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INSTITUTE OF OBSTETRICIANS
& GYNAECOLOGISTS
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

CLINICAL PRACTICE GUIDELINE

MANAGEMENT OF URINARY TRACT INFECTIONS IN PREGNANCY

Institute of Obstetricians and Gynaecologists,
Royal College of Physicians of Ireland
and the
Clinical Strategy and Programmes Division,
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Appendix 4: Treatment options for pyelonephritis in pregnancy 26

1. Revision History

Version No.	Date	Modified By	Description
1.0			

2. Key recommendations

1. Screening for asymptomatic bacteriuria should be performed ideally at 12 to 16 weeks gestation on all women.
2. Imaging of the renal tract may be warranted where pyelonephritis recurs or is slow to respond to treatment.
3. Do not prescribe trimethoprim for pregnant women with established folate deficiency or women taking folate antagonists.
4. Take a single sample for urine culture before empiric treatment is started.
5. Women with symptomatic bacteriuria with systemic signs of infection should be admitted for intravenous antibiotics pending the result of blood cultures and the urine culture.
6. When choosing an antimicrobial regimen it is important to consider issues of teratogenicity and absorption.
7. In cases where a clinical improvement fails to occur with 24 hours of instigating treatment or where there are additional co-morbidities additional senior medical and microbiology advice should be sought.
8. A repeat urine culture should be sent a week after the antimicrobial treatment is finished to ensure that the bacteriuria has cleared.
9. Nitrofurantoin can be used for prophylaxis but should be avoided near term or when delivery is imminent because of the risk of neonatal haemolysis.

3. Purpose and Scope

The purpose of this guideline is to provide multidisciplinary recommendations for the management of women with asymptomatic bacteriuria and urinary tract infections in pregnancy.

These guidelines are intended for healthcare professionals, particularly those in training, who are working in HSE-funded obstetric and gynaecological services. They are designed to guide clinical judgment but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the woman.

This guideline is part of a suite of guidelines that have been developed under the auspices of the HSE Clinical Programme in Obstetrics and Gynaecology and should be read in conjunction with other guidelines including; [IMEWS](#), [Guideline for the Critically Ill Woman in Obstetrics](#), [Bacterial Infection Specific to Pregnancy](#) and [Sepsis Management](#).

4. Background and introduction

Urinary tract infections (UTIs) are one of the most frequent complications during pregnancy (Overturf et al., 1992). Traditionally UTI is classified as either involving the lower urinary tract (acute cystitis) or the upper urinary tract (acute pyelonephritis). A predisposing factor or precursor to UTI is bacteriuria.

Asymptomatic bacteriuria is defined as the presence of a positive urine culture in an asymptomatic person and occurs in 2 to 7 percent of all pregnancies (Patterson and Andriole, 1997). Asymptomatic bacteriuria rates in the pregnant and non-pregnant population are similar, however bacteriuria during pregnancy has a greater tendency to progress to ascending infection than in the non-pregnant woman (Stenqvist et al., 1987, Smaill and Vazquez, 2007). This is because pregnancy is associated with a rapid increase in progesterone levels which leads to ureteric dilatation and urinary stasis which increases the risk of bacteriuria. Mechanical pressure from the gravid uterus and the physiological changes that occur in pregnancy further increase the risk of asymptomatic bacteriuria and in turn ascending infection (Perera, 2009).

Asymptomatic bacteriuria is associated with an increased risk of adverse fetal outcomes. In particular, an increased risk of preterm birth and an increased risk of delivering a low birth weight infant (Millar and Cox, 1997). Furthermore, studies have also shown that treatment of asymptomatic bacteriuria during pregnancy reduces the incidence of these complications (Villar et al., 1998). The prompt recognition and treatment of bacteriuria therefore should limit the risk of progression to ascending infection and the risk of these adverse maternal and fetal outcomes (Smaill and Vazquez, 2007, Rouse et al., 1995).

5. Methodology

Pubmed and the Cochrane Database of Systematic reviews were searched using the terms "pregnancy", "lower urinary tract infection", "lower uti", "pyelonephritis", "asymptomatic bacteriuria", "cystitis", "urethritis", "upper urinary tract infection", "upper uti" and "renal abscess" (Appendices 1 and 2). The limits used were human subjects, English language and published between 1994 and 2014. Several study types were included and these were clinical trials, comparative studies, guidelines, meta-analyses, observational studies, practice guidelines and systematic reviews.

The principal guideline developers were Dr Richard Drew (Rotunda Hospital and Royal College of Surgeons in Ireland) and Dr Sharon Cooley (Rotunda Hospital).

Written invited responses were received from the following; Dr. Susmita Sarma (University Hospital Galway), Dr. Paul Hughes (Kerry General Hospital), Dr. Declan Keane (National Maternity Hospital, Dublin), Ms. Karn Cliffe (Midwife, Drogheda), Ms. Cinnny Cusack (Physiotherapy) and Prof. Michael Turner (HSE Programme for Obstetrics and Gynaecology).

6. Clinical guidelines on Management of Urinary Tract infections in Pregnancy

6.1 Terminology

Abbreviations

BD	Twice daily
CI	Confidence Interval
IV	Intravenous
OD	Once daily
PO	Take orally
QDS	Four times daily
RR	Risk ratio
TDS	Three times daily
UTI	Urinary tract infection

6.2 Signs and symptoms

Asymptomatic bacteriuria is symptomless. Ascending infection may present in pregnancy with lower abdominal pain, frequency, dysuria, haematuria, vomiting or pyrexia and in cases where Pyelonephritis has occurred signs of systemic infection may be present in addition to flank pain (Table 1).

In severe pyelonephritis there is a significant risk of progression to systemic sepsis and in some cases acute respiratory distress. Untreated pyelonephritis may lead to abscess formation and suppuration (i.e. discharging pus) (Cunningham and Lucas, 1994, Towers et al., 1991).

In pregnancy urinary frequency is common as the bladder and gravid uterus compete for space in the pelvis. Unfortunately, UTI symptomatology changes in pregnancy and dysuria may not be present. In some cases vomiting may recur or increase in frequency and may be the only indication that infection is present. Current clinical diagnostic algorithms for the detection of UTI when applied to the pregnant woman have disappointing have low specificity and positive predictive values (Jido, 2014).

Asymptomatic bacteriuria	Lower UTI/cystitis	Upper UTI/pyelonephritis
No clinical signs or symptoms	Frequency	Pyrexia
	Dysuria	Loin pain
	Low grade fever	Dysuria
	Suprapubic pain	Rigors
		Clinical signs of septic shock

Table 1: Clinical signs and symptoms of urinary tract infections

6.3 Laboratory diagnosis

Screening for asymptomatic bacteriuria should be performed ideally at 12 to 16 weeks gestation on all women.

The diagnosis of asymptomatic bacteriuria is made following isolation of a significant growth of one bacterial species in a "clean catch" specimen of urine. A clean catch specimen involves collection of a mid-stream specimen of urine after cleaning of the perineum in order to minimise contamination by skin flora.

Urine microscopy and culture remain the gold standard in detection of asymptomatic bacteriuria. However, it can take 48 hours to obtain a result. Rapid screening tests have been developed. Urine reagent dipstick testing provides a cheap, rapid and easy test for asymptomatic bacteriuria, however, studies have reported sensitivity rates between 50 and 90% with a specificity of 83 to 94% (Etherington and James, 1993, Pastore et al., 1999). Another study comparing centrifugation and Gram-staining of urine, urinalysis and reagent strip testing in isolation and in combination showed high false negative rates with urinalysis (19.4%) and reagent strip testing (52.8%) and low specificity of the centrifuged Gram-stained smear (7.7%) when compared with the reported 80% sensitivity with urine culture (Pastore et al., 1999, McNair et al., 2000, Shelton et al., 2001) The additional value of urine culture is in the identification of an appropriate antibiotic for treatment using antibiotic sensitivity testing.

6.4 Radiological investigations

Imaging of the renal tract may be warranted where pyelonephritis recurs or is slow to respond to treatment. This is to identify renal anomalies or calculi. It should also be used in cases where a renal abscess is suspected, haematuria persists or malignancy is suspected. Ultrasound (US) is the primary radiological investigation of choice for evaluation of the renal tract in pregnancy (Masselli et al., 2014).

6.5 Non-pharmacological measures and antimicrobial prophylaxis

Pyelonephritis may recur during pregnancy. One study showed a recurrence rate of approximately 20% during the pregnancy or the postnatal period (McCormick et al, 2008). A Cochrane review in 2008 of ten studies showed that cranberry juice does decrease the number of UTIs over twelve months, but no data exists as to the optimum timing and quantity of cranberry juice that needs to be consumed to prevent infection (Jepson and Craig, 2008).

The focus on prevention of recurrence has focused on pharmacological and non-pharmacological measures. A Cochrane Review showed that low dose oral nitrofurantoin in combination with increased clinic review and surveillance has not shown any superiority over increased surveillance only in the prevention of recurrence of UTI. In addition, no difference was observed in the incidence of preterm birth in this group (Schneeberger et al, 2012).

The use of nitrofurantoin and a close surveillance policy did lead to a reduced rate of asymptomatic bacteriuria and highlighted the need for a large randomised controlled trial to determine which measures, if any, can reduce the risk of recurrent UTIs.

6.6 Clinical management

Asymptomatic Bacteriuria

- Antibiotic treatment of asymptomatic bacteriuria in pregnancy reduces the risk of urinary tract infection, preterm delivery and low-birth weight infants.
- All women should be screened for asymptomatic bacteriuria at the first antenatal visit.
- Treat women with a positive urine culture for bacteriuria detected during pregnancy with an appropriate antibiotic for the bacteria isolated and the trimester of pregnancy
- Refer to local and national guidelines for the choice of antibiotic in pregnancy
- A seven day course of treatment is normally sufficient
- Do not prescribe trimethoprim for pregnant women with established folate deficiency or women taking folate antagonists.

Symptomatic Bacteriuria

- Urine culture is the investigation of choice in symptomatic bacteriuria.
- Treat symptomatic bacteriuria with an antibiotic in accordance with local guidance.
- Take a single sample for urine culture before empiric treatment is started.
- Women with symptomatic bacteriuria with systemic signs of infection should be admitted for intravenous antibiotics pending the result of blood cultures and the urine culture
- In cases where a clinical improvement fails to occur with 24 hours of instigating treatment or where there are additional co-morbidities additional senior medical and microbiology advice should be sought
- Renal imaging should be considered if renal pathology is suspected or in cases that recur

7. Pharmacological management

7.1 General Principles of antimicrobial use

Choosing the right antimicrobial is an essential part of managing pregnant patients with urinary tract infections. It is not only important to choose the right drug, but also consideration should be given to selecting the right dose and treatment duration. By effectively treating urinary tract infections it is hoped to reduce the risk of maternal sepsis, pyelonephritis, preterm labour and also adverse outcomes for the fetus. Consideration should also be given to potential teratogenicity when choosing an antimicrobial. This may be more difficult in the setting of penicillin allergy but the risks and benefits should be explained to the patient.

Guidelines currently exist for prescribing for UTIs in pregnancy in Primary Care and these are available on www.antibioticprescribing.ie (last accessed 30/12/14). It is also important that antimicrobials are used correctly to minimise risk of antimicrobial resistance emerging in the population. The issue of antimicrobial resistance is addressed in more detail in "Guidelines for antimicrobial stewardship in hospitals in Ireland written by the Society for Antimicrobial Resistance in Ireland Hospital Antimicrobial Stewardship Working Group (Group, 2009).

Some of the key recommendations in this document for all acute hospitals are:

- Each hospital should have an antimicrobial stewardship team who can support the correct use of antimicrobials in pyelonephritis cases
- All acute hospitals must have 24-hour access to expert advice from medical microbiologists or infectious disease physicians for the management of infections
- All acute hospitals must have one or more clinical pharmacists with responsibility for antimicrobial use in the hospital

- Patients should be informed of the rationale for prescribing antimicrobials, and informed of any associated risks or adverse effects
- Laboratories should carry out local surveillance of antimicrobial resistance, including annual review of antibiograms as appropriate. Susceptibility results should be released in a restrictive manner where possible. All hospitals should have local or regional antimicrobial prescribing guidelines based where possible on local antimicrobial resistance data.

7.2 Asymptomatic bacteriuria

The main evidence for treating asymptomatic bacteriuria in pregnancy to prevent adverse maternal and fetal outcomes arises from a Cochrane Review in 2000 which showed that when antimicrobial treatment was compared to placebo or no treatment it was effective in (Smaill, 2000):

- Clearing asymptomatic bacteriuria (risk ratio (RR) 0.25, 95% confidence interval (CI) 0.14 to 0.48)
- Reducing risk of pyelonephritis (RR 0.23, 95% CI 0.13 to 0.41)
- Reducing the incidence of low birth weight babies (RR 0.66, 95% CI 0.49 to 0.89)

A Cochrane review of different antimicrobial treatment regimens of asymptomatic bacteriuria in pregnancy did not find significant differences in terms of outcome between several regimens and suggested that issues such as local susceptibility results, cost and side effects should be taken into account (Guinto et al., 2010). A third Cochrane review which focused on duration of antimicrobial treatment in asymptomatic bacteriuria in pregnancy reviewed 13 studies, involving over 1622 women. It found that a one-day regimen is significantly less effective than a seven-day regimen, and that current practice should be to treat patients for seven days (Widmer et al., 2011).

There have been several trials which have shown that the following regimens are effective in the treatment of asymptomatic bacteriuria in pregnancy.

- Co-amoxiclav 625mg TDS for 5 days (Usta et al., 2011) or for 7 days (Estebanez et al., 2009)
- Cefuroxime axetil 250mg BD (Bayrak et al., 2007) or 500mg BD for 5 days (Usta et al., 2011)
- Cefaclor 500mg for 5-7 days for women with mild penicillin hypersensitivity (Stamatiou et al., 2007)
- Fosfomycin 3g stat dose (Estebanez et al., 2009, Bayrak et al., 2007, Usta et al., 2011, Zinner, 1990, Thoumsin et al., 1990). Second of these studies done in 2nd trimester only
- Nitrofurantoin 100mg BD PO for 7 days (Thoumsin et al., 1990)

When choosing an antimicrobial regimen it is important to consider issues of teratogenicity and absorption. The recommendations are included in Table 1.

7.3 Lower UTI (cystitis) in pregnancy

A Cochrane review of treatment of symptomatic urinary tract infections in pregnancy found that there was insufficient evidence to recommend any specific drug regimen, and that all the studied regimens were shown to be very effective (Vazquez and Abalos, 2011). The HSE guidelines for prescribing in Primary Care recommend that nitrofurantoin or fosfomycin can be used for treatment. Scottish guidelines also exist on this topic, SIGN guidelines (Network, 2012).

There are limited studies available on treatment of symptomatic lower UTIs in pregnancy and the one study found in our search had two regimens which were shown to be equivalent:

- Fosfomycin 3g stat dose PO (Krcmery et al., 2001)
- Ceftibuten 400mg PO for 3 days (Krcmery et al., 2001)

For treatment of symptomatic UTIs in pregnancy it is recommended to treat for seven days, except in the case where fosfomycin is used. A repeat urine culture should be sent a week after the antimicrobial treatment is finished to ensure that the bacteriuria has cleared. For treatment options see Table 2.

Treatment options for asymptomatic bacteriuria or lower urinary tract infection (cystitis) in pregnancy <i>(Note: Always review antimicrobial choice in light of susceptibility results from previous samples and from the current admission)</i>		
Drug	Dose*	Notes
Nitrofurantoin	50mg QDS or 100mg BD PO x 7 days (Note the 100mg BD option is only for slow release Macrobid preparation)	<ul style="list-style-type: none"> • Not suitable to be given after 36 weeks gestation or if delivery is imminent because of risk of haemolysis in the newborn and subsequent jaundice (Nordeng et al., 2013) • Not suitable if patient has renal failure • Don't use if the patient has a history of glucose-6-phosphate dehydrogenase (G6PD)-deficiency as it can lead to haemolysis (Chan et al., 1976)
Amoxicillin	500mg TDS PO x 7 days	<ul style="list-style-type: none"> • Not suitable in penicillin allergy • Not suitable for empirical treatment of UTIs and should only be used when susceptibility results are available • Good treatment option for Group B Streptococcal bacteriuria as it has better absorption than oral penicillin
Fosfomycin	3g stat PO dose	<ul style="list-style-type: none"> • May be useful for patients with multi-drug resistant organisms (e.g. extended spectrum β-lactamases) • May be useful in patients who are felt not to be likely to comply with a seven day treatment course

Co-amoxiclav	625mg TDS PO x 5-7 days	<ul style="list-style-type: none"> • Not suitable in penicillin allergy • Risk of necrotising enterocolitis in neonates (Kenyon et al., 2001b, Kenyon et al., 2001a)
Cefuroxime axetil	500mg BD PO x 7 days	<ul style="list-style-type: none"> • Not suitable in severe penicillin allergy but can be used in mild penicillin allergy according to local guidelines
Cephalexin	500mg BD or TDS PO x 7 days	<ul style="list-style-type: none"> • Not suitable in severe penicillin allergy but can be used in mild penicillin allergy according to local guidelines

Table 2: Treatment options for asymptomatic bacteriuria in pregnancy *

Dose recommended presumes normal renal and hepatic function. If the woman has renal or liver failure then discuss with Infection Specialist and/or Antibiotic Pharmacist.

7.4 Upper UTI (pyelonephritis) in pregnancy

Several international guidelines exist. A small study of 67 women compared IV treatment alone until the patient was 48 hours afebrile to IV treatment with PO antimicrobials afterwards to finish a total of 10 days treatment (Brost et al., 1996). It found that in the women with no additional oral antimicrobials had a 12.9% chance of readmission for pyelonephritis in the 2 week period after the infection, as opposed to a 5.6% readmission rate in the women that received oral antimicrobials to finish the 10 day course of treatment.

There are limited trial data available for the management of antenatal pyelonephritis, however, the regimens that have been used are shown below.

- Ceftriaxone 1g daily until 48 hours afebrile then oral cephalexin 500mg QDS for 10 days(Sanchez-Ramos et al., 1995)
- Cefazolin 1g or 2g TDS until 48 hours afebrile then oral cephalexin 500mg QDS for 10 days(Millar et al., 1995, Sanchez-Ramos et al., 1995)
- Ceftriaxone 1g IM for 2 doses then oral cephalexin 500mg QDS for 10 days(Wing et al., 1999, Millar et al., 1995)

A concern with out-patient management in the initial stages is that the woman may progress into labour and they should be admitted for at least 48 hours if pyelonephritis is suspected. A concern with using ceftriaxone 1g dose is that when women are in the third trimester they may be under-dosed and larger doses (up to 2g once daily) should be considered. There is also uncertainty around the frequency of dosing of gentamicin in pregnancy. The recommendations for the antimicrobial treatment of pyelonephritis in pregnancy is shown in Table 3.

Treatment of pyelonephritis in pregnancy <i>(Note: Always review antimicrobial choice in light of susceptibility results from previous samples and from the current admission)</i>		
	Treatment schedule	Notes
1 st line	Ceftriaxone 1-2g OD IV until the patient is 48 hours afebrile; then change to cephalexin 500mg QDS PO for 10 days	<ul style="list-style-type: none"> Consider adding in gentamicin if the patient is systemically unwell, having rigors or has hypotension Not suitable for severe penicillin allergy but can be used for mild penicillin allergy as per local guidelines Consider using ceftriaxone 2g dose in 2nd/3rd trimesters due to increased body weight
2 nd line	Clindamycin 900mg TDS IV or Vancomycin 1g BD IV (depending on Group B Streptococcus susceptibility result if available) AND Gentamicin 1.5mg/kg TDS or 5mg/kg OD IV until the patient is 48 hours afebrile THEN change to a PO alternative depending on susceptibility results and risk of teratogenicity	<ul style="list-style-type: none"> Can be used for penicillin allergy Choice of oral option should be done in discussion with Clinical Microbiology in view of susceptibility results Fosfomycin and nitrofurantoin are not suitable oral options for pyelonephritis Booking weight should be used to calculate the gentamicin dose Follow local guidelines for the maximum dose allowable (usually 480mg/day) and also for how to monitor levels for toxicity The decision to use vancomycin or clindamycin depends on the susceptibility results for Group B Streptococcus if present.
3 rd line	Ciprofloxacin 750mg BD PO for 7 days	<ul style="list-style-type: none"> This is usually restricted to post partum women because of teratogenicity concerns Advise women of potential issues if breastfeeding Need to ensure local resistance rates to ciprofloxacin are at least <10% Note that this has only limited action against Group B Streptococcus. Seek expert advice

Table 3: Treatment options for pyelonephritis in pregnancy.

7.5 Antimicrobial prophylaxis for urinary tract infections in pregnancy

Antimicrobial prophylaxis should be considered also in women in the following groups

- Pyelonephritis in this pregnancy
- Known renal structural abnormality leading to urinary stasis
- Recurrent urinary tract infections (Epp et al., 2010)

The use of antimicrobial prophylaxis for recurrent UTIs or following pyelonephritis is a difficult area and there are not clear evidence based indications at present. Nitrofurantoin can be used for prophylaxis but should be avoided near term or when delivery is imminent because of the risk of neonatal haemolysis. The use of broad spectrum antimicrobials such as co-amoxiclav and cephalexin should be done following assessment of the benefits of prophylaxis against the risk of generating antimicrobial resistance in the patient leading to more limited treatment options at a later stage. Further research is needed in this area and it has been highlighted in the research questions section.

7.6 Special situations

7.6.1 Renal transplant patients and patients with previous reconstructive renal surgery

These women should be managed on a case by case basis between the nephrologist, obstetrician and the transplant team with support from Clinical Microbiology/Infectious diseases consultants as required. Consideration should be given to following the guidelines of the European Best Practice Guidelines for renal transplantation Section IV.10 Pregnancy in renal transplant recipients (transplantation, 2002). For patients who have had previous renal reconstructive surgery it is important that they have their urine checked regularly and are managed carefully on a case-by-case basis.

7.6.2 Renal Calculi

These women warrant particular close follow up as they will have a higher risk for developing recurrent pyelonephritis and sepsis. Although no international guidelines exist there are two observational studies which review options for treatment of renal calculi in pregnancy (Hoscan et al., 2012, Rosenberg et al., 2011). Close discussion between nephrology, obstetrics and urology is required and women should be managed on a case-by-case basis.

7.6.3 Patients with bacteraemia as a result of pyelonephritis

These women may need longer courses of intravenous antimicrobials depending on their clinical condition and the state of the fetus. Early switching to PO antimicrobials may not be appropriate and these cases should be discussed between the obstetric team and the local infection specialists.

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9. Implementation Strategy

- Distribution of guideline to all members of the Institute and to all maternity units.
- Distribution to the Director of the Acute Hospitals for dissemination through line management in all acute hospitals.
- Implementation through HSE Obstetrics and Gynaecology programme local implementation boards.
- Distribution to other interested parties and professional bodies.

10. Qualifying statement

These guidelines have been prepared to promote and facilitate standardisation and consistency of practice using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion
- Advising women of their choices and ensure informed consent is obtained
- Meeting all legislative requirements and maintaining standards of professional conduct
- Applying standard precautions and additional precautions, as necessary, when delivering care
- Documenting all care in accordance with local and mandatory requirements.

11. Auditable Standards

- Number of patients with pyelonephritis re-admitted with urinary tract infections in same pregnancy
- Neonatal outcome in cases of antenatally diagnosed pyelonephritis
- Incidence of multi-drug resistant organisms causing pyelonephritis (e.g. extended spectrum β -lactamase)

12. Research questions

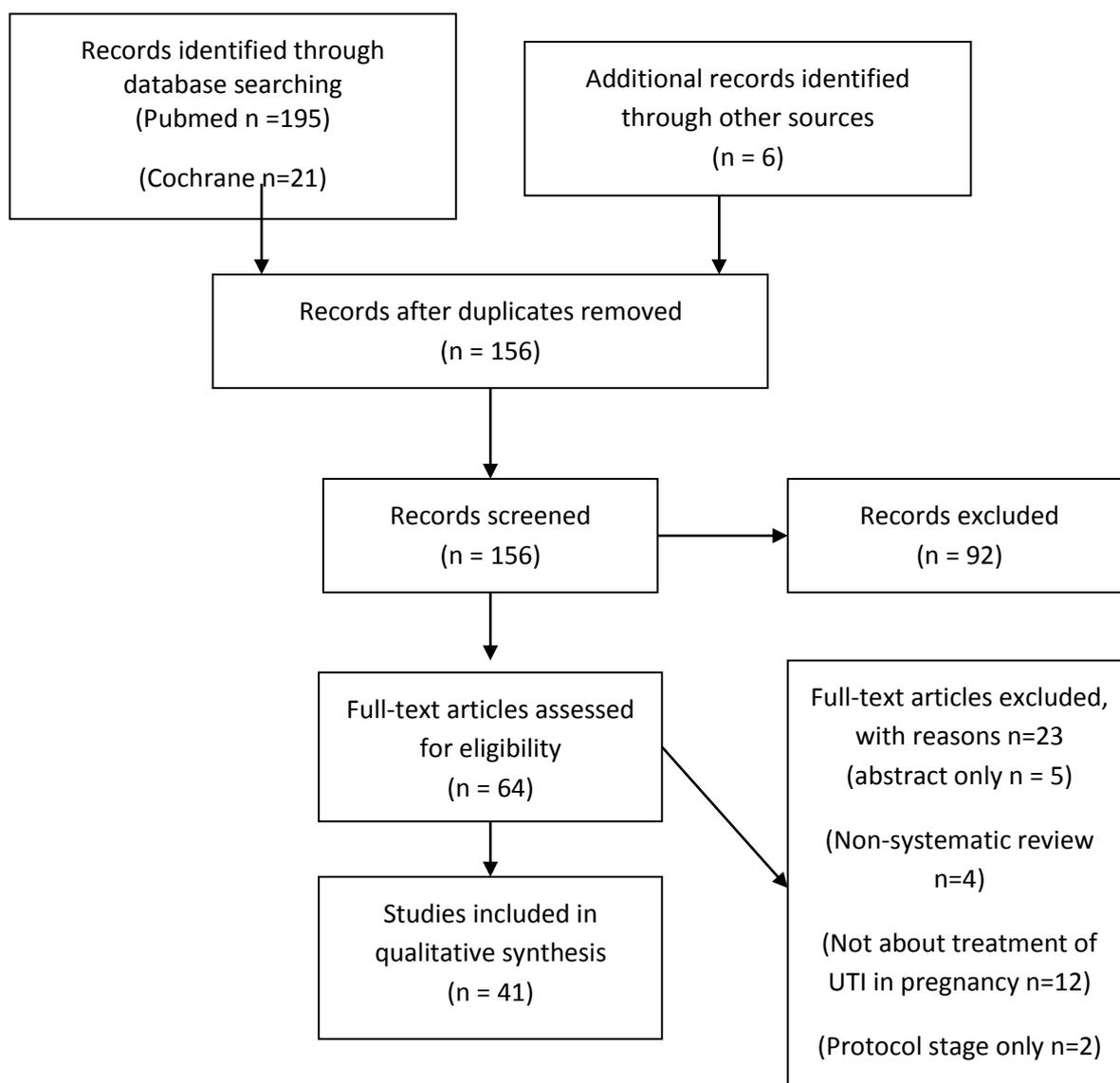
1. What is the optimal dose of ceftriaxone to use when treating pregnant patients for pyelonephritis in the antenatal period; 1g or 2g once daily?
2. What is the best dosing strategy for gentamicin in pregnant patients at each trimester; 1.5mg/kg TDS or 5mg/kg once daily?
3. At what gestation should it be recommended to stop nitrofurantoin prophylaxis?
4. Is intravenous co-amoxiclav equally as safe and effective as third generation cephalosporins for pyelonephritis in pregnancy?
5. When should antimicrobial prophylaxis be used in pregnancy to reduce the incidence of urinary tract infections? When should antimicrobial prophylaxis be stopped; either at term or post-partum?

13. Appendices

Appendix 1: Details of search criteria



PRISMA 2009 Flow Diagram



Appendix 2: Detailed search strategy

Pubmed limits	
Date of search	19/11/2014
Language	English
Subject	Human
Years	1994-2014
Study types	Clinical Trial, comparative study, guideline, meta-analysis, observational study, practice guideline, systematic review

Pubmed		
Search	Query	Items found
#1	Search (pregnancy) AND asymptomatic bacteriuria Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	54
#2	Search (pregnancy) AND asymptomatic bacteriuria	509
#3	Search (pregnancy) AND cystitis Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	16
#4	Search (pregnancy) AND cystitis	326
#5	Search (pregnancy) AND urethritis Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews;	14

	Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	
#6	Search (pregnancy) AND urethritis	277
#7	Search (pregnancy) AND lower uti Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	7
#8	Search (pregnancy) AND lower uti	41
#9	Search (pregnancy) AND lower urinary tract infection Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	46
#10	Search (pregnancy) AND lower urinary tract infection	335
#11	Search (pregnancy) AND upper uti Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	0
#12	Search (pregnancy) AND upper uti Schema: all Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	0
#13	Search (pregnancy) AND upper uti	13
#14	Search (pregnancy) AND upper urinary tract infection Filters: Clinical Trial; Comparative Study;	6

	Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	
#15	Search (pregnancy) AND upper urinary tract infection	141
#16	Search (pregnancy) AND pyelonephritis Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	51
#17	Search (pregnancy) AND pyelonephritis	1588
#18	Search (pregnancy) AND renal abscess Filters: Clinical Trial; Comparative Study; Observational Study; Randomized Controlled Trial; Systematic Reviews; Guideline; Meta-Analysis; Practice Guideline; Publication date from 1994/01/01 to 2014/12/31; Humans; English	1
#19	Search (pregnancy) AND renal abscess	50
Cochrane	(Titles, abstracts and keywords)	
#1	Pregnancy and asymptomatic bacteriuria	6
#2	Pregnancy and cystitis	1
#3	Pregnancy and urethritis	0
#4	Pregnancy and lower UTI	1
#5	Pregnancy and lower urinary tract infection	8
#6	Pregnancy and upper UTI	0
#7	Pregnancy and upper urinary tract infection	0
#8	pregnancy and pyelonephritis	5
#9	Pregnancy and renal abscess	0
		21
International guidelines		
	Total number	6

Appendix 3: Treatment options for asymptomatic bacteriuria and lower urinary tract infection in pregnancy

Treatment options for asymptomatic bacteriuria or lower urinary tract infection (cystitis) in pregnancy <i>(Note: Always review antimicrobial choice in light of susceptibility results from previous samples and from the current admission)</i>		
Drug	Dose*	Notes
Nitrofurantoin	50mg QDS or 100mg BD PO x 7 days (Note the 100mg BD option is only for slow release Macrobid preparation)	<ul style="list-style-type: none"> • Not suitable to be given after 36 weeks gestation or if delivery is imminent because of risk of haemolysis in the newborn and subsequent jaundice (Nordeng et al., 2013) • Not suitable if patient has renal failure • Don't use if the patient has a history of G6PD-deficiency as it can lead to haemolysis (Chan et al., 1976)
Amoxicillin	500mg TDS PO x 7 days	<ul style="list-style-type: none"> • Not suitable in penicillin allergy • Not suitable for empirical treatment of UTIs and should only be used when susceptibility results are available • Good treatment option for Group B Streptococcal bacteriuria as it has better absorption than oral penicillin
Fosfomycin	3g stat PO dose	<ul style="list-style-type: none"> • May be useful for patients with multi-drug resistant organisms (e.g. extended spectrum β-lactamases) • May be useful in patients who are felt not to be likely to comply with a seven day treatment course
Co-amoxiclav	625mg TDS PO x 5-7 days	<ul style="list-style-type: none"> • Not suitable in penicillin allergy • Risk of necrotising enterocolitis in neonates (Kenyon et al., 2001b, Kenyon et al., 2001a)
Cefuroxime axetil	500mg BD PO x 7 days	<ul style="list-style-type: none"> • Not suitable in severe penicillin allergy but can be used in mild penicillin allergy according to local guidelines
Cephalexin	500mg BD or TDS PO x 7 days	<ul style="list-style-type: none"> • Not suitable in severe penicillin allergy but can be used in mild penicillin allergy according to local guidelines

Appendix 4: Treatment options for pyelonephritis in pregnancy

Treatment of pyelonephritis in pregnancy (Note: Always review antimicrobial choice in light of susceptibility results from previous samples and from the current admission)		
	Treatment schedule	Notes
1 st line	Ceftriaxone 1-2g OD IV until the patient is 48 hours afebrile; then change to cephalexin 500mg QDS PO for 10 days	<ul style="list-style-type: none"> Consider adding in gentamicin if the patient is systemically unwell, having rigors or has hypotension Not suitable for severe penicillin allergy but can be used for mild penicillin allergy as per local guidelines Consider using ceftriaxone 2g dose in 2nd/3rd trimesters due to increased body weight
2 nd line	Clindamycin 900mg TDS IV or Vancomycin 1g BD IV (depending on Group B Streptococcus susceptibility result if available) AND Gentamicin 1.5mg/kg TDS or 5mg/kg OD IV until the patient is 48 hours afebrile THEN change to a PO alternative depending on susceptibility results and risk of teratogenicity	<ul style="list-style-type: none"> Can be used for penicillin allergy Choice of oral option should be done in discussion with Clinical Microbiology in view of susceptibility results Fosfomycin and nitrofurantoin are not suitable oral options for pyelonephritis Booking weight should be used to calculate the gentamicin dose Follow local guidelines for the maximum dose allowable (usually 480mg/day) and also for how to monitor levels for toxicity The decision to use vancomycin or clindamycin depends on the susceptibility results for Group B Streptococcus if present.
3 rd line	Ciprofloxacin 750mg BD PO for 7 days	<ul style="list-style-type: none"> This is restricted only to women post-partum Advise women of potential issues if breastfeeding Need to ensure local resistance rates to ciprofloxacin are at least <10% Note that this has only limited action against Group B Streptococcus. Seek expert advice.