Antibiotics for asymptomatic bacteriuria in pregnancy (Review)

Smaill F, Vazquez JC

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2007, Issue 4

http://www.thecochranelibrary.com

TABLE OF CONTENTS

Antibiotics for asymptomatic bacteriuria in pregnancy (Review)

Smaill F, Vazquez JC

This record should be cited as:
Smaill F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: CD000490. DOI: 10.1002/14651858.CD000490.pub2.

This version first published online: 18 April 2007 in Issue 2, 2007.
Date of most recent substantive amendment: 04 January 2007

ABSTRACT

Background
Asymptomatic bacteriuria occurs in 2% to 10% of pregnancies and, if not treated, up to 30% of mothers will develop acute pyelonephritis. Asymptomatic bacteriuria has been associated with low birthweight and preterm delivery.

Objectives
To assess the effect of antibiotic treatment for asymptomatic bacteriuria on persistent bacteriuria during pregnancy, the development of pyelonephritis and the risk of low birthweight and preterm delivery.

Search strategy
We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (January 2007).

Selection criteria
Randomized trials comparing antibiotic treatment with placebo or no treatment in pregnant women with asymptomatic bacteriuria found on antenatal screening.

Data collection and analysis
We assessed trial quality.

Main results
Fourteen studies were included. Overall the study quality was poor. Antibiotic treatment compared to placebo or no treatment was effective in clearing asymptomatic bacteriuria (risk ratio (RR) 0.25, 95% confidence interval (CI) 0.14 to 0.48). The incidence of pyelonephritis was reduced (RR 0.23, 95% CI 0.13 to 0.41). Antibiotic treatment was also associated with a reduction in the incidence of low birthweight babies (RR 0.66, 95% CI 0.49 to 0.89) but a difference in preterm delivery was not seen.

Authors' conclusions
Antibiotic treatment is effective in reducing the risk of pyelonephritis in pregnancy. A reduction in low birthweight is consistent with current theories about the role of infection in adverse pregnancy outcomes, but this association should be interpreted with caution given the poor quality of the included studies.

PLAIN LANGUAGE SUMMARY

Antibiotics can reduce the risk of kidney infections in pregnant women who have a urine infection but no symptoms of infection

A urine infection without any of the typical symptoms associated with an acute urine infection (asymptomatic bacteriuria) occurs in 2% to 10% of pregnancies. It may lead to kidney infection (pyelonephritis) in the mother and may possibly contribute to low birthweight babies and preterm birth (before 38 weeks). The review of trials on antibiotic treatment for these women with no symptoms but high bacterial counts in their urine found 14 studies involving 2302 women. Most of the trials were of poor quality. Antibiotics were effective

in clearing asymptomatic bacteriuria and reducing the incidence of symptomatic kidney infection in the mother. The incidence of low birthweight seemed also to be reduced. None of the studies adequately assessed adverse effects of treatment. More research is needed.

BACKGROUND

Asymptomatic bacteriuria, generally defined as true bacteriuria in the absence of specific symptoms of acute urinary tract infection, occurs in 2% to 10% of all pregnancies (Whalley 1967). While rates from more recent studies, including observational studies from developing countries, fall within this range (McNair 2000; Mohammad 2002; Bandyopadhyay 2005; McIsaac 2005; Tugrul 2005; Fatima 2006), the prevalence of asymptomatic bacteriuria was reported to be as high as 86.6% in a population from Nigeria that included Staphylococcus aureus as a uropathogen (Akerele 2001). The prevalence of infection is most closely related to socioeconomic status and is similar in both pregnant and non-pregnant women (Turck 1962; Whalley 1967). Other contributing factors recognized as associated with an increased risk for bacteriuria include a history of recurrent urinary tract infections, diabetes and anatomical abnormalities of the urinary tract.

The original criterion for diagnosing asymptomatic bacteriuria was more than 100,000 bacteria/ml on two consecutive clean catch samples (Kass 1960a). The detection of more than 100,000 bacterial/ml in a single voided midstream urine is accepted as an adequate and more practical alternative, although there is only an 80% probability the woman has true bacteriuria, increasing to 95% if two or more consecutive cultures are positive for the same organism (Kass 1960a). Because the performance of rapid urine screening tests in pregnancy is poor, quantitative culture remains the gold standard for diagnosis (Bachman 1993; Tincello 1998; McNair 2000; Garingalo-Molina).

E. coli is the most common pathogen associated with asymptomatic bacteriuria, representing at least 80% of isolates. Other organisms include other gram negative bacteria and group B streptococci. These bacteria colonize the vaginal introitus and periurethral area. Uropathogenic gram negative bacteria possess specific virulence factors that enhance both colonization and invasion of the urinary tract; for example, the P-fimbriae of certain strains of E. coli (Stenqvist 1987; Eisenstein 1988). Maternal urinary tract infection with group B streptococci is associated with vaginal colonization with the organism.

While asymptomatic bacteriuria in non-pregnant women is generally benign, obstruction to the flow of urine in pregnancy leads to stasis and increases the likelihood that pyelonephritis will complicate asymptomatic bacteriuria. If asymptomatic bacteriuria is untreated, 30% of mothers develop acute pyelonephritis compared with 1.8% of non-bacteriuric controls (Whalley 1967). Mechanical compression from the enlarging uterus is the principal cause of hydroureter and hydronephrosis, but smooth muscle relaxation induced by progesterone may also play a role (Sobel 1995). Differences in urine pH and osmolality and pregnancy-induced glycosuria and aminoaciduria may facilitate bacterial growth. Clinical signs of pyelonephritis include fever, chills, costo-vertebral tenderness, dysuria and frequency. Nausea and vomiting are common and if infection is associated with bacteremia, women may present with high fever, shaking chills and low blood pressure. Maternal complications include maternal respiratory insufficiency, septicemia, renal dysfunction and anemia (Hill 2005) and. in the pre-antibiotic era, acute pyelonephiritis was associated with a 20% to 50% incidence of preterm birth.

The relationship between asymptomatic bacteriuria, low birthweight and preterm delivery is controversial. Evidence is accumulating that pro-inflammatory cytokines secreted by maternal or fetal monocytes or macrophages in response to bacterial products (for example, endotoxin) may initiate labour (Gomez 1997) and that intrauterine infection is associated with preterm delivery (Goldenberg 2000). Findings from the Cardiff Birth Survey, which prospectively studied 25,844 births, reported that asymptomatic bacteriuria, adjusted for demographic and social factors, was not associated with preterm delivery (odds ratio (OR) 1.2; 95% confidence interval (CI) 0.9 to 1.5) (Meis 1995). However, when preterm births were categorized into medically indicated or spontaneous preterm births, there was a significant association between bacteriuria and medically indicated preterm births (OR 2.03; 95% CI 1.5 to 2.8) but not for spontaneous preterm births (OR 1.07; 95% CI 0.78 to 1.46) (Meis 1995a) and the authors concluded that if asymptomatic bacteruria does not progress to pyelonephritis, it is not associated with preterm birth. Results of a meta-analysis of 17 cohort studies showed an association between asymptomatic bacteriuria and low birthweight and preterm birth but failed to resolve the question whether or not asymptomatic bacteriuria was merely a marker for low socioeconomic status, which is associated with low birthweight (Romero 1989). Studies of the effect of treatment of asymptomatic bacteriuria could provide the answer.

Screening for and treatment of asymptomatic bacteriuria in pregnancy has become a standard of obstetric care and most antenatal guidelines include routine screening for asymptomatic bacteriuria. Using a decision analysis, screening for and treatment of asymptomatic bacteriuria to prevent pyelonephritis has been shown to be cost-effective over a wide range of estimates, although the cost-benefit is diminished if the rate of asymptomatic bacteriuria is less than 2% (Wadland 1989; Rouse 1995). The low prevalence of infection in certain populations, the cost of different screening tests and uncertainty about the benefits of treatment in decreasing

adverse outcomes of pregnancy have, however, been used to argue against screening and treatment as universal recommendations.

OBJECTIVES

To evaluate the effect of antibiotic treatment for asymptomatic bacteriuria in pregnancy on:
(i) persistent bacteriuria during pregnancy and after delivery;
(ii) the development of symptomatic infection (pyelonephritis);
(iii) the risk of preterm delivery and low birthweight.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

We included all trials where the intention was to allocate participants to treatment or no treatment without bias. Trials were included where a quasi-randomized method of allocation (e.g. alternation) was used.

Types of participants

Pregnant women found on antenatal screening to have asymptomatic bacteriuria, as defined by the study authors, at any stage of pregnancy.

Types of intervention

We included studies if any antibiotic regimen was compared with no treatment for asymptomatic bacteriuria.

Types of outcome measures

We included studies with information on persistence of bacteriuria, development of pyelonephritis, incidence of low birthweight or preterm delivery, or rate of bacteriuria long term (defined as at least three to six months postpartum).

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (January 2007).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:
(1) quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
(2) monthly searches of MEDLINE;
(3) handsearches of 30 journals and the proceedings of major conferences;
(4) weekly current awareness search of a further 37 journals.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.

We did not apply any language restrictions.

METHODS OF THE REVIEW

Selection of studies

We assessed all potential studies identified for inclusion as a result of the search strategy.

Data extraction and management

One of the review authors abstracted information on method of allocation, characteristics of participants, type of intervention and outcomes from eligible studies using a standard form. We used the Review Manager software (RevMan 2003) to enter all the data.

Assessment of methodological quality of included studies

We assessed the validity of each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2005). We described methods used for generation of the randomization sequence for each trial.

(1) Selection bias (randomization and allocation concealment)
A quality score was assigned for each trial, using the following criteria:
(A) adequate concealment of allocation: such as telephone randomization, consecutively numbered sealed opaque envelopes;
(B) unclear whether adequate concealment of allocation: such as list or table used, sealed envelopes, or study did not report any concealment approach;
(C) inadequate concealment of allocation: such as open list of random number tables, use of case record numbers, dates of birth, days of the week, alternation or coin toss.

(2) Attrition bias (loss of participants)
We described completeness to follow up for each trial and included reasons for loss of participants, for example, withdrawals, dropouts, protocol deviations when reported.

(3) Performance bias (blinding of participants, researchers and outcome assessment)

Blinding of participants, caregivers and outcome assessment, including use of placebo, was assessed and described, or reported as 'not stated'.

Measures of treatment effect
We used a fixed-effect meta-analysis to combine data where there was no significant heterogeneity among trials using the Review Manager software (RevMan 2003). For dichotomous data, we presented the results as risk ratio with 95% confidence intervals.

Assessment of heterogeneity
We applied tests of heterogeneity among trials using the I^2 statistic. Where we identified substantial heterogeneity among the trials, we used a random-effects meta-analysis and explored the source of the heterogeneity by sensitivity analysis where appropriate.

Dealing with missing data
We performed an available case analysis, including data on only those participants whose results were known. The proportion of participants who did not provide outcome data was noted in the table of 'Characteristics of included studies'. Participants with available data were analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention.

Subgroup analyses
We performed a subgroup analysis based on the duration of the course of antibiotics given (single dose, short course, intermediate duration or antibiotics continued to delivery).

DESCRIPTION OF STUDIES

For details *see* 'Characteristics of included studies'. Fourteen studies met the inclusion criteria and were included. One study enrolled only women with group B streptococci in the urine (Thomsen 1987). Where there was more than one published reference that in the opinion of the review author referred to the same study, information was abstracted from whichever reference provided the necessary details of the study.

All participants were enrolled from hospital-based clinics. Most studies enrolled women at the first antenatal visit. Where there were microbiological criteria, bacteriuria was usually defined as at least one clean catch, midstream or catheterized urine specimen with more than 100,000 bacteria/ml on culture. Several studies required confirmation with a second culture; one study included women with a colony count of more than 10,000 bacteria/ml on two occasions.

Several different antibiotic regimens were used for treatment (*see* 'Characteristics of included studies' for details). Treatment was either a single dose (n = 1), given for three to seven days (n = 4), for three weeks (n = 1), for six weeks (n = 1), continued until term (n = 5) or until up to six weeks after delivery (n = 2). In some studies, repeat antibiotic courses and alternative agents for persisting or resistant organisms were used.

Most studies (n = 11) included the outcome of pyelonephritis. The outcome of low birthweight was reported in seven studies. In many of the studies, prematurity was defined as birth weight less than 2500 g, rather than a gestational age less than 38 weeks. Where there was no definition of prematurity provided by the authors, it was assumed that the results referred to a birth weight of less than 2500 g based on the period when these studies were conducted (1960s) when the standard definition of prematurity was low birthweight. In three studies, the outcome of preterm delivery was reported, although in each study a slightly different gestational age to define preterm delivery was used (*see* 'Characteristics of included studies' table for details).

Three studies measured rates of bacteriuria long term: one between three and nine months postpartum, one at six months and one at 10 to 14 years.

Four studies were excluded (*see* 'Characteristics of excluded studies' table for details).

METHODOLOGICAL QUALITY

For most studies there was only a brief and incomplete description of the research methods, which made it difficult to assess the methodological quality of the studies. Overall, however, the studies were not methodologically strong and in no study was there adequate concealment of allocation. There was no statement in any study that allocation was centrally controlled and in the only study that referred to the use of sealed envelopes (Little 1966), the envelope was drawn from a pool of sealed envelopes rather than a consecutively numbered pile. For the other studies, there was no description of the method of randomization or the method was clearly inadequate: in four studies women were allocated to treatment by alternation, and in one study a coin toss was used. In nine of the 14 studies, the control group received a placebo; no treatment was given to the control group in the others. In those studies without placebo, no mention was made that the observer was blinded to treatment allocation, making it more likely that performance and detection biases were also present.

The description of the characteristics of the study groups was also poor. In only one study (Thomsen 1987) were the similarities in age, parity and socioeconomic status between the treatment and no treatment groups adequately described; in the study from Kass 1960a the racial distribution of the two groups was described and was comparable; in four other studies (Mulla 1960; Elder 1966; Gold 1966; Elder 1971) the urinary bacterial isolates for the two groups were listed but otherwise there was no attempt to demonstrate the comparability of the study groups. No study included the rates of maternal smoking, a recognized risk for low birthweight. There was no description of the presence of co-existing

genital infections, although one study excluded women with positive serology for syphilis (Pathak 1969). Details on the management of recurrent urinary tract infection or persistent infection, the treatment of symptomatic lower urinary tract infection (cystitis) and concurrent antibiotic administration were incomplete. Some studies included twin deliveries while other studies excluded these.

There was no consistent application of standard definitions for the measured outcomes. Persistent bacteriuria at follow up was not usually described further. Pyelonephritis usually referred to symptoms of loin pain, fever, dysuria or frequency, with or without a significant urine culture. While rates of low birthweight were usually reported, most studies described this as "prematurity". For those studies that reported rates of preterm deliveries, the definition of preterm delivery was inconsistent, and there were insufficient data presented in any of the studies to compare gestational age between treatment and control groups.

RESULTS

Antibiotic treatment is effective in clearing asymptomatic bacteriuria (risk ratio (RR) 0.25; 95% confidence interval (CI) 0.14 to 0.48), although this estimate of treatment effect must be interpreted cautiously. Five of the 14 studies reported this result. Without treatment, asymptomatic bacteriuria persisted in 66% of women. Although there was significant statistical heterogeneity among trials, likely explained by differences in study design and the definition of persistent bacteriuria, the direction of the effect was consistent.

Antibiotic treatment was effective in reducing the incidence of pyelonephritis in women with asymptomatic bacteriuria (RR 0.23; 95% CI 0.13 to 0.41). Again there was significant heterogeneity among the studies. A reduction in the incidence of low birthweight was also seen with treatment (RR 0.66; 95% CI 0.49 to 0.89). There was no evidence of a reduction in preterm delivery (RR 0.37; 95% CI 0.10 to 1.36) when this was defined as a gestational age of less than 38 weeks. Only three studies, including one that only enrolled women with group B streptococcal bacteriuria, reported this outcome. Treatment with antibiotics had no effect on the incidence of bacteriuria long term (results reported in one study at between three and nine months postpartum, one at six months and one at 10 to 14 years).

Duration of antibiotic treatment was not associated with any of the outcome measures. Because there was significant heterogeneity within certain subgroups, a formal meta-regression to test for an association between duration of treatment and treatment effect was not performed. We performed a sensitivity analysis including only those studies that used a placebo. Using a random-effects model, there remained a statistically significant benefit of antibiotic treatment on the development of pyelonephritis (RR 0.17; 95% CI 0.09 to 0.31) but not low birthweight (RR 0.64; 95% CI 0.35 to 1.16). When only the placebo-controlled studies were included, the statistically significant heterogeneity among trials was no longer seen.

In no study was the method of allocation concealment considered adequate. Because the method of randomization was not sufficiently described for most of the other studies, we did not perform a sensitivity analysis that excluded the quasi-randomized studies.

For the outcome of pyelonephritis, there was an association between study year and treatment effect, with the more recent studies associated with less treatment effect. In large part, this can be explained by the decrease in prevalence of pyelonephritis over time although there may be other differences in obstetrical management that might explain this observation.

In none of the studies was the adverse effects of antibiotics carefully considered.

DISCUSSION

While the results of these studies are consistent, yielding reductions in the incidence of pyelonephritis and low birthweight with treatment of asymptomatic bacteriuria, important methodological considerations limit the strength of the conclusions. When all studies are included significant heterogeneity among the studies was observed which may be partly explained by study quality. When only those studies that used a placebo were analysed, heterogeneity was no longer statistically significant. Duration of antibiotic treatment did not appear to explain any heterogeneity.

The overall incidence of pyelonephritis in the untreated group was 21%, but ranged from 2.5% to 36%. While different definitions of pyelonephritis could explain some of this variation, there may be other factors, for example type of organism, socioeconomic status, other care given in pregnancy, that, if defined, could identify groups of women with asymptomatic bacteriuria with different risks of developing pyelonephritis. In the absence of this type of information, however, the presence of asymptomatic bacteriuria itself defines a population at risk of pyelonephritis. Overall, the number of women needed to treat to prevent one episode of pyelonephritis is seven (95% CI 6 to 8) and treatment of asymptomatic bacteriuria will lead to approximately a 75% reduction in the incidence of pyelonephritis.

The studies reported here (with only three exceptions) date from the 1960s and 1970s; microbiological methodology for the diagnosis of bacteriuria has not significantly changed over this interval. Although not all of the antibiotics used in these studies remain available currently and the use of tetracycline is now contraindicated in pregnancy, it is valid to assume that the results are applicable to other antibiotics active against urinary pathogens that are safe in pregnancy. A Cochrane Review of treatments for symptomatic urinary tract infections during pregnancy concluded

that although antibiotic treatment is effective for the cure of urinary tract infections, there are insufficient data to recommend any specific regimen (Vazquez 2003). The choice of a sulfonamide or sulfonamide-containing combination, a penicillin, cephalosporin or nitrofurantoin, based on the results of susceptibility testing, are appropriate regimens for the management of asymptomatic bacteriuria. Increasing antibiotic resistance, however, complicates the choice of empiric regimens and is likely to become an increasing problem. There have been few recent surveys of antibiotic resistance in urinary isolates from women with asymptomatic bacteriuria, but results from surveys of antibiotic susceptibility in pathogens causing community-acquired uncomplicated urinary tract infections suggests considerable regional variation. Resistance to ampicillin in E. coli in a survey of European countries and Canada averaged 29.8% but was as high as 53.9% in Spain (Kahlmeter 2003).

Although the analysis did show a statistically significant reduction in the incidence of low birthweight, the poor methodological quality of the studies means conclusions for this outcome should be drawn cautiously. There was no association between treatment and preterm delivery, but only three studies reported this outcome. While preterm deliveries are associated with low birthweight, some low birthweight infants are small for gestational age as a consequence of intrauterine growth retardation, for which there are many possible etiologies. The reduction in the incidence of low birthweight with antibiotic treatment is consistent with current theories about the role of infection as a cause of adverse pregnancy outcomes, but a greater understanding of the basic mechanisms by which the treatment of bacteriuria could lead to a reduction in low birthweight is required. Prevention of pyelonephritis, which in early studies prior to the availability of effective antimicrobial therapy was associated with preterm delivery, may be a factor, but treatment of bacteriuria with antibiotics may also eradicate organisms colonizing the cervix and vagina that are associated with adverse pregnancy outcomes. The relationship between genital infections such as bacterial vaginosis and preterm labour was not recognized when these studies on the treatment of asymptomatic bacteriuria were originally designed.

In none of the studies reviewed were the adverse effects of antibiotics systematically collected. The incidence of allergic reactions, vaginal yeast infections, gastrointestinal side-effects and the development of bacterial resistance, were not considered, nor were neonatal outcomes collected. While it is not possible to compare the benefits versus the disadvantages of antibiotic therapy from these studies, it is unlikely that the expected side-effects from a short course of antibiotics would be significant.

AUTHORS' CONCLUSIONS

Implications for practice

Antibiotic treatment of asymptomatic bacteriuria is indicated to reduce the risk of pyelonephritis in pregnancy. A recent prospective longitudinal study over a two-year period from 2000 to 2001 reports an incidence of hospitalization for acute pyelonephritis in pregnancy of 1.4%, less than the 3% to 4% rate reported in the early 1970s before screening for asymptomatic bacteriuria became routine (Hill 2005).

The optimal time to perform the urine culture is unknown; it seems reasonable to perform the urine culture and treat, as done in these studies, at the first prenatal visit but a single culture before 20 weeks may miss more than half of women with asymptomatic bacteriuria (McIsaac 2005).

Seven of the studies continued antibiotics until term; one additional study treated women for six weeks, while the majority of the rest gave treatment for three to seven days. Both continuous treatment and short-course therapy strategies show a statistically significant benefit in the reduction of pyelonephritis. A small randomized study that compared intermittent therapy with continuous treatment confirmed that both strategies were equally effective (Whalley 1977). While short-course therapy of asymptomatic bacteriuria has become accepted practice, the optimal duration of treatment is unknown and standard treatment regimens are currently recommended (Villar 2000). The choice of antibiotic should be guided by antimicrobial susceptibility testing, but this decision is becoming more difficult because of increasing rates of antimicrobial resistance to commonly prescribed antibiotics.

In the studies included in this review, insufficient data were presented to determine the effectiveness of treatment to prevent recurrent bacteriuria during the pregnancy. Although it is recommended that a urine culture be done following treatment, with retreatment as necessary, the studies did not specifically evaluate the effectiveness of this strategy.

Implications for research

A better understanding of the basic mechanisms by which treatment of asymptomatic bacteriuria could prevent low birthweight is required. Any study of the relationship between other infections and adverse outcomes of pregnancy needs to control for asymptomatic bacteriuria and its treatment but it is unlikely that the particular contribution of asymptomatic bacteriuria to preterm delivery and low birthweight will ever be conclusively determined.

The studies included in this review generally used a urine colony count of more than 100,000 bacteria/ml to identify patients. Although lower colony counts have been shown to be associated with active infection in other populations (Stamm 1982), their significance in pregnancy has not been established. Treatment of asymptomatic pregnant women with lower colony counts is not

currently recommended, but further study of appropriate strategies to manage these women is warranted.

Quantitative urine culture of a midstream or clean catch urine is the gold standard for detecting asymptomatic bacteriuria in pregnancy, but this test is expensive and may not always be available in all clinical settings. Although rapid urine screening tests, for example, urine microscopy and urine dipstick, have not been shown to perform satisfactorily in this population, their use may be cost-beneficial (Rouse 1995). Any new urine screening test that is developed needs to be evaluated in the context of screening for asymptomatic bacteriuria of pregnancy.

None of these studies adequately addressed when the most appropriate time is to perform the initial screening culture, how often to repeat a negative culture and how best to monitor women initially treated for asymptomatic bacteriuria. There is a need to define the appropriate frequency of follow-up cultures and re-treatment strategies.

Despite almost uniform national guidelines, there is little evidence of adherence to screening recommendations. There is a need to evaluate screening for asymptomatic bacteriuria as a measure of quality of care.

While there are no new data to indicate that women should not be screened for asymptomatic bacteriuria, it is difficult to estimate accurately the cost-effectiveness of screening for asymptomatic bacteriuria without up-to-date information on the prevalence of asymptomatic bacteriuria. There needs to be prospective evaluation of cost-effective diagnostic algorithms, that include risk factors, in these different populations. Because of the association between antibiotic treatment and the prevention of pyelonephritis and low birthweight, additional large-scale randomized trials of asymptomatic bacteriuria, which include a 'no treatment' arm, where the participants are similar to those included in these original studies, cannot be advocated, despite the methodological shortcomings of the studies included here. Preventing inappropriate antibiotic use has, however, become an important aspect of programs to decrease the development of antimicrobial resistance. This new concern gives an impetus to researchers to identify a population of women with asymptomatic bacteriuria in whom antibiotic treatment may not be necessary. If a population could be defined where the risk of the development of pyelonephritis was low, a carefully designed randomized placebo-controlled trial with close monitoring of outcomes, including the adverse effects of antimicrobial therapy, could be legitimately performed and provide useful information on alternative management strategies.

POTENTIAL CONFLICT OF INTEREST

None known.

ACKNOWLEDGEMENTS

None.

SOURCES OF SUPPORT

External sources of support

- No sources of support supplied

Internal sources of support

- No sources of support supplied

REFERENCES

References to studies included in this review

Brumfitt 1975 *{published data only}*

* Brumfitt W. The effects of bacteriuria in pregnancy on maternal and fetal health. *Kidney International* 1975;**8**:S113–S119.

Condie AP, Williams JD, Reeves DS, Brumfitt W. Complications of bacteriuria in pregnancy. Urinary tract infection, Proceedings of the First National Symposium; 1968 April; London. London: Oxford University Press, 1968:148–59.

Williams JD, Reeves DS, Condie AP, Franklin ISN, Leigh DA, Brumfitt W. The treatment of bacteriuria in pregnancy. In: O'GradyF, BrumfittW editor(s). *Urinary tract infection, Proceedings of the First National Symposium; 1968 April; London*. London: Oxford University Press, 1968:160–9.

Elder 1966 *{published data only}*

Elder HA, Santamarina BAG, Smith SA, Kass EH. Use of sulfasymazine in the treatment of bacteriuria of pregnancy. *Antimicrobial Agents and Chemotherapy* 1966;**6**:142–8.

Elder 1971 *{published data only}*

Elder HA, Santamarina BAG, Smith S, Kass EH. The natural history of asymptomatic bacteriuria during pregnancy: the effect of tetracycline on the clinical course and the outcome of pregnancy. *American Journal of Obstetrics and Gynecology* 1971;**111**:441–62.

Foley 1987 *{published data only}*

Foley ME, Farquharson R, Stronge JM. Is screening for bacteriuria in pregnancy worth while?. *BMJ* 1987;**295**:270.

Furness 1975 *{published data only}*

Furness ET, McDonald PJ, Beasley NV. Urinary antiseptics in asymptomatic bacteriuria of pregnancy. *New Zealand Medical Journal* 1975;**81**:417–9.

Gold 1966 *{published data only}*

Gold EM, Traub FB, Daichman I, Terris M. Asymptomatic bacteriuria during pregnancy. *Obstetrics & Gynecology* 1966;**27**:206–9.

Kass 1960 *{published data only}*

Kass EH. Pyelonephritis and bacteriuria. A major problem in preventive medicine. *Annals of Internal Medicine* 1962;**56**:46–53.

Kass EH. The role of asymptomatic bacteriuria in the pathogenesis of pyelonephritis. In: QuinnEL, KassEH editor(s). *Biology of pyelonephritis*. Boston: Little Brown and Company, 1960:399–412.

Savage WE, Hajj SN, Kass EH. Demographic and prognostic characteristics of bacteriuria in pregnancy. *Medicine (Baltimore)* 1967;**46**: 385–407.

Zinner SH, Kass EH. Long term (10 to 14 years) follow-up of bacteriuria of pregnancy. *New England Journal of Medicine* 1971;**285**: 820–4.

Kincaid-Smith 1965 *{published data only}*

Kincaid-Smith P, Bullen M. Bacteriuria in pregnancy. *Lancet* 1965; **1**:1382–7.

Little 1966 *{published data only}*

Little PJ. The incidence of urinary infection in 5000 pregnant women. *Lancet* 1966;**2**:925–8.

Mulla 1960 *{published data only}*

Mulla N. Bacteriuria in pregnancy. *Obstetrics & Gynecology* 1960;**16**: 89–92.

Pathak 1969 *{published data only}*

Pathak UN, Tang K, Williams LL, Stuart KL. Bacteriuria of pregnancy: results of treatment. *Journal of Infectious Diseases* 1969;**120** (1):91–5.

Thomsen 1987 *{published data only}*

Thomsen AC, Morup L, Brogaard Hansen K. Antibiotic elimination of group-B streptococci in urine in prevention of preterm labour. *Lancet* 1987;**1**:591–3.

Williams 1969 *{published data only}*

Williams GL, Campbell H, Davies KJ. Urinary concentrating ability in women with asymptomatic bacteriuria in pregnancy. *BMJ* 1969; **3**:212–5.

Wren 1969 *{published data only}*

Wren BG. Subclinical renal infection and prematurity. *Medical Journal of Australia* 1969;**2**:596–600.

References to studies excluded from this review

Calderon-Jaimes 1989

Calderon-Jaimes EC, Arredondo-Garcia JLA, Olvera-Salinas JO, Echaniz-Aviles GE, Conde-Gonzalez CC, Hernandez-Nevarez PH. Urinary infecion prevention during pregnancy in patients with asymptomatic bacteriuria. *Ginecologia y Obstetricia de Mexico* 1989; **57**:90–7.

LeBlanc 1964

LeBlanc AL, McGanity WJ. The impact of bacteriuria in pregnancy - a survey of 1300 pregnant patients. *Biologie Medicale* 1964;**22**:336–47.

Mohammad 2002

Mohammad M, Mahdy ZA, Omar J, Maan N, Jamil MA. Laboratory aspects of asymptomatic bacteriuria in pregnancy. *Southeast Asian Journal of Tropical Medicine and Public Health* 2002;**33**(3):575–80.

Sanderson 1984

Sanderson P, Menday P. Pivmecillinam for bacteriuria in pregnancy. *Journal of Antimicrobial Chemotherapy* 1984;**13**:383–8.

Additional references

Akerele 2001

Akerele J, Abhulimen P, Okonofua F. Prevalance of asymptomatic bacteriuria among pregnant women in Benin City, Nigeria. *Journal of Obstetrics and Gynaecology* 2001;**21**(2):141–4.

Bachman 1993

Bachman JW, Heise RH, Naessens JM, Timmerman MG. A study of various tests to detect asymptomatic urinary tract infections in an obstetric population. *JAMA* 1993;**270**:1971–4.

Bandyopadhyay 2005

Bandyopadhyay S, Thakur JS, Ray P, Kumar R. High prevalence of bacteriuria in pregnancy and its screening methods in north India. *Journal of the Indian Medical Association* 2005;**103**(5):259-62, 266.

Eisenstein 1988

Eisenstein BI, Jones GW. The spectrum of infections and pathogenic mechanisms of Escherichia coli. *Advances in Internal Medicine* 1988; **33**:231–52.

Fatima 2006

Fatima N, Ishrat S. Frequency and risk factors of asymptomatic bacteriuria during pregnancy. *Journal of the College of Physicians and Surgeons Pakistan* 2006;**16**(4):273–5.

Garingalo-Molina

Garingalo-Molina FD. Asymptomatic bacteriuria among pregnant women: overview of diagnostic approaches. *Philippine Journal of Microbiology and Infectious Diseases* 2000;**29**:177–86.

Goldenberg 2000

Goldberg RL, Hauth JC, Andrews WW. Mechanisms of disease: intrauterine infection and preterm delivery. *New England Journal of Medicine* 2000;**342**(20):1500–7.

Gomez 1997

Gomez R, Romero R, Edwin SS, David C. Pathogenesis of preterm labor and preterm premature rupture of membranes associated with intraamniotic infection. *Infectious Disease Clinics of North America* 1997;**11**(1):135–76.

Higgins 2005

Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions 4.2.4 [updated March 2005]. In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons, Ltd.

Hill 2005

Hill JB, Sheffield JS, McIntire DD, Wendel GD. Acute pyelonephritis in pregnancy. *Obstetrics & Gynecology* 2005;**105**(1):18–23.

Kahlmeter 2003

Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. *Journal of Antimicrobial Chemotherapy* 2003;**51**: 69–76.

Kass 1960a

Kass EH. The role of asymptomatic bacteriuria in the pathogenesis of pyelonephritis. In: QuinnEL, KassEH editor(s). *Biology of pyelonephritis*. Boston: Little, Brown and Co, 1960:399–412.

McIsaac 2005
McIsaac W, Carroll JC, Biringer A, Bernstein P, Lyons E, Low DE, et al. Screening for asymptomatic bacteriuria in pregnancy. *Journal of Obstetrics and Gynaecology Canada: JOGC* 2005;**27**(1):20–4.

McNair 2000
McNair RD, MacDonald SR, Dooley SL, Peterson LR. Evaluation of the centrifuged and Gram-stained smear, urinalysis, and reagent strip testing to detect asymptomatic bacteriuria in obstetric patients. *American Journal of Obstetrics and Gynecology* 2000;**182**(5):1076–9. [MedLine: 10819832].

Meis 1995
Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC, et al. Factors associated with preterm birth in Cardiff, Wales. I. Univariable and multivariable analysis. *American Journal of Obstetrics and Gynecology* 1995;**173**(2):590–6.

Meis 1995a
Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC, et al. Factors associated with preterm birth in Cardiff, Wales. II. Indicated and spontaneous preterm birth. *American Journal of Obstetrics and Gynecology* 1995;**173**(2):597–602.

RevMan 2003
The Cochrane Collaboratioon. Review Manager (RevMan). 4.2 for Windows. Oxford, England: The Cochrane Collaboratioon, 2003.

Romero 1989
Romero R, Oyarzun E, Mazor M, Sirtori M, Hobbins JC. Meta-analysis of the relationship between asymptomatic bacteriuria and preterm delivery/low birth weight. *Obstetrics & Gynecology* 1989;**73**: 577–82.

Rouse 1995
Rouse DJ, Andrews WW, Goldenberg RL, Owen J. Screening and treatment of asymptomatic bacteriuria of pregnancy to prevent pyelonephritis: a cost-effectiveness and cost-beneficial analysis. *Obstetrics & Gynecology* 1995;**86**:119–23.

Sobel 1995
Sobel JD, Kaye D. Urinary tract infections. In: MandellGL, BennettJE, DolinR editor(s). *Mandell, Douglas and Bennett's principles and practice of infectious diseases*. 4th Edition. New York: Churchill Livingstone, 1995:662–90.

Stamm 1982
Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK. Diagnosis of coliform infection in acutely dysuric women. *New England Journal of Medicine* 1982;**307**:463–8.

Stenqvist 1987
Stenqvist K, Sandberg T, Lidin-Janson G, Orskov F, Orskov L, Svanborg-Eden C. Virulence factors of Escherichia coli in urinary isolates from pregnant women. *Journal of Infectious Diseases* 1987;**156**(6): 870–7.

Tincello 1998
Tincello DG, Richmond DH. Evaluation of reagent strips in detecting asymptomatic bacteriuria in early pregnancy: prospective case series. *BMJ* 1998;**316**:435–7. [MedLine: 9492667].

Tugrul 2005
Tugrul S, Oral O, Kumru P, Kose D, Alkan A, Yildirim G. Evaluation and importance of asymptomatic bacteriuria in pregnancy. *Clinical and Experimental Obstetrics and Gynecology* 2005;**32**(4):237–40.

Turck 1962
Turck M, Goff BS, Petersdorf RG. Bacteriuria in pregnancy; relationship to socioeconomic factors. *New England Journal of Medicine* 1962;**266**:857–60.

Vazquez 2003
Vazquez JC, Villar J. Treatments for symptomatic urinary tract infections during pregnancy. *Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD002256. DOI: 10.1002/14651858.CD002256.

Villar 2000
Villar J, Widmer M, Lydon-Rochelle MT, Gulmezoglu AM, Roganti A. Duration of treatment for asymptomtic bacteriuria during pregnancy. *Cochrane Database of Systematic Reviews* 2000, Issue 2. Art. No.: CD000491. DOI:10.1002/14651858.CD000491.

Wadland 1989
Wadland WC, Plante DA. Screening for asymptomatic bacteriuria in pregnancy. A decision and cost analysis. *Journal of Family Practice* 1989;**29**:372–6.

Whalley 1967
Whalley P. Bacteriuria of pregnancy. *American Journal of Obstetrics and Gynecology* 1967;**97**:723–38.

Whalley 1977
Whalley PJ, Cunningham FG. Short-term versus continuous antimicrobial therapy for asymptomatic bacteriuria in pregnancy. *Obstetrics & Gynecology* 1977;**49**:262–5.

References to other published versions of this review

CDSR 2001
Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database of Systematic Reviews* 2001, Issue 2. Art. No.: CD000490. DOI:10.1002/14651858.CD000490.

Smaill 1993
Smaill F. Antibiotic vs no treatment for asymptomatic bacteriuria. [revised 22 April 1993]. In: Enkin MW, Keirse MJNC, Renfrew MJ, Neilson JP, Crowther C editor(s). Pregnancy and Childbirth Module. In: The Cochrane Pregnancy and Childbirth Database [database on disk and CDROM]. The Cochrane Collaboration; Issue 2, Oxford: Update Software; 1995.

* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Brumfitt 1975
Methods	Allocation: "randomly chosen" (not further described). Blinding: "double-blinded" (not further described). Study period: 1967-1968 (estimated).
Participants	Inclusion criteria: Bacteriuric (clean-catch urine) at first antenatal visit; microbiological criteria not stated. Setting: London and Birmingham, UK (only Birmingham participants reported for outcome of pyelonephritis). Number of subjects: n = 425.
Interventions	Sulphonamide (sulphormethoxine 2 g single dose) vs placebo (see report by Williams et al 1968 for description of treatment regimen).
Outcomes	Low birthweight (< 2500 g). Pyelonephritis (loin pain, fever or rigors; >100,000 bacteria/ml).
Notes	Outcome of low birthweight reported by Brumfitt (see report by Brumfitt 1975); n = 425). Outcome of pyelonephritis reported by Condie et al (see report by Condie 1968) for Birmingham cohort only; n = 173. Data on persistent bacteriuria provided for treatment group only. No women lost to follow up.
Allocation concealment	B – Unclear

Study	Elder 1966
Methods	Allocation: "assigned by a random scheme". Blinding: not stated (placebo used). Study period: June 1965 - March 1966.
Participants	Inclusion criteria: bacteriuria (same bacterial species in first three uncontaminated clean voided urine specimens, with two samples > 100,000 bacteria/ml and one sample > 10,000 bacteria/ml). Setting: Boston City Hospital, US. Number of participants: n = 122.
Interventions	Sulfasymazine 0.5 g daily until delivery (n = 54) or placebo (n = 52).
Outcomes	Persistent bacteriuria (after 3 weeks of treatment) and before delivery.
Notes	Two women lost to follow up in treatment group; three women dropped out in placebo group. 7/52 subjects in the placebo group developed "asymptomatic" pyelonephritis (not further defined and not included as an outcome). One adverse event reported in treatment group (vomiting); no rash, pruritus or photosensitivity; no newborn kernicterus diagnosed.
Allocation concealment	B – Unclear

Study	Elder 1971
Methods	Allocation: alternate allocation of participants. Blinding: not stated (placebo used). Study period: January 1963 - July 1965.
Participants	Inclusion criteria: bacteriuric (> 100,000 bacteria/ml x 2) at first prenatal visit.

Characteristics of included studies (*Continued*)

	Setting: Boston City Hospital. Number of participants: n = 281.
Interventions	Tetracycline 250 mg qid x 6 weeks vs matching placebo.
Outcomes	Persistent bacteriuria. Pyelonephritis (fever with signs and symptoms localized to the urinary tract). Low birthweight (< 2500 g). Mean gestational age (38.46 weeks in treated group n = 107 vs 38.25 weeks in placebo group n = 122 (calculated from numbers in paper)).
Notes	Tetracycline associated with staining of teeth in one-third of children. No women lost to follow up for outcome of pyelonephritis; 3 women (1%) lost to follow up for outcome of persistent bacteriuria and low birth weight. Outcome of persistent bacteriuria in placebo group does not include women who developed pyelonephritis. Only live births included in outcome of low birth weight.
Allocation concealment	C – Inadequate

Study	**Foley 1987**
Methods	Allocation: "toss of a coin". Blinding: not stated (no placebo). Study period: 1985.
Participants	Inclusion: bacteriuric (> 100,000 bacteria/ml x 1; midstream urine) at first prenatal visit. Setting: Dublin, Ireland. Number of participants: n = 220.
Interventions	Sulphamethizole 300 mg or nitrofurantoin 150 mg daily x 3 days (based on susceptibility of the organism); re-treatment or maintenance treatment as necessary. Control group received no treatment.
Outcomes	Persistent bacteriuria (at follow up). "Admitted with pyelonephritis".
Notes	Loss to follow up: 19%. Actual numbers for outcome of persistent bacteriuria not provided.
Allocation concealment	C – Inadequate

Study	**Furness 1975**
Methods	Allocation: "by random allocation" (not further described). Blinding: not stated (no placebo). Study period: not stated.
Participants	Inclusion: bacteriuric (> 100,000 bacteria/ml x 1 or > 10,000 bacteria/ml x 2; midstream urine) at second antenatal visit. Setting: South Australia. Enrollment period: not stated. Number of participants: n = 206.
Interventions	Menthenamine mandelate or methenamine hippurate 1 g qid vs no treatment. Treatment continued until delivery.
Outcomes	Pyelonephritis (frequency and burning on micturition, pyrexia or loin tenderness and significant bacteriuria). Preterm delivery (defined as less than or equal to 38 weeks' gestation).
Notes	Women randomized to either menthenamine mandelate (n = 69), methenamine hippurate (n = 70) or no treatment (n = 67); for analyses, treatment groups combined. Unable to separate incidence of pyelonephritis during pregnancy and puerperium; results combined.

	Loss to follow up: all women included in outcome of pyelonephritis; 17% loss to follow up for outcome of low birthweight.
Allocation concealment	B – Unclear

Study	**Gold 1966**
Methods	Allocation: odd or even study number. Blinding: not stated (placebo used). Study period: February 1962 - December 1964.
Participants	Inclusion criteria: bacteriuria (> 100,000 bacteria/ml x 2: midstream urine) at any prenatal visit. Setting: New York, NY (85% non-white). Number of participants: n = 65.
Interventions	Sulfadimethoxine 500 mg daily; sulfadiazine 1 g tid after 36 weeks vs placebo. Treatment continued until delivery.
Outcomes	Persistent bacteriuria. Pyelonephritis. Preterm delivery (not defined further).
Notes	Only antepartum episodes of pyelonephritis included. No loss to follow up.
Allocation concealment	C – Inadequate

Study	**Kass 1960**
Methods	Allocation: alternate allocation. Blinding: not stated (placebo used). Study period: October 1956 - April 1960.
Participants	Inclusion: bacteriuric (> 100,000 bacteria/ml at first prenatal visit, confirmed x 2). Exclusion: > 32 weeks' gestation. Setting: Boston City Hospital, US (approximately 50% black). Number of participants: n = 214 (includes 11 women identified through Renal Clinic).
Interventions	Sulfamethoxypyridazine 500 mg daily or placebo; nitrofurantoin for failures. Treatment continued until term.
Outcomes	Pyelonephritis (dysuria, frequency and flank pain, fever or chills). Low birthweight (< 2500 g) Long-term persistence of bacteriuria (10-14 years).
Notes	For outcome of low birthweight, results are given for total number of deliveries (3 twin deliveries in placebo group vs none in treated group). Loss to follow up: 23 (11%) for outcomes of pyelonephritis and low birthweight; 69 (34%) for long-term persistence of bacteriuria.
Allocation concealment	C – Inadequate

Study	**Kincaid-Smith 1965**
Methods	Allocation: "randomly" (not described further). Blinding: double-blinded. Study period: 1964-1965.
Participants	Inclusion criteria: bacteriuria (> 100,000 bacteria/ml x 2, mid-stream urine) at first antenatal visit (< 26 weeks). Setting: Melbourne, Australia. Number of participants: n = 145.

Characteristics of included studies (*Continued*)

Interventions	Sulphamethoxydiazine 500 mg daily or sulphadimidine 1 g tid (after 30 weeks) vs placebo. Treatment continued until delivery. Ampicillin or nitrofurantoin given if organism known to be resistant.
Outcomes	Pyelonephritis (loin pain or tenderness, with or without pyrexia and rigors, with or without dysuria and frequency). Preterm delivery (birthweight < 2500 g). Bacteriuria long term (6 months after delivery).
Notes	240 women initially identified as bacteriuric; no information available on 55 women randomized to treatment (treatment allocation not provided) but not included in the analysis because of poor compliance. 29/145 women randomized to treatment but bacteriuria not confirmed on second culture and not included in outcomes reported for this analysis. For outcome of long-term persistence of bacteriuria, 102 women (70%) lost to follow up.
Allocation concealment	B – Unclear

Study	**Little 1966**
Methods	Allocation: drawn from a pool of sealed envelopes. Blinding: not stated (placebo used). Study period: 1962-1965.
Participants	Inclusion criteria: bacteriuria (> 100,000 bacteria/ml x 2, midstream urine) at first prenatal visit. Setting: London, England. Number of participants: n = 265.
Interventions	Sulphamethoxypyridazine 500 mg or (later) nitrofurantoin 100 mg daily continued until 6 weeks after delivery or placebo. Ampicillin or nitrofurantoin were alternatives for failures.
Outcomes	Pyelonephritis (loin pain and tenderness, fever and > 100,000 bacteria/ml). Low birthweight (< 2500 g).
Notes	No loss to follow up.
Allocation concealment	B – Unclear

Study	**Mulla 1960**
Methods	Allocation: "randomly divided" (not further described). Blinding: not stated (no placebo). Study period: Not stated.
Participants	Inclusion: bacteriuria at 30-32 weeks; microbiological criteria not stated. Setting: Ohio, US. Number of participants: n = 100.
Interventions	Sulfadimethoxine 250 mg bid x 7 days vs no treatment.
Outcomes	Pyelonephritis (criteria for diagnosis not given; described as "cystopyelitis").
Notes	Half (13/26) infections developed postpartum; only antepartum infections included in analysis. No loss to follow up.
Allocation concealment	B – Unclear

Study	**Pathak 1969**
Methods	Allocation: "on a random basis" (not further described). Blinding: not stated (placebo used). Study period: not stated.
Participants	Inclusion: bacteriuria (> 100,000 bacteria/ml x 2); < 24 weeks' gestation; BP < 130/90 mmHg.

Characteristics of included studies (*Continued*)

	Setting: Kingston, Jamaica. Number of participants: n = 178.
Interventions	Nitrofurantoin 100 mg bid x 3 weeks; 400 mg in four doses for further 4 days for those who did not respond vs identical appearing placebo.
Outcomes	Clearance of bacteriuria; pyelonephritis (criteria not described).
Notes	12/88 women in treatment group and 14/90 in control group not included in analysis (positive treponemal serology n = 21; defaulted from clinic n = 5). Rates for preterm delivery only presented by bacteriuric status, not treatment group. Rates for postpartum bacteriuria available for 69 women.
Allocation concealment	B – Unclear

Study	**Thomsen 1987**
Methods	Allocation: "randomly allocated" (not further described). Blinding: 'double-blinded' (not further described). Study period: October 1984-October 1986.
Participants	Inclusion: positive midstream urine culture for group B streptococcus at 27 - 31 weeks' gestation. Setting: University Hospital, Denmark. Number of participants: n = 69.
Interventions	Penicillin 10 million IU tid x 6 days or placebo tablets; retreated if repeat cultures positive.
Outcomes	Preterm delivery (< 37 weeks' gestation). Mean gestational age (39.6 weeks in treatment group n = 37 vs 36.2 weeks in placebo group n = 32)
Notes	All mothers positive for group B streptococcus at delivery and their babies were treated with antibiotics. No loss to follow up.
Allocation concealment	B – Unclear

Study	**Williams 1969**
Methods	Allocation: "at random" (not further described). Blinding: not stated (no placebo). Study period: 1967.
Participants	Inclusion: bacteriuria (> 100,000 bacteria/ml x 2, midstream urine) at first antenatal visit. Setting: University Hospital, Cardiff, Wales. Number of subjects: n = 163.
Interventions	Sulphadimidine 1 g tid x 7 days or no treatment; nitrofurantoin 100 mg bid or ampicillin 250 mg tid x 7 days for failures.
Outcomes	Pyelonephritis (loin pain with tenderness or fever, or both).
Notes	No loss to follow up.
Allocation concealment	B – Unclear

Study	**Wren 1969**
Methods	Allocation: alternate allocation. Blinding: not stated (no placebo). Study period: November 1965-December 1968.
Participants	Inclusion: Bacteriuria (midstream urine) x 2 at initial antenatal visits; microbiological criteria not stated. Setting: University hospital, New South Wales, Australia. Number of participants: n = 183.

Interventions	Nitrofurantoin 100 mg bid x 2 weeks, then ampicillin 250 mg q6h x 1 week, then sulphurazole 500 mg q6h x 4 weeks, then nalidixic acid 500 mg q6h x 2 weeks, then repeated until 1-6 weeks after delivery or no treatment.
Outcomes	Preterm delivery (< 37 weeks) or low birthweight (< 2500 g).
Notes	Loss to follow up: 5%.
Allocation concealment	C – Inadequate

Please attend closely to the study period for patient enrollment (found under 'Method'); in several instances there were significant delays between the enrollment period and the published report.
bid: twice a day
BP: blood pressure
IU: international unit
qid: four times a day
q6h: every 6 hours
tid: three times a day
vs: versus

Characteristics of excluded studies

Study	Reason for exclusion
Calderon-Jaimes 1989	Women "divided" in two groups; no further description of how participants were allocated to treatment or no treatment.
LeBlanc 1964	Both asymptomatic and symptomatic women were randomized; results for the asymptomatic bacteriuric women are not provided separately. For the outcome of pyelonephritis in the no treatment group, the outcome for women who were not treated as well as women who discontinued treatment have been combined.
Mohammad 2002	Observational study describing incidence of bacteriuria; no details on treatment provided
Sanderson 1984	All bacteriuric women were treated with antibiotics. Those women successfully treated were randomised to prophylactic pivampicillin or no treatment for up to three months.

ANALYSES

Comparison 01. Antibiotic versus no treatment for asymptomatic bacteriuria

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Persistent bacteriuria	5	820	Relative Risk (Random) 95% CI	0.25 [0.14, 0.48]
02 Development of pyelonephritis	11	1955	Relative Risk (Random) 95% CI	0.23 [0.13, 0.41]
03 Birthweight < 2500 g	7	1502	Relative Risk (Fixed) 95% CI	0.66 [0.49, 0.89]
04 Preterm delivery < 38 weeks	3	412	Odds Ratio (Random) 95% CI	0.37 [0.10, 1.36]
05 Bacteriuria (long term)	3	417	Relative Risk (Fixed) 95% CI	0.89 [0.58, 1.38]

Comparison 02. Single dose versus no treatment for asymptomatic bacteriuria

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Development of pyelonephritis	1	173	Relative Risk (Random) 95% CI	0.44 [0.21, 0.92]
02 Birthweight < 2500 g	1	413	Relative Risk (Random) 95% CI	0.65 [0.36, 1.18]

Comparison 03. Short course (3-7 days) versus no treatment for asymptomatic bacteriuria

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Persistent bacteriuria	1	69	Relative Risk (Random) 95% CI	0.30 [0.17, 0.54]
02 Development of pyelonephritis	4	552	Relative Risk (Random) 95% CI	0.42 [0.13, 1.35]
03 Birthweight < 2500 g	1	69	Relative Risk (Random) 95% CI	0.14 [0.03, 0.60]

Comparison 04. Intermediate course (3-6 weeks) versus no treatment for asymptomatic bacteriuria

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Persistent bacteriuria	2	433	Relative Risk (Random) 95% CI	0.11 [0.04, 0.28]
02 Development of pyelonephritis	2	433	Relative Risk (Random) 95% CI	0.17 [0.08, 0.37]
03 Birthweight < 2500 g	1	278	Relative Risk (Random) 95% CI	1.09 [0.55, 2.14]

Comparison 05. Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Persistent bacteriuria	2	167	Relative Risk (Random) 95% CI	0.35 [0.19, 0.62]
02 Development of pyelonephritis	5	895	Relative Risk (Random) 95% CI	0.16 [0.04, 0.57]
03 Birthweight < 2500 g	5	862	Relative Risk (Random) 95% CI	0.56 [0.33, 0.96]
04 Preterm delivery < 38 weeks	1	173	Relative Risk (Random) 95% CI	0.36 [0.14, 0.95]
05 Bacteriuria (long term)	2	348	Relative Risk (Random) 95% CI	0.98 [0.58, 1.65]

Comparison 06. Antibiotic versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Persistent bacteriuria	4	600	Relative Risk (Random) 95% CI	0.21 [0.10, 0.42]
02 Development of pyelonephritis	7	1266	Relative Risk (Random) 95% CI	0.17 [0.09, 0.31]
03 Birthweight < 2500 g	4	689	Relative Risk (Random) 95% CI	0.64 [0.35, 1.16]

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Bacterial Agents [*therapeutic use]; Bacteriuria [complications; *drug therapy]; Confidence Intervals; Odds Ratio; Pregnancy Complications, Infectious [*drug therapy]; Pyelonephritis [etiology]; Randomized Controlled Trials

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title Antibiotics for asymptomatic bacteriuria in pregnancy

Authors Smaill F, Vazquez JC

Contribution of author(s) Fiona Smaill had the major responsibility for the preparation of this review. Dr Vazquez reviewed drafts of the review and provided suggestions for revisions.

Issue protocol first published 1997/4

Review first published	1997/4
Date of most recent amendment	21 February 2007
Date of most recent SUBSTANTIVE amendment	04 January 2007
What's New	January 2007 This review has been extensively rewritten. Low birthweight has been separated from preterm delivery as outcomes; subgroup and sensitivity analyses are descibed and heterogeneity of studies discussed. We updated the search and identified two new studies. One additional study (Elder 1966) has been included and another excluded (Mohammad 2002). We have moved the LeBlanc 1964 study to the excluded studies because this study did not meet the inclusion criteria. The conclusions remain unchanged.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	31 January 2007
Date authors' conclusions section amended	Information not supplied by author
Contact address	Dr Fiona Smaill Professor Department of Pathology and Molecular Medicine, Faculty of Health Sciences McMaster University Room 2N16 1200 Main Street West Hamilton Ontario L8N 3Z5 CANADA E-mail: smaill@mcmaster.ca Tel: +1 905 5212100 Fax: +1 905 5215099
DOI	10.1002/14651858.CD000490.pub2
Cochrane Library number	CD000490
Editorial group	Cochrane Pregnancy and Childbirth Group
Editorial group code	HM-PREG

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Antibiotic versus no treatment for asymptomatic bacteriuria, Outcome 01 Persistent bacteriuria

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 01 Antibiotic versus no treatment for asymptomatic bacteriuria

Outcome: 01 Persistent bacteriuria

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Elder 1966	13/52	48/50		21.5	0.26 [0.16, 0.42]
Elder 1971	14/133	98/148		21.1	0.16 [0.10, 0.26]
Foley 1987	27/100	62/120		22.6	0.52 [0.36, 0.75]
Gold 1966	12/35	22/30		21.1	0.47 [0.28, 0.78]
Pathak 1969	3/76	49/76		13.8	0.06 [0.02, 0.19]
Total (95% CI)	396	424		100.0	0.25 [0.14, 0.48]

Total events: 69 (Treatment), 279 (Control)

Test for heterogeneity chi-square=28.82 df=4 p=<0.0001 I^2 =86.1%

Test for overall effect z=4.26 p=0.00002

Analysis 01.02. Comparison 01 Antibiotic versus no treatment for asymptomatic bacteriuria, Outcome 02 Development of pyelonephritis

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 01 Antibiotic versus no treatment for asymptomatic bacteriuria

Outcome: 02 Development of pyelonephritis

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Brumfitt 1975	9/87	20/86		13.0	0.44 [0.21, 0.92]
Elder 1971	4/133	27/148		10.8	0.16 [0.06, 0.46]
Foley 1987	3/100	3/120		7.4	1.20 [0.25, 5.82]
Furness 1975	23/139	17/67		14.2	0.65 [0.37, 1.14]
Gold 1966	0/35	2/30		3.0	0.17 [0.01, 3.45]
Kass 1960	1/106	26/108		5.6	0.04 [0.01, 0.28]
Kincaid-Smith 1965	2/61	20/55		8.3	0.09 [0.02, 0.37]
Little 1966	4/124	35/141		10.9	0.13 [0.05, 0.36]
Mulla 1960	1/50	12/50		5.5	0.08 [0.01, 0.62]
Pathak 1969	3/76	17/76		9.7	0.18 [0.05, 0.58]
Williams 1969	5/85	18/78		11.4	0.25 [0.10, 0.65]

(*Continued . . .*)

(. . . *Continued*)

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Total (95% CI)	996	959		100.0	0.23 [0.13, 0.41]
Total events: 55 (Treatment), 197 (Control)					
Test for heterogeneity chi-square=27.86 df=10 p=0.002 I^2 =64.1%					
Test for overall effect z=4.97 p<0.00001					

Analysis 01.03. Comparison 01 Antibiotic versus no treatment for asymptomatic bacteriuria, Outcome 03 Birthweight < 2500 g

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 01 Antibiotic versus no treatment for asymptomatic bacteriuria

Outcome: 03 Birthweight < 2500 g

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Brumfitt 1975	18/235	21/178		24.5	0.65 [0.36, 1.18]
Elder 1971	15/133	15/145		14.7	1.09 [0.55, 2.14]
Gold 1966	2/35	0/30		0.6	4.31 [0.21, 86.32]
Kass 1960	7/93	21/98		21.0	0.35 [0.16, 0.79]
Kincaid-Smith 1965	9/61	12/56		12.9	0.69 [0.31, 1.51]
Little 1966	10/124	13/141		12.5	0.87 [0.40, 1.92]
Wren 1969	4/83	14/90		13.8	0.31 [0.11, 0.90]
Total (95% CI)	764	738		100.0	0.66 [0.49, 0.89]
Total events: 65 (Treatment), 96 (Control)					
Test for heterogeneity chi-square=8.39 df=6 p=0.21 I^2 =28.5%					
Test for overall effect z=2.75 p=0.006					

Analysis 01.04. Comparison 01 Antibiotic versus no treatment for asymptomatic bacteriuria, Outcome 04 Preterm delivery < 38 weeks

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 01 Antibiotic versus no treatment for asymptomatic bacteriuria

Outcome: 04 Preterm delivery < 38 weeks

Study	Treatment n/N	Control n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
Furness 1975	24/118	10/52		38.2	1.07 [0.47, 2.44]
Thomsen 1987	2/37	12/32		27.0	0.10 [0.02, 0.47]
Wren 1969	5/83	15/90		34.8	0.32 [0.11, 0.93]
Total (95% CI)	238	174		100.0	0.37 [0.10, 1.36]
Total events: 31 (Treatment), 37 (Control)					
Test for heterogeneity chi-square=8.21 df=2 p=0.02 I^2 =75.6%					
Test for overall effect z=1.50 p=0.1					

Analysis 01.05. Comparison 01 Antibiotic versus no treatment for asymptomatic bacteriuria, Outcome 05 Bacteriuria (long term)

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 01 Antibiotic versus no treatment for asymptomatic bacteriuria

Outcome: 05 Bacteriuria (long term)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kass 1960	18/103	18/100		51.7	0.97 [0.54, 1.76]
Kincaid-Smith 1965	6/72	6/73		16.9	1.01 [0.34, 3.00]
Pathak 1969	6/24	16/45		31.5	0.70 [0.32, 1.56]
Total (95% CI)	199	218		100.0	0.89 [0.58, 1.38]
Total events: 30 (Treatment), 40 (Control)					
Test for heterogeneity chi-square=0.48 df=2 p=0.79 I^2 =0.0%					
Test for overall effect z=0.51 p=0.6					

Analysis 02.01. Comparison 02 Single dose versus no treatment for asymptomatic bacteriuria, Outcome 01 Development of pyelonephritis

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 02 Single dose versus no treatment for asymptomatic bacteriuria

Outcome: 01 Development of pyelonephritis

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Brumfitt 1975	9/87	20/86		100.0	0.44 [0.21, 0.92]
Total (95% CI)	87	86		100.0	0.44 [0.21, 0.92]
Total events: 9 (Treatment), 20 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.18 p=0.03					

Analysis 02.02. Comparison 02 Single dose versus no treatment for asymptomatic bacteriuria, Outcome 02 Birthweight < 2500 g

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 02 Single dose versus no treatment for asymptomatic bacteriuria

Outcome: 02 Birthweight < 2500 g

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Brumfitt 1975	18/235	21/178		100.0	0.65 [0.36, 1.18]
Total (95% CI)	235	178		100.0	0.65 [0.36, 1.18]
Total events: 18 (Treatment), 21 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.41 p=0.2					

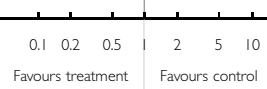
Analysis 03.01. Comparison 03 Short course (3-7 days) versus no treatment for asymptomatic bacteriuria, Outcome 01 Persistent bacteriuria

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 03 Short course (3-7 days) versus no treatment for asymptomatic bacteriuria

Outcome: 01 Persistent bacteriuria

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Thomsen 1987	9/37	26/32		100.0	0.30 [0.17, 0.54]
Total (95% CI)	37	32		100.0	0.30 [0.17, 0.54]
Total events: 9 (Treatment), 26 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.99 p=0.00007					



Analysis 03.02. Comparison 03 Short course (3-7 days) versus no treatment for asymptomatic bacteriuria, Outcome 02 Development of pyelonephritis

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 03 Short course (3-7 days) versus no treatment for asymptomatic bacteriuria

Outcome: 02 Development of pyelonephritis

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Foley 1987	3/100	3/120		27.5	1.20 [0.25, 5.82]
Mulla 1960	1/50	9/50		20.7	0.11 [0.01, 0.84]
Thomsen 1987	1/37	0/32		10.9	2.61 [0.11, 61.80]
Williams 1969	5/85	18/78		40.9	0.25 [0.10, 0.65]
Total (95% CI)	272	280		100.0	0.42 [0.13, 1.35]
Total events: 10 (Treatment), 30 (Control)					
Test for heterogeneity chi-square=5.58 df=3 p=0.13 I^2 =46.2%					
Test for overall effect z=1.45 p=0.1					

Analysis 03.03. Comparison 03 Short course (3-7 days) versus no treatment for asymptomatic bacteriuria, Outcome 03 Birthweight < 2500 g

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 03 Short course (3-7 days) versus no treatment for asymptomatic bacteriuria

Outcome: 03 Birthweight < 2500 g

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Thomsen 1987	2/37	12/32		100.0	0.14 [0.03, 0.60]
Total (95% CI)	37	32		100.0	0.14 [0.03, 0.60]
Total events: 2 (Treatment), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.67 p=0.008					

Analysis 04.01. Comparison 04 Intermediate course (3-6 weeks) versus no treatment for asymptomatic bacteriuria, Outcome 01 Persistent bacteriuria

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 04 Intermediate course (3-6 weeks) versus no treatment for asymptomatic bacteriuria

Outcome: 01 Persistent bacteriuria

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Elder 1971	14/133	98/148		63.7	0.16 [0.10, 0.26]
Pathak 1969	3/76	49/76		36.3	0.06 [0.02, 0.19]
Total (95% CI)	209	224		100.0	0.11 [0.04, 0.28]
Total events: 17 (Treatment), 147 (Control)					
Test for heterogeneity chi-square=2.41 df=1 p=0.12 I^2 =58.5%					
Test for overall effect z=4.66 p<0.00001					

Analysis 04.02. Comparison 04 Intermediate course (3-6 weeks) versus no treatment for asymptomatic bacteriuria, Outcome 02 Development of pyelonephritis

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 04 Intermediate course (3-6 weeks) versus no treatment for asymptomatic bacteriuria

Outcome: 02 Development of pyelonephritis

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Elder 1971	4/133	27/148		57.3	0.16 [0.06, 0.46]
Pathak 1969	3/76	17/76		42.7	0.18 [0.05, 0.58]
Total (95% CI)	209	224		100.0	0.17 [0.08, 0.37]

Total events: 7 (Treatment), 44 (Control)

Test for heterogeneity chi-square=0.01 df=1 p=0.93 I^2 =0.0%

Test for overall effect z=4.49 p<0.00001

Analysis 04.03. Comparison 04 Intermediate course (3-6 weeks) versus no treatment for asymptomatic bacteriuria, Outcome 03 Birthweight < 2500 g

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 04 Intermediate course (3-6 weeks) versus no treatment for asymptomatic bacteriuria

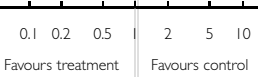
Outcome: 03 Birthweight < 2500 g

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Elder 1971	15/133	15/145		100.0	1.09 [0.55, 2.14]
Total (95% CI)	133	145		100.0	1.09 [0.55, 2.14]

Total events: 15 (Treatment), 15 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=0.25 p=0.8



Analysis 05.01. Comparison 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria, Outcome 01 Persistent bacteriuria

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria

Outcome: 01 Persistent bacteriuria

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Elder 1966	13/52	48/50		51.2	0.26 [0.16, 0.42]
Gold 1966	12/35	22/30		48.8	0.47 [0.28, 0.78]
Total (95% CI)	87	80		100.0	0.35 [0.19, 0.62]
Total events: 25 (Treatment), 70 (Control)					
Test for heterogeneity chi-square=2.79 df=1 p=0.09 I^2 =64.1%					
Test for overall effect z=3.59 p=0.0003					

Analysis 05.02. Comparison 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria, Outcome 02 Development of pyelonephritis

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria

Outcome: 02 Development of pyelonephritis

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Furness 1975	23/139	17/67		26.8	0.65 [0.37, 1.14]
Gold 1966	0/35	2/30		11.1	0.17 [0.01, 3.45]
Kass 1960	1/106	26/108		16.9	0.04 [0.01, 0.28]
Kincaid-Smith 1965	2/72	21/73		21.1	0.10 [0.02, 0.40]
Little 1966	4/124	35/141		24.1	0.13 [0.05, 0.36]
Total (95% CI)	476	419		100.0	0.16 [0.04, 0.57]
Total events: 30 (Treatment), 101 (Control)					
Test for heterogeneity chi-square=20.31 df=4 p=0.0004 I^2 =80.3%					
Test for overall effect z=2.81 p=0.005					

Analysis 05.03. Comparison 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria, Outcome 03 Birthweight < 2500 g

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria

Outcome: 03 Birthweight < 2500 g

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Gold 1966	2/35	0/30		3.0	4.31 [0.21, 86.32]
Kass 1960	7/106	21/108		25.7	0.34 [0.15, 0.77]
Kincaid-Smith 1965	9/72	13/73		26.7	0.70 [0.32, 1.54]
Little 1966	10/124	13/141		26.6	0.87 [0.40, 1.92]
Wren 1969	4/83	14/90		17.9	0.31 [0.11, 0.90]
Total (95% CI)	420	442		100.0	0.56 [0.33, 0.96]

Total events: 32 (Treatment), 61 (Control)

Test for heterogeneity chi-square=5.96 df=4 p=0.20 I^2 =32.9%

Test for overall effect z=2.10 p=0.04

Analysis 05.04. Comparison 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria, Outcome 04 Preterm delivery < 38 weeks

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria

Outcome: 04 Preterm delivery < 38 weeks

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Wren 1969	5/83	15/90		100.0	0.36 [0.14, 0.95]
Total (95% CI)	83	90		100.0	0.36 [0.14, 0.95]

Total events: 5 (Treatment), 15 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=2.06 p=0.04

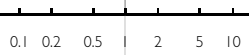
Analysis 05.05. Comparison 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria, Outcome 05 Bacteriuria (long term)

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 05 Continuous antibiotic therapy versus no treatment for asymptomatic bacteriuria

Outcome: 05 Bacteriuria (long term)

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Kass 1960	18/103	18/100		77.0	0.97 [0.54, 1.76]
Kincaid-Smith 1965	6/72	6/73		23.0	1.01 [0.34, 3.00]
Total (95% CI)	175	173		100.0	0.98 [0.58, 1.65]
Total events: 24 (Treatment), 24 (Control)					
Test for heterogeneity chi-square=0.00 df=1 p=0.95 I^2 =0.0%					
Test for overall effect z=0.07 p=0.9					



Analysis 06.01. Comparison 06 Antibiotic versus placebo, Outcome 01 Persistent bacteriuria

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 06 Antibiotic versus placebo

Outcome: 01 Persistent bacteriuria

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Elder 1966	13/52	48/50		27.7	0.26 [0.16, 0.42]
Elder 1971	14/133	98/148		27.2	0.16 [0.10, 0.26]
Gold 1966	12/35	22/30		27.3	0.47 [0.28, 0.78]
Pathak 1969	3/76	49/76		17.8	0.06 [0.02, 0.19]
Total (95% CI)	296	304		100.0	0.21 [0.10, 0.42]
Total events: 42 (Treatment), 217 (Control)					
Test for heterogeneity chi-square=17.71 df=3 p=0.0005 I^2 =83.1%					
Test for overall effect z=4.33 p=0.00001					

Analysis 06.02. Comparison 06 Antibiotic versus placebo, Outcome 02 Development of pyelonephritis

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 06 Antibiotic versus placebo

Outcome: 02 Development of pyelonephritis

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Brumfitt 1975	9/87	20/86		24.4	0.44 [0.21, 0.92]
Elder 1971	4/133	27/148		18.1	0.16 [0.06, 0.46]
Gold 1966	0/35	2/30		3.7	0.17 [0.01, 3.45]
Kass 1960	1/106	26/108		7.5	0.04 [0.01, 0.28]
Kincaid-Smith 1965	2/61	20/55		12.4	0.09 [0.02, 0.37]
Little 1966	4/124	35/141		18.5	0.13 [0.05, 0.36]
Pathak 1969	3/76	17/76		15.4	0.18 [0.05, 0.58]
Total (95% CI)	622	644		100.0	0.17 [0.09, 0.31]

Total events: 23 (Treatment), 147 (Control)

Test for heterogeneity chi-square=10.13 df=6 p=0.12 I^2 =40.8%

Test for overall effect z=5.75 p<0.00001

Analysis 06.03. Comparison 06 Antibiotic versus placebo, Outcome 03 Birthweight < 2500 g

Review: Antibiotics for asymptomatic bacteriuria in pregnancy

Comparison: 06 Antibiotic versus placebo

Outcome: 03 Birthweight < 2500 g

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Gold 1966	2/35	0/30		3.7	4.31 [0.21, 86.32]
Kass 1960	7/106	21/108		31.3	0.34 [0.15, 0.77]
Kincaid-Smith 1965	9/72	13/73		32.6	0.70 [0.32, 1.54]
Little 1966	10/124	13/141		32.4	0.87 [0.40, 1.92]
Total (95% CI)	337	352		100.0	0.64 [0.35, 1.16]

Total events: 28 (Treatment), 47 (Control)

Test for heterogeneity chi-square=4.54 df=3 p=0.21 I^2 =33.9%

Test for overall effect z=1.46 p=0.1