial contamination.

Given the small number of studies and sample size addressing the two topics, no firm conclusions can be drawn from this review. However, the results suggest that a non-irritant solution such as sterile water is acceptable for periurethral cleansing in children prior to urinary catheterization and/or midstream urine collection.

**Keywords**

Urinary catheterization, cleaning solution, pediatrics, urinary tract infection, systematic review
Chapter 1: Introduction to the Study

Situating the Study- a matter of patient safety
When a patient is admitted to a healthcare facility or receives care from a healthcare professional in the home or community, the expectation is that no additional harm (nosocomial or iatrogenic) will occur. The Patient Safety literature however informs us that the rate of nosocomial infections is alarming. External forces such as a climate of zero tolerance for nosocomial infections and the establishment of national and international agencies focused on patient safety have resulted in a flurry of clinical reviews; surveys and research attempting to identify how to minimize hospital acquired infections.

Reducing the rate of nosocomial acquired infections has become a campaign adopted on a global scale. Leading international institutions such as the Institute of Healthcare Initiatives (IHI), Joanna Briggs Institute of Evidence Based Healthcare have developed evidence based bundles aimed at reducing the rate of nosocomial infection that have been readily adopted by healthcare institutions around the world. The success of these evidence-based bundles arises from their simplicity. Typically comprised of no more than five to eight steps, these evidence bundles inform the multidisciplinary team about what techniques, solutions, systems and processes have significantly contributed to reducing the rate of nosocomial infection.

Urinary tract infections are the most common bacterial infections among pediatrics patients.[1] The majority of evidence bundles for UTI’s are informed on research conducted on adult populations. In the 1950’s Kass developed criteria that were to become the universal definition of a urinary tract infection: a “pure urine culture of $\geq 10^5$ cfu/mL of a uropathogen.[2, 3] As healthcare agencies throughout the world attempted to implement best practice guidelines to reduce the rate of nosocomial infections it became important to establish a shared understanding of key performance indicators (KPI’s) with which they could benchmark across institutions. These KPI’s for Urinary Tract Infection’s (UTI’s) were established by the Centers for Disease Control and Prevention (CDC) in 2009 for defining a urinary tract infection, see appendix 7. In the literature prior to 2009, bacterial contamination of urine specimens is discussed in one of three ways: sterile, contaminated or positive. A sterile culture is described as producing no growth. However, when interpreting results of contaminated or positive cultures there is a significant difference amongst authors primarily because the number of Colony Forming Units (CFU) used to confirm the presence of a uropathogen is often dependent
upon the institution’s microbiology protocol for processing urine cultures. This review only included data from positive samples.

The Joint Commission National Patient Safety Goals for 2012 include the implementation of best practice recommendations to reduce the rate of nosocomial infections arising from urinary catheterization. These best practice recommendations arise from the work undertaken by IHI to collate the evidence from clinical research (predominately on adult patients) into evidence bundles.[4-6] There has only been one published study in a pediatric population that assessed the effectiveness of different solutions in cleansing the periurethral meatus prior to urethral catheterization.[7] Additional research is urgently needed to ensure best practice recommendations are available to guide clinicians in the care of the pediatric patient.

**Structure of Thesis**

Having positioned the relevance of this research to the reader the remainder of this thesis occurs in four additional chapters. Chapter two establishes the importance for the review and highlights the many recommendations to prevent catheter associated urinary tract infections and contamination of midstream urine samples. It examines the extant of the literature regarding adult patients' best practice recommendations and in doing so demonstrates the dearth of research on this topic for the pediatric population. Chapter three describes the protocol for the systematic review as defined by Joanna Briggs Institute standards. Chapter four provides the reader with a breakdown of the data from each of the included studies both in graphic (meta-analysis) and narrative form. The final chapter interprets the data and discusses the implications for practice; and draws a set of conclusions to guide the healthcare provider about the status of the evidence related to this subject.

**Abbreviations:**

CAUTI: catheter associated urinary tract infections

CFU / mL urine: Colony forming units

CCU: clean catch urine

Non-CCU: non clean catch urine
Chapter 2: Background to the Study

This chapter provides an overview of the healthcare literature and research as it relates to techniques that minimize the contamination of urinary catheters during insertion and of the urine sample during midstream urine collection. The literature spans four decades and subsequently demonstrates a change in practice as new knowledge emerges. The methodological quality and report of research varies significantly.

Acquisition of a Urinary Tract Infection (UTI) in children is associated with numerous factors such as faecal incontinence; children less than one year of age which is generally linked to a developing immune system; anatomical features i.e. foreskin; voiding dysfunction (unrecognized urostasis) and periurethral colonisation.[8-11] Gender has been identified as another risk factor for example males less than one year of age are more prone to experience urinary tract infections than females of the same age group, however after the age of one the odds are reversed.[12] Periurethral colonisation occurs when there is a disturbance of the normal microbial flora by a virulent organism.[13] During the initial months of a child’s life, periurethral colonisation is at its highest.[14] Evidence suggests that older children who present with repeated urinary tract infection suffer persistent periurethral colonisation.[15]

Periurethral Cleansing

Periurethral cleansing is a process in which tissue surrounding the urethra is cleansed prior to sample collection or urethral catheterisation. Periurethral cleansing is important to reduce contamination of midstream urine collection and contamination of urinary catheter during insertion. The literature is divided in determining the optimum approach to periurethral cleansing prior to urinary catheterisation and/or specimen collection. On the one hand the recommendation is to use a strict aseptic technique whilst others suggest that a simple clean non-sterile procedure is sufficient. Solution recommendations range from soap and water to antiseptic solution i.e. Chlorhexidine Gluconate or Povidone-iodine.[4, 6, 7, 16, 17] Antiseptics solutions are valued for their ability to destroy microbes or hinder their growth. However such solutions have their inherent limitations in particular the damage they cause to the delicate mucosa of the child’s periurethra.[18] The antiseptic solutions may irritate the skin and result in either a skin burn or superficial ulceration and result in discomfort during insertion all of which damages the inherent physiological barriers to infection. Antiseptics solutions have also been documented to bring about residual contamination of urine that in turn affects the accuracy of bacterial counts.[19]
The approach to urine collection and sampling varies across healthcare institutions. The cost and/or invasive nature of the device typically influence the choice. The practice in many institutions is to cleanse the periurethral area with some form of antiseptic solution e.g. 10% povidone iodine or Chlorhexidine Gluconate which are irritating to the periurethral and urethral mucus membrane, particularly in children, often causing skin ulceration, burns and inflammation.[18] Principle collection methods for mid stream urine sampling for the pediatric patient include adhesive bag sampling, urine collection pads, clean catch sampling, urethral catheterization, and suprapubic aspiration.[20]. Urine collection devices are somewhat challenging in terms of leakage and patient comfort. Prolonged exposure of a urine sample within a pad and the perineal flora and or periurethral colonization (which is at its highest during the first few months of a child’s life) are thought to significantly attribute to the urine contamination rates.[14, 20]

Concern exists over the potential for some collection techniques to mask infection i.e. the urine collection pad, by enabling heavy mixed growth of bacteria.[21] Such contamination rates can result in unnecessary investigation, i.e. greater need for re-sampling, thus increasing the child’s exposure to prolonged infection and risk of long-term renal disease.[21] The clean catch midstream technique has been reported to be time consuming to explain, error prone and therefore costly.[22] Data from adult studies have reported that there is no statistical difference between midstream clean catch and midstream non-clean catch urine samples.[23-25] Catheterisation and suprapubic aspiration as a rule are considered the most consistent method to obtain an uncontaminated urine specimen.[26] However, both methods are considered invasive and are most frequently performed on patients who are considered critically ill. Aspiration has been labeled as the gold standard method for urine collection.[27] Its popularity as a comparison to collecting methods was evident by the number of citations found in the initial literature review.

**Urinary Tract Infection (UTI)**

Urinary tract infection is one of the most common bacterial infections in children and can lead to significant morbidity, long-standing health related problems into adulthood and potential mortality.[1, 28] If the infection results in renal scarring, various long-term risks include hypertension, renal insufficiency and may proceed to terminal renal failure. Urinary tract infection therefore negatively impacts the individual’s quality of life with associated long-term health care cost.[29-34]
A urinary tract infection is a microbial infection of one or more components / organs comprising of the renal system, i.e. bladder, kidneys, urethra or ureters. Early diagnosis of urinary tract infection is paramount to preserve kidney function. The goal or primary focus of medical management is for prompt diagnosis, upon confirmation it is essential that treatment is commenced without delay. Delays in confirmation of diagnosis and treatment expose the child to greater chances of permanent renal damage. The severity of the child’s illness generally determines the course of medical management. Lindert et al based the need for hospitalized management on the following criteria, a child less than three months of age or unable to tolerate oral fluids / medications, immunocompromised, or dehydrated, as an inpatients they should commence treatment with parenteral antibiotics and rehydration therapy. The pharmaceutical cost associated with inpatient management is reported to be double that of outpatient management. Hospitalization of children diagnosed with urinary tract infection is necessary in up to 2-3% of all cases.

The literature suggests that children’s renal status should be investigated after their first confirmed urinary tract infection. Recurrent urinary tract infections may suggest abnormalities within the renal system or undiagnosed complications. The literature also suggests that the probability of infants (as opposed older children) presenting with underlying congenital genitourinary malformation are more likely to require additional medical follow up. The following three examples are discussed most extensively throughout the literature, urinary stasis, renal scarring and reflux.

Urinary stasis commonly refers to the obstruction to the flow of urine at any point within the renal system. Causative factors listed as being outflow obstruction, constipation, renal stones or bladder dysfunction.

Renal scarring, in some children renal scarring is link with future health complication i.e. poor renal development, recurrent infections, hypertension and end stage renal disease. Lindert, et al postulate that the degree of scarring is “dependent upon the age at which the child first sustained a urinary tract infection”. In a study conducted by Ditchfield et al they concluded that renal scarring was two times more likely in children with urinary tract infections under the age of two years. Jacobson et al conducted a retrospective study of 30 children diagnosed with renal scarring; ten percent of these children had progressed to end stage renal disease.

Reflux is a condition when urine moves from the bladder retrograde into the ureters or
Urinary tract infections in children are often hard to diagnose as symptoms are generally non-specific, consequently such infections are easily missed. General clinical signs and symptoms for children less than two years of age are described as fever or pyrexia of unknown origins, irritability, nausea and vomiting, diarrhea, failure to thrive. Children older than two are generally able to communicate symptoms such as supra-pubic tenderness or urine frequency. Similarly a child could present to a health care facility with an infection of the urinary tract however present as asymptomatic, i.e. with no clinical symptoms suggestive of infection. Infants who present to health care facilities with atypical symptoms of urinary tract infection are confronted with a greater chance in the delay of diagnosis. Therefore the younger patient populations are at greater risk in developing complications at result in aggressive medical management. A study undertaken in the United States in 2001 looked at using a clinical decision rule, i.e. the presence of 2 or more of 5 predetermined variables, a score of 2 or more lead to identification of 95% of children with UTI and removal of 30% of unnecessary urine cultures.

The internationally recognized standard for diagnosis of urinary tract infection is a urine culture. However collecting uncontaminated urine samples from children is often problematic. There are many clinical procedures / interventions that can be carried out to obtain urine sample for bacterial analysis. From invasive procedures such as supra-pubic aspiration, urethral catheterisation, to the less invasive techniques for example the clean catch or bag method. The different methods for urine sampling / collection are not without faults as all are just as susceptible to contamination. Pryles writes that in 1922 Helmholz and Milleken were among the first to conclude that the risk of urine specimen contamination during the collection process was “so great that the presence of organisms in the urine” was inconclusive of true urinary tract infection. The fundamental principle of all procedures is to ensure that the urine sample is not contaminated, by bacteria/viruses that are external to the body. The most effective approach to minimising contamination is performing periurethral cleansing.

The negative implications associated with contamination of urine samples are the false-positive or false negative results. Inaccurate urine collection may result in miss or over diagnosis of urinary tract infection and result in inappropriate hospital admissions for the non infected child. Of greatest concern is that we therefore expose children to either unnecessary
treatment / investigations or children fail to receive appropriate evidenced based health care in a timely manner to prevent renal damage.[48, 49] Both scenarios result in additional psychological stress to both child and family.[46] Contaminated specimens can fail to reveal true infections, resulting in the need to repeat the procedure and impacting the organisational financially.

**Socioeconomic Implications**
According to Spencer and colleagues the socioeconomic implication of pediatric urinary tract infections within the United States is considerable and rising at a rapid rate.[43] Within the last decade hospital admission rates (50,000 admission / year and length of stay (3.1 days ± 0.1 days) have stayed comparatively constant. From 2002 approximately 2% of all pediatric hospital admissions are directly linked to a urinary tract infection. [43] Data was extrapolated from the Kid’s Inpatient Database (KID) to produce a retrospective analysis of urinary tract infection with in the United States for children less than 18 years of age admitted to a health care setting with the primary diagnosis of urinary tract infection.

The KID data reports that there is a higher incidence of females requiring hospitalization than their counterpart. Additionally the probability of children less than 1 year of age requiring hospitalization is 2.5 time more than older children.[43] This was substantiated by two independent community studies that stated children less than 1 year of age are more predisposed to developing a urinary tract infection than older children.[50, 51] Boys less than 1 year of age have a greater risk for urinary tract infections than girls (2.7% versus 0.7%) cited in Lindert.[12] Uncircumcised infants are 10 times more likely to develop a urinary tract infection before 6 months of age when compare to circumcised boys.[52] Major causes contributing to the expanding health care costs have been linked to avoidable hospitalization and inappropriate or delays to commencement of treatment. The financial impact for United States hospitals and pediatric inpatient urinary tract management in 2006 exceeded $520 million.[53]

**Bag Collection**
The bag collection method is where a sterile urinary collection bag is attached to the child’s perineum, this technique is generally reserved for babies and infants. Once the child has voided the bag is removed and the urine is collected for analysis. Bagged urine collections are clearly the most convenient and without question the least invasive however, contamination rates are as high as 10%.[54] False positive rates have been reported as high as 50-60 %.[55] Regardless of meticulous periurethral cleansing and timely removal of the collect bag, Crain et
In 1976, a group of 30 sick infants and children were enrolled into a study that over a course of 6 hours collected three urine specimens (bag, clean catch and supra-pubic aspiration). Following microbiological analysis of the specimens the authors concluded that bag collection was considerably inferior to clean catch and supra-pubic urine sampling techniques. A study conducted by Al Orifi et al comparing contaminated urine specimens obtained by clean void bag method versus urethral catheterisation concluded that risks associated with bag urine cultures fails to surpass the benefits. Additionally they were able to demonstrate that despite close monitoring i.e. timely removal of collected specimen, it did not reduce the contamination rate.

**Midstream**

Midstream urine sampling was introduced into the health care arena during the later part of the 1950s. Prior to that urinary catheterisation was seen to be the customary approach for urine specimen collection. Midstream urine sampling procedure commenced as the result of two publications challenging the benefits associated with urinary catheterisation. Midstream urine sampling techniques have been reported in the literature as either clean catch or non-clean catch. Clean catch urine specimen involves periurethral cleansing prior to specimen collection. Non-clean catch urine collection is without periurethral cleansing. Both midstream urine collection methods require the child to void into a sterile specimen container. It is commonly acknowledged that despite how meticulous the technique / procedure is undertaken, these specimens are commonly contaminated by periurethral flora. This urine collection technique is not easy to perform on young child and is generally set aside for older children who are able to follow set instructions. Contamination risk associated with midstream procedures is parents or the child inadvertently contaminating the interior of the sterile collection container.

A study conducted by Amir et al compared results of urine cultures from midstream urine collection to that of supra-pubic aspiration from circumcised male infants. Prior to collecting the midstream urine sample the penis was cleansed with an antiseptic solution 0.05% cetrimide plus 0.01% chlorhexidine gluconate. Interestingly the results produced more or less identical finding. However, it is emphasized that the reliability is limited to only circumcised males as results of from uncircumcised infants were noted to be erroneous. Lohr et al conducted a study to review the effects of meatal cleansing and midstream urine contamination rates from
The study compared clean catch and non-clean catch technique and concluded that neither form of periurethral cleansing had significant effect on the rate of positive cultures. These results are further supported by a study conducted on females aged 14 years and above. Participants were either assigned to a clean catch or a non-clean catch midstream collection technique. The results demonstrated that periurethral urethral cleansing failed to significantly lower contamination of midstream urine samples from perineal flora. However, results of a study undertaken by Vaillancourt et al, whom like Lohr et al compared clean catch and non-clean catch in toilet trained children, suggest that the perineum should be cleaned with soap prior to midstream urine collection.

**Urethral Catheterization**

Urethral catheterization requires that a drainage tube (catheter) to be inserted via the urethra into the bladder. Urethral catheterization is frequently performed on those patients unable to follow instruction on performing midstream urine collection. The advantage of performing urinary catheterisation to acquire urine sample is that the success rate come within reach of 100%. Similarly urine specimens collected from urinary catheterization are not without risk of contamination from periurethral flora. It is recommended that the first few milliliters of urine be discarded. A risk factor associated with urinary catheterization is that as a direct result of the insertion process the sterile bladder maybe become inoculated with bacteria, resulting in an iatrogenic urinary tract infection. There is a high correlation with this iatrogenic infection and the catheterisation of uncircumcised boys. Lindehall et al identify urethral trauma in boys as a major complication to urinary catheterisation. Although the incidence is minimal, Turner reports of catheter knotting as a complication to urinary catheterisation. Generally the procedure is regarded as unpleasant, painful and challenging to carry out on young children, all of which exacerbates child and parental anxiety. Adult data suggests that each day a urinary catheter remains insitu there is in the region of a 5% increase risk for the development of a bacteriuria. To date there has only been one study conducted on the pediatric population that compares urinary infection rates with two types of cleansing solutions. However significant research has been undertaken to determine the effects within the adult population. Three studies, two relatively recent compared periurethral cleansing in adults with water and a antiseptic solution, the results demonstrated that later does not reduce the incidence or risk of urinary tract infection.

**Supra-pubic Aspiration**

In order to collect a urine sample from the bladder via supra-pubic aspiration, a needle is
inserted just above the symphysis pubis. This technique was first reported in 1956 by Guze et al.[68] Supra-pubic aspiration is frequently referred to as the reference or gold standard method for urine collection.[69, 70] The success rate associated with blind aspirations varies between 25 to 60%. As a means to overcome the low success rate, O’Callaghan recommended the use of portable ultrasound.[71] Additional shortcomings are firstly the procedure is painful and secondly it is not without complication. The most frequently identified complication is bleeding and supra-pubic hematoma.[72-74] Additional complications reported have been identified as the following, supra-pubic abscess and bowel perforation.[75-77] Urine sample collected from this technique cannot be considered contaminated from periurethral flora as the needle is introduced directly into the bladder rather than being exposed to the urethra.[12] Consequently, the detection of any micro-organisms in a urine sample collected from a supra-pubic aspirate is commonly referred to or diagnosed as significant bacteriuria.[70] The likelihood of a confirmed diagnosis of urinary tract infection from urine obtained from supra-pubic aspiration is approximately 99%.[11]

**Processing of Urine Cultures**

It is recommended that once a urine sample is collected then the specimen is transported to a microbiology facility for processing within two hours, or stored at 4°C during the transportation to a testing facility. Without careful attention being paid to these guidelines on sample transport and storage, proliferation of pre-existing bacteria within the urine, resulting in inaccurate colony counts can result. In order to inoculate the urine specimen onto the agar plate, laboratory staff use calibrated loops. It is essential that these loops are routinely inspected and calibrated, as even fine adjustments can result in considerable errors.[78] Cultures are generally examined from anywhere between 18 to 24 hours and at 48 hours of incubation. Results of the culture are expressed as colony forming units per millilitre (cfu/mL). Clinician’s engage in research are beginning to challenge the universally accepted diagnostic threshold developed by Kass in 1957. A recent report makes reference to Kass’s criteria being too low and as a consequence there is a ~ 7.2 % false positive rate. The recommendation is to increase the threshold from ≥105 to ≥106 cfu/ml which could help to reduce the rate of false-positives samples and their associated costs (fiscal and quality of life) to the patient and healthcare institution.[78]

**Key Definitions**

The CDC defines UTIs as, when a patient presents with either symptomatic urinary tract infection or asymptomatic bacteremic urinary tract infection criteria.[29] In the United States in 2002, adults and children outside of intensive care units represented 32% of all healthcare
associated UTIs. UTI can be classified as being associated with or without urinary catheter placement (see appendix 7 for UTI criteria). According to the Center for Disease Control and Prevention (CDC), 30% of all infections reported by acute care hospitals are urinary tract related, with the majority of these associated with urinary catheterisation.[79, 80] Urinary catheterisation occurs when a drainage tube (catheter) is inserted via the urethra into the bladder. Urinary catheters are connected to a closed collection system and the duration of placement is generally dependent upon catheter selection. Urinary catheter placement falls within two categories - short term or long-term urethral catheters. Catheter placement less than 30 days is generally considered short-term catheterisation. Additionally urinary catheterisation can be performed as an intermittent procedure. A disposable urinary catheter is inserted into the bladder, which allows for urine to drain. This procedure is repeated several times a day and is generally undertaken by the patient as a clean technique.

Nosocomial urinary tract infections in children occur with varying frequency, with approximately 60-80% of these infections being strongly correlated with urethral instrumentation.[8, 9, 34] Infections which develop as a direct result of urethral catheterisation are commonly referred to as Catheter Associated Urinary Tract Infections (CAUTI). Catheter associated urinary tract infections continue to be a major cause of mortality in hospitalized patients.[28] Statistics from the 2006 National Health & Safety Network identified the mean CAUTI rate to be 3.1-7.5 infections per 1000 catheter days.[81] Statistics comparing Healthcare Associated Infection (HAI) and mortality in 2002 demonstrated that UTI equates to the greatest number of infections of all HAI.[79] Risk factors associated with the development of a nosocomial urinary tract infection have been identified as duration of catheter placement, females, no systemic antibiotic cover and catheter and drainage bag disconnection.[82] The literature search identified the few studies have published on the incidence of nosocomial urinary tract infection within the pediatric population.[83, 84]

Escherichia Coli and Candida species of bacteria continue to be identified as the two major pathogens associated with pediatric UTI’s.[85] Whether from endogenous or exogenous sources, the infecting microorganisms gain access to the urinary tract by several routes. The normally sterile urinary tract is defended from infection by several complementary activities: “normal flora” living on intact mucosa; a competent immune system; and frequent and complete voiding of urine.[34, 86, 87] Microorganisms that comprise the “normal flora” of the meatus or distal urethra can be introduced directly into the bladder when a catheter is inserted. With indwelling catheters, infecting microorganisms can migrate to the bladder along the internal
lumen of the catheter after the collection bag or the catheter-drainage tube junction has been “compromised” and contaminated in the process i.e. during drainage bag changes or accidental dislodgement etc.[88]

International consensus on infection prevention recommendations focus on prevention strategies such as limiting urinary catheter use, adhering to aseptic technique during catheter insertion and care and maintenance of a closed system with unobstructed urinary flow.[8-10, 34, 86] The implementation of the above recommendations in reducing CAUTI in terms of infections and mortality equates to 380,000 less infections and 9000 preventable deaths annually.[89] Saint and colleague’s research in 1998 look at the efficacy of silver alloy-coated urinary catheters in preventing urinary tract infections. The results from a meta-analysis demonstrated these catheters to be effective in preventing bacteriuria.[90] Silver alloy-coated urinary catheters are not routinely placed in children, consequently there are no report studies.

To date considerable research has been published regarding adults and CAUTI best practice recommendations. However, when reviewing the literature regarding the procedures for catheter insertion, there is a lack of quality, summarized evidence related to periurethral cleansing for the prevention of catheter-associated urinary tract infections in pediatric patients and further research is recommended.[34] Likewise there is no general consensus where to clean or not to clean and the overall effects on contamination rates of midstream urine collection.

**Conclusion**

Following a search of Medline, Cinahl, Cochrane and the JBI library of systematic reviews, no systematic reviews regarding pediatric urinary catheterization or midstream urine collection were identified as being published or underway on this topic.

In order to ensure our pediatric population is receiving evidence based health care, it is prudent to systematically review the existing research to determine the most suitable periurethral solution to be utilised in the process of midstream urine collection and urinary catheterisation. Determining what the evidence base is has long-term benefits towards reducing the rates of UTI and contaminated urine samples. All of which helps to reduce the cost (fiscally and quality of life) associated this area of care for the pediatric patient.
Chapter 3. Study Design and Methods

This chapter provides detail about the JBI-MAStARI method used to conduct this systematic review. This reviews objectives, inclusion and exclusion criteria, as well as primary and secondary outcomes are discussed in the following sections. Of note is the change in practice across the decades in how to best define UTI and therefore measure the effectiveness of various interventions on reducing UTI and/or contamination of mid stream urine samples. In the 1980s a positive urine culture was defined as growing at least one urinary tract pathogen with a colony count of > 104 CFU/ml of urine.[61] In 2009 the CDC’s definition reflects a greater appreciation of the complexity in measuring a UTI. The CDC standards are broken into 5 categories as detailed in Appendix 7. Discussed is the impact that this variance in the measurement of UTI (the primary outcome of interest for this review) has had on the number of research studies that met the stated inclusion criteria for this review.

JBI-MAStARI method of conducting a Systematic Reviews

The Joanna Briggs Institute for Evidence Based Healthcare has been a constructive voice amidst the global conversation on evidence based healthcare. The JBI Institute promotes a broader view of evidence, and in doing so has developed theories, methodologies and rigorous processes for the critical appraisal and synthesis of these diverse forms of evidence in order to aid in clinical decision-making in health care. These processes relate to the synthesis of quantitative evidence, qualitative evidence, the results of economic analyses and expert opinion and text.

The JBI-CReMS software has a number of analytical modules which are chosen according to the type of research methods accepted to be in the review. The primary outcome of a systematic review is the presentation of the best available evidence for the question being asked. To achieve this outcome requires a concise question that has been structured according to the acronym PICO which stands for Patient/Intervention/Comparison/Outcome.

The question in turn structures the review protocol which includes a clearly stated objective(s), inclusion and exclusion criteria plus primary and secondary outcomes of interest. The existing literature and research on the subject should inform the content of the protocol. Nevertheless, a common experience for authors conducting systematic reviews is determining which outcome(s) best demonstrate the effectiveness of the intervention under review.

Given that this review questions was about determine the evidence base for the effectiveness of an intervention: ‘type of solution used to cleanse the periurethral area prior to insertion of a
catheter or collection of urine sample' the research methods best able to answer this question are experimental in design. The JBI-CReMs analytic module recommended for analyzing the data from experimental studies is JBI-MAStARI. JBI-MAStARI is designed to assist with the following critical steps of a systematic review.[91]:

**Critical appraisal of the studies retrieved,**

- Extracting data from the primary research regarding participants, the intervention, the outcome measures and results.

Pooling the results. Statistical analysis (meta-analysis) occurs according to the quality of the included studies. If pooling of data from different studies is not possible then the JBI-MAStARI recommended approach is to provide a narrative summary of the results. This narrative summary is critical for informing the reader about the current state of evidence for the question in hand.

The following headings are reflective of the protocol structure and standards as set out in the JBI-CReMS software for systematic reviews. The software guides the reviewer to conduct their review according to the rigorous standards held by the JBI Institute. The JBI systematic review process begins with the development of a proposal or protocol that is peer reviewed and approved by the Institute. A rigorous and extensive search of the international literature on the review question is undertaken, which are then assessed for their applicability to the question and appraised using standardised tools to ensure that only the results of the highest quality research are included in the final review. Formal training is required for the successful use of the JBI-CReMs software. This training occurred as part of the course work for the successful completion of the Masters of Clinical Science, of which this thesis is the final assessment.

**Review Objective**

The objective of this review was to synthesize the best available evidence related to periurethral cleansing solutions to prevent contamination of mid stream urine collection and/or catheter associated urinary tract infection in pediatric patients.

**Inclusion criteria**

**Types of participants**

There is no general consensus regarding the upper age range when defining pediatrics. The American Academy of Pediatric policy identifies pediatrics from the foetus to 21 years of age.[92] This review considered:
• Studies involving children from the age of 1 month to 18 years with a short-term indwelling urethral catheter. Short-term catheterisation is defined as less than 30 days of catheterisation in any hospital setting.
• And / or children from the age of 1 month to 18 years who require midstream urine sample in any controlled environment supervised by medical personnel.

**Interventions**
Any cleansing solution e.g. Soap, 10% Povidone-Iodine, Sterile Water, Chlorhexidine Gluconate or saline.

**Comparators**
Any alternate method (solution or no solution) to the intervention.

**Primary Outcome**
The primary outcome of interest was the incidence of urinary tract infection, as determined by urine culture.

For the purposes of this review, urinary tract infection is defined as:

- >105 colony forming units (CFU)/mL of urine
- >104 CFU/mL, with clinical indicators of UTI i.e. Pyrexia (≤38°C) or suprapubic tenderness.
- Bacteriuria >103 CFU/mL. [93]

Or

For studies completed after January 2009, use of the criteria established by the CDC (Appendix 8).[29] For the purpose of this review bacterial contamination is defined as:

- A culture growing one organism with >104 CFU/mL urine is defined as a positive culture.

**Secondary Outcome:**
The presence of urethral meatus trauma i.e. burns, redness

**Type of studies**
This review considered randomised controlled trials that report the incidence of catheter associated urinary tract infections and compare periurethral cleansing solutions prior to catheterisation. Meatal cleansing and the rate of bacterial contamination of midstream urine samples. In the absence of RCTs other research designs, such as non-randomised controlled
trials, surveys, case control, and observational, will be considered for inclusion to enable the identification of current best evidence regarding the effects of periurethral cleansing on urinary tract infection and specimen contamination rates.

**Exclusion criteria**
- Studies involving anti-microbial impregnated catheters
- Children currently receiving antibiotic therapy
- Immunocompromised patients
- Paediatrics under 1 month of age

**Search strategy**
The search strategy was designed to find both published and unpublished studies. A three-step search strategy was utilized:

1. An initial limited search of MEDLINE and CINAHL was undertaken followed by
2. Analysis of the text words contained in the title and abstract, and of the index terms used to describe article. A second search using all identified keywords and index terms was then undertaken across all included databases.
3. Finally, the reference list of all identified reports and articles was searched for additional studies.

English was the only language considered

**Databases Searched**
The principle databases used to collate healthcare research publications and reports were searched for this review:

- CINAHL
- MEDLINE
- Embase

**Unpublished studies or Grey Literature**
A well appreciated form of bias in healthcare research is what is referred to as publication bias. Prior to the error of evidence-based healthcare the preference of researches and journals is to only publish positive outcomes. A systematic review therefore needs to demonstrate the process for minimizing publication bias. It is therefore important to demonstrate how unpublished research was accessed.
Academic thesis or dissertations are a good point to commence this search for the grey literature and two excellent databases have been established to collate this research:

- Dissertation Abstracts International
- Mednar

Initial keywords used:
Using the acronym PICO helps to establish the core concepts and therefore the key words used to build the search strategy used for the systematic searching of the subject matter databases listed above. The key words chosen to focus the search strategy for this review were:

- Urinary
- Catheter
- Bladder catheterization/catheterisation
- Cleaning solution
- Anti-septic/antiseptic solution
- Children
- Pediatrics / Paediatrics
- Infants
- Urinary tract infection
- Periurethral
- Perineal cleansing
- Midstream clean catch
- Midstream clean collection
- Contamination rates
- Clean void urine
- Urine culture

Methods of the Review

Assessment of methodological quality
Just because it is published does not mean it is valid research! Recommendations that are based on published research can be of different quality. The credibility of a systematic review is dependent on the criteria used to assess the internal and external validity of the included studies. Since poor quality evidence can lead to recommendations that are not in the patients
best interest, it is essential to know whether a recommendation is strong (we can be confident about the recommendation) or weak (we cannot be confident).[94]

The process to critically appraise the methodological quality for this review was threefold:

1. Papers selected for retrieval were assessed by two independent reviewers
2. The use of a standardised critical appraisal instruments comprised of ten questions from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument (JBI- MASTARI) (Appendix 3)
3. According to the results of the critical appraisal each paper was graded accordingly:
   i.   Low : < 5/10 ii.   High: > 5/10

Any disagreements that arose between the reviewers were resolved through discussion, or with a third reviewer.

Data collection
The outcomes for a systematic review are dependent on the raw data derived from published or unpublished research reports. If the required data is not available every effort is made to contact the primary authors to determine if they can forward to the review authors the required data. A structured data extraction tool from JBI-MAStARI (Appendix VI) was used by each review author to extract the required data for this review. The data extracted included specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

Data synthesis
The primary benefit of a systematic review is in its ability to synthesis (combine) the data from a number of individual studies towards increasing the number of participant data available to determine the overall estimate of effect. Data synthesis however can only occur if the individual studies are similar in participant sample, research method and analysis. If the individual studies are disparate in these criteria then a high degree of heterogeneity is introduced into the review sample- often likened to trying to compare apples with oranges.

Data synthesis was only possible for 2 of the 3 included studies in this review. [95, 96] (see Table 1 below which displays Meta Synthesis) To minimize data entry errors, two people entered the results on separate occasions into the JBI MASTARI database. Given that the data type for these studies was categorical, relative risk was used to produce a combine estimate of
effect for the type of periurethral cleansing solution used to reduced the rate of contamination during mid stream urine collection. Heterogeneity was assessed using the standard Chi-square test. Given that only one RCT was included in this review no pooling of data was possible and therefore the results are presented in narrative form.

Conflicts of interest
There was no actual or perceived conflict of interest associated either with the topic selection, or the methods used to undertake the systematic review.

Conclusion
This chapter presented the JBI-MAStARI method used to conduct this systematic review. JBI systematic reviews begin with the development of a proposal or protocol that is peer reviewed and approved by the Institute. A rigorous and extensive search of the international literature following a three step process is undertaken in the subject matter databases best suited for the question being asked. Once located the studies are assessed for their applicability to the protocol criteria and appraised using standardised tools to ensure that only the results of the highest quality research are included. Clarification of the inclusion and exclusion criteria in addition to details about data collection and synthesis according to the JBI standards was provided.
Chapter 4: Results

Introduction
Chapter four reports the results of the systematic review, describing the studies, both included and excluded, and the conclusions extracted, according to their levels of credibility. The results of the synthesis are reported by presenting data from the randomized control trial in narrative form, whilst the two descriptive studies are discussed by interpreting the results of the forest plot for the meta-analysis depicted in Figure 2.

Description of studies
To date, the majority of studies available in the literature that address this question for the pediatric patient are descriptive in nature. On the hierarchy of evidence for clinical effectiveness, descriptive studies sit at a level 3 to 5. The type of research design classified as descriptive are:

- Case controlled studies
- Cohort Studies
- Case Series and Case Reports

Changing clinical practice on level 3-5 is not recommended. The systematic search of suitable studies to include in this review commenced in May 2010 to April 2011. A research librarian was consulted in the initial stages of planning, and the search strategy is detailed in Appendix 5. From the search of the literature a total of 414 articles were identified as potentially relevant to the review. The titles were screened and those that were not relevant were eliminated. Forty-six papers were duplicates and therefore eliminated.

From 368 articles, 8 were assessed in detail against the protocol eligibility criteria. Of the eight additional data was needed for three of the studies before they could be included. Attempts to seek clarification by contacting the author were unsuccessful, resulting in the exclusion of three studies. The primary reason for exclusion was that efforts to obtain data on the pediatric participants of their individual studies were unsuccessful. Using the methodological quality criteria available in MASTARI two studies were considered for exclusion, as they rated low.

An additional four articles were identified through hand-searching which included the following steps:

- Identification of leading professional journals/books
• Carefully review of the table of contents
• Carefully review of reference list/bibliography of included articles

One of these was a literature review comparing sampling techniques but with no mention of periurethral cleansing [20]. The other three required additional information:

1. the population studied by Unlu et al [57] was aged 18 - 73 years.
2. the population studied by Schlager et al [25] was aged 10 - 19 years; data were requested between 10 to 18 years.
3. the population studied by Bradbury et al [97] was aged 16 – 75 years; data was requested from 16 to 18 years.

Additional data was sought from each of the primary authors however all efforts were unsuccessful, resulting in the final exclusion of these three studies.

The study selection process is illustrated in Figure 1; a total of only 3 studies met the inclusion criteria: one randomized control trial (RCT) [7] and two descriptive studies [95, 96] These three studies were conducted in Canada [7], Costa Rica [96] and the United States of America [95] and were published (in English) between 1986 and 2009. Details of the excluded studies are shown in Appendix 4. An additional search was undertaken by reviewing the references cited in each of the included articles. No articles reviewed at this time were included in the review.

The two descriptive studies used the same inclusion criteria and the same definitions for a positive culture – i.e. a culture growing one organism with ≤10⁴ CFU / ml urine. Similarly the collection of clean catch urine was followed in both these studies by meatal cleansing with 2% Castile soap. Meta-analysis was conducted only on the two descriptive studies.
Citations (records) identified through database searching:
Midstream urine collection n= 255
Urinary catheterization n= 159, Total n= 414

Studies excluded after duplication:
Midstream urine collection n= 9
Urinary catheterization n= 37 n=46
Total n= 46

Studies excluded after review of title and abstract, and failure to meet eligibility criteria:
Midstream urine collection n= 239
Urinary catheterization n= 121
Total n= 360

Full text retrieved against eligibility criteria:
Midstream urine collection n= 7
Urinary catheterization n= 1 n=8

Studies meeting all eligibility criteria:
Midstream urine collection n= 2
Urinary catheterization n= 1

Studies excluded as did not meet eligibility criteria:
Midstream urine collection n= 5
Urinary catheterization n= 0 n= 5

Final number of studies retrieved meeting all eligibility criteria and assessed for methodological quality:
Midstream urine collection n= 2
Urinary catheterization n= 1, Total n= 3

Additional studies retrieved from hand search:
Midstream urine collection n= 4
Urinary catheterization n= 0
Studies included n= 0

Studies included:
Midstream urine collection n= 2
Urinary catheterization n= 1
Total n=3

Figure1: Flow diagram of the search results and study selection of the studies
**Methodological quality**

Of the three studies that fulfilled the protocol inclusion/exclusion criteria, two are classified as descriptive/case-series according to the appraisal criteria in MAStARI and one a randomized control trial.[7, 95, 96] Overall the three studies lacked rigor in their design and reporting of outcomes. Within the randomized control trial, study allocation concealment was undertaken by means of a computer generated number sealed in an envelope[7]. However, no details are provided in the published report about how or if blinding of the outcome assessors and intention to treat analysis were carried out. The data for all enrolled participants were included in the analyses and final results. Demographic data and clinical presentations were noted to be similar in both groups. There was no indication that there had been any prior effort to estimate required sample sizes using power analysis, and reported patient sample sizes were similar across all three studies. The two descriptive studies failed to demonstrate appropriate use of statistical analysis[95, 96] and they lacked clear descriptions of demographics, cultural and socioeconomic backgrounds. All the included studies had small sample sizes and the sampling method was not clearly stated. The RCT study received ethics approval from their institutional review board and participant consent was obtained prior to study enrollment[7]. Both descriptive studies lacked clear identification of confounding factors and/or strategies incorporated to deal with them, and only one documented that written consent was obtained.[96]

All collected urine samples in the RCT were sent immediately to an onsite microbiology laboratory for processing. When Lohr et al, collected urine samples at a local elementary school, they were immediately stored on ice and transported to the same facility within one hour of collection.[95] In addition to urine cultures, two of the included studies [7, 95] completed a urinalysis as an additional means of determining the presence of infection. All urinalyses by Lohr et al [95] were negative despite 3 producing positive urine sample cultures. The breakdown analysis of positive cultures by Al Farsi et al [7] is unclear in its description of what percentage were negative for leucocytes and nitrates when assessed via urinalysis dipstick.

**Sample sizes**

The study by Al Farsi et al [7] recruited one hundred & eighty-six consenting pediatric patients. The two descriptive studies [95, 96] together recruited, two hundred & one pediatric patients. The number of pediatric patients in each of the three studies ranged from ninety-nine to one hundred & eighty six, with the total number of three hundred & eighty seven pediatric patients.
Study setting
The randomized control trial comparing periurethral cleansing solutions prior to urinary catheterization was conducted within an Emergency Department of a tertiary care pediatric hospital in Toronto, Canada. [7] This department performs approximately 2,000 urinary catheterisations per year [7]. The two descriptive studies were conducted in the following settings: Pediatric Clinic in Costa Rica [96], Children’s Medical Centre Clinic and a local elementary school within the United States.[95]

Pediatric patients
The question of whether or not circumcision has an effect on the contamination rates in mid-stream urine collection was raised by the results of the 1986 study by Lohr et al [95], since only 4% of the sample population were circumcised. In 1988, Saez-Llorens et al [96] reported results from 99 uncircumcised boys with the conclusion that circumcision had no negative effect on the rate of contamination post-meatal cleansing. Information such as demographics, ethnicity, socioeconomic and cultural background of study participants was not consistently provided. The three included studies met the inclusion/exclusion criteria for age and the condition that the children were not receiving antibiotic therapy. The boys ranged in age from two to fifteen years in both descriptive studies.[95, 96] Eighty-seven percent of the participants studied by Al-Farsi et al were under 12 months of age [7]; this indicated that the relevance of female patients was slightly higher (55%).[7] One study reported reasons for excluding children who failed to meet the inclusion criteria; the main reason for exclusion was they were considered very ill and any delay to acquire consent was considered unethical.[7] Of the three studies reviewed here, the number of different pathogens isolated from the urine cultures varied from one to seven, with no single pathogen identified across the three study groups; however Al-Faris et al [7] reported that E. coli was the most common pathogen identified and seen in both their control and comparison groups. This is comparable to what is reported elsewhere in the literature.[85]

Solutions
Al Farsi et al [7] studied urinary infection rates in children whose periurethral area was cleansed prior to urinary catheter insertion with either sterile water or 10% povidone-iodine.[7] The principle reason for urinary catheterization is this study was to acquire a urine sample for the analysis and diagnosis of a urinary tract infection. The two descriptive studies undertaken by Saez-Llorens [96] and Lohr et al [95] were undertaken to ascertain whether or not meatal cleansing influences the rate of bacterial contamination of midstream urine specimens.[95, 96]
Periurethral cleansing was achieved with the use of a 2% Castile soap. The culture media within the two descriptive studies were identical, using trypticase soy agar with 5% sheep blood and MacConkey agar.[95, 96]

**Techniques of Periurethral Cleansing**

The randomized control trial required participants to undergo urethral catheterization.[7] Standard hospital protocol for urinary catheter insertion was followed in both the sterile water and Povidone-iodine groups. The patients were placed in a dorsal recumbent position with knees bent and soles of their feet together.[7] The sterile drape was positioned to ensure the periurethral/urethral meatus area was visible. The catheter tip was lubricated and the non-lubricated end was positioned to ensure that the urine sample drained into a sterile collection container. The labia minora were separated during the cleansing process of all female patients. To expose the urethral opening of those uncircumcised patients gentle tension was applied to the foreskin. Al-Farsi details that in both groups the perineal area was swabbed from front to back, center to outward 3 times, and the tip of the penis was cleaned from the urethral opening backward toward the body 3 times with cotton balls soaked in either 10% Povidone-Iodine or sterile water.[7] The urine sample was immediately tested within the emergency department and transported to microbiology for relevant processing.

Saez-Llorens et al [96] replicated the same study method undertaken by Lohr et al [95] for urine specimen collection obtained with and without mental cleansing; the only difference was that the patient populations studied by Saez-Llorens et al were uncircumcised. Prior to urine specimen collection, participants from the study by Lohr et al [95] were individually instructed by health care personnel on the procedure for midstream urine collection but unlike the patients studied by Saez-Llorens [96] during the collection process not all participants were supervised. The first urine sample was without mental cleansing and designated as a non-clean-catch urine sample. The specimen was collected in a sterile wide-mouth container with a screw-lid. The second specimen was collected following mental cleansing with 2% Castile Soap and designated as a clean-catch urine sample. Because the patients studied by Saez-Llorens et al [96] were not circumcised, the foreskin was retracted prior to mental cleansing and specimen collection. If the child suffered from Phimosis (the foreskin cannot be fully retracted over the glans penis exposing the urethral opening), mental cleansing could not take place [96]. The procedure was performed using a standard prepackaged urine collection kit. In both studies the second specimen was collected between 24 and 30 hours after the initial sample.
<table>
<thead>
<tr>
<th>Study one</th>
<th>Study two</th>
<th>Study three</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Author</strong></td>
<td>Al-Farsi et al, 2009</td>
<td>Saez-Llorens et al. 1988</td>
</tr>
<tr>
<td><strong>Research Focus</strong></td>
<td>Urinary catheterisation</td>
<td>Mid Stream</td>
</tr>
<tr>
<td><strong>Study Design</strong></td>
<td>RCT</td>
<td>Descriptive</td>
</tr>
<tr>
<td><strong>Study population</strong></td>
<td>N=186; Canada</td>
<td>N=99, Costa Rica</td>
</tr>
<tr>
<td></td>
<td>Males: 78</td>
<td>Males: 99</td>
</tr>
<tr>
<td></td>
<td>Female: 108</td>
<td>Uncircumcised:99</td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Sterile Water: n = 92</td>
<td>No peri urethral cleansing</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>10% Povidone-Iodine: n=94</td>
<td>2% Castile Soap &amp; Water</td>
</tr>
<tr>
<td><strong>Outcome measures</strong></td>
<td>Rate of UTI as/ 50 x 10⁶ CFU/ L</td>
<td>CFU* &gt; 10⁴/ml urine</td>
</tr>
<tr>
<td><strong>Intervention results</strong></td>
<td>18%</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Comparator results</strong></td>
<td>16%</td>
<td>2%</td>
</tr>
<tr>
<td><strong>P Value</strong></td>
<td>0.03</td>
<td>0.2 (Fisher)</td>
</tr>
</tbody>
</table>

Table 1: Individual study data and results (*CFU: Colony Forming Units)

A Forest Plot (Figure 2) was used to analyze the data from the two descriptive / case-series studies. This shows that the Risk Ratios and the associated 95% confidence intervals the two individual studies are 1.00 (0.14, 6.96) [95] and 1.15 (0.07, 18.06) [94]. According to these analyses, neither study was able to demonstrate a significant clinical effect. Judging from the large confidence intervals associated with these studies, both studies would appear to be significantly underpowered, so that their results are inconclusive. The results from a meta analysis shown in the same figure support the findings of the individual studies. The overall Risk Ratio is 1.05 (0.21, 5.11), and although the p-value is extremely non-significant (p=0.9602), nonetheless the wide confidence limits indicate that no firm conclusions should be derived from these results.
Conclusion

This chapter provided a detailed discussion of the methodological quality and synthesis of the included studies. Overall the methodological quality of the included studies is rated as poor, primarily because of the paucity of raw data from published research reports. This chapter highlights the lack of methodologically sound research available to direct the decision-making efforts of healthcare professionals related to the most effective method for periutethral cleansing in the pediatric patient.
Chapter 5: Discussion and Conclusions

Introduction
This review has focused on the study of the best available evidence for determining the optimum method and solution for (i) periurethral and (ii) periurethral cleansing in the management of midstream urine sample contamination and the prevention of catheter-associated urinary tract infection respectively, in pediatric patients.

The paediatric patients included in the three reviewed studies were aged between a few weeks and 15 years, with most being under 12 months of age in the study conducted by Al Farsi et al.[7] Two included studies evaluated or investigated the effects of periurethral cleansing on contamination rates midstream urine collection and one study compared two different cleansing solution.

Three articles met the required inclusion criteria. In two of the studies, midstream urine specimens were collected from healthy male children. Each study provided clear criteria to specify a urine specimen as being positive, contaminated or sterile [7, 95, 96] although the analyses undertaken in this review only focused on positive results. One study within the review compared urinary infection rates and periurethral cleansing with sterile water versus an antiseptic solution. Within the two other (descriptive) studies, intervention and comparator and therefore allowing a meta-analysis to be conducted to determine the affects of meatal cleansing and the rate of contamination in midstream urine specimens.

The primary outcome measured was the incidence of urinary tract infection, as determined by the colony forming units in the urine culture. The results of the two studies included in the meta-analysis are represented in the Forest Plot of Figure 2. Of note is the fact that both studies used the same research protocol and analysis but in two different population [96] is a replication of the other.[95] The combined relative risk (RR) calculated for the two studies is 1.05, however the p –value is non-significant and therefore there is no evidence of a genuine effect. Neither of these studies included female patients which raises the question if there is a gender difference in the presentation and management of this condition. The only available RCT concludes with the statement that sterile water is not inferior to 10% Povidone-Iodine for cleansing in the periurethral area prior to bladder catheterisation in infants and children.[7]p659

However, this recommendation is based on a single study, which was substantially underpowered. As only 3 studies were included in the review this clearly demonstrates there is an urgent need for further research in the pediatric population on the use of appropriate periurethral cleansing prior to urinary catheterization and midstream urine collection.
Implications for Practice
Given the findings from this review there is some evidence to suggest that implementing the following interventions would not negatively impact the quality of patient outcomes.

Periurethral Cleansing Prior to Urinary Catheterisation
The rates of UTI when using sterile water versus 10% povidone-iodine as the cleansing solution prior to urinary catheterization are comparable. The same outcomes have been found in the adult based research for example three different studies conducted by Cheung et al.; Webster et al. and Nasiriana et al [4, 6, 67] demonstrated that there was no increase risk of acquiring a urinary tract infection if periurethral cleansing was undertaken with potable water. Consequently, if there is no associated risk of developing a urinary tract infection when cleansing with sterile water, the cost benefit in the form of both fiscal (cost of antiseptic solutions) and quality of life (non irritant of periurethral mucosa) is worthy of consideration. In addition, in countries where the accessibility to antiseptic solutions is limited, this evidence is worthy of further investigation through a large well-designed RCT.

Bacterial contamination of mid stream urine collection
The available research in this area considered suitable to include in this review was conducted in pediatric males either circumcised or not with a meta-analysis demonstrating a non-significant trend in favor for no cleansing solution required. These studies are descriptive in design and therefore sit at a level of evidence 3-5. A change in clinical practice is therefore not recommended.

Implications for research
Despite the fact that the results favour periurethral cleansing with sterile water as opposed to an antiseptic based solution when performing urinary catheterisation and that meatal cleansing does not significantly decrease the rate of bacterial contamination of midstream urine samples in boys, this review clearly demonstrates the need for more research within the pediatric population.

Comprehensive work has been undertaken to guide multi-disciplinary care for adult populations and urinary catheter insertion and ongoing management. The Joint Commission’s recent recommendation identifies that during 2012, JACHO and JCIA accredited healthcare organizations must plan for the full implementation of the National Patient Safety Goals (NPSG) #07.06.01 by January 1, 2013.[5] This NPSG calls for the implementation of evidence-based practices to prevent indwelling catheter- associated urinary tract infections (CAUTI). Of concern is there concluding statement that these guidelines are not applicable to pediatric
populations as the research needed to support and change in practice in the form of evidence bundles is not available for the pediatric population. It is therefore of critical importance that a well designed RCT is undertaken to demonstrate the effectiveness of periurethral cleansing solution(s) on reducing either the rate of nosocomial infection during urinary catheterisation in the pediatrics patients and/or the contamination of mid-stream urine samples. The results of this review suggest that the comparators for this RCT need to be sterile water; soap and water and an antiseptic solution.

Conclusions

The only available RCT evidence suggests that sterile water is sufficient for periurethral cleansing prior to urinary catheterization. However, this recommendation is based on a single study, which was substantially underpowered and therefore is not worthy to effect and change in practice. The available research regarding effective solutions to minimize the contamination of mid-stream urine samples is of a descriptive nature and therefore not worthy of recommending a change in practice. Given the rising awareness of recipients of healthcare and the subsequent zero tolerance of nosocomial infections, there is an urgent need for further research in the pediatric population on the use of appropriate periurethral cleansing prior to urinary catheterization and/or midstream urine collection.
References
4. Cheung K Fau - Leung, P., et al., Water versus antiseptic periurethral cleansing before catheterization among home care patients: a randomized controlled trial. (1527-3296 (Electronic)).
25. Schlager, T.A., D.E. Smith, and L.G. Donowitz, Perineal cleansing does not reduce contamination of urine samples from pregnant adolescents. Pediatr Infect Dis J,


Appendix I: MASTARI Critical Appraisal Instrument

NOTE:
This appendix is included on pages 35-37 of the print copy of the thesis held in the University of Adelaide Library.
Appendix II: Final assessment of included studies

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Appendix III: MASTARI data extraction instruments

NOTE:
This appendix is included on pages 39-40 of the print copy of the thesis held in the University of Adelaide Library.
Appendix IV: List of excluded studies

Reason for Exclusion: Unable to contact author for further information

Reason for Exclusion: Unable to contact author for further information

Reason for Exclusion: Unable to contact author for further information

Reason for Exclusion: Literature review

Reason for Exclusion: Undertaking the quality assessment study rate low

Reason for Exclusion: Unable to contact author for further information

Reason for Exclusion: Unable to contact author for further information

Reason for Exclusion: Unable to contact author for further information

Reason for Exclusion: Undertaking the quality assessment study rate low
Appendix V: Comprehensive search strategies

Core Concepts to identify Keywords for Urinary Catheterization

Urinary catheterization
Urinary catheterization
Urinary catheter Urethral catheter
Urinary tract infections
Urinary tract infection
Bacteriuria
Catheter-related infections
Catheter-related infection

Children
child
infant
infancy
adolesc*
teens*
pediatric*
paediatric
pediatric nursing paediatrics

Disinfectants
Povidone-iodine
Chlorhexidine
Gluconate
Anti-infective agents
Anti-infective
Disinfection
Saline
Isotonic solutions
Saline solution, hypertonic
Saline solution
Sterile water
Water
Antiseptic
Antisepsis
Asepsis

Periurethral
Periuthra*
Perineum
Perineal
Meatus
Meatal
Core Concepts to identify Keywords Midstream Urine Collection

Midstream urine

Mid stream

Midstream

Disinfectants

Povidone-iodine

Chlorhexidine Gluconate

Anti-infective agents

Anti-infective

Disinfection

Saline

Isotonic solutions

Saline solution, hypertonic

Saline solution

Sterile water

Water

Antiseptic

Antisepsis

Asepsis

Periurethral Periuthra*

Perineum

Perineal
Meatus
Meatal

Infection

Urinary tract infection

Bacteriuria

Anti-Infective Agents, Urinary

Sources and search strategy used to locate Studies Urinary Catheterization

PubMed


Sources and search strategy used to locate Studies Midstream Urine Collection

PubMed


midstream[tiab] OR mid stream[tiab]


To obtain relevant Urinary Catheterization articles search included only periurethral cleansing

**PubMed**

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PubMed
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