NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review consultation document

Review of Clinical Guideline (CG54) - Urinary tract infection in children

1. Background information

Guideline issue date: 2007
3 year review: 2010
National Collaborating Centre: Women's and Children's Health

2. Consideration of the evidence

Literature search

From initial intelligence gathering and a high-level randomised control trial (RCT) search clinical areas were identified to inform the development of clinical questions for focused searches. Through this stage of the process 71 studies were identified relevant to the guideline scope. The identified studies were related to the following clinical areas within the guideline:

- Urine collection and diagnosis of urinary tract infection (UTI)
- Acute management of UTI (antibiotic treatment and symptomatic treatment)
- Long-term management of UTI (prophylactic antibiotics, imaging tests for structural abnormality, renal scarring and vesicoureteral reflux and surgical management of vesicoureteral reflux)

Six clinical questions were developed based on the clinical areas above, qualitative feedback from other NICE departments and the views expressed by the Guideline Development Group, for more focused literature searches. The results of the focused searches are summarised in the table below. All references identified through the initial intelligence gathering, high-level RCT search and the focused searches can be viewed in Appendix I.

Clinical area 1: Diagnosis of UTI in children		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q1: In infants and children with suspected UTI, which method of urine collection is most clinically effective and cost effective?	Through the focused search 10 studies relevant to the clinical question were identified. Literature was identified evaluating different urine collection methods in children including urine collection bags, clean catch specimens, urethral catheterization and suprapubic aspiration. The identified evidence does not change the direction of current guideline recommendations. No new evidence was identified relating to the cost effectiveness of urine collection methods.	No new evidence was identified which would change the direction of current guideline recommendations.
Q2: In infants and children with suspected UTI, which is the most diagnostically accurate,	Through the focused search 12 studies relevant to the clinical question were identified. Literature was identified relating to the use of microscopy, culture, dipstick	No new evidence was identified which would change the direction of current guideline

clinically effective and cost effective urine test for detecting UTI? (NICE research recommendation)	testing and flow cytometry for detection of UTI in children. One meta-analysis was identified which aimed to determine the diagnostic performance of urine dipstick testing in children with suspected UTI compared with microscopy. The study indicated that urine dipstick testing can be recommended for diagnosis of UTI in children over two years of age however the study reiterated the research recommendation given in the guideline concluding that further studies, stratified by age and comparing urine dipstick testing with microscopy are required. In terms of localisation of UTI using laboratory tests, several studies were identified evaluating C-reactive protein, serum procalcitonin, interleukin-6 and interleukin-8 as biomarkers. Further research is needed to evaluate the effectiveness of procalcitonin and other inflammatory markers in localising UTI.	recommendations.

Clinical area 2: Acute management of UTI		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q1: In infants and children with UTI, which is the most clinically effective and cost effective antibiotic treatment regime or symptomatic treatment regime in addition to antibiotics for treatment of UTI?	Twelve studies were identified through the focused search relating to this clinical question. Literature was identified evaluating antibiotic treatment for UTI. Some studies were identified focusing on short versus long courses of antibiotic therapy however, more conclusive evidence is required to determine the optimal duration of therapy. No new evidence was identified which would warrant an update of the guideline recommendations at this time. In terms of symptomatic treatment of UTI in children, two RCTs and a systematic review were identified focusing on the clinical effectiveness of cranberry products. The RCTs reported inconsistent results whilst the systematic review was unable to identify good quality evidence focusing on the effectiveness of cranberry juice in treatment of UTIs. As such, no conclusive evidence on the effectiveness of cranberry products was	No new evidence was identified which would change the direction of current guideline recommendations.

	identified.	
Clinical area 3: Long-term management of UTI		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q1: In infants and children who have had a UTI, how effective is the use of prophylactic antibiotics? (NICE research recommendation)	Through the focused search 12 studies relevant to the clinical question were identified. Literature (including several RCTs) was identified evaluating the efficacy of antibiotic prophylaxis for UTI in children. The RCTs reported varying conclusions whilst systematic reviews concluded that evidence is lacking relating to the efficacy of prophylactic antibiotics for UTI in children. Therefore, the current body of evidence does not seem to be conclusive. As such, no sufficient conclusive new evidence was identified which would warrant an update of the guideline recommendations at this time.	No conclusive evidence was identified that would invalidate current guideline recommendations.
Q2: In infants and children who have had a UTI, what are the most	Through the focused search 23 studies relevant to the clinical question were identified.	No conclusive evidence was identified that would invalidate current

effective and cost effective imaging tests for diagnosing structural abnormality and vesicoureteral reflux? (NICE research recommendation)	Literature was identified which compared imaging tests including ultrasound, dimercaptosuccinic acid scintigraphy and voiding cystourethrography for diagnosing structural abnormality, renal scarring and vesicoureteral reflux. The identified studies compared different imaging tests and reported inconsistent results and as such, the current body of evidence does not seem conclusive. Few studies were identified which examined the diagnostic accuracy of magnetic resonance imaging (MRI) for UTI. This was a research area identified in the guideline and as such, further research is required to investigate the diagnostic accuracy and cost-effectiveness of MRI as an imaging test for UTI. No sufficient conclusive new evidence was identified which would warrant an update of the guideline recommendations at this time.	guideline recommendations.
Q3: How does surgical management of vesicoureteral reflux compare with conservative	Through the focused search 8 studies relevant to the clinical question were identified. Several RCTs were identified comparing antibiotic prophylaxis, endoscopic treatment or surveillance as the control group in children with grade III or	No conclusive evidence was identified that would invalidate current guideline recommendations.

management? (NICE research recommendation)	IV vesicoureteral reflux. One RCT reported on development of new renal defects in the three treatment groups; one study focused on the recurrent UTI pattern and another RCT reported on vesicoureteral reflux outcomes. In all studies follow-up was undertaken at two years. In general, the RCTs demonstrated that endoscopic treatment and antibiotic prophylaxis were more beneficial compared with surveillance. However, the difference between endoscopic and prophylaxis groups did not reach statistical significance in the RCTs analysing UTI pattern and renal defects whilst the RCT focusing on vesicoureteral reflux outcomes did not detect a statistically significant difference between the prophylaxis and surveillance groups. In addition, in one of the identified RCTs concerns were highlighted relating to endoscopic treatment complications and recurrence of dilating vesicoureteral reflux after two years. As such, no sufficient conclusive new evidence was identified which would warrant an update of the guideline recommendations at this time. A retrospective cohort study compared endoscopic treatment with antibiotic prophylaxis finding endoscopic treatment to be of benefit. Due to	

	the retrospective nature of the study no treatment randomisation was performed. As such, no sufficient conclusive new evidence was identified which would warrant an update of the guideline recommendations at this time. Literature was identified which compared endoscopic treatment with open surgical management of vesicoureteral reflux. Both treatments were found to be of benefit. In one study, however, recurrent bacteriuria was observed more often after endoscopic treatment whilst pyelonephritis was observed more frequently following surgical treatment. As such, the current body of evidence does not seem to be conclusive at this time. One study was identified which conducted a cost-utility analysis of treatment algorithms for moderate grade vesicoureteral reflux (grades II and III). The results of the study indicated that a non-interventional approach constitutes the least costly treatment for moderate grade vesicoureteral reflux. Therefore, no new evidence was identified which would warrant an update of the guideline recommendations at this time.	

	Surgical interventions for vesicoureteral reflux was a research area identified by the guideline. As such, well-designed randomised placebo-controlled trials are required to determine the effectiveness of prophylaxis or various surgical procedures for the management of vesicoureteral reflux in preventing recurrent UTI or renal parenchymal defects.	

Several ongoing clinical trials (publication dates unknown) were identified focusing on diagnosis of UTI in children; effectiveness of antibiotic prophylaxis; antibiotic treatment (including short-term therapy and oral versus intravenous regimens);symptomatic treatment (including cranberry juice in prevention of UTI and possible interactions with antibiotic treatment) and comparisons of endoscopic versus open surgery for reflux. The results of these trials have not been published at this time but may contribute towards the evidence base relating to diagnosis and treatment of UTI in children in the next update review.

In conclusion, no new conclusive evidence was identified that would invalidate current guideline recommendations.

Guideline Development Group and National Collaborating Centre perspective

A questionnaire was distributed to Guideline Development Group (GDG) members and the National Collaborating Centre (NCC) to consult them on the need for an update of the guideline.

Six responses were received with respondents highlighting that since publication of the guideline more literature has become available on urine collection, antibiotic prophylaxis, antibiotic treatment, imaging tests, nitrite and white blood cell testing and the possible role of procalcitonin and interleukin-8 in diagnosis. In addition, respondents highlighted that a Health Technology Assessment project entitled: The diagnosis of urinary tract infection in young children (DUTY) study is underway with a proposed publication date of 2014. Furthermore, the randomised intervention for children with vesicoureteral reflux (RIVUR) trial was highlighted. The aim of this trial is to determine whether children with vesicoureteral reflux should be treated with long-term antibiotics.

Respondents also drew attention to variations in current practice and acknowledged that the guideline has not been universally implemented. GDG members also stated that a multi-centre audit of guideline implementation has been funded by the Healthcare Quality Improvement Partnership (HQIP) with results to follow.

Feedback from the GDG and NCC contributed towards the development of the clinical questions for the focused searches.

Implementation and post publication feedback

In total, 22 enquiries were received from post-publication feedback, most of which were routine. Key themes emerging from post-publication feedback included enquiries relating to diagnosis (including the use of dipstick tests) and treatment of UTI in children. This feedback contributed towards the development of the clinical questions for the focused searches.

Implementation feedback indicated that various organisations found some of the recommendations set out in the guideline confusing.

No new evidence was identified through post publication enquiries or implementation feedback that would indicate a need to update the guideline.

Relationship to other NICE guidance

The following NICE guidance is related to CG54:

Guidance	Review date
CG47: Feverish illness in children, 2007	Currently scheduled for a consideration for an update (Dec 2010).

Anti-discrimination and equalities considerations

No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation. The original scope provides advice on diagnosis and management of UTI in children from birth up to the age of 16 with first or recurrent upper or lower UTI who are not already known to have underlying uropathy.

Conclusion

Through the process no additional areas were identified which were not covered in the original guideline scope or would indicate a significant change in clinical practice. There are no factors described above which would invalidate or change the direction of current guideline recommendations. Variations in practice are reported to still exist however conclusive new evidence is required particularly in the research areas identified by the guideline. The UTI in children guideline should not be updated at this time.

3. Review recommendation

The guideline should not be updated at this time.

The guideline will be reviewed again according to current processes.

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18.11.10

Appendix I

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