UTIC – STAKEHOLDER COMMENTS FROM CONSULTATION

Status	Organisation	Order no.	Document	Section no.	Page no.	Comment	Response
SH	Action for Sick Children					This organisation was approached but did not respond.	
SH	Addenbrookes NHS Trust					This organisation was approached but did not respond.	
SH	Airedale General Hospital - Acute Trust					This organisation was approached but did not respond.	
SH	Anglesey Local Health Board					This organisation was approached but did not respond.	
SH	Association for Continence Advice					This organisation was approached but did not respond.	
SH	Association of Breastfeeding Mothers					This organisation was approached but did not respond.	
SH	Association of Medical Microbiologists	1	FULL	General		The Association of Medical Microbiologists welcomes the opportunity to comment on the draft guidelines. Members have made the following comments:	Thank you for your comments.
SH	Association of Medical Microbiologists	2	FULL	4.6.1		The consensus view is that borate is an acceptable and appropriate preservative if the urine cannot be examined promptly or refrigerated throughout transport to the laboratory. We wish to emphasise the importance of filling the container to the indicated level to ensure the concentration of borate is not excessive and inhibitory	Thank you for your comments.

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SH	Association of Medical Microbiologists	3	FULL	4.6.1		Impact of borate on dipsticks: contrary to reference 149 there is evidence from one of the dipstick manufacturers (Bayer) that borate may inhibit the detection of leucocyte esterase and this has been confirmed by unpublished investigation in the laboratory of one of our members. Ideally specimens should be collected in containers without borate if dipstick testing is to be undertaken (and then transferred to borate containers if culture is required). It is also important to note that Bayer recommend (on their package insert) that fresh urine must be tested within two hours. We believe that this advice is widely ignored and this delay may give misleading results, particularly in the presence of borate.	Thank you for your comment. We have amended the text and recommendations to indicate the importance of using fresh urine when testing with dipsticks.
SH	Association of Medical Microbiologists	3a	FULL	4.7.2		It may be helpful to give guidance on the level of pyuria as most laboratories report quantitative or semi-quantitative white cell counts. There may be value in adding a comment on the role (or otherwise) of quantitative cell counts in the diagnosis of infection.	Thank you for your comment. Studies analysed used different levels of pyuria. Precise guidance on the level of pyuria is outside our scope and should be agreed between local laboratories and the clinical services they support. In general when using higher cut-off levels of pyuria the number of false positives is reduced but the risk of false negative values will be increased. The algorithm will still function effectively but the likelihood ratios will be slightly different.
SH	Association of Medical Microbiologists	4	FULL	4.7.3.		Several members noted that it was common practice for paediatricians to request two or three urine samples (particularly in acute hospitalised patients) taken in rapid succession to confirm urinary tract infection (even if the first specimen was diagnostic). Guidance on the number of urine samples required to confirm urinary tract infection would be welcomed.	Thank you for your comments. The guideline has been developed on the basis that a single sample is usual practice. The uncertainty of some samples is recognised but guidance has been provided to help the clinician decide on whether or not to treat on a case-by-case basis. The RCP guidance of 1991 advised a second sample before treatment was started.

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SH	Association of Medical Microbiologists	5	FULL	4.7.6		The Association believes that urine cultures should be undertaken in children over three years of age with their first urinary tract infection. This is to ensure that the causative organism is identified and that appropriate susceptibility testing is undertaken. There is a limited range of antimicrobials licensed for use in children and the Association considers that knowledge of antimicrobial susceptibility is an important aspect of treatment.	We considered the risks and benefits of universal urine culture to monitor children with UTI. We believe undertaking urine culture for children over 3 years with a first episode of cystitis is unnecessary, unless there are complicating issues such as those listed in the recommendations. See Table 4.19. In addition, there is a recommendation that laboratories should monitor resistance patterns of urinary pathogens and make this information routinely available to prescribers.
SH	Association of Medical Microbiologists	6	FULL	*5.3*		Some doubts have been expressed on the recommendation not to treat asymptomatic infections, particularly in younger children where evidence of symptoms may not be available. Two older reports: DCL Savage et al and SR Meadow et al (both in BMJ 12 July 1969) indicated that many children with 'asymptomatic' bacteriuria do have symptoms on closer questioning and some of these had renal damage.	Detecting children who do not present with symptoms would require a screening programme and this is outside the scope of the guideline. If children are attending a GP or hospital follow-up appointment and have the sort of symptoms described by the papers quoted they would not be asymptomatic. This guideline has not suggested that symptomatic children attending for care should not have their symptoms addressed or their urine tested. However, the guideline does not recommend collecting urine from children without symptoms.
SH	Association of Medical Microbiologists	7	NICE	1.1.6.5		Table 2 - It might be helpful to explain that nitrite tests may be negative with certain organisms such as Enterococci spp.or Pseudomonas spp	This has been addressed in the text
SH	Association of Paediatric Emergency Medicine					This organisation was approached but did not respond.	
SH	Association of the British Pharmaceuticals Industry,(ABPI)					This organisation was approached but did not respond.	

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SH	Bard Limited					This organisation was approached but did not respond.	
SH	Barnet PCT					This organisation was approached but did not respond.	
SH	Barnsley PCT					This organisation was approached but did not respond.	
SH	Barts and the London NHS Trust - London					This organisation was approached but did not respond.	
SH	Bayer Healthcare PLC					This organisation was approached but did not respond.	
SH	Bedfordshire & Hertfordshire NHS Strategic Health Authority					This organisation was approached but did not respond.	
SH	Birmingham Children's Hospital					This organisation was approached but did not respond.	
SH	British Association for Accident and Emergency Medicine					This organisation was approached but did not respond.	

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SH	British Association for Paediatric Nephrology	1	Full/NICE	General		General The guideline was discussed at the General Meeting of the British Association for Paediatric Nephrology on Friday 8th December 2006 after members had been circulated in advance to invite their comments. (At the time of the request for comment by NICE, the Standards and Guidelines Committee of the British Association for Paediatric Nephrology had not been established. This committee becomes fully functional in early 2007) Members identified a number of methodological flaws. The selection of reference material was incomplete and arbitrary. Statistical methods were inappropriate. Terminology was not well defined or evidence based (for example clinical definitions of “systemically unwell”, “severely unwell”)	Thank you for your comments. As the methodological flaws have not been detailed it is not possible to provide a detailed response. The search criteria were clearly described in the methodology section. They were not arbitrary and they were agreed within the Guideline Development Group (GDG). The GDG have carefully reviewed the statistical methods with help and advice from senior members of the technical team and have not identified any statistical flaws. However, the positive and negative predictive values have been recalculated and expressed as Likelihood ratios for clarity in response to a comment from the NCC peer reviewer. This has not altered the outcome of evaluation of evidence from any section. The clinical terms for illness severity have been defined in accordance with the recently published guideline on fever. These definitions have been used consistently throughout the UTIC documents. The glossary has been amended to include some additional definitions.

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						The detailed criticism produced by the NCC peer reviewer was strongly endorsed. Because the methodological flaws are fundamental to the review process, it was considered inappropriate for the BAPN to go on to respond to some of the details point-by point. However, members endorsed the following general comments: · In infants and children, UTI is a common condition, with wide variations related to age, gender, family history and other factors. A small proportion have potentially serious renal lesions, some congenital, some acquired and infection-related. The opportunity to prevent the development or limit the progression of structural damage by rapid diagnosis and treatment of UTI has not been seriously addressed or recommended.	 Replies to Reviewer.doc The guideline contains several references to the importance of prompt diagnosis and treatment. The text has been amended to ensure that these points are clearer. However, there were already many references to this point and the overall strategy of the guideline was to support rapid diagnosis and treatment of UTI, particularly if there is a risk of acute pyelonephritis. This point was made in the first paragraph of the introduction, as well as elsewhere. Additional discussion about the importance of rapid diagnosis and treatment has now been added to Section 3.1.2 in the Introduction, to emphasise this point, and Section 3.1.6 specifically deals with this question: '3.1.6 Back to first steps: dealing with underdiagnosis of UTIs'. Within the epidemiology there is a paragraph within Section 3.3.11 on possible effects of delay in treatment. Long-term complications are described in Section 3.3.12 The aims of diagnosis is described in Section 4.1.1 paragraph 2 Recommendations in Section 4.8 on symptoms and signs state that 'Infants and children presenting with unexplained fever of 38 °C or higher should have a urine sample tested after 24 hours at the latest' and that

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							‘Infants and children with signs and symptoms suggestive of UTI should have a urine sample tested for infection’. This is so that the diagnosis can be made and treatment given, thus providing the opportunity to prevent long-term complications. Since the Guideline on feverish illness in children became available the risk of serious illness described in that document has been used in this guideline, instead of the terms used previously such as "serious illness" and "severely ill. The fever guideline has been aligned with the UTI guideline with regard to diagnosis and treatment of UTI and there is extensive cross referencing. (Section 4.8) The guideline chairs have ensured that both guidelines are complementary and in particular the fever guideline indicates that UTI should be considered in febrile children without obvious cause. Urine should be collected from all children in the amber or red illness risk categories and from green cases if they have urinary symptoms or are referred to a paediatric specialist. Fever lasting 5 days falls into the amber category. The urine testing strategy tables, 4.17–4.20, recommend methods that provide an immediate answer (dipstick testing and urgent microscopy) (Section 4.8) so that decisions and treatment can be made immediately. An audit of current practice showed that a very high proportion of cases of UTI are overlooked in secondary care when relying on culture. This new advice represents a significant reduction in the time delay from urine collection to diagnosis.

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							The tables 4.17–4.20 on urine testing outcomes also indicate whether or not to start treatment. There is clear clinical guidance on when a child should be considered to be at risk of acute pyelonephritis (fever of 38 °C or over or any UTI with fever and loin pain) with additional advice on how to confirm this with tests on the rare occasions when this is considered necessary (Section4.8). Current practice in the UK (RCP guideline 1991) does not make this distinction clearly. The best opportunities for preventing renal damage are to ensure early diagnosis and treatment in this group. The treatment section gives clear advice on how to manage children with significant illness risk through cross reference to the fever guideline. (Section 5.3) There is clear advice on route, duration, specialist referral and setting for treatment for children under 3 months, and those likely to have acute pyelonephritis, i.e. those at greatest risk of renal damage. (Section 5.3). The imaging strategy is clearly directed at the most high risk children while minimising the burden of imaging to low risk cases. See chapter 6, particularly the introduction, section 6.4.1, translation, section 6.4.5., and Tables 6.13, 6.14 and 6.15 in Section 6.4.
						The guideline excludes children with underlying obstruction or neurogenic bladder, but UTI is often how they present, so the guideline needs to be able to identify these children accurately. This group is at a high risk	We agree with this statement. This is why the selective imaging strategy above has been recommended. Opportunities to detect neurogenic bladder following the first or recurrent UTI arise through history, physical

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						of acquired structural kidney disease. A reduction in imaging is welcome, but the guideline must be able to identify children with, or at risk of, structural kidney disease whose clinical management would then be different. There is particular concern about minimising imaging in neonates and infants.	signs, age at presentation, severity of illness, recurrence of UTI and culture of atypical organisms. Ultrasound is advised either early, in the highest risk cases with atypcal illness, or within 6 weeks of UTI for infants under 6months and for older children with recurrent UTI. Views of the bladder including bladder emptying have been recommended. The imaging strategy specifically aims to identify children at greatest risk of congenital or acquired renal lesions by targeting those under 6 months, those with severe illness, those with recurrent UTIs and those with specific risk features on history or examination as above. In particular, the tests aim to identify those who might benefit from interventions such as relief of obstruction. (Section 6.4, Tables 6.12–6.15) There is a significant set of data on prophylaxis with a conspicuous absence of evidence of benefit to clinically important outcome measures. Some critics of the draft guideline have misinterpreted the lack of evidence of benefit as a lack of evidence. There were 9 randomised controlled studies with over 1000 randomised patients. However, within these studies there was no evidence that imaging and prophylaxis resulted in fewer episodes of acute symptomatic UTI or reduction in new scar formation. The GDG has taken the view that it is not justifiable to subject healthy children (without signs and symptoms associated with an increased risk of underlying renal disease or uropathy and who have fully recovered from an

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							illness) to imaging tests, long-term treatment and follow-up which may be burdensome, has risks and has no proven benefit. This is explained in the translation of the imaging section and the prophylaxis section. The GDG considered the fact that placebo-controlled trials are ongoing or under development as an argument for not continuing with the current practice of imaging and prophylaxis in healthy children but would expect to amend the guideline if evidence of benefit emerges. It is possible that the results of such studies would be similar to the results of existing published studies. One of the stakeholders for the RCPCH who is a BAPN member mentioned the preliminary results of trials presented in Palermo in 2006 at the ESPN meeting which show no benefit so far. (See comments No.14 from RCPCH and our reply) The identification of anomalies, in apparently healthy children, which do not lead to effective therapy has not been a priority. In the absence of clear evidence of risk to the child from the legacy of UTI or benefit from the imaging and prophylaxis this is seen as inappropriate and over-invasive. In the absence of evidence of benefit from prophylaxis or re-implantation of the ureter the imperative for imaging tests was reduced. In particular, where patients were subdivided into those with VUR and those without VUR the results of randomised controlled trials did not reach significance but found more acute symptomatic UTIs and more new scars in the treatment groups than in the control group

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							(Figures 6.1 and 6.3). This has not supported the view of some critics that this reduction of imaging is dangerous. The current rate of diagnosis and referral from primary care is unknown but some studies suggest that there is significant under-diagnosis (Coulthard et al, 2003) and incomplete referral.
						The guideline alters the pattern of referral between primary care and paediatric services without addressing the issue of skills in diagnosis and management in these different settings.	This guideline aims to improve the primary diagnosis and treatment but has not identified good reasons for referral to secondary care in the majority of children who have recovered normally from UTI. The value of long-term follow up is unknown, but it is an imposition to families of low-risk children. The guideline specifically states that children with abnormalities of structure or function should be referred to a paediatric specialist and lists the features that should prompt a referral. The GDG believe this will result in a smaller number of more appropriate referrals. The NICE implementation team will develop an implementation support plan and a suite of practical support tools which will involve working with key stakeholders to identify areas of most significant change, their impact and how these can be supported.
						Low-dose antibiotic prophylaxis is dismissed as an effective management because there is 'no good evidence' for it. This is premature as current studies are underway that will clarify this point.	The GDG looked carefully at the evidence on prophylaxis on two separate occasions using two different approaches and two separate researchers. They did not consider that there was sufficient evidence of benefit either for the prevention of acute symptomatic UTIs or for prevention the acquisition of new renal parenchymal defects to recommend this to healthy

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							children at low risk of long-term problems. (Section 6.3) In the absence of any evidence of benefit the GDG took the view that use of prophylaxis was inappropriate in healthy children who had recovered from their acute UTI and are at low risk of renal disease. The risks of imaging and antibiotics outweigh any likely benefits. Long-term low-dose prophylaxis is of unproven benefit even for children at increased risk of long-term renal morbidity. However, the option to use it in higher risk children has not been excluded. (Section 6.3 recommendations) There was published and anecdotal evidence of risks and side effects both to the individual and to the population at large of common side effects from the medication recommended. Under these circumstances the GDG did not consider that this form of management should be offered routinely to healthy infants and children after recovery from a UTI. The fact that controlled studies are underway supports the GDG view that there is a lack of adequate evidence for benefit. The outcome of these trials will be an important input to any future guidance.
SH	British Association of Paediatric Surgeons					This organisation was approached but did not respond.	
SH	British National Formulary (BNF)					This organisation was approached but did not respond.	

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SH	British Nuclear Medicine Society	1	Full	6.3.2		To suggest that DMSA may be used to identify VUR is obtuse. Reflux only becomes potentially important if there is renal damage and recurrent UTI. So the question should be reversed in that how good is the DMSA scan in identifying children who need a MCUG.	Thank you for your comments. This section has not been included in the revised version.
SH	British Nuclear Medicine Society	2	Full	6.3.2	310	When imaging is required to detect reflux in pre toilet trained boys, an MCUG is recommended so that the urethra is also imaged. In girls cystosonography is a valid alternative' Does this refer to pre-toilet trained girls only. If however this refers to all girls, then this is unacceptable as the catheterization of the older girl should be avoided unless strongly directed by the clinical state.	Agree - MCUG (or cystosonography) should mainly only apply to infants After toilet training an indirect radionuclide cystogram should be used (if reflux needs to be identified). However, in this guideline we have not recommended the routine use of tests to look for VUR in children over 6 months.
SH	British Nuclear Medicine Society	3	Full	6.4		Gold standard is the pig work as only this way do you know what is true positive and true negative	The GDG did not consider animal work to be indicative of a gold standard for imaging in children.
SH	British Nuclear Medicine Society	5	Full	6.5.5	325	If defects on ultrasound are identified, they appear relatively specific and in the clinical context of a child who has had a urinary tract infection could obviate the need for a DMSA scan.' This statement has not been justified in the preceding sections. There is a high false positive and false negative rate with ultrasound. If ultrasound detects a defect then this is an indication for a DMSA to confirm the defect, assess the function of this 'damaged' kidney, and ensure the opposite kidney is normal. As this is a small group of children, so the number of children undergoing a DMSA scan will not be high. The radiation burden from a DMSA scan is 0.9 mSv, this is not regarded as a 'high' exposure	A DMSA scan was not recommended as this would not alter management.
SH	British Psychological					This organisation was approached but did not respond.	

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	Society, The						
SH	British Society for Antimicrobial Chemotherapy					This organisation was approached but did not respond.	
SH	British Society of Paediatric Radiology	1	NICE	13.3.1		This discusses the use of DMSA to detect renal scarring. The guidance suggests it being performed six months following the UTI. The guidance regarding DMSA with repeat infections is obscure and inconclusive. There is no comment on the use of DMSA in the more acute phase with possible repeat examinations being performed on those children who are positive. The evidence of a six month wait is not wholly conclusive. Could the delay be three months or nine months?	Thank you for your comments. The importance of detecting renal scarring has been reduced by the lack of impact this has on effective interventions. Where DMSA is deemed to be appropriate because the risk of scarring is more than minimal the view of the GDG was that it should not be done too soon as there is a relationship between time from UTI and the extent of the renal parenchymal defects seen. If the child is having recurrent UTIs one option is to postpone the DMSA scan. However, if this happens repeatedly it might be better to do the Scans anyway and note the time from UTI.
SH	British Society of Paediatric Radiology	2	NICE	1.3.2		This discusses the use of MCUG. The guidance indicates that three days of prophylactic antibiotics should be given. Is there evidence for this? A survey performed by the BSPR shows that the use of prophylaxis and its dosage is very variable across the UK. Could the advice just refer to local practice. What is the type and dose of antibiotic needed?	This advice has been retained.
SH	British Society of Paediatric Radiology	3	NICE	General		The document implies that the child is otherwise well with no other pathologies. There is little comment on bladder dysfunction and neuropathic bladders. There is little comment on children with a single kidney.	Children with neuropathic bladders were excluded from the scope of this guideline. The guideline aimed to give general and practical advice for the majority of children who get UTIs and does not cover children known to have urological abnormalities. Dysfunctional voiding is addressed in the section on recurrent UTIs. The imaging strategy is not designed to detect all possible renal anomalies but aims to detect those that have significant treatment

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							implications such as obstruction and neurogenic bladder. The majority of single kidneys are now detected by antenatal ultrasound.
SH	BSUG					This organisation was approached but did not respond.	
SH	Calderdale and Huddersfield Acute Trust					This organisation was approached but did not respond.	
SH	CEMACH					This organisation was approached but did not respond.	
SH	Centre for Reviews and Dissemination	1	General			First of all, congratulations on producing such a comprehensive doccument in what apeared to me to be an impossible time frame. I am suitably impressed. The general and detailed comments attached refer only to those sections upon which I am qualified to comment, i.e. those relating to diagnostic tests and based largely upon our HTA review. I have highlighted in bold those comments which refer to transcription errors in the data presented from our HTA review, or errors in the interpretation of the data. These significantly effect the meaning of what is presented, and therefore need to be addressed. The remainder refer to minor errors, or issues of presentation and consistency.	Thank you for your comments.
SH	Centre for Reviews and Dissemination	2	Full	general		The text contains many examples of un-supported statements, often assigning numerical values. This should be checked carefully throughout and references added where necessary.	Thank you for your observations.

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SH	Centre for Reviews and Dissemination	3	Full	Glossary	71	Summary receiver operator characteristic (SROC), should be receiver operating characteristic, which is given correctly in the definition. However, SROC is then defined as "recommended to represent the performance of a diagnostic test, based on data from a meta-analysis." This is not strictly true, as it is one recommended method, to be used in specific circumstances. Also, this 'definition' does not describe what the SROC curve represents; a proper definition is needed here.	Thank you for your comments.
SH	Centre for Reviews and Dissemination	4	Full	1.7	89	The list of "outcome measures used in the guideline" should included the measures of diagnostic accuracy (e.g. sensitivity, specificity, likelihood ratios) used as outcome measures in chapters 4 and 6.	We have added 'Measures of Diagnostic Accuracy' to the list of outcome measures.
SH	Centre for Reviews and Dissemination	5	Full	general		Something missing here?	Apologies for this oversight. All tables and figures have now been referenced accurately.
SH	Centre for Reviews and Dissemination	6	Full	general		Some sections in chapters 4 and 6 include summaries of the methodological quality of studies (as provided in the systematic review to which they refer) and some do not; consistency is required.	The text and recommendations have been amended. However, the need for additional information is also dependent on the context.
SH	Centre for Reviews and Dissemination	7	Full	general		Similarly, there is a lack of consistency throughout chapters 4 and 6 with respect to the number of decimal places quoted for measures of diagnostic performance such as sensitivity and specificity.	We have amended all measures of diagnostic performance to two decimal places.
SH	Centre for Reviews and Dissemination	8	Full	general		Chapters 4 and 6: Where ranges are quoted for sensitivity, specificity and likelihood ratios, the corresponding paired values are often missing. I have tried to list all instances below, but this should be checked carefully throughout.	This has been amended where appropriate.

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SH	Centre for Reviews and Dissemination	9	Full	general		Chapters 4 and 6: Some sections quote pooled LR with 95% CI and some also quote median LR with IQR; consistency is needed. Personally, given the heterogeneity of the data, I would prefer to see median with IQR (though I recognise that I am guilty of using pooled values in the original document).	The reporting in the guideline is dependent on how the included papers reported their findings, but consistency has been ensured as much as possible.
SH	Centre for Reviews and Dissemination	10	Full	general		Chapters 4 and 6: Where data from additional studies are reported alongside data from the HTA report (upon which the bulk of these chapters is based), I think it would improve clarity if these studies were described in relation to the HTA. i.e. Are they: published since the HTA, excluded by the HTA (outside its remit), or within the remit and date of the HTA but missed by it.	We do not usually do this, but we have clarified this where needed.
SH	Centre for Reviews and Dissemination	11	Full	4.3	91	Summary recommendations do not mention how children should be tested (combination dipstick is mentioned elsewhere). It would be useful to have this in summary as well as main text. I recently came across a 3 year old who had waited (without treatment) for a week for laboratory results.	. Acting on a positive result as described in your comment is an implementation issue and not a matter for the guideline.
SH	Centre for Reviews and Dissemination	12	Full	4.1	155, line 21	“condition its management” should read “condition and its management”	Amended to read 'condition and its management'.
SH	Centre for Reviews and Dissemination	13	Full	4.3	156, line 4	Sentence state “ranges from” but does not close statement.	This has been amended.
SH	Centre for Reviews and Dissemination	14	Full	4.4.1	180, line 10	10 studies should be 5 studies	This has been amended and now reads 5 studies.
SH	Centre for Reviews and Dissemination	15	Full	4.4.1	180, line 15	“sensitivity of 87%” should be “sensitivity of 64%”	This has been amended.
SH	Centre for Reviews and	16	Full	4.5.1	185, line 14	Pooled negative likelihood ratio “17.8 (interquartile range 6.6, 19.5)” should	This has been amended.

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	Dissemination					read “0.23 (95% CI 0.18, 0.30)”	
SH	Centre for Reviews and Dissemination	17	Full	4.5.7	193, line 14-17	This is a repetition of section 4.5.5, pg 189-90. These data only need to be presented once.	This has been amended - these data are now under the heading 'Early compared to late stream samples'.
SH	Centre for Reviews and Dissemination	18	Full	4.7	210, line 7	I am not sure that it is reasonable to describe microscopy as a test for which a result is “immediately” available, especially in the context of UK primary care.	The role of the GDG is to recommend the best test given the available evidence. Issues such as delivery of service will be addressed through the NICE implementation process.
SH	Centre for Reviews and Dissemination	19	Full	4.7.1	213, line 9	“Positive likelihood ratios ranged from 2.6 (LR- 12.5)” should read “Positive likelihood ratios ranged from 2.6 (LR- 0.39)”	This has been amended.
SH	Centre for Reviews and Dissemination	20	Full	4.7.1	214	It is important that some note be made of the practical application of the glucose test. Its operating principle requires a physiologically concentrated urine specimen (i.e. first void of the morning, concentrated in the bladder overnight) at can therefore never be useful in pre-toilet trained children.	Thank you for your comment.
SH	Centre for Reviews and Dissemination	21	Full	4.7.1	215, line 17-18	The values for likelihood ratio ranges are missing their corresponding pairs.	. This has been amended.
SH	Centre for Reviews and Dissemination	22	Full	4.7.1	216, line 6-7	Sentences should read “Sensitivity ranged from 30% (specificity 100%) to 89.2% (specificity 97.6%). Specificity ranged from 89.2% (sensitivity 87%) to 100% (sensitivity 30-88%).	This has been amended.
SH	Centre for Reviews and Dissemination	23	Full	4.7.1	216, line 7-8	The values for likelihood ratio ranges are missing their corresponding pairs.	This has been amended.
SH	Centre for Reviews and Dissemination	24	Full	4.7.1	220, line 7-8	“However, a negative result for either nitrite or LE has the highest negative likelihood ration and will be most useful in excluding UTI.” 1. Surely you mean lowest negative likelihood ration? 2. The above statement contradicts the recommendation in the summary section that both results negative be treated as ruling out UTI. I think the	We conducted further analyses on the data included in the HTA, and came to new conclusion, clarifying these issues.

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						confusion may be arising because the nitrite OR LE positive = positive result combination gives the lowest negative LR. For this combination a negative test result (that used to rule out disease) would be defined as both LE and nitrite negative. You therefore need to be very careful with phrasing.	
SH	Centre for Reviews and Dissemination	25	Full	4.7.2	221, line 1-2	"28 studies" should be "27 studies" and "25 studies" should be "24 studies"	This has been amended.
SH	Centre for Reviews and Dissemination	26	Full	4.7.2	221, line 10	Sensitivity and specificity ranges are missing their corresponding paired values.	This has been amended.
SH	Centre for Reviews and Dissemination	27	Full	4.7.2	222, line 15-17	Sensitivity and specificity ranges and likelihood ratio ranges are missing their corresponding paired values.	This has been amended.
SH	Centre for Reviews and Dissemination	28	Full	4.7.2	224, line 19-21	Sensitivity and specificity ranges and likelihood ratio ranges are missing their corresponding paired values.	This has been amended.
SH	Centre for Reviews and Dissemination	29	Full	4.7.2	225, line 15-17	Sensitivity and specificity ranges and likelihood ratio ranges are missing their corresponding paired values.	This has been amended.
SH	Centre for Reviews and Dissemination	30	Full	4.7.2	226, line 6-8	Evidence summary - "However, the pooled likelihood ratios show that a negative result for either pyuria or bacteriuria is better for ruling out UTI than dipstick testing." Don't think that the data allows you to be so certain about this. Even if significant difference could be demonstrated (which I doubt is the case), data would be generated from an indirect comparison (the performance data for dipsticks and that for microscopy come from different studies, which are unlikely to be equivalent in their key characteristics). Also, the original review summary for this section suggest that only a combination of both tests negative is potentially useful for ruling out UTI. I think we have a similar confusion here	We conducted further analyses on the data included in the HTA, and came to new conclusion, clarifying these issues.

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						to that described above for dipstick tests (a low negative LR arising from the combination where either test positive is defined as a positive result is associated with a negative result defined by both tests negative)	
SH	Centre for Reviews and Dissemination	31	Full	4.7.3	227, line 3-5	Sensitivity and specificity ranges and likelihood ratio ranges are missing their corresponding paired values. Also need to make it clear that these data are for the eight dipslide studies.	This has been amended.
SH	Centre for Reviews and Dissemination	32	Full	4.7.3	228-229	Evidence summary - "The pooled negative likelihood ratio for culture is 0.23 which shows that culture is no better for ruling out UTI than dipstick testing…"	Thank you for pointing this out. The quoted negative likelihood ratio is for dipslide culture in comparison with laboratory-based culture. i.e. What this result shows, if anything, is that dipslide methods do not compare well with conventional culture methods for ruling out UTI. It does not give any information about the performance of conventional culture methods, either in their own right or in comparison to dipstick or microscopy. This has been amended in the text.
SH	Centre for Reviews and Dissemination	33	Full	4.7.3	229	Evidence summary - Please reference the figure used on this page.	This has been amended.
SH	Centre for Reviews and Dissemination	34	Full	4.7.6	237-238	It should be made clear that the entry for "culture" in this table refers to a comparison of dipslide culture with conventional, laboratory-based culture methods, and does not reflect the diagnostic performance of culture per. se.	Thank you for pointing this out. The quoted negative likelihood ratio is for dipslide culture in comparison with laboratory-based culture. i.e. What this result shows, if anything, is that dipslide methods do not compare well with conventional culture methods for ruling out UTI. It does not give any information about the performance of conventional culture methods, either in their own right or in comparison to dipstick or microscopy. This has been amended in the text.
SH	Centre for Reviews and	35	Full	4.7.6	238, line 2-4	As described above, care is needed when explaining how combination tests	We conducted further analyses on the data included in the HTA, and came to

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	Dissemination					are used to rule out disease: where the OR combination defines a positive test and this gives the lowest negative LR, the definition of a negative test (useful to rule out) is both tests negative.	new conclusion, clarifying these issues.
SH	Centre for Reviews and Dissemination	36	Full	4.7.6	240, line 3-10	I think care is needed when interpreting the relative positive LRs for nitrite and LE derived from our review. In the first place these incorporate a highly heterogeneous range of results. In the second place, and linked to the first point, the two tests may perform differently in different circumstances in ways which could not be captured by the available data. e.g. Nitrite is a bacterial metabolite and LE is a product of cellular inflammatory response, it may therefore be that these two substances appear in the urine in different time frames post infection (just one, currently un-testable, possible explanation for heterogeneity).	We conducted further analyses on the data included in the HTA, and came to new conclusion, clarifying these issues.
SH	Centre for Reviews and Dissemination	37	Full	4.7.6	242, line 1	Research recommendation - “leukocyte” should read “leukocyte esterase”	This has been amended.
SH	Centre for Reviews and Dissemination	38	Full	4.8	242, line 14-15	“A systematic review identified 10 studies assessing various clinical features for the localisation of UTI in children.” Should read “A systematic review identified 5 studies assessing various clinical features for the localisation of UTI in children.” Also, no results are reported for these studies.	The GDG decided that clinical features of UTI constituted things such as body temperature and physical symptoms - The 5 studies you refer to are in section 4.4.17 ' Localisation of UTI by symptoms' and signs The seven studies drawn from the HTA in this section (4. 7.2 Localisation of UTI by laboratory tests) are about using CRP to diagnose/localise UTI - these 7 papers appear in the 'Localisation' section of the HTA, however for the purposes of this guideline and because of the additional papers located (on the use of procalcitonin), the GDG felt these studies were better placed in this

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							section.
SH	Centre for Reviews and Dissemination	39	Full	4.8	247-248	Translation - I am not convinced that this section represents a “translation” of the data presented. It may well be practice to differentiate between upper and lower tract UTI using clinical findings, but the data from the systematic review cited (but not reported) do not provide any evidence to support this. Also, units are missing from some of the CRP thresholds quoted.	The tests for localisation have not been recommended as tools to differentiate upper from lower UTI.
SH	Centre for Reviews and Dissemination	40	Full	6.1	290, line 6-9	The statement about the association between VUR and the development of renal scarring requires referencing or qualifying. I don’t think that there is clear cut evidence of association (but am happy to be proved wrong).	Seethe Epidemiology section. There is good evidence that VUR is associated with more scarring, but only animal studies show cause and effect.
SH	Centre for Reviews and Dissemination	41	Full	6.1	291, line 15-22	There is an absence of referencing in this paragraph, in the presence of some quite explicit, quantitative statements.	See the Epidemiology section. The introduction to the imaging section has been extensively re-written so that this comment is no longer applicable. Some information on this topic is available in the background and epidemiology sections, sections 3.2.5 and 3.3.11.

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SH	Centre for Reviews and Dissemination	42	Full	6.1	293, line 3-4	"It is based almost completely on a Health Technology Appraisal which looked solely at technical (and not clinical) utility of these tests." This statement is not accurate. The HTA did look at clinical utility, but found almost no evidence (looking and not finding is not the same as not looking). One study (abstract only) on clinical utility was identified and described and I think it is important that it be included in this document (I cannot find mention of it, but may have missed it). This is the Paul Dick study (RCT), which found that routine investigation of children for reflux did not improve outcome.	Dick and Feldman - not included by NICE because it is an SR of non-intervention studies. It is referenced in the Epidemiology section. This is an excluded study but would be useful to include here. We have included the HTA, and therefore we cannot include any study that is already included in the HTA, as this will result in presentation of the same data twice. The HTA recommended no further investigation of children with first UTIs between 2-5 years of age.
SH	Centre for Reviews and Dissemination	43	full	6.3.1		Why does the section on contrast enhanced ultrasound include a description of the methodological quality of studies included in the systematic review cited, whilst the section on conventional ultrasound does not?	Methodological quality data has now been included in the conventional ultrasound section.
SH	Centre for Reviews and Dissemination	44	Full	6.3.1	295, line 22	"The pooled positive likelihood ratio was 1.9 (95% CI: 11.2, 2.9)" should read "The pooled positive likelihood ratio was 1.9 (95% CI: 1.2, 2.9)"	This has been amended.
SH	Centre for Reviews and Dissemination	45	Full	6.3.1	296, line 2	"the median negative likelihood ratio was 1.4 (IQR 0.58 to 0.98)" should read "the median negative likelihood ratio was 0.79 (IQR 0.58 to 0.98)"	This has been amended.
SH	Centre for Reviews and Dissemination	46	Full	6.3.1	296, line 3-4	The systematic review from which these data are derived does not report calculated PPV and NPV values and I don't think that they are particularly helpful here. However, if you must include them, then the prevalence data used to derive them needs to be given alongside.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	47	Full	6.3.1	298, line 13	"8 studies did not include sufficient detail of the reference standard…" should read "9 studies did not include	This has been amended.

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						sufficient detail of the reference standard…"	
SH	Centre for Reviews and Dissemination	48	Full	6.3.1	299, line 9-10	The systematic review from which these data are derived does not report calculated PPV and NPV values and I don't think that they are particularly helpful here. However, if you must include them, then the prevalence data used to derive them needs to be given alongside.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	49	Full	6.3.1		Consistency: The term interquartile range is sometimes used in full and sometimes abbreviated to IQR.	This has been amended - the term now appears as IQR.
SH	Centre for Reviews and Dissemination	50	Full	6.3.1	301	The table reproduced on pg 301 has a superscript "3" inserted into the middle of the word "presence" on its top line.	This has been amended.
SH	Centre for Reviews and Dissemination	51	Full	6.3.1.1		Figure legend has an additional 1 in its numbering, and series label has "contrast" misspelled as "contrasr"	This has been amended.
SH	Centre for Reviews and Dissemination	52	Full	6.3.2	304	The table reproduced on pg 304 has the title "DMSA vs MCUG", but includes data from a study (Oostenbrink) that is of risk scoring (not DMSA) vs MCUG.	The Oostenbrink study has now been placed in Table 6.6 ('Other Investigations for VUR' Section 6.3.44.
SH	Centre for Reviews and Dissemination	53	Full	6.3.3.1	306	The entry for the "Reference standard; definition of a positive result" is missing for the second data set from the Cavanagh study and should read "MCUG; presence of reflux". This is important, as without it the table appears to quote two different data sets for the same comparison.	This has been amended.
SH	Centre for Reviews and Dissemination	54	Full	6.3.4	307, line 5	"A systematic review identified 7 studies…" should read "A systematic review identified 6 studies". This is the correct number for the set described as "other" in the original HTA report, with the DMSA studies treated separately (as has been done in this report). If you want to discuss only imaging tests, as suggested by the opening paragraph,	Thank you for your comment. We have amended the text as suggested.

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						then the correct number would be 4. Currently, the table 6.3.4.1, which is associated with this section, contains data for all four imaging studies (discussed in the text), plus one study of a risk score (Oostenbrink, not mentioned in the text), and omits the data for a study of biochemical tests (Johnson, also not mentioned in the text). It is therefore not clear what is intended. The whole section requires careful checking for accuracy and consistency.	
SH	Centre for Reviews and Dissemination	55	Full	6.3	310	Translation - I am unclear of the justification for the statement that direct and indirect cystography can be used to detect reflux. The diagnostic performance data cited for these methods is poor, particularly in relation to indirect cystography which (in the limited number of studies available) had very poor sensitivity. In my view the statements about cystography in this section should be given justification or removed.	This section has been amended to say that there was little evidence.
SH	Centre for Reviews and Dissemination	56	Full	6.4	311, line 18-19	As previously indicated, PPV and NPV should only be reported along side the prevalence values used to derive them.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	57	Full	6.4	312	The table on this page is mislabelled. It also appears to be a reproduction from the HTA report cited elsewhere, but is not cited as such. Care is needed over copyright issues throughout this document.	This table has been amended .
SH	Centre for Reviews and Dissemination	58	Full	6.5.1	314, line 21-22	As previously indicated, PPV and NPV should only be reported along side the prevalence values used to derive them.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	59	Full	6.5.1	315	Again, the table reproduced on this page appears without appropriate citation.	This has been amended.
SH	Centre for Reviews and	60	Full	6.5.2	316, line 7	If you are going to present PPV and NPV please also present the LRs and	We agree - all predictive values have been removed from the guideline text

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	Dissemination					prevalence values used to derive them.	and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	61	Full	6.5.2	317	Another un-cited table.	This has been amended.
SH	Centre for Reviews and Dissemination	62	Full	6.5.3	318, line 3-10	PPV and NPV values again used without important data on their derivation.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	63	Full	6.5.3	319	Another un-cited table, and this one is also missing the second data set from the Ditchfield study (which is referred to in the text above it).	This has been amended - the second data set is now included.
SH	Centre for Reviews and Dissemination	64	Full	6.5.4	320	PPV and NPV values again used without important data on their derivation.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	65	Full	6.5.4	321	Another un-cited table.	This has been amended.
SH	Centre for Reviews and Dissemination	66	Full	6.5.5	323	PPV and NPV values again used without important data on their derivation.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	67	Full	6.5.5	323	The second study referred to in this section is described as evaluating the presence of defects on MAG3 for the detection of renal scarring. It is, in fact a study of the accuracy of reflux, identified by indirect radionuclide cystography (MAG3), for the detection of scarring. This needs to be corrected.	This has been amended and now reads - 'The second study evaluated the accuracy of reflux, identified by indirect radionuclide cystography (MAG3), for the detection of scarring.'
SH	Centre for Reviews and Dissemination	68	Full	6.5	325	The statement “DMSA is the most accurate method for detecting renal parenchymal defects in children who have had a UTI” seems rather non-sensical in this context. This report has only included studies which used DMSA as the reference standard in this section; implying a starting assumption that DMSA is the most accurate method. However, to state this does not sum up the data presented. In fact DMSA is the one tests upon whose actual accuracy the data presented shed no light at all.	This section has now been amended.

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SH	Centre for Reviews and Dissemination	69	Full	6.5	325	I think care is needed when stating that ultrasound and MAG3 can be used to detect the presence of renal parenchymal defects. The accuracy data cited for MAG3 are sparse and show poor performance. The ability of ultrasound to rule-in scarring needs to be distinguished from its relatively poor performance in ruling-out scarring.	MAG3 has been removed from the evidence statement.
SH	Centre for Reviews and Dissemination	70	Full	6.6.6	326, line 13-14	"In 14 of the 18 studies the scintigraphic standard was DMSA." In fact, all 18 studies used DMSA (14 studies used acute DMSA, and 4 gave no information about timing)	This has been amended and now reads 'A systematic review assessed the diagnostic accuracy of ultrasound in 18 studies reporting 28 data sets where renal scintigraphy was the reference standard. 14 studies used acute DMSA, and 4 gave no information about timing.
SH	Centre for Reviews and Dissemination	71	Full	6.6.1	327, line 7-8	PPV and NPV values again used without important data on their derivation.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.
SH	Centre for Reviews and Dissemination	72	Full	6.6.1	327, line 10-11	Why suddenly use a reference to ROC plots (which are not shown) to refer to heterogeneity, when throughout the rest of the report this has been done using LRs and p values?	Agree - this sentence has been removed.
SH	Centre for Reviews and Dissemination	73	Full	6.6.1	328-329	Another un-cited table.	This has been amended.
SH	Centre for Reviews and Dissemination	74	Full	6.6.2	332, 19-20	"ROC curves showed that all studies included indicate that MGUG is a poor test for localising UTI." This seems a strange way of expressing the point, as ROC curves were not used in the systematic review cited (plots of individual study results in ROC space only), and are not used in the guideline. The data presented are sufficient to make the point.	Agree - this sentence has been removed.
SH	Centre for Reviews and Dissemination	75	Full	6.6.2	332, line 21-22	PPV and NPV values again used without important data on their derivation.	We agree - all predictive values have been removed from the guideline text and replaced with likelihood ratios.

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SH	Centre for Reviews and Dissemination	76	Full	6.6.2	333	Another un-cited table.	This has been amended.
SH	Centre for Reviews and Dissemination	77	Full	6.6.2	334	The section entitled “other imaging studies”, beginning on page 334, is still under section 6.6.2 MCUG; it probably needs a new section number.	This has been amended and now has a new section number.
SH	Centre for Reviews and Dissemination	78	Full	6.6.2	334, line 15-16	“These studies report sensitivities ranging from 75% to 100% and specificities ranging from 9% to 44%.” should read “These studies report sensitivities ranging from 9% to 42% and specificities ranging from 75% to 100%.”	This has been amended.
SH	Centre for Reviews and Dissemination	79	Full	6.6.2	336	Another un-cited table. Also, this table contains data from a study of cystography for the localisation of UTI, which is not mentioned anywhere in the text.	The table is now cited. The data for the study using cystography is mentioned in the previous paragraph.
SH	Centre for Reviews and Dissemination	80	Full	6.6	337, line 6-7	“Power Doppler ultrasonography increases the predictive value of ultrasound.” The data presented do not support this statement; please justify.	For localisation of infection - the GDG considered that PD did increase predictive value.
SH	Centre for Reviews and Dissemination	81	Full	6.6	338, line 7-9	“When acute imaging is performed then, ultrasound, including power Doppler evaluation because it is readily available, less invasive and does not involve ionising radiation.” This statement contradicts the recommendation given below it: “In the rare instances where it is clinically important to confirm or exclude upper tract infection a DMSA scan is recommended.”	This section has been reworded.
SH	CIS'ters					This organisation was approached but did not respond.	
SH	Coloplast Limited					This organisation was approached but did not respond.	
SH	Commission for Social Care Inspection					This organisation was approached but did not respond.	
SH	Connecting for					This organisation was approached but	

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	Health					did not respond.	
SH	Conwy & Denbighshire Acute Trust					This organisation was approached but did not respond.	
SH	Co-operative Pharmacy Association					This organisation was approached but did not respond.	
SH	Cornwall & Isles of Scilly PCT					This organisation was approached but did not respond.	
SH	Craven Harrogate and Rural District PCT					This organisation was approached but did not respond.	
SH	Croydon PCT					This organisation was approached but did not respond.	
SH	Department of Health	1	General			I would like to confirm that the Department of Health has no comments to make on this document.	
SH	East Cambridgeshire and Fenland Primary Care Trust					This organisation was approached but did not respond.	
SH	Eastbourne Downs Primary Care Trust					This organisation was approached but did not respond.	
SH	Faculty of Public Health					This organisation was approached but did not respond.	
SH	Gloucestershire Acute Trust					This organisation was approached but did not respond.	
SH	Good Hope Hospitals NHS Trust					This organisation was approached but did not respond.	
SH	Great Ormond Street Hospital for Children NHS Trust					This organisation was approached but did not respond.	
SH	Hampshire Partnership NHS Trust					This organisation was approached but did not respond.	
SH	Health Protection	1	Full	General		The Infection Control Team at HPS have reviewed this guideline with	Thank you for your comments. UTI is not an infectious disease in that the

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	Agency					particular reference to the infection control elements that would be expected, in line with the nature of the document. The review process has revealed that no infection control precautions have been included within the guideline. We feel that there are clear areas in which infection control measures should either be considered for inclusion or cross reference, for example in Chapter 4.5 on urine collection via catheter or Suprapubic aspiration (SPA). It is therefore recommended that infection control precautions should be included in the appropriate sections of the document, in line with current UK Infection Control guidelines for example (see below). National Institute for Health and Clinical Excellence 2003, Infection control, prevention of healthcare associated infection in primary and community care, NICE, England Evidence Based Practice in Infection Control, 2001, Guidelines for Preventing Hospital-acquired Infections, Guidelines for preventing infections associated with the insertion and maintenance of short-term indwelling urethral catheters in acute care, EPIC, England [available online] Evidence Based Practice in Infection Control, 2006, National Evidence-based Guidelines for Preventing Healthcare Associated Infections in NHS Hospitals in England, EPIC2, England [out for consultation] NHS Quality Improvement Scotland, 2004, Best Practice Statement, Urinary Catheterisation & catheter care, Scotland. Health Protection Scotland, 2006, Model Infection Control	infecting organisms are believed to arise from the patients' own gut flora. This is outside our scope. Please refer to the NICE guideline on Infection control.

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						Policies, HPS, Glasgow [available online]. This reference is included because these policies underpin the fundamental infection control measures that should be applied at all times. (Standard Infection Control Precautions) The document is well written and the inclusion of evidence summaries, followed by translations and recommendations enables the evidence surrounding each recommendation to be clearly identified. We would welcome and value this guideline. However, consideration of the possible inclusion of appropriate infection control elements, to strengthen the information and provide a consistent message in the UK would be valuable. We would be happy to understand why infection control was not included in the document and would welcome any comment or discussion regarding this.	
SH	Healthcare Commission					This organisation was approached but did not respond.	
SH	Heart of England NHS Foundation Trust					This organisation was approached but did not respond.	
SH	Hertfordshire Partnership NHS Trust					This organisation was approached but did not respond.	
SH	Hospital Infection Society					This organisation was approached but did not respond.	
SH	Infection Control Nurses Association of the British Isles					This organisation was approached but did not respond.	
SH	Institute of biomedical Science					This organisation was approached but did not respond.	

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SH	King's College Acute Trust	1	NICE Algorithm	General		The main practical problem with UTI in children is potential mis-interpretation of specimen culture results so that many children are referred with what is NOT a UTI at all despite a positive urine culture. The diagnostic algorithm is quite useful for this, but the most difficult group are in fact children under the age of 3 years where the algorithm discounts the value of urine stix analysis completely. These guidelines don't help us to resolve this and weigh the value of urine examination results in making a decision.	Thank you for your comments. We agree. Studies of Incidence have (recently) acknowledged this.
SH	King's College Acute Trust	2	NICE algorithm			There is also no answer as to what should happen about bag specimens of urine, although this is how most urine is collected in small children.	The guideline recommends clean catch urine as the preferred method, but resorting to pads or bags if a clean catch sample cannot be obtained. The data on washed up potties was not considered secure enough to use as evidence for analysis. This does not mean that this method is invalid but that it requires further study.
SH	King's College Acute Trust	3	NICE Algorithm			The statement about systemically well children as being children who have a suspected UTI but are systemically well, doesn't really match with my experience of the clinical problem. Most younger children in whom one might suspect UTI, have systemic symptoms, and who is to say that their temperature has/has not been over 38 degrees?- most parents do not record temperature. This means, that it may be practically impossible to exclude systemic features from consideration even when they are not present at the time of examination.	The fever guideline advises that fever reported by parents should be acknowledged and that the temperature should be measured by any health professional managing a sick or febrile child. In addition the illness risk should be assessed using the criteria they have suggested. We acknowledge that many children under 12 months with UTI have a fever. UTI accounts for around 5% of these children and over 10% if there is no obvious cause for the fever.
SH	King's College Acute Trust	4	NICE Algorithm			Ultrasound scanning. The quality of renal ultrasound scanning really cannot be ascribed a national standard, and yet this algorithm treats renal	No benefit was identified from DMSA scanning or identification of VUR in the majority of children with first time UTI. Therefore these imaging tests have not

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						ultrasound scanning is if it was quality assured. I have worked in hospitals where I could not rely on the interpretation of ultrasound findings- King's is fortunately especially good, but I have had patients with proven 13% renal function on one side referred with "normal Ultrasound findings" reported in other hospitals. What also has happened to the risk of undiagnosed vesicoureteric reflux in infants under the age of 1 year, and the use of prophylactic antibiotics?	been recommended except in the highest risk groups. In these groups there is the greatest likelihood of identifying a lesion that will benefit from an intervention. The aim of ultrasound is to identify the presence of obstruction or bladder emptying problems. The identification of other abnormalities has not been shown to influence outcomes.
SH	King's College Acute Trust	5	algorithm			As an experienced paediatrician, I am not happy about the algorithm because it does not help to deal with the practical issues particularly in the younger child, and leaves many questions unanswered. I am particularly concerned about the degree of confidence placed on ultrasound assessment, and the possibility for downgrading a child into the "systemically well" category when this may not be warranted.	No benefit has been identified from additional imaging investigations except in the relatively uncommon situation of a child with recurrent attacks of acute pyelonephritis.
SH	Leeds Teaching Hospitals NHS Trust					This organisation was approached but did not respond.	
SH	Liverpool PCT					This organisation was approached but did not respond.	
SH	Luton and Dunstable Hospital NHS Trust	1	NICE	1.1.2.2.		Please add: “even if only one sign or symptom persists” to the last sentence	Thank you for your comments. This has been amended and the recommendations reworded.
SH	Luton and Dunstable Hospital NHS Trust	2	NICE	1.1.2.3	9-10, table 1	Offensive urine has clearly been shown not to be an indicator of urinary tract infection in several studies. This item should therefore be excluded from the list of signs and symptoms. Struthers S, Scanlon J, Parker K, Goddard J, Hallett R. Parental reporting of smelly urine and urinary tract infection. Arch	Offensive urine was one of the symptoms evaluated in the evidence and is represented in the table because it was cited in the evidence reviewed.

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						Dis Child 2003;88:250-2. Midthun SJ, Paur R, Lindseth G. Urinary tract infections. Does the smell really tell? J Gerontol Nurs 2004;30:4-9.	
SH	Luton and Dunstable Hospital NHS Trust	3	NICE	1.3.5.2	16-17	Imaging in children who are systemically unwell: Children toilet trained and older. It is inappropriate and not supported by evidence not to perform a DMSA scan in children with severe UTI when they are toilet trained and older. While some forms of vesicoureteric reflux are age dependent, renal scarring is not and severe pyelonephritis can cause renal scarring at any age. Renal scarring occurs in kidneys without vesicoureteric reflux. The following study and review show this very clearly: Ataei N, Madani A, Habibi R, Khorasani M. Evaluation of acute pyelonephritis with DMSA scans in children presenting after the age of 5 years. Pediatr Nephrol 2005;20:1439-44. Jakobsson B, Jacobson SH, Hjalmas K. Vesico-ureteric reflux and other risk factors for renal damage: identification of high-and low-risk children. Acta Paediatr Suppl. 1999;88:31-9. In children with recurrent cystitis a DMSA scan is not justified (See column "Recurrent UTI").	The advice on when to perform a DMSA scan is based on a reduction in imaging from current practice while focussing tests on the small number of children who are at greatest risk of scarring.
SH	Luton and Dunstable Hospital NHS Trust	4	NICE	1.2.1.3.	14	In pyelonephritis or septicemia due to UTI it should be recommended to use an antibiotic the organism (mostly E.coli) is likely to be sensitive to like a third generation cephalosporine and not an antibiotic with a high percentage of resistant strains like trimethoprim or amoxycillin.	The treatment of severely ill children will be informed by the fever guideline. The treatment of acute pyelonephritis has been clarified and examples given.
SH	Maidstone and Tunbridge Wells					This organisation was approached but did not respond.	

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	NHS Trust						
SH	Medicines and Healthcare Products Regulatory Agency (MHRA)					This organisation was approached but did not respond.	
SH	Mid Essex Hospitals NHS Trust	1	NICE	1.1.4	11	(a)Establishing a diagnosis of UTI is the most difficult task that we face in the management of UTI in children. In infants < 1year and who is systemically unwell and in whom we suspect UTI SPA urine or catheter urine should be the preferred method. (b)I have not seen good data to confirm that "urine collectio pads" are as good as "clean catch urine" (c) Please specify what other proven non-invasive methods are available to collect reliable sample	Thank you for your comments. The GDG agree with your comment. Urine collection is difficult and tests on non-invasive urine samples are often inconclusive. Data on urine collection and testing methods are incomplete for the most critical and difficult age group. Hence a pragmatic approach has been taken, using evidence-based information where available and supplementing this with the clinical experience of the GDG members.
SH	Mid Essex Hospitals NHS Trust	2	NICE	1.2.4	15	The guideline does not discuss whether antibiotic prophylaxis is indicated in children with VUR	The guideline recommends that children with VUR should be referred to a specialist. Prophylaxis is not routinely recommended but has not been ruled out for selected cases if the specialist feels this might be beneficial.
SH	Mid Essex Hospitals NHS Trust	3	NICE	1.2.1	13-14	It will be better if the guideline names the antibiotics recommended for treatment	The most suitable antibiotic cannot be concluded from the studies retrieved in children. The GDG advised that there should be a local policy informed by monitoring local sensitivity patterns. Some pragmatic suggestions have been included in the revised version.
SH	Mid Essex Hospitals NHS Trust	4	NICE	General		In infants 0-6 months with atypical UTI/recurrent UTI and in whom US has ruled out any dilatation - what will a very invasive test like MCUG contribute?	The decision was based on the view that current imaging is excessive and that invasive tests like MCUG should be carried out only in a more selected group of patients. There is a higher incidence of urethral valves and the most severe grades of VUR in infants presenting with UTIs in the first 6 months of life.

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SH	Mid Essex Hospitals NHS Trust (2)	1	Full	2	91, line 6	This says urine should be checked with any of the suggested symptoms or signs. I feel this should be done only if the symptoms and signs are unexplained. If there is an obvious diagnosis waiting for a urine sample can cause unnecessary and detrimental delay	This has been clarified in the revised document.
SH	Mid Essex Hospitals NHS Trust (2)	2	Full		91, line 8	Similar thoughts as above	This has been clarified in the revised document.
	Mid Essex Hospitals NHS Trust (2)	3	Full	2	92, line 9	Pad samples, I feel, should only be used for ruling out UTI. If the pad sample is positive, if the child is well I would try and get clean catch urine; if the child is unwell invasive method should be used to get urine if applicable. A positive diagnosis of UTI, I feel, should only be made on a clean catch method, mid stream or invasive method	Thank you for your comment.
SH	Mid Essex Hospitals NHS Trust (2)	4	Full	2	101, line 7-9	In this section it says about not sending urine culture for first time urinary infection even if dipstick neg or positive. How can we say first time urinary infection when the urine dip is neg? I would prefer children with first time urinary symptoms rather than infection	We agree except that symptoms are vague: the concept is fine, but an adequate definition may be difficult.
SH	Mid Essex Hospitals NHS Trust (2)	5	Full	2		Page 101 line 14 This line contradicts with the above statement where it says not to send urine even if the dip is positive for leuc/Nitrates.	We have amended the text and recommendations to clarify this.
SH	Mid Essex Hospitals NHS Trust (2)	6	Full	General		The reason now we do not as much abnormalities in investigations for UTI as 10 years before is because of the effective antenatal screening which picks out most of the congenital renal abnormalities and vesicoureteric reflux. The 1991 RCP guideline was effective for that decade . Now the antenatal screening is too effective that it is even	This point has been addressed in the revised guideline.

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						picking up minor renal pelvic dilatation, which settles in the first few months of life. This group of children with congenital renal abnormalities are separated out and investigated separately now. Hence children (for which this guideline applies) who presents with first time UTI has got a good pair of kidneys to start with and do not need as extensive investigations as in 1990s. I feel this is the main reason for this updated guideline and should be emphasised early in the guideline.	
SH	National Kidney Federation (NFK)					This organisation was approached but did not respond.	
SH	National Kidney Research Fund, The					This organisation was approached but did not respond.	
SH	National Patient Safety Agency					This organisation was approached but did not respond.	
SH	National Public Health Service - Wales					This organisation was approached but did not respond.	
SH	Neonatal & Paediatric Pharmacists Group (NPPG)	1	NICE	1.2.1.5		IM is missing from " should be considered"	Thank you for your comments. The text and recommendations have been amended.
SH	Neonatal & Paediatric Pharmacists Group (NPPG)	2	NICE	1.3		For MCUG – Should this be clearer. Would "Treatment doses of prophylactic antibiotics be given for 3 days with MCUG taking place on the second day." be more appropriate?	Thank you for this suggestion. This recommendation has been reworded.

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SH	Neonatal & Paediatric Pharmacists Group (NPPG)	3	Full	5.2		Current recommendations from PRODIGY vary greatly from the proposed new NICE recommendations. There are quite a number of studies comparing short duration and long duration antibiotics, not all agree that the shorter course is acceptable. Bearing in mind the dangers of pyelonephritis and renal scaring is it safe to move to the shorter treatment regimes with out further randomised controlled trials. Some papers for longer treatment. Ron Keren, MD, MPH and Eugenia Chan, MD, MPH. A Meta-analysis of Randomized, Controlled Trials Comparing Short- and Long-Course Antibiotic Therapy for Urinary Tract Infections in Children. PEDIATRICS Vol. 109 No. 5 May 2002, pp. e70 R Keren and E Chan. Short versus standard duration antibiotic treatment for UTIs: a comparison of two meta-analyses. Archives of Disease in Childhood 2003;88:89-91	The GDG considered the evidence available and concluded that 3 days of treatment was satisfactory and safe for children at low risk of acute pyelonephritis, which was defined as not having a fever over 38 °C and not having loin pain or tenderness. If in doubt cases should be managed according to the proposals for acute pyelonephritis. The decisions of this guideline have been made independently of any decisions made in other guidelines.
SH	Neonatal & Paediatric Pharmacists Group (NPPG)	4	Full	5.5.3		Not using prophylactic antibiotics as currently recommended by PRODIGY will present a great change in practice. While there is not a great level evidence in favour of prophylaxis. Without further well designed randomised controlled trails is it safe to omit antibiotic prophylaxis, which may protect the few children that may present at risk of further infection, with structural abnormalities etc.	The view of the GDG was that children should not be routinely subjected to treatments of unproven value.
SH	Newcastle PCT					This organisation was approached but did not respond.	

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SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	1	FULL NICE	General		The comments collated below are from the Department of Paediatric Nephrology and Paediatricians in Department of Paediatrics within the Newcastle Upon Tyne Hospitals Trust. In addition a number of individual paediatric consultants who are part of the Regional paediatric service who refer cases to Newcastle Upon Tyne Hospitals have added comments.	Thank you for your comments.
SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	2	FULL NICE	General		Urinary tract infection (UTI) in childhood is a common problem encountered by almost all clinicians active in paediatrics. There has been for many years considerable debate particularly relating to diagnosis and investigation of childhood UTI. It is widely acknowledged that there is a paucity of evidence in many areas and UTI has therefore been managed by clinicians using a mixture of evidence based medicine and consensus view. The NICE guidelines propose a markedly different approach to that proposed by the last UK consensus document prepared by the Royal College of Physicians in 1991. There is agreement that the RCP document is in need review and updating. However our examination of the Guidelines reveals severe methodological errors in a number of areas (some of which are detailed below). These serve to undermine our confidence in the methodological and statistical basis of the whole document. The conclusions reached in the document can only be as reliable as the processes used to reach those conclusions. A number of processes in this document are severely flawed and therefore whatever conclusions are reached we are	Each point has been answered separately below.

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						concerned that they are also be severely flawed. We would recommend a full and thorough review and revision of this document and would be happy to contribute further details to that process.	
SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	3	Full	1.7	83	"*It was not possible to supply GDG members with the original papers from which the technical team developed the systematic reviews. Evidence statements translations and recommendations were based on these reviews. Additionally, the guideline is in draft form and the imperative to enter into consultation means the GDG feel the document is work in progress*" We are concerned by this statement found on page 83 as it implies that members of the GDG have had some doubts about the strategies and methods employed to include or reject publications and evidence and that they were dependant on reviews produced by technical staff. The statement also implies that members of the GDG were not happy with the current version of the guidelines. We are concerned by this and it undermines confidence in the document. There is, in our view, a huge difference between a draft version of a guideline and "work in progress". We would like further exploration of the reasons behind the inclusion of this statement on page 83.	Problems described on page 83 of the consultation document have been addressed. The original papers were available for review before each meeting. During the last 4 months of the guideline development Abstracts, a of all papers were made available on the web site. Copyright arrangements were increased. Members were formally invited to review any papers that they had not been able to see previously and still needed to review. Reviews were carried out and revisited by trained evidence specialists.
SH	Newcastle Upon	4	FULL	Urine		There is concern amongst	It is the same concept as the argument

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	Tyne Hospitals NHS Foundation Trust		NICE	testing		paediatricians about both over and under diagnosis of UTI and an acknowledgement that any recommendations about subsequent management and investigation are dependant on actually getting the diagnosis correct in the first place. The guidelines propose significant changes from current practice regarding diagnosis of UTI which do not appear to improve diagnostic accuracy. We are concerned about the quality of the evidence presented to substantiate recommendations on diagnosis. We are concerned about the use of statistics particularly in this section. We note the absence of a statistician on the GDG and would urge NICE to commission a full statistical review of the evidence cited. We are also concerned that a number of publications that we are personally familiar with have been excluded from analysis and wish to question further the selection process used by the GDG.	about risk - decisions in UTI are dependent on our concerns for individual children based on a complex judgement on risk stratification.

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SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	5	Full NICE	5.5.3	286	When NICE considers the introduction of a new treatment or device then it is appropriate & logical to propose it should not be introduced (ie current practice should not be changed) if there is insufficient evidence to support its use. In the UTI guideline NICE appears to not be using the same criteria. For example: recommendations regarding the use of prophylactic antibiotics, which are currently widely used. Some publications and evidence on this which we are familiar with appears to have been discarded (see comments above regarding our concerns about the selection of reference material by the GDG). Where insufficient good evidence has been found then the guideline proposes a change from current practice to actually recommend not using prophylaxis. This is illogical. The logical conclusion on the evidence they have cited would be to say "insufficient evidence to either recommend or not recommend the use of prophylactic antibiotics". The guideline thus appears to be using insufficient evidence to equate to negative evidence. Again a review by a statistician about this use of statistics is needed.	The GDG considered that we should not do things to healthy children that have no evidence of benefit or insufficient evidence to show benefit. This applies to both widespread use of long-term low-dose antibiotics and imaging investigations.

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SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	6	FULL NICE	6.5		There is conflict in the statement about DMSA being the “most sensitive method for detecting renal parenchymal defects” but then recommending this should not be used because of the burden of ionizing radiation. Evidence of the harm of this burden is not given. DMSAs are in common use by paediatricians and the radiation dose, if compared to background radiation, is not currently considered particularly high by clinicians who explain this test on a daily basis to their patients and families. The guideline appears to be recommending a less good test on the grounds of the hazard posed by the better test but without providing evidence for this. The issue does however underline the importance again of making the correct diagnosis and only subjecting children who may benefit from investigation to it.	In this analysis DMSA was the most sensitive test but this does not mean it should be used routinely in all children with UTI. Harm from radiation is a statistical concept - but radiology professional guidance states that if there is no benefit to patients then radiation should not be used. We are not saying don't use DMSA, just use it in a defined small group of children who are at greatest risk of having a modifiable abnormality, and not routinely.
SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	7	FULL NICE	General		Where there is insufficient evidence then good clinical practice is forced to rely on clinical experience and consensus view of experts. There is little evidence or detail of any process that NICE has undertaken for obtaining a consensus view in these situations where there is insufficient evidence. Having examined the membership details of the GDG it is clear that the GDG itself would not be in a position to formulate an expert consensus view because of the experience of the individual members of the GDC. Therefore the GDG / NICE either has to state there is insufficient evidence and therefore no recommendation can be made or it has to convene expert groups to tackle specific areas to	The processes for identifying evidence, evaluating it and supplementing decisions by a consensus within the GDG have been described in detail in the methodology section. All the members of the GDG had regular experience of diagnosing and treating UTI in children of various ages. The membership was chosen to cover a wide range of clinical areas. The level of evidence is clearly stated within each evidence summary.

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						produce a consensus view.	
SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	8	Full NICE			The British Association of Paediatric Nephrology has recently circulated its membership with a review by Dr M Coulthard of the UTI guidelines. The guidelines and his review have been widely debated within the department of paediatric nephrology. There is unanimous agreement with the comments made in his report which deals in great detail with some parts of the guidelines the department had felt uneasy about. We agree with his findings that there are serious limitations in the processes used including selection and exclusion of reference papers and interpretation of statistics. In addition conclusions are drawn which do not relate to the evidence presented and there is inappropriate use of lack of evidence to support major changes in practice. The guidelines which propose major changes in current practice are seriously flawed.	Dr M Coulthard was a reviewer for the National Collaborating Centre for Women and Children's Health and a response to his comments will be managed by them. The GDG considered that it is better not to subject healthy children to imaging and treatments that have no evidence of benefit and clearly identified drawbacks. The GDG carefully considered these issues in the light of available evidence including clinical practice and local and national audits. The members considered that it was not sufficient to justify former or future management strategies on historic or current practice. The previous guideline developed by the RCP was not developed using the rigorous approach now recommended by NICE. The National Audit showed that there was a large amount of imaging and prophylaxis but little evidence that this influenced effective interventions. It also showed that 50% of children under two with fever admitted to hospital and found to have a positive urine sample did not receive a diagnosis of UTI or receive any

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							treatment or follow-up.
SH	Newcastle Upon Tyne Hospitals NHS Foundation Trust	9	NICE			Comment from Regional General Paediatrician regarding investigation after UTI "I would say however that it would be very disappointing if NICE loses the opportunity to produce a valid balanced review of the available evidence in this controversial area. They should highlight both what is known and what is not, so that parents and practitioners can make a choice based on facts."	The levels of evidence are clearly stated after each systematic review.
SH	NHS Direct					This organisation was approached but did not respond.	
SH	NHS Pathways					This organisation was approached but did not respond.	
SH	NHS Quality Improvement Scotland					This organisation was approached but did not respond.	
SH	North Tyneside Primary Care Trust					This organisation was approached but did not respond.	
SH	Northwest London Hospitals NHS Trust					This organisation was approached but did not respond.	
SH	Nottingham City Hospital					This organisation was approached but did not respond.	
SH	PERIGON					This organisation was approached but	

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	(formerly The NHS Modernisation Agency)					did not respond.	
SH	Powys Local Health Board					This organisation was approached but did not respond.	
SH	Princess Alexandra Hospital NHS Trust					This organisation was approached but did not respond.	
SH	Prodigy					This organisation was approached but did not respond.	
SH	PromoCon (Disabled Living)	1	Full	5.5.2	39	The term encopresis relates ONLY to voluntary soiling or the passage of a normal stool in an inappropriate place and is usually related to behaviour issues, also known as 'functional non-retentive soiling'. In this context 'involuntary' soiling or 'functional retentive soiling' relates to 'over flow soiling' in conjunction with constipation and relates to soiling over which the child has no control	Thank you for your comments. The definition has now been taken from a medical dictionary.
SH	PromoCon (Disabled Living)	2	Full	4.7	101	Line no 7-9 appear to contradict line 14 'urine samples should not be routinely sent for culture…which is negative or positive for both….'	This section has been revised and should be clearer. Essentially both N and LE positive rules in UTI and both negative rules out UTI. N+LE+ does not require urine to be sent for culture in first-time UTI. Where UTI has not been ruled in or out, i.e. one positive and one negative, a microscopy and culture is recommended.
SH	PromoCon (Disabled Living)	3	Full	4.7.6	241	Again line 7-9 appear to contradict line 14	We have amended the text and recommendations to clarify this.
SH	PromoCon (Disabled Living)	4	Algorithm	general		Useful concise overview but a little difficult to read – may be clearer in full size A4	The algorithm has been simplified and redrawn.
SH	PromoCon (Disabled Living)	5	General			As a practitioner I would find this guidance very useful	Thank you for your comments.
SH	Q-Med (UK) Ltd	1	Full			See attached document.	See comments on attached Word

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							document.
SH	Q-Med (UK) Ltd	1	FULL	Section 7		It is implied that because VUR tends to resolve spontaneously, and that kidney damage appears congenital, there is little ground for treating VUR on the basis of protecting renal function. However, in children prone to UTIs, the presence of VUR increases the risk of an infection spreading to the upper urinary tract and developing into pyelonephritis.[1] This condition is associated with a risk of renal damage, and there is an established association between increased occurrence of UTIs and increased risk of renal scarring.[2] In children who may have already experienced some degree of renal damage, it is important to protect the weakened renal system from the possibility of further insult resulting from later urinary tract infections. In addition to the risks of renal damage, upper urinary tract infections are associated with considerable morbidity. Infants and young children suffering severe pyelonephritis can become acutely ill, and many require hospitalisation. Significant costs are then incurred, relating to medication, physician time, potential hospital stay, children's absence from school and parental time off work to care for their children. The draft guideline states that STING may be an option in children where surgical treatment is judged necessary. The STING procedure has an entirely different profile from open surgery (ureteral reimplantation). It is less invasive and has a low complication rate. For example, "Endoscopic	While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.

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						treatment of vesicoureteral reflux with dextranomer/hyaluronic acid copolymer [Deflux® gel] was free from complications in all 310 procedures performed in our study"[3] A few patients may experience mild pain after treatment, but this was reported in less than 4% of patients in one study.[4] Ultrasound studies have shown a lack of ureteral obstruction or significant renal parenchymal changes following Deflux injection. [4] In contrast, with open surgery post-operative pain is likely and significant adverse events such as obstruction are possible.[1] Ureteral reimplantation is a major procedure requiring hospitalization, whereas the STING procedure is a minor procedure that can be performed as a day case. Therefore the Deflux procedure is far less traumatic for children undergoing the procedure than open surgery. In terms of effectiveness, cure rates reported with STING (Deflux) in studies published over the last 3 years are considerably higher than the 75% quoted in the report (over 80% of children may be cured following a single Deflux procedure).[5-7] This is likely related to the use of a modified injection procedure (hydrodistention-implantation technique, HIT).[5] The outcomes now achieved with Deflux approach cure rates reported with open surgery. Overall, therefore, we believe that the STING procedure is a far more viable treatment option than open surgery for VUR. Evidence indicates a rate of UTIs following treatment with Deflux that is similar to that in the general population,	

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						and lower than that with either antibiotic prophylaxis or open surgery.[3, 8] Pharmacoeconomic data support the use of Deflux, indicating that it is more cost-effective than either open surgery or antibiotic prophylaxis.[9, 10] The guideline as it currently stands rightly indicates various disadvantages with both antibiotic prophylaxis (resistance, breakthrough infections, non-compliance) and open surgery (major procedure requiring hospitalisation, risks of significant adverse events). There is also acknowledgement of the issues surrounding MCUG investigation. The STING procedure offers the possibility of avoiding most of the potential disadvantages of open surgery and antibiotic prophylaxis, while still providing cure in the majority of children with VUR (once cured, future MCUG investigations are unlikely to be needed). The draft guideline concludes that surgical management of VUR is not routinely recommended, with the implication that long-term antibiotic prophylaxis is supported. While we agree that the use of open surgery should not be routinely recommended, we would that the STING procedure by offering reduced invasiveness and improved safety, but similar efficacy, should be considered as a first-line treatment in place of long-term antibiotic prophylaxis. Numerous publications in the literature support	

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						this conclusion.[6, 11-13] 1. Kirsch AJ, Hensle TW, Scherz HC, Koyle MA. **Injection therapy: advancing the treatment of vesicoureteral reflux.** *J Ped Urol* in press. 2. American Academy of Pediatrics. **Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children.** American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection. *Pediatrics* 1999; **103**: 843-52. 3. Läckgren G, Wåhlin N, Sköldenberg E, Stenberg A. **Long-term follow-up of children treated with dextranomer/hyaluronic acid copolymer for vesicoureteral reflux.** *J Urol* 2001; **166**: 1887-92. 4. Yu RN, Jones EA and Roth DR **Renal ultrasound studies after endoscopic injection of dextranomer/hyaluronic acid copolymer for vesicoureteral reflux**. *Urology* 2006; **68**: 866-8 5. Kirsch AJ, Perez-Brayfield M, Smith EA, Scherz HC. **The modified STING procedure to correct vesicoureteral reflux: improved results with submucosal implantation within the intramural ureter.**	

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						J Urol 2004; **171**: 2413-6. 6. Yu RN, Roth DR. **Treatment of vesicoureteral reflux using endoscopic injection of nonanimal stabilized hyaluronic acid/dextranomer gel: initial experience in pediatric patients by a single surgeon.** *Pediatrics* 2006; **118**: 698-703. 7. Puri P, Chertin B, Velayudham M, Dass L, Colhoun E. **Treatment of vesicoureteral reflux by endoscopic injection of dextranomer/hyaluronic acid copolymer: preliminary results.** *J Urol* 2003; **170**: 1541-4. 8. Hensle TW, Hyun G, Grogg AL, Manan B. **Assessing the effectiveness of endoscopic injections in treating patients with vesicoureteral reflux for the reduction of urinary tract infections.** Presented at the 2006 Annual Meeting of the American Academy of Pediatrics, Atlanta, GA. 2006. 9. Kobelt G, Canning DA, Hensle TW, Lackgren G. **The cost-effectiveness of endoscopic injection of dextranomer/ hyaluronic acid copolymer for vesicoureteral reflux.** *J Urol* 2003; **169**: 1480-4. 10. Nicklasson L, Högård S. **Cost-analysis of management strategies for children with vesico-ureteric reflux.** *Acta Paediatr Suppl* 1999; **88**: 79-86.	

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						11. Capozza N, Lais A, Matarazzo E, Nappo S, Patricolo M, Caione P. **Treatment of vesico-ureteric reflux: a new algorithm based on parental preference.** *BJU Int* 2003; **92**: 285-8. 12. Läckgren G. **Endoscopic treatment of vesicoureteral reflux and urinary incontinence in children.** *AUA Update Series* 2003; **Volume XXII, Lesson 37**: 294-9. 13. Stenberg A, Hensle TW, Läckgren G. **Vesicoureteral reflux: a new treatment algorithm.** *Curr Urol Rep* 2002; **3**: 107-14.	
SH	Q-Med (UK) Ltd	2	FULL	2.2	Chapter 3.4 Page 96	"The development of mild renal scarring seems to mainly depend on urinary tract infections, while moderate and severe scarring are also associated with high grade reflux and male sex. Early detection and treatment may prevent further urinary tract infections as well as reflux related kidney damage." **Renal Scarring in Familial Vesicoureteral Reflux: Is Prevention Possible?** Martina E. Pirker, Eric Colhoun and Prem Puri *The Journal of Urology 2006 Vol. 176, 1842-1846.*	The link between vesicoureteric reflux, urinary tract infections and renal scarring remains unclear. Because the guideline focuses primarily on children with urinary tract infection, it is most appropriate for the research recommendation to remain in this form.
SH	Q-Med (UK) Ltd	3	FULL	2.2	Chapter 5.5.3 Page 96	"Dextranomer/hyaluronic acid (Dx/HA) copolymer has favourable properties for endoscopic treatment of vesico-ureteral reflux (VUR). This open, randomized study was performed to	The Guideline Development Group carefully considered surgical options for children with VUR and concluded that further randomised controlled trials are required before this procedure can

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						compare the efficacy and safety of Dx/HA copolymer with antibiotic prophylaxis in children with VUR." "Endoscopic treatment with Dx/HA copolymer was more effective than antibiotic prophylaxis in alleviating childhood VUR, and there were no safety concerns with either treatment." **Dextranomer/hyaluronic acid copolymer implantation for vesico-ureteral reflux: a randomized comparison with antibiotic prophylaxis** Capozza N. and Caione P. *The Journal of Pediatrics 2002; 140: 230-4.* "This retrospective analysis was conducted using the nationally representative PharMetrics Integrated Medical and Pharmaceutical database encompassing 45 million lives…There were 140 patients prescribed antibiotics and 48 Dx/HA patients matched in the analysis with a VUR diagnosis between January 2000 to December 2004. The average number of UTIs per year was 0.69 in the antibiotics cohort and 0.42 in the Dx/HA cohort, respectively…UTIs were observed in 25% of the Dx/HA patients vs 45% of the patients treated with antibiotics" "The use of antibiotic prophylaxis in the treatment of VUR resulted in 79% more UTIs when compared to endoscopic injection with Dx/HA. Based on the number of UTIs observed, treatment with endoscopic injection of Dx/HA offers better outcomes than treatment with prophylactic antibiotics."	be recommended in a national guideline. The GDG concluded that "Studies evaluating the long term benefits of the STING are pending, but in children where surgical treatment of reflux is judged to be necessary, this procedure might be an option." The GDG did not feel it was appropriate to recommend STING for children in the UK based on one, relatively small RCT. While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.

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						Assessing the effectiveness of endoscopic injections in treating patients with vesicoureteral reflux for the reduction of urinary tract infections Terry W. Hensle, Grace Hyun, Amy L. Grogg, Manan B. Shah. *Poster presented at the 2006 Annual Meeting of the American Academy of Pediatrics, Atlanta, GA. October 7-10, 2006.*	
SH	Q-Med (UK) Ltd	4	FULL	2.2	Chapter 7 Page 97	"Endoscopic correction is a safe, effective, minimally invasive outpatient procedure for high grade vesicoureteral reflux in infants. Early correction of vesicoureteral reflux may provide protection from reflux associated damage and prolonged antibiotic use." **Endoscopic Treatment of High Grade Vesicoureteral Reflux in Infants** Michael J. Dawrant, Nochiparambil Mohanan and Prem Puri *The Journal of Uology 2006 Vol.176, 1847-1850.* "The use of antibiotic prophylaxis in the treatment of VUR resulted in 79% more UTIs when compared to endoscopic injection with Dx/HA. Based on the number of UTIs observed, treatment with endoscopic injection of Dx/HA offers better outcomes than treatment with prophylactic antibiotics." **Assessing the effectiveness of endoscopic injections in treating patients with vesicoureteral reflux for the reduction of urinary tract infections** Terry W. Hensle, Grace Hyun, Amy L. Grogg, Manan B. Shah. *Poster presented at the 2006 Annual Meeting of the American Academy of Pediatrics, Atlanta, GA. October 7-10, 2006.*	While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.

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						"Of the 692 patients 18 (2.6%) had symptomatic UTIs during followup. In 2 patients UTI was an indicator of persistent high grade reflux. Therefore, followup VCUG should be performed if a symptomatic UTI occurs after endoscopic treatment for VUR even if the 3-month followup cystogram shows reflux resolution. The incidence of UTI in the population without persistent reflux was 2.3% in girls and 0.29% in boys. Considering the median followup of 24 months, these rates are comparable with the annual incidence of 0.9% to 1.4% in girls and 0.1% to 0.2% in boys reported in the general population." **Subureteral Dextranomer/Hyaluronic Acid Injection as First Line Treatment in the Management of High Grade Vesicoureteral Reflux** Prem Puri, Martina Pirker, Nochiparambil Mohanan, Michal Dawrant, Laxman Dass and Eric Colhoun *The Journal of Urology Vol. 176, 1856-1860, October 2006.* This final citation highlights the effectiveness of endoscopic subureteral injection of Deflux® for prevention/reduction of UTI episodes. Please refer to the full clinical paper for further details on the study.	
SH	Q-Med (UK) Ltd	5	FULL	3.4.8	Page 137	"A total of 120 children with VUR were endoscopically treated between June 2, 2003, and January 18, 2005…After the initial treatment, 6 patients were lost to follow-up, and 7 had not yet undergone a postoperative VCUG…Therefore the efficacy population consisted of 107 patients, in	While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.

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						whom 162 refluxing ureters were treated." "Reflux was resolved in 88 patients (82.2%) after a single NASHA/Dx gel treatment. After the second implantation, the number of patients free from reflux increased to 97 (90.7%)." "Nevertheless, the lowest grade-specific resolution rate (grade IV) was 68%, meaning the majority of patients can expect a positive outcome." "The present study has shown that VUR may be cured by endoscopic injection of NASHA/Dx gel in a high proportion of patients. Therefore, endoscopic treatment with NASHA/Dx gel is a valuable treatment option for children with VUR and should be considered as a first-line treatment in place of antibiotic prophylaxis." **Treatment of Vesicoureteral Reflux Using Endoscopic Injection of Nonanimal Stabilized Hyaluronic Acid/Dextranomer Gel: Initial Experience in Pediatric Patients by a Single Surgeon** Richard N. Yu and David R. Roth *Pediatrics 2006; 118;698-78.*	
SH	Q-Med (UK) Ltd	6	FULL	7	Page 346 Rows 1-5	"The use of antibiotic prophylaxis in the treatment of VUR resulted in 79% more UTIs when compared to endoscopic injection with Dx/HA. Based on the number of UTIs observed, treatment with endoscopic injection of Dx/HA offers better outcomes than treatment with prophylactic antibiotics." **Assessing the effectiveness of endoscopic injections in treating patients with vesicoureteral reflux for the reduction of urinary tract infections** Terry W. Hensle, Grace	While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.

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						Hyun, Amy L. Grogg, Manan B. Shah. *Poster presented at the 2006 Annual Meeting of the American Academy of Pediatrics, Atlanta, GA. October 7-10, 2006.*	
SH	Q-Med (UK) Ltd	7	FULL	7	Page 346 Rows 9-14	"Endoscopic subureteral injection of Deflux® is excellent first line treatment in children with high grade vesicoureteral reflux. This 15-minute outpatient procedure is safe and simple to perform, and it can be easily repeated in failed cases." **Subureteral Dextranomer/Hyaluronic Acid Injection as First Line Treatment in the Management of High Grade Vesicoureteral Reflux** Prem Puri, Martina Pirker, Nochiparambil Mohanan, Michal Dawrant, Laxman Dass and Eric Colhoun *The Journal of Urology Vol. 176, 1856-1860, October 2006.* "The majority of patients undergoing minimally invasive therapy for VUR with Dx/HA are cured after 1 treatment. The modified STING is our preferred method of implant injection for the correction of VUR and in our hands produces a resolution rate of 89% (92% of ureters.)" **The Modified Sting Procedure to Correct Vesicoureteral Reflux: Improved Results with Submucosal Implantation within the Intramural Ureter** Andrew J. Kirsch, Marcos Perez-Brayfield, Edwin A. Smith and Hal C. Scherz. *The Journal of Urology Vol 171, 2413-2416, June 2004.* "The present study has shown that VUR may be cured by endoscopic	While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.

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						injection of NASHA/Dx gel in a high proportion of patients. Therefore, endoscopic treatment with NASHA/Dx gel is a valuable treatment option for children with VUR and should be considered as a first-line treatment in place of antibiotic prophylaxis." **Treatment of Vesicoureteral Reflux Using Endoscopic Injection of Nonanimal Stabilized Hyaluronic Acid/Dextranomer Gel: Initial Experience in Pediatric Patients by a Single Surgeon** Richard N. Yu and David R. Roth *Pediatrics 2006; 118;698-78.*	
SH	Q-Med (UK) Ltd	8	FULL	7	Page 346 Rows 18-19	"The majority of patients undergoing minimally invasive therapy for VUR with Dx/HA are cured after 1 treatment. The modified STING is our preferred method of implant injection for the correction of VUR and in our hands produces a resolution rate of 89% (92% of ureters.)" **The Modified Sting Procedure to Correct Vesicoureteral Reflux: Improved Results with Submucosal Implantation within the Intramural Ureter** Andres J. Kirsch, Marcos Perez-Brayfield, Edwin A. Smith and Hal C. Scherz. *The Journal of Urology Vol 171, 2413-2416, June 2004.*	While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.
SH	Queen Elizabeth Hospital NHS Trust (Woolwich)					This organisation was approached but did not respond.	
SH	Regional Public Health Group - London					This organisation was approached but did not respond.	
SH	Rotherham Primary Care Trust					This organisation was approached but did not respond.	

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SH	Royal Bolton Hospitals NHS Trust					This organisation was approached but did not respond.	
SH	Royal College of General Practitioners	1	Full			Firstly, congratulations to the authors for producing such a comprehensive and generally clearly written guideline. I think it makes excellent use of the available evidence and communicates this in practical and logical steps highlighting the deficiencies in the literature well. Hence my comments are minor and do not alter the overall guideline in any way. They are listed below roughly in order of importance.	Thank you for your comments.
SH	Royal College of General Practitioners	2	Full	4.3	179, table 4.3.2	Abdominal pain cannot be reported by a neonate and hence this should be removed from the neonate column. Also I would suggest that rigors should be inserted below fever for children in preverbal and verbal columns. I would add rash (suggestive of circulatory shock) that could include cyanosis pallor and mottling.	The symptom tables were derived from published papers giving evidence. Signs of severe illness and septicaemia are described in the fever guideline.
SH	Royal College of General Practitioners	3	Full	6.6 algorithm 2.5		I could not find this	The algorithm has been simplified and redrawn.
SH	Royal College of General Practitioners	4	Full	3.4.3	128/168, linne 14	Perhaps it is worthwhile flagging up that the studies that we have are over 25 years old (i.e 1979 to 1990) This supports their conclusions later that a well conducted cohort study is badly needed in this area. Also most of the published research is limited by being set within the secondary care setting and not in primary care where 90% of clinical contacts with children take place. Elsewhere this is acknowledged (eg 4.5 p182)	The Dickinson study in General Practice was 1979. All references include the date of publication. The studies on which the summary data are based are post-1990. The cohort study suggested is to address long-term risk (rather than incidence). The best incidence studies were population based-, so although the researchers were from secondary care, their population was typical of the whole of the local population.

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SH	Royal College of General Practitioners	5	Full	5.2		It is a minor point but this paragraph begins with 3 bullet points. I would make the last sentence 'Severely ill children…' a 4th separately bulleted point	We could not identify this problem.
SH	Royal College of General Practitioners	6	Full	6.6	heading	Typo error Localisation sp	Thank you for this comment.
SH	Royal College of General Practitioners	7	Full	4.4.2	182	Recommendation 4th bulleted point - 'Ill appearing' could be better put as 'appears ill'	Terms of illness severity have been aligned with the terms used in the fever guideline.
SH	Royal College of General Practitioners	8	Full			Rather than even trying to read 680 pages I have simply looked at the diagnosis section which is most relevant to my work as a GP. One of the areas I have worked with has been in the use of microscopy in general practice. This skill is easily developed and as a GP tutor I am keen to look at opportunities to roll out this skill into routine practice. For the under 3s this is invaluable in practice and is manageable and practical within the routine surgery. I would be sorry if NICE did not flag up the significant benefits in early accurate diagnosis (and immediate exclusion of UTI in feverish kids with no obvious source of infection). PBC provides opportunities to fund practices with the microscopes and provide training. I am also a little dubious about the accuracy of the dip stix testing. It may be that things have improved but I believe they have significant false positive and negative results--which might have potentially serious consequences if too much weight is placed on their accuracy.	Thank you for your comment. A more detailed analysis of the data on dipstick testing in children under 2 years has suggested that dipsticks are less effective in this age group and the guideline has been amended accordingly to recommend microscopy and culture in children under 3 years. The guideline does not dictate where the microscopy and culture should take place and would not rule out use of microscopy within the surgery if staff were suitably trained and skilled. Many GPs will not be keen on this, but for those who are prepared to put in the effort, we think they will be rewarded with improved management.

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SH	Royal College of General Practitioners	9	All	General		Throughout all documents, you have used 3 years as a distinction. However, the wording may be open to interpretation. That is, you have used “Children under 3” and “Children over 3”. What about the 3 year old? I would argue that to be absolutely clear, throughout the documents you should use “Children under 3” and “Children aged 3 or more” (or some such wording”	This has been addressed in the Guideline.
SH	Royal College of General Practitioners Wales					This organisation was approached but did not respond.	
SH	Royal College of Nursing	1	Full	4.7		The table that shows the results of the dipstick seems good and helpful. However, consider that there are fundamental flaws in the statistical methodology. It appears to be currently based on adult work with no age stratification.	Thank you for your comments. We have amended the text and recommendations to clarify this.
SH	Royal College of Nursing	2	Full	4.7	218-219 and 229 and 241	In the guideline the developers state that dipstick negative results are 100% accurate except for under 2 yrs when they are 95% accurate. The guideline therefore recommends urine cultures for under 3 yrs by group consensus. Why are the 2-3yrs included in this recommendation anyway? We could not find any evidence for this other than the group consensus. (See comments below) For the under 2yrs 95% accurate seems good, if the families are given advice for on what to do if symptoms do not abate or worsen. In our view, to stop dipstick on the under 3yrs would have big effects on waiting times and costs, for little clinical impact it seems.	We have amended the text and recommendations to clarify this.
SH	Royal College of Nursing	3	Full	4.7		Concerned that the evidence upon which fundamental management is	We have amended the text and recommendations to clarify this.

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						based i.e. dipsticks, is flawed since it represents work mainly done in the adult population and is not age stratified. The younger the child, the more likely the dipstick is to be negative - it is this age group that is most likely to sustain renal scaring.	
SH	Royal College of Nursing	4	Full	4.7		Dipsticks are not reliable at ruling out a diagnosis of UTI in children, and it is this age group which appears to be most at risk of sustaining permanent damage from renal scarring - it is probably safer to send a urine sample for culture rather than relying on dipsticks to rule out a UTI.	We have amended the text and recommendations to clarify this.
	Royal College of Nursing	5	Full	4.5	183, line 7-9 and 199, line 5-6	Use of cotton wool balls i.e. that amongst other things should not be used as they have bactericidal agents incorporated. Some clinicians use STERILE cotton wool balls from CSSD packets and question whether these may have bacteriocidal agents. There is evidence to suggest that there is. (see below (Lancet 27.August 1994-letter Vernon.S et al) Letter written to Lancet 2004 states that fatty acids produced during their manufacture are anti bacterial, reducing some bacteria by c.75% which was added during manufacture therefore rendering cotton wool balls unsuitable. This was not referenced in the draft document because it is outside NICE's guideline methodology.	The guideline recommends that cotton wool balls should not be used.
SH	Royal College of Nursing	6	NICE	1.1.4	12 and 13	The above points are also included in the care pathway / algorithm and testing It is important that the definitions given in the glossary are correctly stated.	Thank you for your comment.
SH	Royal College of Nursing	7	Full	Glossary	39	The term encopresis relates ONLY to voluntary soiling or the passage of a normal stool in an inappropriate place	The definition has been reviewed by the GDG.

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						and is usually related to behaviour issues, also known as 'functional non-retentive soiling'. In this context 'involuntary' soiling or 'functional retentive soiling' relates to 'over flow soiling' in conjunction with constipation and relates to soiling over which the child has no control.	
SH	Royal College of Nursing	8	Full	2.3	101, line 7-9	Line no 7-9 appear to contradict line 14 'urine samples should not be routinely sent for culture…which is negative or positive for both….'	We have amended the text and recommendations to clarify this.
SH	Royal College of Nursing	9	Full	Page 241		Again line 7-9 appear to contradict line 14	We have amended the text and recommendations to clarify this.
SH	Royal College of Nursing	10	Algorithm			Useful concise overview but a little difficult to read – may be clearer in full size A4. Also consider that the Algorithm is probably flawed in view of methodological concerns.	The algorithm has been simplified and redrawn
SH	Royal College of Nursing	11	Full	General		We are concerned that this document is based on some research carried out in entirely different health care settings and yet evidence from the UK has been disregarded because it does not fit NICE guideline criteria.	Some of the studies retrieved were from different countries. However this was taken in to account when interpreting the evidence. The healthcare settings in different countries are likely to have a significant bearing on the rates of UTI and pyelonephritis.
SH	Royal College of Nursing	12	Full	General		Also concerned that the approach adopted appears to swing too far in the opposite direction to previous understanding of the management of UTI in children without adequate evidence to support the proposed approach and excludes any concept of prevention of renal scarring and later progressive renal pathology in spite of strong experience to the contrary.	The guideline aims to minimise the risk of renal scarring by ensuring good early detection and treatment of each UTI in all age groups. In the absence of evidence that long-term interventions such as prophylaxis in healthy children are effective the GDG did not think it was justified to continue the current imaging strategies.
SH	Royal College of Nursing	13	Full	General		In general, practitioners would find guidance on this topic very useful if developed from sound evidence – however some GPs and others have advised that they find the current	Current practice fails to diagnose a high proportion of children with UTI in both primary and secondary care. The guideline is designed to improve this. The National Audit showed that 50% of

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						Alogrithim confusing. We are however concerned by methodological issues, including the selection of evidence and what would appear to be flawed analysis of findings upon which recommendations are made, with some aspects potentially being solely based upon review group members assumptions and opinions. We would urge NICE to review the content of this particular guidance and recommendations further, particularly as it would appear that the recommendations would result in a failure to diagnose 10% of children who have a UTI and we are conscious of the fact that early renal scarring can have a significant impact upon renal function later in life, with a requirement for intervention to the extent of renal transplantation.	children under 2 admitted to hospitals in England and found to have a UTI on culture did not receive any treatment or diagnosis as a result of poor implementation of existing guidelines. In the North East their nurse-led programme led to a fourfold increase in rate of UTI diagnosis suggesting that without this service UTIs may have been underdiagnosed- and under-treated. The GDG considered that the best strategy for minimising the risk of scarring was to ensure that each child with a symptomatic UTI is diagnosed and treated promptly. The methodology has been described in the guideline in detail. It is not possible to comment on 'flawed analysis' unless precise details of the area of concern are provided.
SH	Royal College of Paediatrics and Child Health	1	General			I wish to congratulate the guideline committee on having produced a guideline which I think combines rational practicality with using the available evidence as much as possible. I my opinion the majority of children present with a UTI in primary care, can be managed in primary care and do not come to any harm. The guideline has ensures that children with more troublesome clinical courses are evaluated in secondary care with more involved investigations and treatments. I do not think that this guideline will lead to undiagnosed pathology like hypertension and renal failure, it will lead to less referrals to secondary care and unnecessary investigations and puts GPs firmly in charge of managing a condition that should be managed in primary care	Thank you for your comments.

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SH	Royal College of Paediatrics and Child Health	2	General			There is no mention of the problem of under-recognition of UTIs by GPs, who are the main clinicians that diagnose and treat this condition. I think it will improve the pick-up rate of UTIs in the community because of the simplicity of the guideline but there could be more direct encouragement of GPs to take urine specimens in children and record UTIs.	The combination of clear guidance from the fever guideline and this guideline should make it much more clear when UTI should be considered and when urine should be collected to test for UTI. The under-diagnosis of UTI is mentioned in the background section and scope.
SH	Royal College of Paediatrics and Child Health	3	Full NICE	4.7.6.2	240 NICE page 12 table 2	The middle two sections are 'probable UTI' and 'may or may not be UTI' respectively. But there is no indication as to whether these episodes should be allotted to UTI or not UTI category as far as follow up and investigation is concerned. Also, In the 'UTI excluded' row, actually UTI is not excluded but simply very unlikely. The guideline wording could reflect this uncertainty, and if data were adequate, even quantify the uncertainty (e.g.: about 1 in 1000 risk of UTI). Similarly the statement at the top of the table – UTI – simply reflects a high probability making UTI 'highly likely'.	We have amended the text and recommendations to clarify this.
SH	Royal College of Paediatrics and Child Health	4	Full NICE	Care Pathway		In the "if symptoms and/or signs of UTI, collect urine" section there is a potential difficulty as follows: - pyrexia is a sign of UTI, collecting urine is often difficult and "if not obtainable" may be accepted too readily and "antibiotic treatment should not be delayed if urine is not obtained" may potentially allow some to approach the issue of pyrexia as needing antibiotics "in case it might be a urinary tract infection".	The pathway through this difficult situation has been described in more detail in the revised document.
SH	Royal College of Paediatrics and Child Health	5	Full NICE	Care Pathway		Not collecting urine < 3 years old could produce a lot of problems - urine is cultured for two reasons - diagnosis and sensitivity information. Even if diagnosis can be satisfactorily	We are well aware of the two reasons for sending urine samples. We considered and discussed risks and benefits including issues around severity of diseases, age, accuracy of

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						undertaken by dipstix not sending urine may produce difficulties in accumulating information about sensitivity in general.	diagnosis and additional information from sending them, and amended the recommendations to clarify this.
SH	Royal College of Paediatrics and Child Health	6	Full	Algorithm		The algorithm states doing an acute ultrasound on an atypical UTI, which includes a non E.coli UTI. Unless we have taken a urine culture (which we aren't necessarily doing on children over 3), we will not know the organism. Also unless this child is admitted it will not be possible to do an ultrasound.	Thank you for your comment. We have amended the text and recommendations to clarify this.
SH	Royal College of Paediatrics and Child Health	7	NICE	General		The recommendations are very clear and reasonable. The tables (3 onwards) are particularly helpful. A minor point is the use of terms that suggest certainty, where there is none.	Thank you for your comments.
SH	Royal College of Paediatrics and Child Health	8	NICE	Introduction	3	The importance of accurate diagnosis depends on the effectiveness of subsequent investigations and follow up in altering the outcome. It may be more easily understood to follow this with a statement to the effect that the evidence of effectiveness of subsequent investigations and follow up in altering the outcome is not well established so a pragmatic approach to the diagnosis of urinary tract infection is often appropriate"	Agree, the introduction has been extensively re-written.
SH	Royal College of Paediatrics and Child Health	9	NICE	Patient-centred care	4	Importance of communication is stressed quite rightly but there is no attempt to produce a temple for written information that might be usable for this purpose. It may be easier to get people to buy into the ideas if there was a sample information sheet that could be adapted for local use.	This will be addressed through the document on advice for carers and the implementation programme.
SH	Royal College of Paediatrics and Child Health	10	NICE	1.1.4.1		A widely acceptable written description of how to collect urine specimens from children might be useful. I have attached the ones I try to use but I am	This will be addressed in the document prepared for patients and parents in greater detail.

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						sure that something much better could be produce to bring clarity to an area where practice varies greatly. One of the advantages of giving this information to parents is that they will be able to draw it to the attention of other medical staff they come across in future.	
SH	Royal College of Paediatrics and Child Health	11	NICE	1.1.5.2		This recommendation could be made more specific e.g. the standard boric acid specimen container required 25 mls of urine to be made up according to the manufactures instructions. It is unusual to be able to collect this volume of urine in children less than ??5 years of age.	Such details are outside our Scope.
SH	Royal College of Paediatrics and Child Health	12	NICE	1.1.6.1		While this is only an outline I think this is such an enormous change in practice that some justification for it needs to be given here - this would probably most readily understood in terms of positive and negative predictive values.	We have amended the text and recommendations to clarify this.
SH	Royal College of Paediatrics and Child Health	13	Full	General		The full report is very comprehensive and thorough. My comments mainly relate to the presentation of the results, particularly how results could be presented more succinctly, retaining the detail in tabular and graphical form. The summary of the research literature would be easier to follow if there were more use of tables to summarise the studies adjacent to the relevant text, to summarise the salient elements of study quality (this is not included anywhere systematically – even in the text narrative) and greater use of Forest plots, and ROC curves, to summarise the results of studies. At present it is impossible to get a sense of the distribution of study results. On page 197 there is a comment about an	Much of the text has been revised. The comments on page 197 have been reviewed.

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						outlying study but as a reader, it is hard to appreciate which study, or how much it differs from the other studies. Greater use of graphical summaries would also save space on the narrative.	
SH	Royal College of Paediatrics and Child Health	14	Full	4.5.1	185	It would be valuable to see the pooled estimates of results, particularly for the ROC curve for dipsticks. The recommendations regarding wider use of dipsticks are quite bold, but are not backed up by a pooled estimate of test performance (from the summary ROC)..	
SH	Royal College of Paediatrics and Child Health	15	Full	2.1	91-98	Fever remains the most powerful symptom for a UTI in children unable to communicate. To facilitate rapid diagnosis and treatment a urine collection should be done on any child under 1 year of age with a significant fever rather than wait for 24-48 hours of symptoms	Any child with a fever should be managed in line with the fever guideline. Urine collection is recommended in any child with a fever and no obvious source of infection after 24 hours at the latest.
SH	Royal College of Paediatrics and Child Health	16	Full	2.1	105-106	I find the advice on localisation of infection confusing. No routine imaging is recommended, yet if ultrasound is acutely performed, Doppler should be used to look for parenchymal involvement	This section has been reworded to improve clarity.
SH	Royal College of Paediatrics and Child Health	17	Full	4.7.1	211-220	Using urine dipsticks for nitrite and LE in stead of using urine culture in children over 3 years of age: 1) Why was 3 years chosen after which to use this diagnostic tool? 2) I think this is a	The revised recommendations have been designed to minimise antibiotic usage in cases of uncertainty to those children who are significantly unwell and in whom there is a high risk of

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						very pragmatic and effective approach to the difficulty of diagnosing UTI in primary care. The evidence is not rock solid and a lot of criticism will ensue. There will be false positive diagnoses of UTIs, but this will not matter since antibiotic treatment is only for 3 days, 1 day longer than it takes to get the urine culture back and realising it is negative. The false negative rate is potentially more concerning: but children are over 3 years of age (less risk of new scars) and not severely ill or systemically unwell. I would add to the advice given to parent to return if the child where a UTI has been ruled out doesn't improve within 24-48 hours.	acute pyelonephritis. In children with a low risk of APN and uncertainty of diagnosis without urinary symptoms it is considered acceptable to await the result of culture which takes 24 hours.
SH	Royal College of Paediatrics and Child Health	18	Full	5.5.3	285	Evidence summary: states there are a number of poor quality studies and they do not provide clear evidence to assess the effectiveness of prophylactic antibiotics in preventing recurrent UTIs. Yet the guideline than translates this into prophylaxis not having an apparent effect. I do not support the use of prophylactic antibiotics, but the guideline must acknowledge that it's recommendation is not based on evidence, but on balancing pros and cons of using prophylaxis.	The GDG considered that we should not do things to healthy children that have no evidence of benefit or insufficient evidence to show benefit. This applies to both widespread use of long-term low-dose antibiotics and imaging investigations.
SH	Royal College of Paediatrics and Child Health	19	Full	6.7	339-341	Why was less than 6 months chosen for the age to investigate infants more intensely? Only 50% of all boys have a UTI before 6 months and a lesser percentage in girls. The median age for infant boys for a UTI is 2.4-4.5 months, for infant girls 6.5 months. Most studies have used 1 year as a cut off point for doing more or less investigations.	The lowering of the age limit cut-off for MCUG was a reduction on current practice based on a lack of evidence for benefit from this intervention and from any subsequent use of prophylactic antibiotics.

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	Royal College of Paediatrics and Child Health	20	Full	6.7.3	340	MCUG should be considered in boys with bilateral hydronephrosis or poor bladder emptying, even if the child is over 6 months. I note there is no mentioning of the MAG-3 scan to assess obstruction and assume this will be used by the paediatric specialist?	The referral points have been made more clear.
	Royal College of Paediatrics and Child Health	21	Full	7	347	Do we need more RCTs to define the effectiveness of surgical procedures for management of VUR in preventing UTI? There seem to be 7 studies providing an answer to this question already.	Published studies were not sufficiently well designed to answer all the questions raised. They largely compared surgery with prophylaxis, which is an alternative management strategy of unproven benefit. Several additional international studies are underway which include a placebo or control arm but until they are published we do not know whether they will adequately answer the question. The design of future studies should be informed by the results of the studies in progress. to ensure optimal design and adequate power
SH	Royal College of Paediatrics and Child Health	22	Full	General		While there are plenty of recommendations for research, audit advice seems to be lacking. This is surprising.	Audit proposals and toolkits will be developed after completion of the guideline.
SH	Royal College of Paediatrics and Child Health	23	Full	General		It is very important that the stakeholding community realises that children with recurrent UTIs or severe UTIs will be investigated and followed. Only those children with a single UTI, who are well, older and respond to treatment are not going to be seen again. Even if these children had a scar or reflux, if they do not develop another UTI than neither prophylactic antibiotics or surgery is ever indicated. The risks of proteinuria, hypertension and renal failure are so small as not to warrant continuous medical attention. This group clearly deserves to be seen in Primary Care only. Further studies are	It is reassuring to hear that research is in progress and that there are no indications so far that treatment and prevention by surgery or prophylaxis will significantly alter outcome. The results of this and other studies will be awaited with interest and amendments to the guideline may be made if necessary.

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						being carried out and were presented at the latest ESPN meeting in Palermo, confirming that low grade reflux does not increase the risk of infection or scarring, therefore prophylaxis is not indicated. Two RCTs comparing prophylaxis or not (plus one endoscopic injection arm) for VUR are being analysed, but preliminary results show no difference in degree of scarring	
SH	Royal College of Pathologists	1	Full	general		The Scoping document 4.3c refers to what diagnostic criteria to use in laboratories this does not appear to be included in the Full version of the guidelines (except regarding CRP). I expected there to be some advice to laboratories regarding microscopy and culture results, in particular around cut off values for significant bacteriuria.	Thank you for your comments. Detailed cut-offs are outside our Scope.
SH	Royal College of Pathologists	2	Full	2.1 4.3	92 and 179	Fever defined as >38°C, the method of temperature taking should be noted	The temperature should be measured as described in the fever guideline.
SH	Royal College of Pathologists	3	Full	2.1 4.5		Urine collection bags are not mentioned in this section as being either suitable or unsuitable	The guideline states that clean catch is the preferred method and that pads are an alternative if clean catch is not possible. Further information about bags is available in the evidence statement
SH	Royal College of Pathologists	4	NICE	1.1.4.1		Urine collection bags are not mentioned in this section as being either suitable or unsuitable	There is a statement saying that if clean catch is not possible other non-invasive methods such as pads should be used.
SH	Royal College of Pathologists	5	Full	2.1 5.2	93 and 264	Treating for 3 days, can I confirm that this applies to all children including neonates	The treatment of children under 3 months has been aligned with the treatment recommendations in the fever guideline for route and choice of

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							antibiotics as the diagnosis is not often confirmed with certainty at the point when treatment starts.
SH	Royal College of Pathologists	6	Full	2.1 5.5.3	93 and 286-287	I would question some of the references used to draw this conclusion although I agree that a formal randomised controlled trial should be done to evaluate the efficacy of prophylactic antibiotics in children and if any high risk groups would benefit. One of the principle papers referred to in the Cochrane review was by Savage et al. (Lancet, 1975 p358-61). It was a controlled trial of therapy in young girls (at the age of 5 entering school) with covert bacteriuria. As use of prophylaxis following the guidance is limited to symptomatic infection I do not think we can apply the findings from this paper. Furthermore, can we exclude any benefit of antibiotics given to younger children who may still be in nappies etc. This paper does however support the chapter 5.3 statement that asymptomatic bacteriuria should not be treated.	This was only one of the papers included. There were also papers which included children after symptomatic UTI.
SH	Royal College of Pathologists	7	NICE	1.1.2.2		UTI should be considered in children with unexplained persistent symptoms or signs, I presume this refers to those signs and symptoms given in the table	Thank you for making this point.
SH	Royal College of Pathologists	8	NICE	1.1.6.1 1.1.6.2	12	Does this imply that dipstick testing should not be done in children less than 3 years? or should, in that group both dipstick testing and culture be performed. I would favour the latter, if the authors feel there is insufficient evidence to rely on dipstick results in this age group. If microscopy is the only method to diagnose UTI then all children less than 3 would have to have access to urgent microscopy or therapy delayed until microscopy and/or culture	The evidence on urine testing in children under 2 was re-evaluated and a recommendation has been made to test urine for UTI using microscopy and culture in all children under 3 years since dipsticks were found to be less reliable in the youngest age groups.

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						results were available.	
SH	Royal College of Pathologists	9	NICE	1.1.6.8	12	I would argue that patients with less certain diagnosis should be cultured and those with a clear cut diagnosis should not. For example, child presents with ? UTI, dipstick equivocal with –ve nitrite and +ve LE, antibiotic gets started, child not improving at 48h, urine gets cultured and culture is negative but is this because of antibiotic therapy or did we have the wrong diagnosis to begin with. 1.1.6.8 appears to contradict 1.1.6.9	Thank you for your comment. We have amended the text and recommendations to clarify this.
SH	Royal College of Pathologists	10	NICE	1.2.1	13	I would like to check that this refers to all children, most studies using a 3 day course of therapy have only included children 6months of age or older. There is a meta-analysis that suggests 7-14 days therapy should be given but this was excluded from the guidelines.	The treatment of children under 3 months has been aligned with the treatment recommendations in the fever guideline for route and choice of antibiotics as the diagnosis is not often confirmed with certainty at the point when treatment starts.
SH	Royal College of Pathologists	11	NICE	1.2.4.1	15	The wording of this suggests that there are indications for prophylaxis, if so, these should be clearly stated.	The GDG have not established criteria for when to use prophylaxis in children with VUR. However, the possibility of continuing with current practice has not been ruled out.
SH	Royal College of Pathologists	12	NICE	1.3.5.2	16-17	It is recommended that prophylaxis be given for 3 days with the MCUG performed on the second day. No reference is given for this however other procedures that involve manipulation of the renal tract either require prophylaxis to be given unless there is documented negative culture results. Could single dose prophylaxis	Thank you, this does apply to MCUG done in all ages. This recommendation is based on consensus opinion due to the lack of evidence regarding whether single dose or multiple dose prophylaxis during an MCUG is the most appropriate treatment regime

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						be given? Finally I presume this applies to MCUG done in all age groups.	
SH	Royal College of Pathologists	13	Full	3.4.12	150, line 20-24	Page 150, line 20-24, the reference given appears not to correlate with the sentence	Thank you for spotting this.
SH	Royal College of Radiologists	1	Full	6.3		The Guidelines suggest that antibiotic prophylaxis should be given for 3 days for an MCUG and the procedure performed on the second day. Is there sound evidence for this? An email survey of current practice in the UK suggests a wide variety of different local practice which varies in the amount of prophylaxis given and the timing. The 3-day prophylactic regime appears to be too prescriptive. It does not advise on the type of antibiotic or the dose. Should the recommendation not be that antibiotic prophylaxis should be used to locally agreed protocols.	The recommendation was based on consensus opinion and will provide consistent practice until further evidence is available.
SH	Royal College of Radiologists	2	Full	6.4		There is limited detail on children with abnormal function and those with neurogenic bladders. There is no detail on the assessment of normal bladder and function and post voiding residues. There is no reference to the International Childrens Continence Society Guidelines 2005 on the terminology and describing bladder function.	Neurogenic bladders are outside the scope. We do need to stress that in toilet-trained children, when an ultrasound is done, the bladder should be imaged after voiding to assess emptying.
SH	Royal College of Radiologists	3	Full	6.4		There is comment about DMSA being performed within 6 months and a comment that this may need to be altered in children with recurrent UTIs. This statement is misleading and could effectively mean a child with recurrent UTIs never undergoes a DMSA. Further more robust and succinct	This has been addressed.

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						advice is needed for these children.	
SH	Royal College of Radiologists	4	Full	6.5	292	The comment on page 292 that it is standard practice in the UK to perform a DMSA after 56 months needs to be substantiated	The rate of renal parenchymal defects is related to the timing of the scan, with earlier scans yielding a higher rate of defects. A delay of 4-6 months reduces the risk of detecting transient renal parenchymal defects.
SH	Royal College of Radiologists	5	Full	6.4		The delay in performing DMSA for 6 months I presume is based on evidence that transient focal nephronia may persist for some months. There does appear to be some evidence that these changes can last up to 9 months. Is there not a case for performing the DMSA earlier and only in the positive cases organising repeat investigations.	As there was no indication of a treatment implication arising from a DMSA scan the advice on DMSA scanning is aimed reducing the number of scans carried out in older children.
SH	Royal College of Radiologists	6	FULL	6.3	310	Page 310 This seems to advocate the use of MCUG over the age of 12 months. This is a very traumatic procedure and can be very stressful in the older child. Apart from the child with bladder dysfunction is there evidence that an MCUG will alter management in the older child?.	MCUG is only recommended routinely in children under 6 months.
SH	Royal College of Surgeons of England					This organisation was approached but did not respond.	
SH	Royal Liverpool Children's Hospital	1	NICE	General		Make clear if no MSU to be sent on systemically well children prior to 3 days treatment – no sample even if dip positive?	Thank you for your comments. The GDG felt that it was not necessary to send a sample in clear-cut cases in children over 3.
SH	Royal Liverpool Children's Hospital	2	NICE	1.3.5.2	16-17	Why mention early DMSA if never indicated?	This point has been addressed.
SH	Royal Liverpool Children's Hospital	3	NICE	1.4.1.1	18	Needs further information in the guide (acknowledged that in full section)	These recommendations were lifted from the full guideline. The revised version makes this issue more clear.

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SH	Royal Liverpool Children's Hospital	4	NICE	1.3.5.2	16-17	Repetition of tables ? necessary	This point has been addressed.
SH	Royal Liverpool Children's Hospital	5	NICE	General		Document rather an algorithm alone should clearly identify when to ref to secondary care.	This has been addressed in the main document.
SH	Royal Liverpool Children's Hospital	6	Algorithm			Drink and adequate amount - expand	This statement has not been changed as there was no evidence on which to base any more detailed advice.
SH	Royal Liverpool Children's Hospital	7	Full	2.3	108	STING – if treatment of VUR is necessary – define terms of necessary as this is the only indication that you appear to suggest a STING is considered an option in treatment	Is this the correct page ref? Current indications for surgery (treatment of VUR) in the UK are symptomatic breakthrough UTIs despite medical management and/or increased renal scarring.
SH	Royal Liverpool Children's Hospital	8	Full NICE	1.1.4.1	11	SPA recommends U/S before attempt how is this to be undertaken out of hours in AE department? Are you advocating the use of portable bladder scanning equipment away from radiological areas?	Catheter samples may be the preferred alternative as used routinely in the USA. Alternatively, departments may wish to have US facilities.
SH	Royal Liverpool Children's Hospital	9	NICE	General		It is recognised these guidelines are for simple UTI and difficult cases will remain outside the scope of this document	Thank you for your comment.
SH	Royal Liverpool Children's Hospital	10	NICE	General		The algorithm from NICE is in disagreement with HTA (http://www.hta.ac.uk/project/1325.asp?src=alr) will there be clear guidelines established as Prodigy also have made recommendations, there will be at least 3 sources of 'expert' advice from appraisal of the same data. Clarification is sought as to the best path to follow.	This guideline has been developed independently of existing guidance. The developers of other guidelines will be free to review and adopt these recommendations if they feel that they are appropriate.
SH	Royal Liverpool Children's Hospital	11	NICE	General		Were there any studies that identified the accuracy of U/S in children in identifying anatomical abnormalities?	As far as we have searched and reviewed, there are no further good quality studies, apart from those already included, that address the question.
SH	Royal United Hospital Bath					This organisation was approached but did not respond.	

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	NHS Trust						
SH	Sandwell & West Birmingham NHS Trust					This organisation was approached but did not respond.	
SH	Scottish Intercollegiate Guidelines Network (SIGN)					This organisation was approached but did not respond.	
SH	Scottish Paediatric Renal Urology Network					This organisation was approached but did not respond.	
SH	Sheffield Children's Hospital Trust	1	NICE FULL	General		We welcome the attempt to rationalise the approach to the diagnosis and management of UTI in childhood. However, we have concerns about the guidelines in some areas, particularly with respect to diagnosis and investigation, especially in the infant and young child. If followed it would significantly alter the way of investigating young infants and very young children with UTI which may have adverse consequences. In addition, conflicting advice is given within the document which could raise concerns about the overall review process and advice given within the document as a whole.	Thank you for your comments. The GDG considered that we should not subject healthy children to interventions that have no evidence of benefit or insufficient evidence to show benefit after many years. This applies to both widespread use of long-term low-dose antibiotics and imaging investigations. It is not clear what is meant here by 'conflicting advice'.
SH	Sheffield Children's Hospital Trust	2	NICE	General		Clarification and emphasis is needed that the document refers in the main to the diagnosis and management of the first UTI in a child.	The document refers to first and recurrent UTIs but does not address management in children known to have a uropathy such as those children with antenatal diagnosis of dilated urinary tract or urethral valves. This is clearly stated in the scope.
SH	Sheffield Children's Hospital Trust	3	NICE	1.1.2.2	09-Jan	Fever as a single feature does not seem to warrant urine culture in those outside of the neonatal period – which we presume to be more than 4 weeks old. The papers listed state that fever is a common presenting feature of UTI in	Fever is the major symptom of UTI in infants and young children. As you have suggested, fever without explanation should prompt urine collection and testing. This applies to children of any age.

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						those that present to secondary care and in particular fever in infants without an identified source of fever may be due to UTI. One of the papers cited describes that fever was the only presenting feature in a significant proportion of those with UTI although the exact age of these individuals was unknown. Thus fever per se, in the absence of an identifiable cause should prompt urine examination, especially in infants. If this is covered by the "unexplained" persistent symptoms or signs, persistent fever per se without other obvious cause needs to be emphasised.	
SH	Sheffield Children's Hospital Trust	4	NICE	1.1.4.2	11	Whilst prompt treatment of an acutely unwell child is necessary, obtaining a sample of urine when there is no other immediately identifiable cause for their illness is to be advocated if they are unwell enough to warrant secondary care review. Invasive methods of obtaining an adequate urine sample in this case should be considered. Definition of an acceptable "delay" under varying circumstances may not be possible but should be considered.	In children who are significantly unwell, such as with amber or red features from the fever guideline and no focus for their infection, a urine sample should be collected. If clean catch sample is not available an invasive sample is indicated. Catheter samples may be the preferred alternative, as used routinely in the USA. Alternatively, departments may wish to have US facilities.
SH	Sheffield Children's Hospital Trust	5	NICE	1.1.6 General	12	There is concern from a microbiological perspective that there will be inadequate surveillance of urine isolates for population purposes in order to give adequate advice about the treatment of UTI and to highlight trends in resistance etc if the number of urine samples for culture is diminished to a significant degree.	It hasn't been a problem for adults in fact, current surveillance is flawed as it over-represents UTI in high-risk groups. The GDG considered the need to culture urine from the perspective of what was required for patient care separately from the need to monitor antibiotic sensitivity within each patient group. Current surveillance methods tend to over-represent the high risk groups since they tend to have more recurrent UTIs.
SH	Sheffield Children's	6	NICE	1.1.6	12	Whilst urine culture results alone cannot be taken in isolation, there is no	We have amended the text and recommendations to clarify this.

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	Hospital Trust					advice regarding interpretation of urine culture results at all in the NICE guideline. It would be helpful if at least some comments and advice could be formulated for the situations where urine is sent for culture.	
SH	Sheffield Children's Hospital Trust	7	NICE	1.1.6.9	13	Clarification of the statement that urine samples should be sent for culture when "clinical symptoms and dipstick tests do not correlate" may be needed. This could be interpreted as meaning that a urine culture should be sent if there are symptoms that could be UTI but the dipstick is "negative". It is presumed that was not the intention of the advice.	We have amended the text and recommendations to clarify this.
SH	Sheffield Children's Hospital Trust	8	NICE	1.1.4.2 1.1.6	11	Advice regarding when to give antibiotics pending culture results in those under 3 years of age is required within the document itself although is stated on the care pathway. A statement that treatment does not need to be delayed until after the culture report is received, as on the pathway, should be considered. It may be felt that it is implicit within the guidelines but this is not clear.	The text and recommendations have been amended.
SH	Sheffield Children's Hospital Trust	9	NICE	1.3.5.1	16	Conflicting advice is given within the document. Should further investigations be considered if systemically well child has recurrent UTI and/or abnormality on ultrasound scan rather than requiring recurrent UTI AND abnormal ultrasound scan as stated. Elsewhere in tables for those over 6 months, late DMSA is indicated if there are three or more episodes of UTI without systemic symptoms/signs – without need for abnormality on ultrasound scan.	The guidance concerns the minimum routine investigations that are recommended. It does not preclude a specialist undertaking additional imaging in specific circumstances. Other appropriate tests are described in the follow-up section.
SH	Sheffield Children's	10	NICE	1.3.5.1	16	Further clarification as to what constitutes an abnormal ultrasound	The guideline aims to ensure that all children with renal anomalies are

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	Hospital Trust					scan may be required.	identified and referred to a paediatric specialist. Management or children with uropathy is outside the scope of the guideline and therefore this level of detail has not been provided.
	Sheffield Children's Hospital Trust	11	Full	6.2	293, line 19	Whilst it is said that the incidence of abnormalities such as obstruction that affect management is very low in children after 6 months of age and in children presenting with mild or moderately severe illness, the evidence that supports this statement is not clear. As this seems to be the main reason that determines the grouping of children into age groups to decide the level of investigation in the first instance it would be helpful if the evidence was clarified.	We have amended the text to clarify these issues. However, there is no study addressing this directly, and in the light of current practice, available limited evidence, and clinical expertise from the GDG members, a cut-off of 6 months was chosen.
SH	Sheffield Children's Hospital Trust	12	NICE	1.3.5.2	16-17	The qualitative assessment of how unwell a child is determines the level of investigation that is undertaken. What is the evidence that the clinical factors that discriminate these groups as described – which may be open to clinical judgement and interpretation – are valid in determining the likelihood of abnormality/risk ?	The illness risk levels have been aligned with the fever guideline. Renal scarring is increased when UTI occurs in young age, recurrent infection and acute pyelonephritis.
SH	Sheffield Children's Hospital Trust	13	NICE	1.3.5.2	16-17	What is the definition of a severe UTI ? Does this mean those that are “severely unwell” as defined elsewhere in document ?	The illness risk levels have been aligned with the fever guideline. Renal scarring is increased when UTI occurs in young age, recurrent infection and acute pyelonephritis.
SH	Sheffield Children's Hospital Trust	14	NICE	1.3.5.2	16-17	What is the reason for not undertaking an early ultrasound scan in those with UTI in circumstances when this could be more easily done early rather than late ? If it can be undertaken early, before discharge for those that are admitted for UTI, why not undertake and then maybe prevent further attendance for parents at a later date ?	The guideline indicates when an early US is essential. If trusts and paediatricians prefer to do all ultrasounds early this is largely an operational issue. However, the kidney will be significantly larger owing to inflammation if the US scan is done during or immediately after an episode of acute pyelonephritis.

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SH	Sheffield Children's Hospital Trust	15	NICE	1.3.5.2	16-17	Table infants aged 0 – 6 months: "If the child responds well to treatment" – this does not take into account how long the symptoms have been present before antibiotics are started and therefore it is difficult to see why the response to treatment should be the deciding factor in determining further investigation, in addition the judgement of responding well to treatment is objective and may need absolute clarification.	The opinion of the GDG was that children who do not respond well to treatment have a higher risk of underlying abnormality. If a diagnosis has been made late this may also be a risk factor and the clinician will be free to use discretion in choosing the best course of action. However, it is difficult to build this into a guideline.
SH	Sheffield Children's Hospital Trust	16	NICE	1.3.5.1 1.3.5.2	16-17	Table infants aged 0 – 6 months: Discrepancy in advice – if abnormality on ultrasound scan – consider late DMSA (1.3.5.1), if abnormality on late ultrasound scan – consider MCUG (table, 1.3.5.2).If a late ultrasound has been undertaken in a baby who has responded well to treatment and abnormality is found, it may be that a DMSA as well a MCUG be considered, depending on ultrasound findings ?	The recommendations have been changed. However, when an abnormality is detected the child moves outside the scope of the guideline and should be referred to a paediatric specialist.
SH	Sheffield Children's Hospital Trust	17	NICE	1.3.5.2	16-17	Table infants aged 0 – 6 months: What is the evidence that prophylactic dose of antibiotics should be given as opposed to treatment dose around the time of an MCU ? . What is the evidence for the length of time for which they should be given ?	In the absence of data on prophylaxis, the recommendation is based on evidence for treatment courses.
SH	Sheffield Children's Hospital Trust	18	NICE	1.3.5.2	16-17	Table infants aged 0 – 6 months: Late DMSA scan – our current practice is to undertake "late" DMSA at 3 months as a compromise between the ideal time and a time which may ensure better compliance with the investigation.	The GDG have recommended 4-6 months after an acute UTI.
SH	Sheffield Children's Hospital Trust	19	NICE	1.3.5.2	16-17	Table 6 months to toilet trained: What is the evidence that this age cut off, ie 6 months, is appropriate and is the response to treatment more important than length of illness before appropriate treatment is started ?	Current practice advises MCUG in all children under 12 months. However, although VUR is present in a third, no benefit has been demonstrated from this imaging investigation.

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SH	Sheffield Children's Hospital Trust	20	NICE	1.3.5.2	16-17	Table 6 months to toilet trained: Indications for MCUG – what is the definition of or what is meant by poor urine flow? Clinical assessment of urine stream on history is likely to be unhelpful. Does this mean an assessment of bladder emptying meant by ultrasound scan?	Poor urinary stream is a significant point in the history and is common in infants with urethral valves. In older, toilet-trained children this would prompt a urinary flow rate and ultrasound in the first place. It is usual to assess bladder emptying when carrying out an ultrasound of the urinary tract.
SH	Sheffield Children's Hospital Trust	21	NICE	1.3.5.2	16-17	Table toilet trained and older: Definition of atypical UTI includes organism grown on culture – but many may not have culture on basis of diagnosis on dipstick testing and they respond to treatment. Therefore how important is it to know the infecting organism or not ?	The list of indications for urine culture has been revised so that in the majority of cases, including those with acute pyelonephritis, an organism will have been identified and cultured.
SH	Sheffield Children's Hospital Trust	22	NICE	1.3.5.2	16-17	Table toilet trained and older: Why not undertake a late DMSA in those who have had a “severe” UTI when it is undertaken in those with recurrent UTI with no systemic symptoms – what is the evidence and relative risk in these two situations ?	Because if there is a good response to treatment and it is a single UTI, the GDG felt that there was no evidence for benefit from prophylaxis or further investigation.
SH	Sheffield Children's Hospital Trust	23	NICE	1.1.6.9	13	What is the definition of recurrent UTI in this situation – the second and subsequent episodes of symptoms suggesting UTI in those who have had UTI diagnosed before on culture or dipstick – ie positive for both nitrite and leucocyte esterase ? Or another definition ?	Recurrent UTI has now been defined in the guideline as two episodes of acute pyelonephritis or three episodes of cystitis.
SH	Sheffield Children's Hospital Trust	24	NICE	1.2.1.5	14	We presume that “im” has been omitted before the words “treatment should be considered”.	The text and recommendations have been amended.
SH	Sheffield Children's Hospital Trust	25	NICE	1.2.3.1		Dysfunctional elimination syndromes – clarification of this in the guideline is needed.	The definition is in the glossary of the full guideline.
SH	Sheffield Children's Hospital Trust	26	NICE	1.2.3.2		Clarification of an adequate amount of fluid would be helpful	There was insufficient evidence on the amount of fluid that was beneficial but limited evidence that low fluid intake was a risk factor. There was no information on benefits of high fluid

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							intake and therefore this has not been mentioned.
SH	Sheffield Children's Hospital Trust	27	NICE	1.3.1.3		The term “simple” UTI can be inferred but would be best to be adequately defined.	This point has been addressed
SH	Sheffield Children's Hospital Trust	28	NICE	1.5.1.3		We would suggest that when results are normal after a single UTI, an outpatient appointment is not necessarily required BUT as outlined elsewhere in care pathway – recurrent UTI may need follow up.	This section includes a recommendation that when results of imaging are normal children and their carers should not be routinely asked to come to a follow-up appointment to be told that the imaging results are normal but should receive a letter to this effect. There is also a recommendation that children with recurrent UTIs will need follow-up.
SH	Sheffield Children's Hospital Trust	29	NICE	Care Pathway		There is a discrepancy between care pathway and NICE guideline in terms of assessment of symptoms and signs.	The algorithm has been derived from the recommendations.
SH	Sheffield Children's Hospital Trust	30	NICE	Care Pathway		Diagnosis of UTI – no advice is given regarding sending urine for culture where dipsticks do not “diagnose” or “disprove” UTI. Needs clarification of other groups where urine culture is needed ie recurrent UTI or make clear that this care pathway is ONLY for the first presentation of possible UTI	The management of indeterminate urine tests has been clarified.
SH	Sheffield South West Primary Care Trust					This organisation was approached but did not respond.	
SH	Society and College of Radiographers					This organisation was approached but did not respond.	
SH	South & Central Huddersfield PCTs					This organisation was approached but did not respond.	
SH	South Birmingham Primary Care Trust					This organisation was approached but did not respond.	
SH	South East Sheffield Primary Care					This organisation was approached but did not respond.	

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	Trust						
SH	South Warwickshire General Hospitals NHS Trust					This organisation was approached but did not respond.	
SH	Southport & Ormskirk Hospital NHS Trust					This organisation was approached but did not respond.	
SH	Specialist Advisory Committee on Antimicrobial Resistance (SACAR)					This organisation was approached but did not respond.	
SH	St Mary's Hospital, Isle of Wight Healthcare NHS Trust					This organisation was approached but did not respond.	
SH	Staffordshire Ambulance HQ					This organisation was approached but did not respond.	
SH	Staffordshire Moorlans Primary Care Trust					This organisation was approached but did not respond.	
SH	Steering Group on Healthcare Associated Infection					This organisation was approached but did not respond.	
	Stockport PCT	1	NICE	1.1.6.7	12	For routine screening for children with continence issues – either at a continence clinic or enuresis clinic (run by school health), what is recommended? The enuresis nurses have been told (prior to NICE guidelines) by microbiology to send urine for C+S as a routine part of the assessment with directions to test for glucose as well (to eliminate undiagnosed diabetes as a cause of	Thank you for your comments. The guideline concerns children who present with acute UTI. The management of children with chronic infection was not addressed in this guideline. The issue of the effectiveness of dipsticks varies with the clinical setting and the infecting bacteria. The problem you have raised is outside the scope of this guideline.

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						incontinence.) I have been dipsticking. In NICE guidelines it states clearly that dipsticking is as accurate as lab tests, but I haven't been able to access the research this is based on. In the Scottish Intercollegiate Guidelines Network.(SIGN) – "management of suspected bacterial urinary tract infection in adults "– guidelines, it indicates that "the quality of evidence for near patient testing with dipsticks was poor" – p7, and this is the understanding of the microbiologist who has told the school nurses to send routine samples of urine for C+S. However, the adult continence service and District Nurses use dipsticks! The children who attend clinics are usually well, but need to have UTI ruled out prior to a programme of care and it would be very useful for a clear national standard for routine urinalysis to be included in the guidelines.	
SH	Tameside and Glossop Acute Trust	1	NICE	1.1.2	9 and 10	The document has a premise that those younger children with UTI who do not complain of pain etc do so because they are preverbal. This is plainly not the case, as they would cry. The reason must be that it is a different pattern of illness than in older children. I believe that the format that you have chosen to separate on the basis of inability to speak is incorrect and should be change to an age separation	Thank you for your comments. The GDG considered this point but have not amended the guideline on this point which is concerned not only with pain but also with the description of symptoms.
SH	Tameside and Glossop Acute Trust	2	NICE	Table 1	9 and 10	Sepsis should be added to common presentations in the neonate	Thank you for your comment.
SH	Tameside and Glossop Acute Trust	3	NICE	1.1.4.1	11	Re use of SPA – you provide good evidence that results are better where ultrasound guidance is used, BUT it is not available at such short notice and implementation of the guideline would	The Guideline is responsible for identifying and recommending the best practice based on available evidence. Implementation issues are the responsibility of the NICE

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						deny many children accurate diagnosis. The guideline should be changed to read that ultrasound guidance should be used WHERE AVAILABLE. It would also be helpful to give a maximum age for the use of SPA (I didn't find this)	implementation team and local trusts.
SH	Tameside and Glossop Acute Trust	4	NICE	1.3.2	15	Detecting reflux – as your contention is that prophylactic antibiotics should not be used, I'm not sure why reflux should be detected and why an MCUG should be ordered in those over 6 months.	The guideline has recommended a significant reduction in the number of children subjected to MCUG and has focussed attention on the youngest and most vulnerable children who are most likely to have significant congenital anomalies, obstruction and severe VUR. This includes infants under 6 months, those with severe illness and those with recurrent infection.
SH	Tameside and Glossop Acute Trust	5	NICE	1.3.5	16-17	Recommendations for imaging – I cannot agree with not requesting a DMSA scan in toilet trained children with a severe UTI – I have picked up several children like this who have had significant scarring	In children at low risk of renal scarring who are not going to be offered any intervention there is no benefit in doing this test.
SH	The David Lewis Centre					This organisation was approached but did not respond.	
SH	The Medway NHS Trust					This organisation was approached but did not respond.	
SH	The North West London Hospitals NHS Trust					This organisation was approached but did not respond.	
SH	The Royal Society of Medicine	1	Full	Algorithm		Very difficult to interpret the section: Follow up of children with UTI. Add to definitions : Systemically well and unwell, using definitions provided in the very first box, top left of pathway under the Identification of Children with UTI. The follow up charts are difficult to interpret. The Age bandings need to be more specific	Thank you for your comments. The algorithms have been re-written and simplified. The follow-up section has been clarified. Systemically well, systemically unwell and seriously ill children have been defined in line with the fever guideline. The age bands have been made more specific.
SH	The Royal Society of	2	Full	Algorithm		Is the care pathway for use in Primary care? If it is needs much clearer	The guideline is intended for use in primary and secondary care. It

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	Medicine					pathways related to Primary care management –	describes when to consider UTI, when and how to collect urine, how to test the urine and how and when to treat or refer to secondary care in infants and children from birth to 16 years.
SH	The Royal Society of Medicine	3	Full	Algorithm		There are no statements of when to refer to local paediatric services and when not – and why -	The text and recommendations have been amended.
SH	The Royal Society of Medicine	4	Full	Algorithm		What does a 'paediatric specialist 'mean – a nephrologist or a secondary care general paediatrician?	This means a paediatrician.
SH	The Royal Society of Medicine	5	Full	Algorithm		Should the Ultrasound and post mict volume always be done by the gp, in the toilet trained child and older, prior to referral.? If these are normal is there sufficient evidence to suggest referral and further investigation is not required.?	We envisage that the ultrasound would be done by a radiologist with experience of working with children and not by a GP. If ultrasound is carried out it is appropriate to look for the factors that are associated with recurrent UTIs, such as poor bladder emptying, since this is amenable to management by measures such as regular toileting and management of constipation. There was no evidence of benefit from interventions in children with normal ultrasound of kidneys and bladder.
SH	The Royal Society of Medicine	6	Full	Algorithm		Could merge the tables 6month to toilet trained, and children toilet trained and older, and just emphasise the need for late DMSA in the younger child with systemic symptoms	The algorithms have been re-written and simplified. The follow-up section has been clarified. Systemically well, systemically unwell and seriously ill children have been defined in line with the fever guideline. The age bands have been made more specific.
SH	The Royal Society of Medicine	7	Full	Algorithm		Why no Mag 3 – especially in the older child instead of the DMSA	No comparative studies were identified that evaluated the effectiveness of MAG 3 for detecting VUR. We are not advocating the routine use of MAG 3 indirect cystography as we have not identified any benefit to the patient from cystography or prophylactic antibiotics with the exception of the very small number of older children with recurrent episodes of acute

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							pyelonephritis and reflux who benefit from surgery.
SH	The Royal West Sussex Trust					This organisation was approached but did not respond.	
SH	The Survivors Trust					This organisation was approached but did not respond.	
SH	UK Specialised Services Public Health Network					This organisation was approached but did not respond.	
SH	University College London Hospitals (UCLH) Acute Trust	1	NICE	general		Overall we found this a very helpful guideline and generally clearly laid out.	Thank you for your comments.
SH	University College London Hospitals (UCLH) Acute Trust	2	NICE	1.1.4.1	11	Because of lack of ultrasound equipment for immediate bedside use in many places, departments will find it difficult to adhere to this guideline if need to do SPA	The Guideline is responsible for identifying and recommending the best practice based on available evidence. Implementation issues are the responsibility of the NICE implementation team and local trusts.
SH	University College London Hospitals (UCLH) Acute Trust	3	NICE	1.3.5.2	16-17	Some departments of radiology are reluctant to do MCUG's on patients over 1 year and recommend Mag3 and indirect cystogram instead.	The guideline only recommends MCUG routinely in infants younger than 6 months. This point has now been included in the guideline.
SH	University College London Hospitals (UCLH) Acute Trust	4	NICE	general		Welcome less invasive, less investigative approach.	Thank you for your comments
SH	University Hospital Birmingham NHS Trust	1	General			Thank you for giving University Hospital Birmingham NHS Foundation Trust the opportunity to comment on the draft of this guideline. We have no comments to make.	Thank you for your comment.

Status	Organisation	Order no.	Document	Section no.	Page no.	Comment	Response
SH	Welsh Assembly Government	1	General			Thank you for giving the Welsh Assembly Government the opportunity to comment on the above appraisal. We are content with the technical detail of the evidence supporting the consultation and have no further comments to make at this stage.	Thank you for your comment.
SH	Welsh Scientific Advisory Committee (WSAC)	1	Full	4.7.6.2	240	Nitrite-negative and LE-positive – diagnostics box should advise culture and microscopy.	Thank you for your comments. We have amended the text and recommendations to clarify this.
SH	Welsh Scientific Advisory Committee (WSAC)	2	Full	4.7.6	241	Second paragraph starting “urine samples….” – the comment “who have a urine dipstick which is negative or positive for both nitrite and leukocyte esterase is confusing – change to “irrespective of leukocyte esterase or nitrite result”.	We have amended the text and recommendations to clarify this.
SH	Welsh Scientific Advisory Committee (WSAC)	3	Full	4.7.6	241	Section headed “urine samples should be sent for culture in” – the recommendation “single positive result for nitrite or leukocyte esterase” needs reflecting on the previous page.	We have amended the text and recommendations to clarify this.
SH	Welsh Scientific Advisory Committee (WSAC)	4	Full	4.7.6	241	Section headed “urine samples should be sent for culture in” - this section does not mention children on prophylaxis or with known abnormalities/recurrent infections – shouldn’t it?	We have amended the text and recommendations to clarify this.
SH	Whipps Cross University Hospital NHS Trust					This organisation was approached but did not respond.	
SH	Wyre Forest Primary Care Trust					This organisation was approached but did not respond.	