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Asymptomatic Bacteriuria in Pregnancy: Systematic Reviews of Screening and Treatment Effectiveness and Patient Preferences

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ABSTRACT (word count=300)

Objective: To systematically review screening and treatment effectiveness, and patient preferences, to inform recommendations by the Canadian Task Force on Preventive Health Care on screening for asymptomatic bacteriuria in pregnancy.

Design: We searched multiple databases (inception – September 2017) and grey literature sources for studies on screening effectiveness and patient preferences. For treatment with antibiotics, we searched three databases for systematic reviews and obtained search results of the Cochrane Pregnancy and Childbirth Group's Trials Register to update a Cochrane review. Study selection, risk of bias assessment, and evaluation of the quality for each outcome using Grading Recommendations Assessment and Development Evidence (GRADE) was completed independently by two reviewers with consensus. Meta-analysis was conducted when appropriate as were analyses based on planned sub-group variables.

Outcomes: For screening and treatment effectiveness: maternal and perinatal mortality, maternal and neonatal sepsis, pyelonephritis, spontaneous abortion, preterm delivery, low birth weight, and serious adverse events. Valuation of outcomes for patient preferences.

Results: Four studies compared outcomes before and after the introduction of a screening program or between different screening programs. All evidence on screening effectiveness was considered very low quality. Women have conflicting opinions about antibiotic use during pregnancy. Fifteen trials compared antibiotic treatment with no treatment or placebo in women with confirmed bacteriuria. Low quality evidence found that treatment lowered rates of pyelonephritis (12 trials, RR 0.24; 95% CI 0.13, 0.42; ARR 17.6%; NNT 6, 95% CI 5, 7) and low birth weight (7 trials, RR 0.63; 95% CI 0.45, 0.90; ARR 4.4%; NNT 23, 95% CI 15, 85).

Conclusions: Antibiotic treatment for women having significant bacteriuria likely reduces the incidence of pyelonephritis and low birth weight, but we are uncertain about the magnitude of the effect and about the extent to which we can apply these results to asymptomatic populations and the screening scenario.

Protocol registration number: CRD42016045263

Keywords: asymptomatic infections, bacteriuria, pregnancy, mass screening, anti-bacterial agents, systematic review, meta-analysis

Strengths and limitations of this study

- Comprehensive search, risk of bias and quality assessments were conducted for all studies.
- Methodological limitations were common across many studies.
- Applicability of results to routine, prenatal care for women is limited by scant and inconsistent reporting of population and screening characteristics among included studies.
- The quality of the body of evidence was low to very low for reported outcomes.
- No direct evidence was available on how women weigh benefits and harms of screening.

BACKGROUND

Asymptomatic bacteriuria (ASB) signifies a significant quantitative count of bacteria in the urine without symptoms of a lower (acute cystitis) or upper urinary tract/kidney (acute pyelonephritis) infection.[1, 2] Prevalence of ASB in premenopausal, ambulatory women is 2-10%,[1] but due to anatomical and physiological changes (e.g., displaced bladder) to the urinary tract in pregnancy there are theoretical reasons to suspect higher rates of ASB during pregnancy and consequently a greater chance of progression to symptomatic UTI and other pregnancy complications (e.g., pyelonephritis, preterm delivery).[1, 3] Numerous risk factors for ASB in pregnancy have been identified (e.g., low socioeconomic status, higher parity, a history of recurrent UTI, diabetes, and anatomical abnormalities of the urinary tract[1, 2, 4]).

Controversy exists over the mechanism linking ASB, pyelonephritis, and adverse perinatal outcomes (i.e., whether ASB affects pregnancy and neonatal outcomes solely through pyelonephritis or also other mechanisms such as prostaglandin activation),[2, 4] and therefore also about whether treatment of ASB with antibiotics will reduce the risk of such adverse outcomes. Additionally, some sources have outlined concerns with incidence and reporting on adverse effects of antibiotic treatment for ASB, UTIs, or antibiotic use in general during pregnancy.[2, 4, 5]

Reports of reduced incidence of pyelonephritis in pregnant women after introduction of routine screening (e.g., 0.3 to 0.57% vs. 1-2%[6]) suggest that these programs have been beneficial. Practices of urine testing may be used to detect conditions in pregnancy other than ASB. There appears to be diversity in screening for ASB with variations in urine testing methods, timing, and collection, as well as treatment protocols (duration, test-for-cure, threshold of bacteria for treatment).

Our reviews examined the following questions:

1) What are the benefits and harms of screening compared with no screening, or different screening methods or algorithms, for ASB in pregnancy?
2) How do women weigh the benefits and harms of screening and treatment of ASB in pregnancy, and how does this outcome valuation inform their decisions to undergo screening?
3) What are the benefits and harms of antibiotic treatment compared with placebo or no treatment for ASB in pregnancy?

METHODS

This series of systematic reviews (SRs) follow methods of the Canadian Task Force on Preventive Health Care (CTFPHC); the protocol was registered with PROSPERO (CRD42016045623) and is available online (Supplement 1).

Search strategy

Preliminary searches for SRs and primary studies in PubMed found one SR on treatment effectiveness, but no relevant studies on screening effectiveness. Comprehensive searches were developed and conducted by our research librarian in bibliographic databases for each question (details in Supplement 2). For screening effectiveness, the following databases were searched (inception to September 2017):

MEDLINE (1946-) via Ovid; Embase (1974-) via Ovid; Cochrane Library; CINAHL (1937-present) via EBSCOhost; and PubMed via NCBI Entrez. For women's outcome valuation, we also searched PsycINFO. Limits were applied for language (English and French) but not study design or publication date. For treatment effectiveness, SRs were searched on October 14, 2016 in PubMed (1946-) via NCBI Entrez, the Cochrane Database of Systematic Reviews (inception-) and the Database of Abstracts of Reviews of Effects (DARE) (inception-2013) via Wiley Cochrane Library. Authors of the SR on treatment[4] provided results of their recent search update (Cochrane Pregnancy and Childbirth Group's Trials Register) in October 2017. Additional studies were identified through contact with experts and grey literature.[7]

Study selection and eligibility criteria

Two reviewers independently screened titles and abstracts, followed by full-text review, using a standard eligibility criteria form and DistillerSR software (Evidence Partners, Ottawa, Canada).[8] The flow of screening and decisions were recorded in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Chart.

The criteria for inclusion (populations, interventions, comparators, outcomes, timing and setting [PICOTS]) for screening and treatment effectiveness, and women's outcome valuation are summarized in Supplement 3.

For treatment effectiveness, existing SRs were eligible based on a) searching more than one database, b) reporting selection criteria, and c) using PICOTS criteria that closely match the current review. The included studies were assessed for eligibility to meet our inclusion criteria, incorporating existing data and extracting additional data as necessary, conducting quality assessments, and performing new meta-analyses and GRADE quality assessments.

Data extraction and risk of bias assessment

One reviewer independently extracted data and another verified data from each included study on study details and relevant PICOTS, including information for patient and intervention subgroups. Authors of included studies were contacted for clarification of study details and outcome data with follow-up as necessary. Intention-to-treat results were recorded whenever possible. For all outcomes, including harms, counts or proportions, and sample size by study arm, were recorded.

Two reviewers independently assessed the risk of bias (ROB) of each included study with disagreements resolved via consensus or third-reviewer consultation. For observational studies on screening effectiveness, the Newcastle-Ottawa Quality Assessment Scale was used; a separate assessment for reporting bias was included due to suspected selective outcome reporting. For cross-sectional studies on women's outcome valuation, the tool developed by the Center for Evidence-based Management[32] was used. For treatment effectiveness, all controlled trials were appraised using the Cochrane Risk of Bias tool.[9]

Data synthesis and analysis

Relative risks (RR) were reported using the DerSimonian and Laird random effects model with Mantel-Haenszel method and corresponding 95% confidence intervals (CI). Sensitivity (for ROB and study design) and subgroup (for pre-defined population and screening characteristic variables) analyses were conducted when possible and appropriate. We report values for statistical heterogeneity (I^2) but did not rely on this for decisions about meta-analysis or subgroup analysis. A minimum of two of the following criteria determined credibility of subgroup investigations: a) visual inspection of forest plot showing a meaningful difference between effect estimates (e.g., clinical decision making on the intervention would differ for each subgroup), b) a reduction in the heterogeneity (I^2) for each subgroup from the original meta-analysis, and c) a statistically significant Chi^2 test for subgroup effects.

Analyses were performed using Review Manager Version 5.3. For outcomes that demonstrated significant effects, absolute risk reduction (ARR) and number needed to screen (NNS) or number needed to treat (NNT), were calculated. The values for NNS or NNT were calculated using absolute numbers from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tables estimated using the control group event rate and RR with the 95% CI obtained from the meta-analysis.[10]

Small-study bias (for meta-analyses with eight or more studies) was assessed using the funnel plot and Egger's test.[11]

Quality assessment

Two reviewers independently assessed the quality of the body of evidence for each outcome using GRADE methodology[12, 13] with disagreements resolved through discussion or consultation with a third reviewer. For evidence on benefits and harms of screening and treatment, quality was assigned initially as high for evidence from RCTs and low for evidence from observational studies. Thereafter, quality was potentially downgraded based on five core domains: study limitations/ROB, inconsistency, indirectness, imprecision, and publication/reporting bias. We did not consider upgrading because of serious concerns with the main domains.[14] Assessments were entered into the GRADEpro software[15] and summarized in GRADE Summary of Findings (SOF) and Evidence Profiles (EP) tables.[16]

RESULTS

Study selection and characteristics

Study flow and selection is in Figure 1. Characteristics of included studies for screening and treatment effectiveness is in Table 1; detailed study information is in Supplement 4.

Screening effectiveness: Four studies (7,611 women)[17-20] were included. One study[17] was published in French. All were non-concurrent cohort studies, comparing outcomes before and after introduction of a screening program.

Women's outcome valuation: No studies were identified that examined how women weigh the benefits and harms of screening and/or treatment of ASB in pregnancy or how their valuation of benefits and harms inform their decisions to undergo screening and treatment. Six surveys and one cross-sectional

study were included: three studies provide information on drug utilization opinions,[21-23] while four studies provide information on perceptions of teratogenic risk.[24-28] One study was a multicenter screening cohort of pregnant women with an embedded RCT of antibiotic treatment for women with significant bacteriuria; cross-sectional findings from the women eligible for treatment are used for information on treatment preference.[22]

Treatment effectiveness: One SR[4] met our inclusion criteria. Contact with the information specialist of the Cochrane Pregnancy and Childbirth Group's Trials Register confirmed one study (Kazemier et al[22]) identified from their ongoing search updates (to October 2017) relevant for treatment effectiveness. Fifteen primary studies[22, 29-42] (2,869 women), mostly published in the 1960s, examined treatment effectiveness for bacteriuria. One study[30] included in the Cochrane review[4] only reported on persistent bacteriuria and therefore was excluded from analysis and the overall body of evidence relevant to our outcomes of interest.

Table 1. Summary of included studies for screening and treatment effectiveness

Study design; ROB (no. of studies)	Setting (no. of studies)	Sample (no. of participants)	Population characteristics (no. of studies)	Screening details (no. of studies)	Treatment details (no. of studies)	Follow-up details (no. of studies)	Outcomes reported (no. of studies)
Studies of screening effectiveness							
Non-concurrent cohort (4) Unclear ROB (3) Low ROB (1)	Countries: France (1) Spain (1) Turkey (1) USA (1) Clinical setting: Hospital (1) Hospital-based midwifery practice (1) Obstetrics clinic, academic (2)	Total=7,611 Screening (2,008) vs. no screening (3,651); Frequent screening (933) vs. one-time screening (1,019)	• <25wks GA (1) • <32wks GA (1) • Predominantly medically underserved and Hispanic women (1) • GDM, range 3-9% (2)	Screened at first visit: • Mean 20wks GA (1) • <32wks GA (1) • Urine culture (4) • $\geq 10^5$ CFU/mL ($\geq 10^8$ CFU/L) (2)	Treatment after sensitivity testing (3)	Follow-up culture, at least once (2)	Pyelonephritis (4) Perinatal mortality (2) Spontaneous abortion (1) Preterm delivery (3) Fetal abnormalities (1)
Studies of treatment effectiveness							
RCT (11) CCT (4) High ROB (11) Unclear ROB (3) Low ROB (1)	Australia (3) Denmark (1) Ireland (1) Jamaica (1) Netherlands (1) UK (3) USA (5) Hospital-based clinics (15)	Total=2,869 Treatment (1,357) vs. no treatment/placebo (1,262)	• First prenatal visit (9) • Second prenatal visit (1) • ≤32 wks GA (9) • ≥50% non-Caucasian ethnicity (3) • 100% Caucasian ethnicity (1) • Low education, range 10-15% (1) • All from lowest income category (1) • Previous UTI, ~40% (1) • Past history of UTI, 10-15% (2) • No urogenital anomalies (2) • No chronic renal insufficiency (1) • ~20% with renal-tract disease or abnormalities (2) • >50% with renal abnormalities (1) • Asymptomatic patients only (4)	• Clean-catch/MSU (13) • 1 urine sample (5) • ≥2 urine samples (10) • Routine urine culture (13) • Urine dipslide device (2) • $\geq 10^5$ CFU/mL in at least one sample (11) • 10^2-10^6 CFU/mL, group B streptococci (1)	Antibiotic treatment: • >1 dose (14) • Up to 1wk (5) • Up to 3wks (1) • Up to 30d (1) • Up to delivery (6) Tested for persistent bacteriuria: • during pregnancy, re-treatment as warranted (7) • after delivery only (1) • during pregnancy and after delivery (3)	Follow-up until: • delivery or postpartum (5) • 10d post-delivery (1) • 6wks post-delivery (4) • >6wks post-delivery (2)	Pyelonephritis (12) Perinatal mortality (6) Spontaneous abortion (2) Neonatal sepsis (1) Preterm delivery (4) Low birth weight (7) Fetal abnormalities (4) Hemolytic anemia (1)

CCT: controlled clinical trial; d: day(s); GA: gestational age; GDM: gestational diabetes mellitus; no: number; RCT: randomized controlled trial; ROB: risk of bias; UTI: urinary tract infection; wks: weeks

ROB and quality assessments

Overall ROB assessments for screening and treatment effectiveness are in Table 1, and reported with quality assessments below; detailed ROB assessments are in Supplement 5.

For women's outcome valuation, all seven studies addressed a focused research question and used a sample representative of this study question, their reported sampling methods could potentially introduce bias and only one of the studies[24] fully accounted for confounding factors through statistical analysis. None of the papers reported that their sample size was based on pre-study considerations while only two papers[23, 28] used survey questions that were considered valid and reliable.

Quality of evidence assessments for screening and treatment effectiveness are in Table 2; detailed GRADE SOF and EP tables and forest plots are in Supplement 6.

Screening effectiveness

Three studies[17, 18, 20] of unclear ROB (5,659 women) found a statistically significant difference for *screening compared with no screening* on the outcome of **pyelonephritis** (RR 0.28; 95% CI 0.15, 0.54; I^2=0%; ARR 1.3%; NNS 77, 95% CI 65, 121; very low quality). One study[19] (1,952 women) with low ROB comparing *screening at all prenatal visits with screening at first prenatal visit only*, found no significant difference for pyelonephritis (RR 1.09; 95% CI 0.27, 4.35; very low quality).

Two studies[17, 20] (724 women) with unclear ROB and suspected reporting bias[43] found no significant difference (RR 1.21, 95% CI 0.01, 102.93, I^2=84%; very low quality) in **perinatal mortality**.
One study of 370 women[17] with unclear ROB but suspected reporting bias found no significant difference (RR 0.96, 95% CI 0.41, 2.27; very low quality) in **spontaneous abortion** at ≤28 weeks of gestation.

Two studies[17, 20] (722 women) with unclear ROB but suspected reporting bias[43] compared *screening with no screening* and found no significant difference (RR 8.70, 95% CI 0.32, 240.07; I^2=80%; very low quality) in **preterm delivery**. The study[19] comparing *different screening algorithms* found a significant difference for preterm delivery (RR 1.57; 95% CI 1.11, 2.23; very low quality) with more preterm deliveries among the group that was screened at all prenatal visits. The study authors did not present a possible hypothesis to explain this result.

One study[20] (372 women) with unclear ROB found no significant difference (RR 1.50, 95% CI 0.25, 8.87; very low quality) in **fetal abnormalities**.

No study reported on maternal mortality, maternal sepsis, neonatal sepsis or low birthweight.

Subgroup analyses were not performed due to insufficient number of studies per category comprising *a priori* subgroups.

Women's outcome valuation

Studies demonstrated varied opinions on antibiotic use during pregnancy, with nearly half of participants from two studies (47-48%) expressing that antibiotics should not be used during pregnancy.[21, 23] Cross-sectional analysis of patients recruited for an RCT of treatment for ASB found similar results, with 61% of 255 women with ASB not wanting to be treated for an asymptomatic condition.[22] Some evidence suggested that women thought penicillin posed a teratogenic risk[24, 26] and that antibiotics were unsafe during pregnancy particularly for the fetus.[25, 27] How these attitudes may inform the women's decisions on whether to screen for ASB was not reported, nor were details on accuracy or understanding of information regarding potential risks and benefits.

Treatment effectiveness

Twelve studies[22, 29, 31-39, 41] (2,017 women) examined the effects of antibiotic treatment and found a significant difference in development of **pyelonephritis** (RR 0.24; 95% CI 0.13, 0.41; I^2=60%; ARR 17.6%; NNT 6, 95% CI 5, 7; low quality) (Figure 2). Three trials explicitly included women without symptoms at baseline (other trials may have included some symptomatic women); sensitivity analysis did not affect the results (3 trials,[22, 38, 41] RR 0.22; 95% CI 0.10, 0.49; I^2=0%). Sensitivity analysis for ROB (removing studies with overall high risk) and study design (removing CCTs) did not change the results.

Subgroup analysis for the number of urine samples—studies using one or more additional cultures to confirm ASB compared with just one culture—appeared to explain the heterogeneity among all studies combined (I^2=60%) for pyelonephritis (RR 0.19, 95% CI 0.11, 0.31; I^2=31% versus RR 0.50, 95% CI 0.19, 1.35; I^2=41%). The test for subgroup differences was not statistically significant (p=0.08), but the heterogeneity in each subgroup was reduced and visual inspection of the forest plots suggests a meaningful difference in effect. There was a statistically significant subgroup difference (Chi^2 p=0.001) when testing for persistent bacteriuria was done during pregnancy and after delivery (RR 0.11, 95% CI 0.05, 0.25; I^2=0%) compared with testing during pregnancy only (RR 0.24, 95% CI 0.13, 0.41; I^2=30%) or with testing only after delivery (RR 0.65, 95% CI 0.37, 1.14). Studies that followed women beyond six weeks after delivery (RR 0.11, 95% CI 0.05, 0.25; I^2=0%) found greater reduction in pyelonephritis than those only following women until delivery or six weeks post-delivery (RR 0.31, 95% CI 0.18, 0.54; I^2=53%; Chi^2 p=0.04).

The funnel plot (Supplement 7) appeared symmetrical; however, Egger's test was inconclusive (p=0.065). The twelve studies with small sample sizes limit the ability to detect or exclude the possibility of small-study bias.

Six studies (1,104 women) examined **perinatal mortality**; one study[22] was at low ROB, three studies[31, 35, 42] were at high ROB, and two studies[36, 37] were unclear. No significant difference was found between groups on perinatal mortality (RR 0.96, 95% CI 0.27, 3.39; I^2=56%; very low quality).

Two studies[33, 42] (379 women) with high ROB reported on **spontaneous abortion** and found no significant difference between groups (RR 0.60, 95% CI 0.11, 3.10; I^2=17%; very low quality).
Two studies[22, 40] (154 women) with low ROB reported on **neonatal sepsis** with no statistically significant difference (very low quality) between groups.

Two studies[22, 40] with low risk of bias and two studies[33, 42] with high ROB (total 533 women) showed no significant difference between groups on **preterm delivery** (RR 0.57, 95% CI 0.21, 1.56; I^2=70%; very low quality).

Seven studies (1,522 women) with two studies[22, 37] at low, three[29, 31, 35] at high and one[36] at unclear ROB examined the effect of treatment on **low birth weight** (Figure 3). There was a statistically significant difference favoring antibiotics (RR 0.63; 95% CI 0.45, 0.90; I^2=20%; ARR 4.4%; NNT 23, 95% CI 15, 85; low quality).

Four studies (821 women; 2 low ROB[22, 37], two high ROB[31, 33]) examined the effect of treatment on **fetal abnormalities**, and found no statistically significant difference between groups (RR 0.49, 95% CI 0.17, 1.43; I^2=0%; very low quality).

One study[31] (265 women) with high ROB (very low quality) reported no cases of **hemolytic anemia** in infants.

No study reported on maternal mortality, maternal sepsis, or maternal harms.

Table 2. Summary of findings for effects of screening and treatment on maternal and neonatal benefits and harms

Screening vs. no screening					
Outcomes	**No. of participants (no. of studies)**	**Absolute difference per 1,000 (95% CI)**		**Risk ratio (95% CI)**	**Quality of evidence (GRADE)**
		Risk with no screening	**Risk with screening**		
Pyelonephritis	5,659 (3)	18	NS*	0.28 (0.15 to 0.54)	Very Low
Perinatal mortality	724 (2)	19	NS*	1.21 (0.01 to 102.93)	Very Low
Spontaneous abortion	370 (1)	55	NS*	0.96 (0.41 to 2.27)	Very Low
Preterm delivery	722 (2)	13	NS*	8.70 (0.32 to 240.07)	Very Low
Neonatal serious harm: fetal abnormalities	372 (1)	11	NS*	1.50 (0.25 to 8.87)	Very Low
Frequent screening vs. one-time screening					
Outcomes	**No. of participants (no. of studies)**	**Absolute difference per 1,000 (95% CI)**		**Risk ratio (95% CI)**	**Quality of evidence (GRADE)**
		Risk with one-time screening	**Risk with frequent screening**		
Pyelonephritis	1,952 (1)	4	NS*	1.09 (0.27 to 4.35)	Very Low
Perinatal mortality	1,952 (1)	49	NS*	1.57 (1.11 to 2.23)	Very Low
Treatment vs. no treatment/placebo					
Outcomes	**No. of participants (no. of studies)**	**Absolute difference per 1,000 (95% CI)**		**Risk ratio (95% CI)**	**Quality of evidence (GRADE)**
		Risk with no treatment	**Risk with treatment**		
Pyelonephritis	2,017 (12)	232	176 fewer (from 137 fewer to 202 fewer)	0.24 (0.13 to 0.41)	Low
Perinatal mortality	1,104 (6)	40	NS*	0.96 (0.27 to 3.39)	Very Low
Spontaneous abortion	379 (2)	33	NS*	0.60 (0.11 to 3.10)	Very Low
Neonatal sepsis	154 (2)	22	NS*	0.22 (0.01 to 4.54)	Very Low
Preterm delivery	533 (4)	158	NS*	0.22 (0.21 to 1.56)	Very Low
Low birth weight	1,522 (7)	118	44 fewer (from 12 fewer to 65 more)	0.63 (0.45 to 0.90)	Low
Neonatal serious harm: fetal abnormalities	821 (4)	19	NS*	0.49 (0.17 to 1.43)	Very Low
Neonatal serious harm: hemolytic anemia	265 (1)	0	NS*	Not estimable	Very Low

CI: confidence interval; GRADE: Grading of Recommendations Assessment, Development and Evaluation; no: number; NS: not significant; vs.: versus

* Results failed to show a difference between intervention groups

CONCLUSIONS & DISCUSSION

This paper reports on three SRs to inform recommendations on screening for ASB in pregnancy. Using the GRADE approach, very low quality was found for most outcomes from studies of screening programs using urine culture, including evidence from one study comparing frequent screening with one-time screening. No direct evidence was found on how women weigh the benefits and harms of screening and/or treatment for ASB and how this valuation might affect their decisions to undergo screening. Low quality evidence for women with significant bacteriuria provides limited confidence that antibiotic treatment reduces the incidence of pyelonephritis and the number of babies born at low birth weight.

Limitations of evidence base and review

Many patient and intervention characteristics were inconsistently reported or unreported, making it difficult to infer direct associations between specific risk or intervention factors and outcomes, as well as limiting potential subgroup analyses. Outcomes were defined variably among studies.

Much of the evidence came from trials on treatment of bacteriuric women (2-10% of screening population), therefore the results fail to incorporate several effects that would be captured in studies of screening effectiveness (e.g. effects on non-screened women who develop symptoms, or on ASB-negative women; effects from non-adherence to screening protocol). Only three studies explicitly reported patients as exclusively asymptomatic pregnant women; among treated patients, the beneficial effects may be larger among symptomatic women compared with asymptomatic women. Early stopping due to low incidence of primary outcomes in one study[22] may have biased effects of treatment.

Comparison with other reviews

Similar to findings of the current review, a recent systematic review by Angelescu et al[43] that examined benefits and harms of screening for ASB in pregnancy found no trials on screening effectiveness. The review authors included four RCTs focused on treatment of ASB.[22 30 38 41] These authors limited inclusion to studies reporting exclusively on treatment in asymptomatic women. We included studies that likely included some women with symptoms, and found no meaningful difference for this variable in subgroup analysis. Angelescu et al[43] examined some intervention characteristics (e.g., treatment regimen and adjunct treatments) and outcomes (e.g., lower urinary tract infection (UTI), very low birth weight <1500g) that were not included in our review. They concluded that there was no reliable evidence on the benefits and harms of screening to support routine screening for ASB using urine culture in pregnant women.[43]

Future research

Although the anticipation of a large RR reduction for pyelonephritis appears to limit the clinical equipoise necessary to conduct RCTs on screening for ASB, such trials may be considered based on: (1) very low quality evidence from screening studies and the linked nature of treatment evidence, particularly concerns about the methodological quality and the applicability of dated trials to current practice, and (2) some evidence suggesting that the incidence of pyelonephritis in untreated ASB (e.g., 2.5% in recent screening

cohort study[22]) may be substantially lower than that reported in historical literature and most of the available treatment trials (median control group incidence of 23%), such that the absolute number of women who benefit from screening may be relatively low. Studies evaluating screening programs should aim to capture data accurately on harms and include a cost-effectiveness analysis, in clearly defined populations, using modern definitions for outcomes.

Better information is needed to determine whether there are important moderating factors for ASB screening, as we attempted to examine in comparing different screening methods/algorithms. Subgroup analyses of studies using one urine culture versus at least one additional confirmatory culture, had some credibility but were limited to reliance on between-study effects. Studies directly examining this, and other factors such as different thresholds for treatment, could provide high-quality data and be informative for how to maximize benefit. Enhanced culture protocols (e.g. expanded spectrum) for detecting the most clinically relevant uropathogens are emerging,[44, 45] and if found to consistently provide better detection of these microorganisms than standard urine culture, studies comparing screening programs differing by these methods are encouraged to determine if they also predict how well treatment reduces the risk for pyelonephritis and other pregnancy complications in asymptomatic women.

More evidence or information about how women weigh the benefits and harms of screening and treatment for ASB in pregnancy would be valuable. It may be useful to use deliberative processes or focus groups to facilitate patients' understanding of results on such benefits and harms; this may be informative to determine whether it is critical to better engage patients in shared decision-making.

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Figures

Figure 1. PRISMA flow diagram of study selection
Figure 2. Forest plot of the effect of antibiotic treatment on incidence of pyelonephritis
Figure 3. Forest plot of the effect of antibiotic treatment on incidence of babies born at low birth weight

Supplementary data

This paper is based on a full report conducted by the Edmonton Evidence Review and Synthesis Centre "Screening for Asymptomatic Bacteriuria in Pregnancy: Systematic Review & Meta-analysis", available at [CTFPHC website link when available].

Supplement 1 – Protocol
Supplement 2 – Search strategy
Supplement 3 – Eligibility criteria
Supplement 4 – Characteristics of included studies
Supplement 5 – Risk of bias assessments for included studies
Supplement 6 – GRADE Summary of Findings & Evidence Profiles tables & forest plots
Supplement 7 – Funnel plot

Contributors: LH, AW, JP, MS, MG, RF, KS and BV critically reviewed and contributed to drafts of the report. AW, JP, MS, MG, KS and BV conducted screening, quality assessments, data extraction and analysis. AW, JP, LH, MS, KS and BV contributed to interpretation of results. All of the authors approved the final version of this report.

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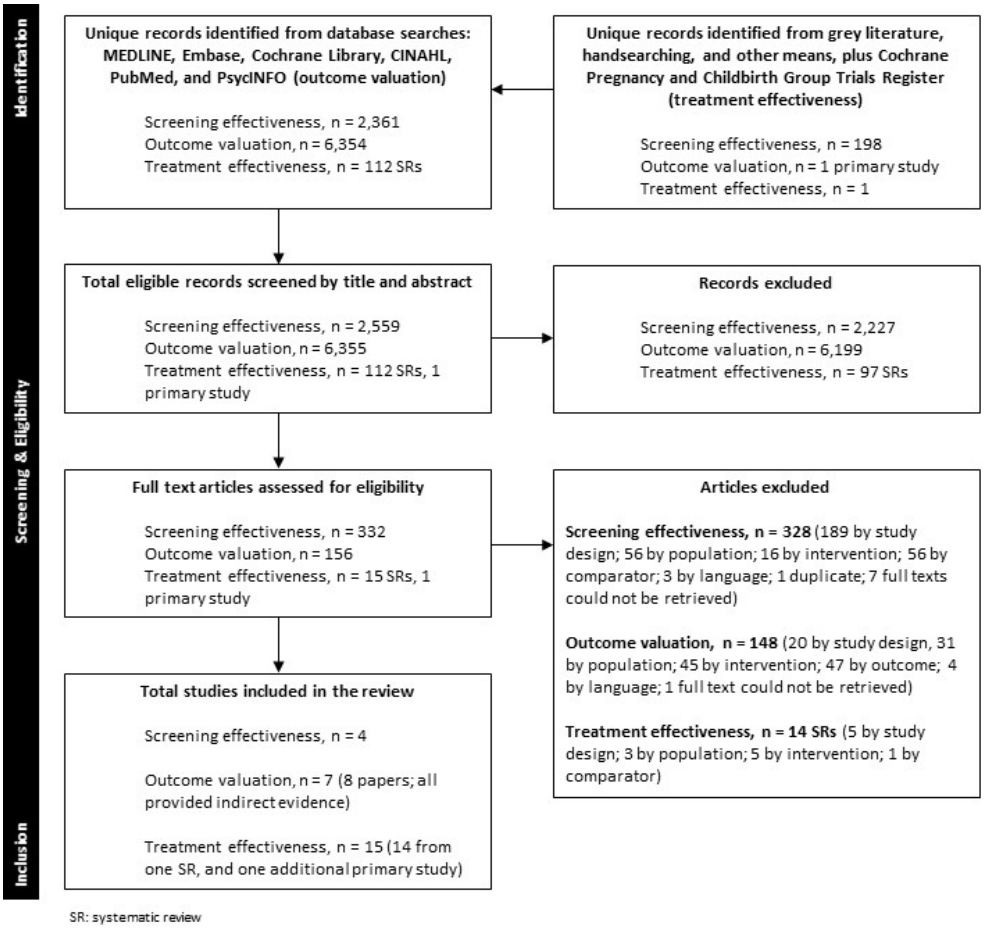

Figure 1. PRISMA flow diagram of study selection

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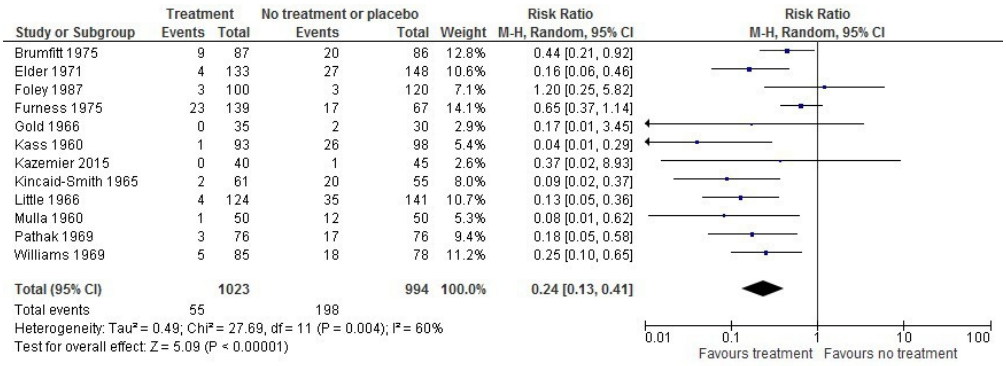

Figure 2. Forest plot of the effect of antibiotic treatment on incidence of pyelonephritis

73x27mm (300 x 300 DPI)

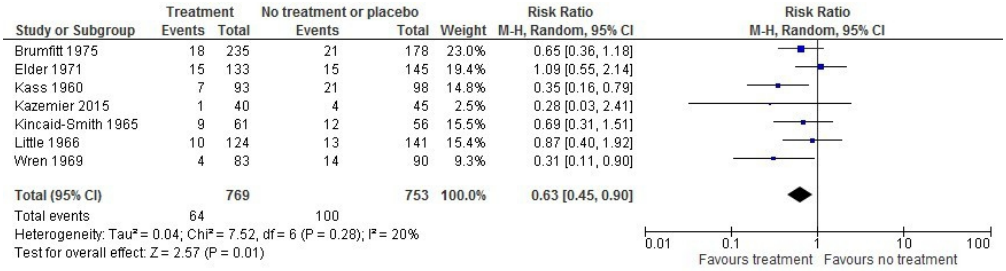

Figure 3. Forest plot of the effect of antibiotic treatment on incidence of babies born at low birth weight

73x20mm (300 x 300 DPI)

Supplement 1. Protocol: Screening for asymptomatic bacteriuria in pregnancy

December 1, 2016

ERSC Project Lead Investigator: Lisa Hartling
ERSC Project Staff: Aireen Wingert, Jennifer Pillay, Robin Featherstone (MLIS), and Ben Vandermeer (Statistician)

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Author Contributions

AW and JP drafted the protocol and RF developed the search strategy and provided text for the protocol. AW, JP, and LH contributed to discussions with the CTFPHC and PHAC on the scope for this work. LH and BV critically reviewed the protocol. All of the authors approved the final version of this protocol.

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PHAC Global Health & Guidance Division Staff: Marion Doull, Alejandra Jaramillo Garcia, Susan Courage, Nicki Sims-Jones

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Section I. Background and Purpose

Asymptomatic Bacteriuria in Pregnancy

Asymptomatic bacteriuria (ASB) - synonymous with asymptomatic urinary tract infection (UTI) - signifies a significant quantitative count of bacteria in the urine without symptoms of a lower (acute cystitis) or upper urinary tract (acute pyelonephritis) infection (1, 2). There is a 2-10% prevalence of ASB in premenopausal, ambulatory women (1), but due to anatomical and physiological changes (e.g., urinary stasis - difficulty emptying the bladder due to extended accumulation of urine) to the urinary tract in pregnancy there are theoretical reasons to suspect a greater chance of progression to symptomatic UTI and other pregnancy complications (e.g., maternal kidney infection, preterm delivery) (1, 3). Numerous risk factors for ASB in pregnancy have been identified, with low socioeconomic status, parity, a history of recurrent UTI, diabetes, and anatomical abnormalities of the urinary tract most cited (1, 2, 4).

Consequences of Untreated Bacteriuria in Pregnancy and Rationale for Review of Screening

There is a potentially greater risk in pregnant women compared to other populations for ASB developing into pyelonephritis (upper urinary tract infection) (3) with its associated inflammation of the renal parenchyma, calices and pelvis (5), although controversy exists. There is significant heterogeneity in reports of the incidence of pyelonephritis in untreated ASB during pregnancy. Some reports suggest low incidences of 1% or less after the introduction of screening and treatment for ASB and 4% or higher before the era of screening and treatment of ASB in pregnancy. Historical reports prior to 1966 indicated up to 40% of pregnant women with ASB developed pyelonephritis. These higher rates were before modern obstetrical care; however, these numbers continue to be cited in current systematic reviews (4) and guidelines (6) of ASB in pregnancy (1, 7). Furthermore, whether there is evidence to support a causal link between ASB and pyelonephritis in contemporary practice is uncertain.

There is an association between clinical signs of pyelonephritis and maternal respiratory insufficiency, septicemia, renal dysfunction and anemia, as well as evidence of a 20 to 50% higher incidence of preterm birth and low birth weight (4, 8). However, controversy exists over the direct link between ASB, pyelonephritis, and adverse perinatal outcomes (e.g., whether ASB affects pregnancy and neonatal outcomes solely through pyelonephritis or also other mechanisms) (2, 4), and also about whether treatment of ASB will reduce the risk of such adverse outcomes. A 2015 Cochrane review (4) found that antibiotic treatment for ASB in pregnancy may greatly reduce the incidence of pyelonephritis, preterm birth, and low birth weight babies. However, the authors' confidence in the findings were low due to poor quality evidence. A preliminary search identified a recent cohort study (9) with an embedded RCT, which found no statistically significant difference between ASB-positive women who were untreated or placebo-treated compared to ASB-negative women in terms of both pyelonephritis and preterm birth (6/208 [2.9%] vs 77/4035 [1.9%]; adjusted odds ratio [OR] 1.5, 95% CI 0.6–3.5).

Although the direct link between pyelonephritis and adverse perinatal outcomes may not be easily resolved (4), some main issues to examine include: 1) which, if any, screening tests and methods (e.g., collection methods, timing) are most accurate, and; 2) whether screening of all pregnant women and treatment for positive cases is effective (9). The effectiveness of screening for reducing risk of pyelonephritis and neonatal and maternal complications need to be examined in an era of modern obstetrical care.

Issues to Consider for Screening Tests

Significant bacteriuria is usually defined by the presence of at least 10^5 colony-forming units (CFU) per mL of urine of a single uropathogen, in two consecutive clean-catch specimens (4, 7). Acceptable thresholds and repetitions considered positive for bacteriuria in pregnancy may vary in practice. The quantitative urine culture is considered to be the gold standard for accurate detection of ASB. However, it is costlier, more labor intensive and more time-consuming compared with other rapid urine screening tests (urinalysis, dipstick nitrite tests) which reportedly have lower sensitivity[1] (1, 2). A preliminary search for recent literature identified a systematic review of onsite tests (point-of-care tests that are widely available in resource-limited settings) compared with urine culture that concluded specificity[2] was high overall but sensitivity was low and therefore onsite tests were not reliable in detecting pregnant women with ASB (10). There is no consistent recommendation for urine specimen collection in pregnancy (clean-catch with or without perineal cleansing) or optimal timing and frequency of screening tests or follow-up cultures (2). It is unclear whether universal screening (with subsequent treatment) for ASB confers benefits, and whether available screening tests for ASB are comparable to the current gold standard (urine culture) for identifying bacteriuric patients. The standard urine culture protocol is evolving with the testing of emerging techniques that may improve the detection of uropathogens (11, 12). However, at this time, urine culture is considered the reference standard. Resource needs for screening may be an important factor to consider. For example, an economic analysis indicated that screening with a dipstick and providing screen positive women treatment with antibiotics remained cost-beneficial for reducing pyelonephritis when prevalence of ASB is <2% or when the proportion of patients with ASB who develop pyelonephritis dropped to 10%, but the cost-benefit was not seen for culture diagnostics where the absolute clinical benefit was shown to be reduced (13).

[1]Sensitivity is a diagnostic test accuracy outcome that refers to how well a test correctly identifies individuals with a disease/condition; [2]Specificity is a diagnostic test accuracy outcome that refers to how well a test correctly identifies individuals without a disease/condition.

Issues to Consider for Harms of Screening

Patients may have preferences for avoiding harms due to screening and treatment in asymptomatic conditions (e.g., test anxiety/distress). Although the harms from screening tests may be considered minimal, harms from antibiotic treatment need to be considered when making decisions about screening practices for ASB in pregnancy. Some sources have outlined concerns with incidence and reporting on adverse effects of antibiotic treatment for ASB, UTIs, or antibiotic use in general during pregnancy (2, 4, 14). Some trials evaluating treatment versus no treatment/placebo of ASB in pregnancy have been critiqued for poorly reporting harms (4), such that making judgments on the net balance of benefits and harms may be difficult. The significance of the expected side effects from a short course of antibiotics may be small although increasingly there are concerns about the effect of antibiotics on the human microbiome and the

immune system. Antimicrobial resistance has certainly made the selection of an antibiotic for an individual woman more difficult (4). Additionally, patients may have preferences for avoiding treatment harms in asymptomatic conditions that need to be considered.

The goal of this review is to determine the effectiveness of screening for ASB among pregnant women. This evidence synthesis will inform recommendations on screening for ASB made by the Canadian Task Force for Preventive Healthcare (CTFPHC). As part of the guideline development process, the CTFPHC will also engage organizational stakeholders and peer-reviewers to gather information on key implementation considerations, such as strategies to help address potential health inequities and any concerns about the acceptability and feasibility of the guideline.

Section II. Recommendations in Other Guidelines and Current Practice

Canadian Organizations

The Society of Obstetricians and Gynecologists of Canada (SOGC), concerned over maternal and perinatal risks associated with ASB, recommends to treat single-strain colony counts of 10^5 CFU/mL (or 10^8 CFU/L) or greater with appropriate antibiotics during pregnancy to prevent adverse outcomes such as pyelonephritis and preterm birth (15). They support a single quantitative culture in any trimester as sufficient and recommend re-treatment with sensitivities for women with recurrent bacteriuria although they do not make recommendations for timing or frequency of re-testing. Similar recommendations apply when group B streptococcal (GBS) bacteria is detected in the urine during screening in pregnancy; separate recommendations (not relevant for this review) are made for screening and treating GBS (at any colony counts) at time of labour or rupture of membranes for prevention of early-onset neonatal GBS disease.

Guidelines from International Organizations

The U.S. Preventive Services Task Force 2008 guideline (16) on screening of ASB in adults recommends all pregnant women be screened at 12 to 16 weeks' gestation (or first prenatal visit) for ASB using a urine culture, and that treatment with antibiotics significantly reduces the incidence of symptomatic maternal urinary tract infections. The evidence informing this reaffirmation of the original recommendation from 2004 is mainly drawn from a Cochrane review of treatment effectiveness (17). The American Academy of Family Physicians (AAFP) (18) endorses the recommendations of the USPSTF. The Infectious Diseases Society of America (6) recommends screening for bacteriuria by urine culture for pregnant women in early pregnancy, and treatment if results are positive, with periodic re-testing for recurrent bacteriuria after therapy. The American Academy of Pediatrics (AAP), jointly with the American College of Obstetricians and Gynecologists (ACOG) recommend to treat ASB and then to test for cure (19).

The UK's National Institute for Health and Care Excellence (NICE) states that women should be offered routine screening for ASB by midstream urine culture early in pregnancy to reduce the risk of developing pyelonephritis (20).

The Scottish Intercollegiate Guidelines Network (SIGN) recommends that pregnant women be tested for ASB by urine culture at the first antenatal visit and culture-positive patients be treated with an antibiotic (21).

Current Practice

Several major healthcare organizations in North America (USPSTF, IDSA, ACOG, AAP, AAFP) advocate screening of pregnant women, and nearly all recommend treating patients who have been confirmed with ASB using antibiotics. In Canada, the current usual practice is to obtain a urine sample at each prenatal visit, where testing may typically be done by culture early in pregnancy and then followed with subsequent testing if indicated. It is clear there is diversity in which of these samples are collected for the presence of significant bacteriuria, how the sample is collected, how presence of bacteriuria is determined, and when sample(s) for ASB is/are collected in pregnancy. It is unclear whether and to what degree practices use screening methods incorporating tests other than urine culture.

Section III. Review Approach and Scope

This review will be completed by the Evidence Review and Synthesis Centre (ERSC) at the University of Alberta. The review will be developed, conducted, and prepared according to the CTFPHC methods (http://canadiantaskforce.ca/methods/methods-manual/). A working group of CTFPHC members was formed for development of the topic, refinement of the key questions and scope, and rating of patient-important outcomes considered most important for creating a recommendation. The CTFPHC will not be involved in the conduct of the review including selection of studies and data analysis, but will comment on the draft report and provide input on the interpretations of findings. The Global Health and Guidelines Division science team at the Public Health Agency of Canada provided assistance and input on CTFPHC methodological considerations during the topic refinement and development of the protocol. Perspectives of patients, and members of the public have been be incorporated regarding prioritization of outcomes (benefits and harms), as well as other aspects of guideline development. A draft version of this protocol was reviewed by nine external topic experts and stakeholders and all comments were considered when finalizing this protocol. This final version of the protocol has been approved by the entire CTFPHC and will be posted on the CTFPHC website and registered with the International Prospective Registry of Systematic Reviews (PROSPERO) database.

Analytical Framework and Staged Approach

Figure 1 is an analytical framework that depicts the structure used to address the Key Questions (KQs) for evaluating the benefits and harms of screening asymptomatic women during pregnancy for bacteriuria.

A staged approach will be followed based on the availability and quality of the body of evidence. Quality of evidence (classified as high, moderate, low, very low) will be assessed using methods developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group (http://www.gradeworkinggroup.org/), whereby high quality evidence relies on precise and consistent effect estimates from studies having few limitations on internal validity (i.e., low bias) and examining directly relevant populations, interventions, comparators, and outcomes (i.e., PICOs) (see Section IV for more details). The staging approach of the

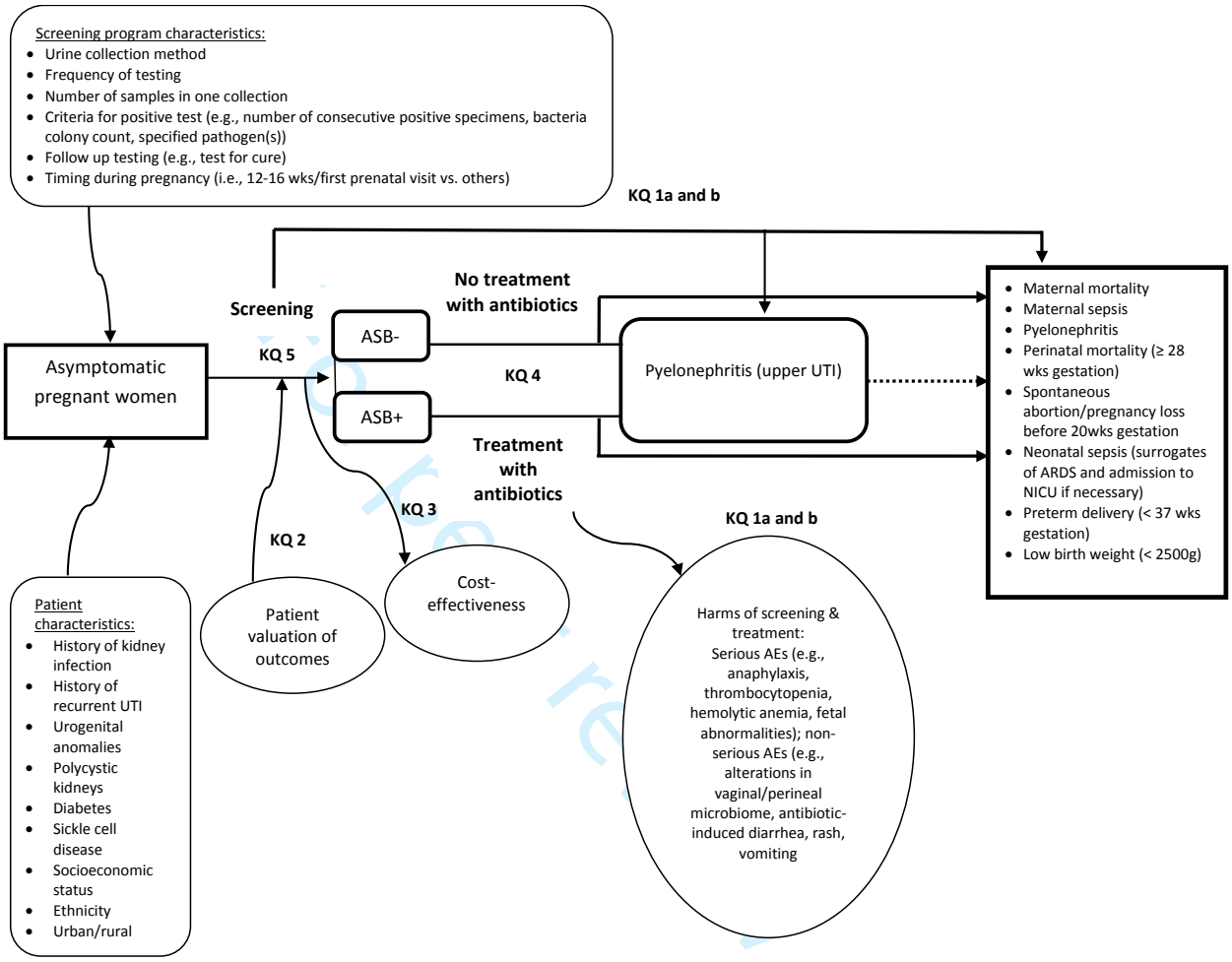
CTFPHC relies on choices made when considering, primarily, the GRADE domains of study limitations and indirectness. Moreover, decisions made during the evidence review are based on the information needs of the CTFPHC for making a screening recommendation based on the balance of critical patient-important benefits and harms.

The most direct and least biased evidence for the effectiveness of screening for ASB will be prioritized. This review will start by examining evidence from randomized-controlled trials (RCTs) on the clinical effectiveness of screening on patient-important outcomes. Staging beyond this point will require careful deliberation with documentation of rationale. If data from the initial stage is scarce for critical benefits or harms the CTFPHC will consider searching for data from (potentially) more biased study designs or indirect evidence (e.g., evidence from observational studies treatment RCTs, test accuracy studies. In cases where evidence on test accuracy and treatment effects will be used to provide indirect evidence on screening effectiveness, the limitations of such an indirect approach will be described. Examining both accuracy and treatment data may not be useful in all cases; for example, if the CTFPHC becomes confident that treatment is ineffective there would be no need to further examine test accuracy. In general, subsequent stages will only be conducted when the evidence from the previous stage(s) is non-existent or of too poor quality (e.g., very low quality based on GRADE tables) for the Task Force to make a screening recommendation based on the balance of patient-important benefits and harms.

For this review, the first stage will focus on identifying and using data from studies directly linking screening for ASB to patient-important benefits and harms (KQ1). Study designs providing the highest internal validity (e.g., RCTs) for this KQ will be preferred with a hierarchy of evidence used after this point if necessary. After RCTs we will consider controlled clinical trials (CCTs; defined for this review as *experimental trials without random allocation but where intervention(s) are introduced, standardized, and allocated objectively [e.g., by date of birth, but not using subjective means such as patient or clinician preferences] by investigators and blinding of participants is typically possible*) and then prospective and retrospective controlled observational studies. This stage will also include examination of KQ2 on women's valuation of benefit and harm outcomes of screening for ASB (and more broadly/indirectly treatment with antibiotics) in pregnancy. The cost-effectiveness of screening for ASB (KQ3) will also be considered only if there is evidence from KQ1 indicating a favorable benefit-harm ratio such that screening may be recommended.

If this first stage does not provide high enough quality of evidence for making a recommendation, the CTFPHC will carefully consider pursuing stage two with documentation of rationale before proceeding. Stage two will commence with examination of effectiveness of treatment of ASB in pregnancy (KQ4). If there is sufficient quality evidence indicating favorable treatment effectiveness from KQ4, an examination of KQ5 on diagnostic test accuracy will be considered in stage 3. Due to the indirectness of evidence provided by KQs 4 and 5 for making recommendations for the clinical effectiveness of screening, we will only seek data from study designs offering the greatest potential for high internal validity. That is, for KQ4 (treatment) we will focus on RCTs, and for KQ5 (test accuracy) we will exclude case-control designs. Where high quality systematic reviews exist examining these indirect evidence links, we will utilize these when possible.

Figure 1. Analytical Framework



AEs: adverse events; ARDS: acute respiratory distress syndrome; ASB: asymptomatic bacteriuria; d: day; g: grams; KQ: key question; NICU: neonatal intensive care unit; UTI: urinary tract infection; wks: weeks

Key Questions (KQs)*

Stage 1:

Benefits and harms of screening

KQ1a: What are the benefits and harms of screening compared with no screening for asymptomatic bacteriuria in pregnancy? Are there subgroup differences with SES or other patient characteristics?

KQ1b: What are the comparative benefits and harms of screening with different screening tests/algorithms for asymptomatic bacteriuria in pregnancy?

Outcome valuation

KQ2a: How do women weigh the benefits and harms of screening and treatment of asymptomatic bacteriuria in pregnancy?
KQ2b: How do women's valuation of benefits and harms of screening and treatment inform their decisions to undergo screening?

Resource use**

KQ3: What is the cost-effectiveness of screening for asymptomatic bacteriuria in pregnancy?

Stage 2:

Treatment

KQ4: What are the benefits and harms of antibiotic treatment compared with no treatment for asymptomatic bacteriuria in pregnancy?

Stage 3:

Diagnostic accuracy of screening tests

KQ5: What is the diagnostic accuracy of screening tests for asymptomatic bacteriuria in pregnancy?

Decision process for staging outlined in section on Analytical Framework and Staged Approach
****Conducted if benefit-harm ratio deemed beneficial based on KQ1***

Section IV. Review Methods

Literature Search

The literature search strategy will be developed and implemented by a research librarian. The search strategy will consist of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords, and will be peer-reviewed. Methodological filters will not be applied to limit retrieval by study design; study designs included for each KQ are identified in the section on inclusion and exclusion criteria. Searches will be restricted by language to include full texts published in English and French, without a publication date restriction.

We will conduct comprehensive searches in bibliographic databases most relevant for each KQ. For evidence informing stage 1 of our review we will perform comprehensive searches for studies meeting our inclusion criteria as described below. For KQ1, we will search MEDLINE (1946-) via Ovid; Embase (1974-) via Ovid; Cochrane Library; CINAHL (1937-present) via EBSCOhost; and PubMed via NCBI Entrez. The detailed search strategy for MEDLINE is reported in Appendix 1 and will be adapted to accommodate the controlled vocabularies of each database. For KQs 2 (women's outcome valuation) and 3 (cost-effectiveness of screening), we will modify the search to include relevant terms and will add suitable databases (e.g. PsycINFO for patient preferences, NHS Economic Evaluation Database [EED] for cost effectiveness). Full search strategies for all databases will be included in the final report.

For evidence used in stages 2 and 3, we are aware of at least one high-quality systematic review for KQs 4 (4) and 5 (10) which we may rely on. For KQ4 on effectiveness of antibiotic treatment compared with no treatment, we anticipate updating a recent Cochrane review of treatment for asymptomatic bacteriuria in pregnancy (4); if an update is not possible, we will follow methods adopted by the CTFPHC for integrating systematic reviews (see Appendix 2). If we update this review, the original search will be updated. For KQ5 (test accuracy), we anticipate using a recent review of screening tests for asymptomatic bacteriuria in pregnancy (10) and any additional reviews that may be identified as similar in scope. While multiple reviews may be considered for KQ5 (test accuracy) if found, we will not attempt to update the search(es) to identify more recent studies. If the scope of any review is narrower (e.g., does not include all interventions applicable to our topic), we may screen the excluded studies list(s) to identify potentially relevant studies for inclusion. To ensure we have identified all potentially relevant systematic reviews relevant to KQs 4 and 5, we will conduct a database search for systematic reviews. We will search PubMed (1946-) via NCBI Entrez, the Cochrane Database of Systematic Reviews (inception-) and the Database of Abstracts of Reviews of Effects (DARE) (inception-2013) via Wiley Cochrane Library to identify systematic reviews, meta-analyses and health technology assessments. Our PubMed search will utilize a search filter from CADTH (https://www.cadth.ca/resources/finding-evidence).

Grey literature will be searched and documented according to CTFPHC methods and will include internet-based searches (via adapted Canadian Agency for Drugs and Therapeutics in Health [CADTH] checklists; https://www.cadth.ca/resources/finding-evidence/grey-matters), electronic libraries (e.g., Health Canada Library, Canadian Electronic Library), and trial registries (ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform). Based on consultation with clinical experts, the following highly relevant conference proceedings will be hand-searched for recent studies not yet published (2014-present): Society of Obstetricians and Gynaecologists of Canada, Association of Medical Microbiology and Infectious Disease Canada, ID Week, and American Society for Microbiology meeting (ICAAC). Clinical and content experts identified by the CTFPHC will be contacted and invited to identify relevant research reports for consideration; websites of relevant Canadian stakeholder organizations will be searched.

Eligibility Criteria

Table 1 outlines the inclusion and exclusion criteria for all KQs, and details are provided below.

Population

Studies will be considered for inclusion in all KQs if they examine pregnant women at any stage of pregnancy where the population represents a “routine screening” scenario (e.g., the majority of patients do not have a degree of signs or symptoms prompting diagnostic testing and/or treatment for upper or lower UTI). It is recognized that many women experience nocturnal and increased frequency of urination, or other symptoms, which do not necessarily indicate bacteriuria or infections. We will include studies where a proportion of, but not all, women have risk factors for UTIs or other outcomes of the review. KQ2 on women’s outcome valuation, we will include studies of women of child-bearing age if no evidence is found from studies with pregnant women; studies will still be required to examine screening or antibiotic treatment during pregnancy.

We will exclude studies *exclusively* including women with conditions that place them at substantially higher than average risk for bacteriuria (i.e., kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infections [UTI], diabetes, sickle-cell disease), or with symptoms of UTI.

***Population subgroups of interest*:** history of kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection (UTI), diabetes, sickle cell disease, socioeconomic status (i.e., education, income), ethnicity (i.e., percent South Asian versus others), and urban/rural setting.

Interventions & Comparators

For clinical effectiveness of screening (KQ1), any screening test/algorithm for ASB will be eligible for inclusion and the comparator is absence of screening (1a) or a different urine test or screening algorithm (1b). Studies that compare urine cultures of differing criteria (e.g., threshold 10^3 CFU/mL versus 10^5 CFU/mL) will also be eligible for inclusion. For women's outcome valuation (KQ2), any screening test for ASB during pregnancy will be eligible for inclusion; indirect evidence about antibiotic treatment during pregnancy broadly will be used if needed. For cost-effectiveness (KQ3), any screening test compared with no screening or another screening test (i.e., urine culture) will be eligible for inclusion; costs must be compared with outcomes/effects such that studies examining costs only will be excluded. For treatment effectiveness (KQ4), any antibiotic treatment for ASB compared to no treatment or placebo will be eligible for inclusion. For diagnostic accuracy (KQ5), any index test compared with a urine culture for detecting ASB will be eligible for inclusion. For all KQs, studies that include screening or treatment for group B streptococcus (GBS) at any time of pregnancy for any of the outcomes of interest will be included.

We will exclude studies exclusively examining urine tests used for screening for other conditions (e.g., proteinuria, glycosuria), and non-urine screening tests (e.g., vaginal/rectal swab culture for GBS testing).

***Screening subgroups of interest*:** urine collection methods (e.g., clean-catch and/or midstream; excluding catheter methods/samples), frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, and timing during pregnancy.

Outcomes

As with the KQs, the outcomes for inclusion for KQ1 (screening effectiveness) and KQ4 (treatment) will be staged to some extent, if necessary. Each outcome has been rated independently by members of the CTFPHC and by women, as per the patient engagement activities of an independent group with expertise in knowledge translation from St. Michael's Hospital in Toronto, Ontario. All patient-important outcomes rated as critical (7 to 9 out of 9) or important (4 to 6 out of 9) for decision making were considered for inclusion. From these ratings, the eight outcomes were rated as critical will be included in stage 1; of three outcomes rated as important, low birth weight (but not hypertension or acute kidney injury) will be included

because in the past (i.e. older studies) this was conceptually considered the same as "pre-term birth", which both the CTFPHC members and patients rated as critical. Considering harms separately, if no evidence is found for any of the outcomes (serious adverse events [AEs]) in stage 1, there will be inclusion of the outcomes (non-serious AEs) from stage 2. This grouped and staged approach to harms will address infrequent reporting, reporting of different harms across studies, and also uncertainty regarding all the potential harms that may be reported. Non-serious AEs, particularly if frequent or severe, are considered important but not critical for decision making by the CTFPHC. This approach acknowledges guidance to limit the number of total outcomes (maximum 7) to those which can be successfully managed cognitively by guideline panels when balancing multiple benefits and harms.

Outcomes for KQs 1 and 4 with ratings:

Benefits (reduced incidence for all):

1. maternal mortality (9)
2. maternal sepsis (8)
3. pyelonephritis (7)
4. perinatal mortality (≥ 28 weeks of gestation (e.g., intrauterine demise, stillbirth, early neonatal death)) (9)
5. spontaneous abortion/pregnancy loss before 20 weeks of gestation (8)
6. neonatal sepsis (if not reported will include surrogate outcomes of acute respiratory distress syndrome [ARDS] or admission to neonatal intensive care unit [NICU]) (8)
7. preterm delivery (live fetus passed < 37 weeks of gestation) (7)
8. low birth weight (< 2500g) (6)

Harms:

1. serious adverse event(s)[a] associated with antibiotic treatment, *including but not limited to*: (7)
    a. anaphylaxis,
    b. thrombocytopenia,
    c. hemolytic anemia,
    d. fetal abnormalities; and,
2. non-serious adverse event(s) associated with treatment, *including but not limited to*: (4)
    a. alterations in vaginal/perineal microbiome (e.g., candidiasis, vaginitis),
    b. antibiotic-induced diarrhea,
    c. rash,
    d. vomiting

[a]Serious adverse event (experience) or reaction is any untoward medical occurrence that: a) results in death, b) is life-threatening, c) requires in-patient hospitalisation or prolongation of existing hospitalisation, d) results in persistent or significant disability/incapacity, or e) is a congenital anomaly/birth defect (Health Canada, 2011);

We will exclude studies that screen pregnant women for group B streptococcus near delivery or at time of rupture of membranes for the prevention or treatment of chorioamnionitis or neonatal GBS (without other outcomes of interest listed above).

Women's outcome valuation (KQ2) include several possible outcomes related to the weighing of benefits and harms of screening and treatment (KQs 1 and 4) and how this may affect their decisions to undergo screening (e.g., relative weight/utilities of benefit and harms; willingness to be screened based on relative value placed on benefits and harms of screening programs or treatment); these outcomes will be based on considerations of the possibility or perceived/expected magnitude of effects for the outcomes identified for KQs 1 and 4.

During focus groups, women identified an additional outcome - psychological distress/anxiety - and rated this as critical (7 out of 9), although it was interpreted differently by some women as either a benefit (e.g., reduction in psychological distress/anxiety by knowing the health status of themselves and their baby) or a harm (e.g., another of many tests and potential worries during pregnancy). Anxiety as a critical outcome will be sought and synthesized within findings from KQ2 on women's valuation of benefits and harms of screening and treatment, as well as within interpretation of test accuracy outcomes from KQ5 (TP, TN, FP, FN) which will be *interpreted based on the CTFPHC judgments* on the magnitude of potential consequences of each (e.g., unnecessary anxiety from high FP, loss of potential benefit in FN) as identified in the section below "Assessment of the Overall Quality of the Evidence using GRADE".

Cost-effectiveness (KQ3) outcomes include cost per quality-adjusted life year (QALYs), incremental cost-effectiveness ratios (ICERs), and net benefit (in dollars from cost-benefit studies.

Diagnostic test accuracy (KQ5) outcomes include: sensitivity, specificity, false positives, false negatives, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio.

Setting, Study Design & Timing

Studies conducted in primary care, or relevant clinical settings (e.g., prisons, remote stations, community health centers, midwifery practice) will be included. For KQ3 on cost-effectiveness we will limit studies to those conducted using data relevant to Canada, thus within countries having a very high Human Development Index (22).

For KQ1 (screening effectiveness), we will include RCTs initially and then, if needed based on the GRADE assessment of overall quality of the evidence, we will search for CCTs (defined in Section III) and then controlled observational studies (i.e., prospective and retrospective cohort, case-control, controlled before-after). For KQ2 (outcome valuation), we will include any study where women are asked to balance the benefits and harms of screening and treatment for ASB and state/choose their willingness to be screened and treated; surveys, experimental designs (e.g., contingent valuation), and qualitative research are examples. Cost-effectiveness (KQ3) will look at any study comparing effects and costs (e.g., cost-effectiveness, cost-utility, cost-benefit) and may include modelling of effects and/or costs. For KQ4 (treatment), we will rely on RCTs. For KQ5 (test accuracy), we will rely on prospective and retrospective studies where a consecutive or random sample of participants receive both the index test(s) and reference standard, or where participants are randomized to different index tests but all receive the reference standard, and

assessment in a cross-sectional manner. We will exclude case-control studies and studies with longitudinal assessment of the reference standard.

For all KQs, case reports and case series (i.e., group of patients selected based on particular outcome) will be excluded as will papers not reporting primary research (e.g. editorials, commentaries, opinion pieces). Conference abstracts will not be eligible for inclusion, but will be captured and serve to help identify full study reports and assess the quality of evidence in relation to potential publication and reporting biases. No limits will be applied to publication year.

Additional considerations

We do not have a minimum sample size for inclusion, nor do we have a minimum threshold for extent of incomplete follow-up or participant attrition; these factors will be considered during assessment of the quality of evidence (e.g., precision domain accounts for sample size across studies), and during sensitivity analyses in cases of substantial heterogeneity in findings at the data synthesis stage (see relevant sections).

Tables 1 to 5. Inclusion and Exclusion Criteria for Key Questions

Table 1. KQ1a, b: Benefits and harms of screening

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions	Any screening program or test Screening subgroups/algorithms, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for group B streptococcus (GBS) testing)
Comparator	KQ1a: No screening (but may include indicated/targeted testing and/or treatment upon development of symptoms or for high-risk groups) KQ1b: A different screening test or algorithm (see intervention subgroups)
Outcomes	*Benefits (reduced incidence for all)*: 1. maternal mortality (9) 2. maternal sepsis (8)\ 3. pyelonephritis (7) 4. perinatal mortality (≥ 28 week's gestation (e.g., intrauterine demise, stillbirth, early neonatal death)) (9) 5. spontaneous abortion/pregnancy loss before 20 week's gestation (8) 6. neonatal sepsis (if not reported will include surrogate outcomes of acute respiratory distress syndrome [ARDS] or admission to neonatal intensive care unit [NICU]) (8) 7. preterm delivery (live fetus passed < 37 week's gestation) (7) 8. low birth weight (< 2500g) (6) *Harms:* 1. serious adverse event(s)[a] associated with antibiotic treatment, *including but not limited to*: (7) a. anaphylaxis,

	b. thrombocytopenia, c. hemolytic anemia, d. fetal abnormalities; and, 2. non-serious adverse event(s) associated with treatment, *including but not limited to*: (4) a. alterations in vaginal/perineal microbiome (e.g., candidiasis, vaginitis), b. antibiotic-induced diarrhea, c. rash, d. vomiting Exclude: screening for GBS near delivery or at time of rupture of membranes for the prevention or treatment of chorioamnionitis or neonatal GBS (without other outcomes of interest in list above)
Study Designs	Staged: RCTs, CCTs, controlled observational (i.e., prospective and retrospective cohorts, case-control, controlled before-after)
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices)
Timeframe	No publication date limits

CCT: controlled clinical trial; KQ: key question; RCT: randomized controlled trial

[a]Serious adverse event (experience) or reaction is any untoward medical occurrence that: a) results in death, b) is life-threatening, c) requires in-patient hospitalisation or prolongation of existing hospitalisation, d) results in persistent or significant disability/incapacity, or e) is a congenital anomaly/birth defect (Health Canada, 2011)

Table 2. KQ2: Outcome valuation

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria; will also accept asymptomatic women who are not pregnant if necessary Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any screening program or test, and any antibiotic; will accept studies on treatment for any bacterial condition in pregnancy Screening subgroups/algorithms, including: urine collection method, frequency of testing, criteria for a positive test (including number of consecutive positive specimens, bacteria colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine *screening* is done for other conditions (e.g., proteinuria, glycosuria), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	Not applicable
Outcomes[§]	Several possible outcomes (e.g., relative weight/utilities of benefit and harms; willingness to be screened based on relative value placed on benefits and harms of screening programs or treatment)
Study Designs	Qualitative, mixed methods, surveys/cross-sectional
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices)
Time frame	No publication date limits

KQ: key question

[§]If there is a very limited quality of evidence base for KQ2 (i.e., in terms of quantity/sample size, methodological quality, inconsistency between studies, or applicability to our population or setting) we will consider including studies examining women's valuation of harms *or* benefits rather than the trade-off between the two. For example, studies examining women's acceptance of screening and/or treatment for ASB when only considering their perspectives on the potential

risks of antibiotic treatment to their baby, or the importance placed on reassurance about the potential to prevent preterm delivery et cetera, could offer some indirect evidence to help the CTFPHC in their deliberations. Likewise, the relative value placed on different benefit or harm outcomes (e.g., serious versus non-serious AEs) could be informative.

Table 3. KQ3: Cost-effectiveness of screening

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any screening program or test Screening subgroups/algorithms, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	No screening (but may include indicated/targeted testing and/or treatment upon development of symptoms or for high-risk groups), or a different screening test or algorithm (see intervention subgroups)
Outcomes	Cost per quality-adjusted life-years (cost per QALY), incremental cost-effectiveness ratio (ICER), net benefit/cost
Study Designs	Economic evaluations
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices); limited to countries rated as having very high Human Development Index (22)
Time frame	No publication date limits

KQ: key question

Table 4. KQ4: Treatment

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any antibiotic Screening subgroups/algorithms, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia,), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	No treatment or placebo
Outcomes*	*Benefits (reduced incidence for all)*: 1. maternal mortality (9)

	2. maternal sepsis (8)\ 3. pyelonephritis (7) 4. perinatal mortality (≥ 28 week's gestation (e.g., intrauterine demise, stillbirth, early neonatal death)) (9) 5. spontaneous abortion/pregnancy loss before 20 week's gestation (8) 6. neonatal sepsis (if not reported will include surrogate outcomes of acute respiratory distress syndrome [ARDS] or admission to neonatal intensive care unit [NICU]) (8) 7. preterm delivery (live fetus passed < 37 week's gestation) (7) 8. low birth weight (< 2500g) (6) *Harms:* 1. serious adverse event(s)[a] associated with antibiotic treatment, *including but not limited to*: (7) a. anaphylaxis, b. thrombocytopenia, c. hemolytic anemia, d. fetal abnormalities; and, 2. non-serious adverse event(s) associated with treatment, *including but not limited to*: (4) a. alterations in vaginal/perineal microbiome (e.g., candidiasis, vaginitis), b. antibiotic-induced diarrhea, c. rash, d. vomiting Exclude: screening for group B streptococcus near delivery or at time of rupture of membranes for the prevention or treatment of chorioamnionitis or neonatal GBS (without other outcomes of interest listed above)
Study Designs	RCTs
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices)
Time frame	No publication date limits

KQ: key question; RCT: randomized controlled trial

[a]Serious adverse event (experience) or reaction is any untoward medical occurrence that: a) results in death, b) is life-threatening, c) requires in-patient hospitalisation or prolongation of existing hospitalisation, d) results in persistent or significant disability/incapacity, or e) is a congenital anomaly/birth defect (Health Canada, 2011)

Table 5. KQ5: Diagnostic accuracy of screening tests

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any index test Screening subgroups/algorithm, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	A urine culture Screening subgroups/algorithm, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy

	Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Outcomes	Sensitivity, specificity, false positives, true positive, false negatives, true negatives, positive and negative likelihood ratios, prevalence/pre-test probability (true positive + false positive)/total number of people)
Study Designs	Prospective and retrospective studies where a consecutive or random sample of participants receive both the index test(s) and the reference standard, or where participants are randomized to different index tests but all receive the reference standard, and assessment in a cross-sectional manner Exclude: case-control studies and studies with longitudinal assessment of the reference standard
Language	English and French

Screening and Selecting Studies for Inclusion

For the database searches, two reviewers will independently screen the titles and abstracts (when available) using broad inclusion/exclusion criteria. Citations will be classified as "include/unsure," "exclude," or "reference" (i.e., conference abstracts, protocols, and systematic reviews). One reviewer will review the "reference" group and will conduct all other searching as outlined in the above section. The full text of all studies classified as "include/unsure" or identified after reviewing the reference citations will be retrieved for full review; two reviewers will independently assess eligibility using a standard form that outlines the inclusion and exclusion criteria. Disagreements on final inclusion of all studies will be resolved through consensus or third party adjudication. For KQs 4 and 5, any existing systematic review(s) identified as relevant will be assessed for eligibility based on whether the authors: i) searched more than one database, ii) report their selection criteria, and iii) use PICOTS criteria that are a close match to that for the relevant KQ. In cases where there is more than one possible review providing results for the same intervention-outcome pair, we will choose one based on: AMSTAR (23) rating (score 8 or higher preferred), comprehensiveness of search (i.e., reports on most or more papers included by other existing reviews), closest match to our PICOTS, most recent date of study inclusion/search, and the quality and extent of reporting on individual study characteristics, data, and quality assessments. All decisions to exclude a study at full text review will be provided. The title/abstract screening and full-text selection processes will be conducted and documented in DistillerSR. The flow of literature and reasons for full text exclusions will be recorded in a PRISMA Flow Chart.

Data Extraction & Reporting

One reviewer will independently extract data from each included study or systematic review into DistillerSR; a second reviewer will verify all data. Disagreements will be resolved through discussion or third-party consultation until consensus is reached.

When using individual studies for a KQ, a narrative summary (with accompanying tables) will be provided to report on all studies by design, country of origin, sample sizes, population(s) (including subgroups), intervention(s)/index tests (including data on thresholds and for subgroup questions), comparator(s)/reference test, setting, and outcome measures, as reported by studies. When there are multiple publications associated with a study we will consider the earliest report of the main (primary) outcome data to be the primary data source. We will extract data from the primary source first and then add outcome data reported in the secondary/associated publications and data sources. We will reference the primary source throughout the evidence report; all associated literature will be tabulated for reference.

When relying on systematic reviews for KQs 4 (treatment) and 5 (test accuracy), we will extract data on the characteristics of the systematic review (PICOTS), the included studies with specifics related to the population (size and characteristics), outcomes evaluated (including definitions and timing of assessment), quality/risk of bias (by domain/construct if available), the methods of analysis (meta-analytical approach and its findings in relation to heterogeneity, if applicable), findings from their syntheses including subgroup analysis and GRADE or other quality assessments if performed across studies, and any limitations noted by the systematic review authors. For KQs 4 and 5, data verification will be completed on 5 to 10% of included studies in any existing systematic review(s), and if satisfied with concordance, we will consider incorporating the reported data on study and participant characteristics without returning to the primary studies. If additional studies are included (e.g., new studies from updated search [KQ4] or excluded studies in the identified systematic review that is subsequently included for current review to ensure coverage of scope [KQ5]), these will be clearly identified and presented.

When using individual studies, we will record intention-to-treat results, if possible. For continuous outcomes measures, we will extract (by arm) the mean baseline and endpoint or change scores, standard deviations (SD) or other measure of variability, and number analyzed. We will not include outcome data from studies that did not provide a follow up change or endpoint mean or data that could be used to calculate follow up scores. If necessary, we will approximate means by medians. If standard deviations are not given, they will be computed from p-values, 95% confidence intervals (95% CIs), standard errors, z-statistics, or t-statistics. If computation is not possible they will be estimated from upper bound p-values, ranges, inter-quartile ranges, or (as a last resort) by imputation using the largest reported SD from the other studies in the same meta-analysis. When computing SDs for change from baseline values, we will assume a correlation of 0.5, unless other information is present in the study that allows us to compute it more precisely. For dichotomous outcomes, we will report counts or proportions, and sample size, by study arm.

For dichotomous data on harms, each adverse event (AE) will be counted as if it represents a unique individual; because a single individual might experience more than one AE, this assumption may overestimate the number of people having an AE. Only numerical data for AEs will be extracted; that is, we will make no assumptions on lack or presence of an AE if this is not reported; authors that report only p-values or that one arm had fewer events than another (but where it is explicit that the outcome was captured in the study) will be contacted (3 times via email) to provide the data.

Data on within-study subgroup analysis will be collected, including: subgroups (independent variables), the type of analysis (e.g., subgroup/stratified or regression analysis), the outcomes assessed (dependent variables), and the authors' conclusions. We will collect data suitable for all patient and intervention subgroups (see Table 1) for performing our own subgroup analyses (e.g., stratified analysis, meta-regression) based on study-level data.

Risk of Bias/Methodological Quality Assessment

Two reviewers will independently assess the risk of bias (ROB) of each included study (KQs 1-3), with disagreements resolved through discussion or third-party consultation to reach consensus. The results for each study and across studies will be reported by each domain and for

the overall ROB score. The ROB for each study will be assessed on an outcome basis where needed, particularly when different outcomes are assumed to have different susceptibilities to bias; for example, subjective outcomes and expected harms are more prone to bias from non-blinding than objective outcomes and unexpected/rare harms.

RCTs and CCTs (theoretically only differing from RCTs by lack of random sequence generation and not by other ROB domains) will be appraised using the Cochrane Risk of Bias tool (24). This tool consists of six domains (sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and "other" sources of bias) and a categorization of the overall risk of bias. Blinding will be assessed separately for patients/providers and outcome assessors taking into account the type of outcome that may be affected (e.g. subjective vs. objective). To assist with outcome reporting bias assessments, we will seek study protocols and studies/data from registries. The overall assessment is based on the responses to individual domains. If one or more individual domains are assessed as having a high risk of bias, the overall score will be rated as high risk of bias. If at least one domain is assessed as unclear, and no domains are assessed as high, the overall score will be rated as unclear risk of bias. The overall risk of bias will be considered low only if all components are rated as having a low risk of bias.

Controlled observational studies will be appraised using the Newcastle-Ottawa Quality Assessment Scale (25); three domains (sample selection, comparability of cohorts, and assessment of outcomes) are evaluated. Each item that is adequately addressed is awarded one star, except for the "comparability of cohorts" item, for which a maximum of two stars can be given. The overall score is calculated by tallying the stars. We will consider a total score of 6 to 8 stars to indicate low ROB, 4 or 5 stars to indicate moderate ROB, and 3 or fewer stars to indicate high ROB.

For diagnostic accuracy studies (KQ5), we will rely on the Quality of Diagnostic Accuracy Studies (QUADAS-2) (26) used to assess ROB. This tool assesses concerns of risk of bias among four domains (patient selection, index test, reference standard, and flow and timing) and concerns of applicability across the first three domains.

If one or more systematic review(s) is used to provide evidence for KQ4 (treatment) or KQ5 (accuracy), we will assess if the review used an explicit tool (e.g., Cochrane ROB [KQ4], QUADAS [KQ5]) for assessing the main sources of potential bias. If so, we will complete assessments on 5 to 10% of included studies to establish concordance before considering the use of assessments reported by each review.

Studies answering KQ2 (outcome valuation) will be evaluated by tools appropriate to their study design: for surveys and qualitative studies we will use tools developed by the Center for Evidence-based Management (http://www.cebma.org/resources-and-tools/what-is-critical-appraisal/). The quality of economic evaluation studies (KQ3) will be assessed using Drummond's checklist for economic evaluation studies (27).

Data Analysis & Synthesis

We will provide summaries of intervention effects for each study by calculating the appropriate statistics based on types of outcomes.

Key Question 1

For pair-wise meta-analysis in KQ1 (screening effectiveness), we will employ a random effects model. For continuous outcomes, we will report a pooled mean difference (MD) when one measurement tool is used, or other options that exist for communicating results when combining two or more outcome scales measuring similar constructs (28, 29). For dichotomous outcomes, we will report relative risks (RR) and risk differences (RD) between groups with corresponding 95% CIs. For those outcomes (e.g. serious adverse events) where at least one intervention group contains zero events, only the risk difference will be used. For calculating the RD, we will use the median baseline risk for the control group in the included studies, although may perform sensitivity analysis using differing baseline risks if thought suitable (30, 31). The decision to pool studies will not be based on the statistical heterogeneity (I^2 statistic will be reported), but rather on interpretation of the clinical and methodological differences between studies. When substantial heterogeneity is suspected, we will conduct sensitivity analyses if appropriate (e.g., in the presence of studies with outlying effect sizes, for studies rated as high risk of bias in some domains such as incomplete outcome data [<80 percent] or lack of allocation concealment, parallel versus cross-over designs). Heterogeneity will also be examined during our planned subgroup analyses for important patient and intervention variables (see Table 1). Where there are at least eight studies in a meta-analysis, we will analyze publication bias both visually using the funnel plot and quantitatively using Egger's test (32). We will not combine results from RCTs with CCTs or controlled observational studies (if used via staging approach for KQ on screening); rather, the latter two will be used to support or provide context for the evidence from RCTs.

Key Questions 2 & 3

For KQs 2 (outcome valuation) and 3 (cost-effectiveness), results will be narratively described in most cases. If more than one study is identified providing numerical values for ranking benefits and/or harms (KQ2) or similar outcomes (KQ3) these will be summarized descriptively and results across studies compared. Thematic analysis may be undertaken for KQ2, including coding data (meaning and context) into descriptive themes that accurately reflect the data and then summarizing this in a narrative format.

Key Questions 4 and 5

When using systematic reviews for stages 2 and 3, any meta-analysis will be reconstructed if possible to provide graphical representation of the findings to support our interpretations. Meta-analysis may be recalculated, if possible, when new studies are found in search updates (KQ4), analysis methods are not thought appropriate (e.g., use of random rather than fixed effects models, ability but no use of HSROC models [see below]) or if further analysis (e.g. between-study stratification) may be possible for subgroups of interest. When substantial methodological heterogeneity was found, we may conduct sensitivity analyses if appropriate and able (e.g., for studies rated as high risk of bias, different study designs) or decide to not use the pooled/combined estimate. If not conducted by the authors and when there are at least eight studies in a meta-analysis, we will if possible analyze publication bias both visually using the

funnel plot and quantitatively using Egger's test (32). If meta-analysis was not performed, we will summarize the findings of the systematic review authors.

For KQ5 (diagnostic accuracy), if individual studies are incorporated we will construct 2 x 2 tables and calculate sensitivity, specificity, and positive and negative likelihood ratios (LR+, LR-). Sensitivity and specificity are measures of test accuracy. Likelihood ratios are used to estimate the increased or decreased probability of disease (i.e., ASB) for a patient and can be used to refine clinical judgement based on varying pre-test probabilities. The larger the LR+, the more accurate the test is and the greater the likelihood of disease following a positive test; the smaller the LR-, the more accurate the test is, the lesser the likelihood of disease following a negative test (33). A LR+ that is >10 indicates a large and often conclusive probability that the condition is present; a LR- that is <0.10 suggests a large and often conclusive probability that the condition is not present. A likelihood ratio of one means that a positive or negative result is equally probable in a patient with and without the disease/condition.

If there are more than three studies and they are clinically homogenous (i.e., timing in pregnancy, thresholds, diagnostic criteria), we will pool data using a hierarchical summary receiver-operator curve (HSROC) and bivariate analysis of sensitivity and specificity (34). The HSROC simultaneously compares the sensitivity and specificity (taking their correlation into account) for all studies comparing a particular screening test with ASB diagnostic criteria. We will use Review Manager Version 5.0 (The Cochrane Collaboration, Copenhagen, Denmark) to perform meta-analyses, and Stata 11.0 (metandi program; StataCorp LP, College Station, TX, USA) to fit the bivariate and HSROC models and produce the pooled estimates of sensitivity, specificity, and likelihood ratios.

The results will be organized by type of screening test. If possible, we will examine the impact of screening before and after 12-16 weeks' gestation and in relation to other intervention subgroups described in Table 5. Sensitivities, specificities, and likelihood ratios and their 95% confidence intervals (CI) will be presented in summary tables that include all screening tests and diagnostic criteria. Based on the findings for sensitivity and specificity and estimates of one or more relevant baseline prevalence, an evidence profile will be generated for the outcomes FN, FP, TN, and TP (30).

Subgroup Analyses

Our primary approach for evaluating differential effect for subgroups will be to record any within-study subgroup analyses performed by study investigators using individual patient data; these results preserve the within-study randomization. Because these results are often based on diverse methodology and may be difficult to interpret across the body of evidence, we will also perform our own subgroup analyses using study-level data, as possible, using formal statistical approaches (e.g., meta-regressions) or by stratifying the results of the pairwise meta-analyses by subgroup variables. When determining whether entire studies fall into a particular subgroup category (e.g., recurrent UTI), we will consider ≥80 percent of the study population meeting the criteria as sufficient. We will employ regression analyses when: for continuous variables (e.g., timing during pregnancy) there are at least six to ten studies reporting on the outcome within a specific subgroup, and for categorical variables (e.g., history of recurrent UTI) there are at least three studies for each category level. The number of sufficient studies serves as a rule of thumb

for the lower bound that investigators can consider for a meta-regression, but power will vary according to the size and variability of the effect. These analyses would rely on study-level data, such that the results would be considered observational in nature.

Assessment of the Overall Quality of the Evidence using GRADE

Two reviewers will independently assess the quality of the body of evidence or confidence in the effect for each outcome of interest (see Table 1) using the GRADE methodology. Discrepancies will be resolved through discussion or third-party consultation to reach consensus. Assessments will be entered into the GRADEPro software and summarized in GRADE evidence profiles, Summary of Findings tables and Evidence to Decision Tables. Footnotes to the tables will explain all decisions. The CTFPHC will then use this evidence on each outcome, to assess the net benefits and harms of each service, consider patient preferences and values, and other elements of the GRADE methodology to develop the recommendations on screening for bacteriuria (feasibility, acceptability and equity).

The general approach is outlined here although methods will align with GRADE guidance (30, 35). When using systematic reviews, GRADE assessments will be based on the individual studies and reporting by review authors (e.g., on ROB assessments and PICOTS characteristics) and upon validation of a sample by the review team. For evidence on the benefits and harms of screening (KQ1), as a starting point the quality is assigned as high for evidence from RCTs and low for evidence from observational studies, when used. For accuracy studies, cross-sectional or cohort studies in patients with diagnostic uncertainty and direct comparison of test results with an appropriate reference standard will be considered high quality. Thereafter, we will examine and potentially downgrade the quality based on five core domains: study limitations/ROB, inconsistency, indirectness, imprecision, and publication/reporting bias. For outcomes where there is evidence from observational studies and no other reason to downgrade the evidence, we will also consider the additional domains of dose-response association, plausible confounding, and strength of association (i.e., large magnitude of effect [i.e., large ≤ 0.5 or ≥ 2.0 or very large RR ≤ 0.2 or ≥ 5.0]), to potentially upgrade the quality (36).

For the *study limitations (risk of bias)* domain RCTs and CCTs may be downgraded one or two levels depending on the proportion of trials (e.g., one very large trial may outweigh two very small trials) assessed as having high ROB for the particular outcome under consideration (37). Evidence from observational studies will be downgraded when most studies have moderate or high ROB. For *inconsistency* (consistent, inconsistent) we will assess the magnitude of the effects of the included studies (e.g., inconsistent when lack of overlap in 95% CIs for some studies) (38). *Indirectness* of the evidence (direct or indirect) is based on evaluating the relevance of the study's PICOs compared to ours for our primary KQ1 (effectiveness of screening); when relying on test accuracy and treatment studies there will be downgrading by at least one level for this domain (36). We will assess *imprecision* (precise or imprecise) on the basis of clinical thresholds and Optimal Information Size (39). For outcomes where clinical thresholds are used/determined, we will typically downgrade this domain once if the entire pooled 95% CI does not cross the threshold (i.e. only one limit of the CI crosses), and downgrade twice if the 95% CI crosses the threshold and no difference (0 MD or 1.0 RR) or does not cross

the threshold at all. Thresholds may be determined a priori (prior to viewing results from studies) but may also be revised post hoc based on careful benefit-harm considerations when considering all outcomes together (e.g., lower benefit threshold in cases of few and minor harms). A precise estimate is one that allows for a clinically useful conclusion. *Reporting bias* (suspected or undetected) will be evaluated with respect to publication bias.

Interpreting these domains when relying on evidence from diagnostic test (KQ5) data has certain considerations, including how certain the CTFPHC is about the consequences of each outcome (FP, FN, TP, TN) in relation to the main outcomes of interest for KQs 1, 2 & 4 (30).

External Review

The evidence review will be peer-reviewed by external content experts (minimum 3) and invited stakeholder organizations (minimum 10), with response to all comments shared with all reviewers approximately two months after posting of the final review.

Planned Schedule and Timeline

Draft protocol approved by CTFPHC members: July 29, 2016
External peer review: August 1-10, 2016
Final protocol: November 30, 2016
Draft evidence review: January 31, 2017
Final evidence review: March 31, 2017

Conflict of Interest Statement

None of the study team members have any known actual or perceived conflicts of interest related to this review.

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Appendix 1. MEDLINE Search Strategy (KQ1 [screening effectiveness])

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Title: PHTF Bacteriuria Screening in Pregnancy

Strategy:

1. Asymptomatic Infections/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
2. Bacteriuria/
3. exp Cystitis/
4. Dysuria/
5. Pyelonephritis/
6. Urinary Tract Infections/
7. bacilluria*.tw,kf.
8. bacteriuria*.tw,kf.
9. cystiti*.tw,kf.
10. (cysto-pyeliti* or cystopyeliti*).tw,kf.
11. dysuria*.tw,kf.
12. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw,kf.
13. (pyelo-cystiti* or pyelocystiti*).tw,kf.
14. (pyelo-nephriti* or pyelonephriti*).tw,kf.
15. (UTI or UTIs).tw,kf.
16. or/1-15 [Combined MeSH & text words for bacteriuria]
17. Antibody-Coated Bacteria Test, Urinary/
18. *Bacteriuria/di, pc, mi, ur
19. exp *Cystitis/di, pc, mi, ur
20. Mass Screening/
21. Microbial Sensitivity Tests/
22. Microscopy/
23. Predictive Value of Tests/
24. *Pyelonephritis/di, pc, mi, ur
25. Reagent Kits, Diagnostic/
26. Reagent Strips/
27. "Sensitivity and Specificity"/
28. Urinalysis/
29. *Urinary Tract Infections/di, pc, mi, ur
30. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw,kf.
31. diagnostic accurac*.tw,kf.
32. culture*.tw,kf.
33. (detect* or predict* or screen*).tw,kf.
34. (dip slide* or dipslide* or dip stick* or dipstick*).tw,kf.
35. (micro-scopy or microscopy).tw,kf.
36. (microb* adj2 test*).tw,kf.
37. ((re-agent* or reagent) adj3 (strip* or test*)).tw,kf.

38. strip* test*.tw,kf.
39. urine test*.tw,kf.
40. (urinalys* or urine analys*).tw,kf.
41. uriscreen.tw,kf.
42. or/17-41 [Combined MeSH & text words for screening]
43. exp Pregnancy/
44. Pregnancy Complications, Infectious/
45. Pregnant Women/
46. Prenatal Care/
47. Prenatal Diagnosis/
48. (antenatal* or pre-natal* or prenatal*).mp.
49. (expect* adj (female? or mother? or wom#n)).tw,kf.
50. pregnan*.mp.
51. or/43-50 [Combined MeSH & text words for pregnancy]
52. and/16,42,51 [Combined searches for bacteriuria, screening & pregnancy]
53. Male/ not (Female/ and Male/)
54. 52 not 53 [Male only records excluded]
55. exp Animals/ not (exp Animals/ and Humans/)
56. 54 not 55 [Animal only records excluded]
57. (comment or editorial or news or newspaper article).pt.
58. (letter not (letter and randomized controlled trial)).pt.
59. 56 not (57 or 58) [Opinion pieces excluded]
60. case reports.pt.
61. 59 not 60 [Case reports excluded]
62. limit 61 to (english or french)
63. remove duplicates from 62

Appendix 2. Methods for Integrating Existing Systematic Reviews into New Reviews

One or more systematic reviews may exist that align with one or more key questions (KQs) of the reviews undertaken to inform CTFPHC guidelines. The CTFPHC and ERSCs have considered the manner in which new reviews conducted for CTFPHC guidelines can benefit from efficiencies by incorporating existing systematic reviews, while maintaining methodological rigor in their own systematic review conduct, closely aligning existing reviews within their review scope (i.e., inclusion/exclusion criteria), and maintaining consistency with other CTFPHC Methods. They have based their approach on work conducted by a methods working group composed of investigators from the Evidence-based Practice Center Program funded by the U.S. Agency for Healthcare Research and Quality.[1,2] A summary of the way the ERSCs will operationalize the 12 AHRQ recommendations (Box 1) to meet their needs is outlined below. This approach differs from situations when "updating" a single existing systematic review is deemed suitable, that is, in some cases a high-quality review will be used to answer one or more of the CTFPHC KQs in entirety, usually without revisions to the review's scope, search for evidence (apart from updating to present), methodological quality/risk of bias assessments, data extraction, or data analysis.

Summary of CTFPHC Approach

The recommendations developed by AHRQ (Box 1) will serve as an overall framework for ERSC reviews, although in most cases existing systematic reviews will be used to build efficiencies in discrete steps within the review process—mainly search and selection of literature, and data extraction—which will not generally include refinement of the scope or data analysis and interpretation. Moreover, we will not in most circumstances include a systematic review itself as a study design for inclusion (unless the intention is to specifically conduct an overview of reviews). The ability to use any given systematic review will largely depend on how it aligns with the CTFPHC review's scope (PICOTS). A further primary consideration will be the comprehensiveness of its search strategy and reporting of literature flow. It is important to note that some CTFPHC reviews need to be complex with multiple stages (e.g., a review of screening effectiveness for patient-important benefits and harms may require including evidence on indirect evidence of test accuracy and treatment) such that existing systematic reviews may exist for one or more discrete stages but not for others. Some key points on the operationalization, and minor revision, by the ERSCs of these recommendations are provided below.

1. **Choosing systematic reviews**: Following the identification of relevant reviews (a search for systematic reviews may be undertaken for some topics), the evidence for each will be mapped to the PICOTS elements and the quality of the review will be assessed (e.g., using the AMSTAR tool which has been evaluated and found effective to discriminate reviews with high and low quality of methods and reporting).[3] Some of the CTFPHC KQs may only have a single existing systematic review for possible incorporation, while others may have more than one; if suitable, a decision between systematic reviews will be based on methodological quality, comprehensiveness and quality of its literature search and reporting (e.g., assessed using PRESS checklist), comprehensiveness of reporting on included studies, and the best fit within the CTFPHC scope and methods. In some cases two or more reviews may be integrated because, together, they capture the full scope of the CTFPHC KQ(s). Rationale will be provided for choices made.

Note: If no review is deemed a good fit for purpose for integration (i.e., de novo process all together appears to be best option) we will at minimum examine available reviews for their search strategies (to ensure that our search strategies are comprehensive) and review their reference lists for identification of studies.

2. **Searching**: Various strategies will be considered. If one or more reviews are fit for purpose (but do not meet criteria for classification as a systematic review update) and cover a scope that is *very similar or broader* than the CTFPHC topic, we may update the search(es) if the last search date was prior to 6 months before commencing our review. When there are multiple reviews being considered, updating the literature to present may involve a new comprehensive search strategy to identify studies published after the date of the earliest existing review; this may reduce complexities when trying to implement, document, and remove duplicates from multiple searches. Alternatively, if the scope of the existing review(s) is *narrower* (e.g., missing an element in PICOTS) or the search *deemed sub-optimal in some manner* (e.g., missing key terms, additional database viewed as highly relevant) we may re-run the existing review's search concurrent with an original (e.g., broader) search and remove the citations previously screened for the other review. If more appropriate, we may update the other review's search and use a new search for the missing PICO element(s) (e.g., one additional intervention) for a longer time period to meet our timeframe. In cases where we feel screening excluded studies lists is appropriate we will also undertake this. Careful consideration will be used to ensure a comprehensive search is conducted regardless of approach taken; moreover, the ERSC librarians will help determine on a case-by-case basis what approach would be feasible for implementation to ensure aims of building efficiencies are possible.
3. **Screening and selection**: We will assess articles included in all relevant reviews (based on full text if necessary) to determine if they meet our inclusion criteria.
4. **Data extraction and methodological quality assessments**: We will consider incorporating the data on study and participant characteristics rather than extracting these data anew; we may also use the review author's risk of bias assessments if the tools/methods are consistent with CTFPHC methods. These steps will create efficiencies but because they are dependent on the quality of the systematic review and extent of reporting, the ERSC staff will verify the data on at least 5 to 10% of studies.[1]
5. **Data analysis**: We will consider using quantitative outcome data from reviews (with verification), but will not typically use meta-analyses or quality (GRADE) assessments of existing reviews.
6. **Reporting**: Transparent reporting of all integration steps used will be included in the evidence review report.

Box 1. Recommendations developed by AHRQ EPCs*[1,2]

*Strength of evidence refers to AHRQ's slightly modified approach to the GRADE quality of evidence approach

1. Existing reviews should be confirmed as systematic reviews through the application of a minimum set of eligibility criteria. We propose that the minimum eligibility criteria for systematic reviews include an explicit and adequate search, application of predefined eligibility criteria to select studies, risk of bias assessment for included studies, and synthesis of results.
2. Criteria to assess the relevance, in terms of question elements and currency, and quality of existing systematic reviews under consideration for inclusion in reviews should be predefined.
3. The quality of relevant existing systematic reviews should be assessed in an explicit manner with a minimum set of quality criteria that include search of multiple sources, use of a generally accepted tool for risk of bias assessment, and sufficient information to assess the strength of the body of evidence that includes the major domains of risk of bias, directness, consistency, precision, and reporting bias.
4. The risk of bias assessments from the existing systematic review may be used when the review described an explicit process, including the use of a tool or method that is compatible with the approach of the current review and that assessed the key sources of potential bias.
5. We suggest that risk of bias assessment be repeated in a sample of studies from an existing review under consideration for inclusion in a new review to confirm concordance with current review team approach.
6. We recommend that at a minimum, reviews should narratively describe findings of the prior review(s), including the number and types of studies included, and the overall findings.
7. We recommend that newly identified studies be clearly distinguished from studies in the existing review(s) when presented in the narrative and any tables (eg, separate tables).
8. Summary tables should include sufficient information to support ratings for overall strength of evidence, including ratings for individual strength of evidence domains (study limitations, consistency, precision, directness, reporting bias). The strength of evidence ratings should be based on the underlying primary evidence, not the number or quality of existing systematic reviews.
9. Using strength of evidence domains as a framework (study limitations, consistency, precision, directness, and reporting bias), review authors should consider how new evidence would change estimates of effect or ratings for strength of evidence. A new quantitative synthesis (ie, pooled estimate) is needed if new studies would change conclusions or strength of evidence judgements, or to obtain a more precise or more up-to-date estimate.
10. In cases where the existing systematic review(s) did not complete strength of evidence grading for a comparison and outcome of interest, the strength of evidence should be assessed for the body of evidence, considering primary studies from prior review(s) and any new studies identified.
11. In cases where no new studies are added to the body of evidence, the strength of evidence assessment from the existing systematic review may be used if conducted using an acceptable grading approach consistent with current review context. In these cases, we suggest that the overall strength of evidence assessment be reviewed, considering the strength of evidence domains, to confirm consistency with current review team assessments.
12. In cases where new studies are added to the body of evidence, the strength of evidence may need to be reassessed on the basis of all studies/evidence.

Appendix 2 References

1. Robinson KA, Chou R, Berkman ND, et al. Integrating bodies of evidence: existing systematic reviews and primary studies. Methods Guide for Effectiveness and Comparative Effectiveness Reviews [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Feb.

2. Robinson KA, Chou R, Berkman ND, et al. Twelve recommendations for integrating existing systematic reviews into new reviews: EPC guidance. J Clin Epidemiol. 2016 Feb;70:38-44. PMID: 26261004.

3. Foisy M, Hartling L. Challenges and considerations involved in using AMSTAR in overviews of reviews. 22nd Cochrane Colloquium. Hyderabad (India); 2014 Sept 21-26.

Supplement 2. Search Strategy

KQ1: Screening Effectiveness
Database: Ovid Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Date Searched: 13 June 2016
Records Retrieved: 1437

1. Asymptomatic Infections/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
2. Bacteriuria/
3. exp Cystitis/
4. Dysuria/
5. Pyelonephritis/
6. Urinary Tract Infections/
7. bacilluria*.tw,kf.
8. bacteriuria*.tw,kf.
9. cystiti*.tw,kf.
10. (cysto-pyeliti* or cystopyeliti*).tw,kf.
11. dysuria*.tw,kf.
12. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw,kf.
13. (pyelo-cystiti* or pyelocystiti*).tw,kf.
14. (pyelo-nephriti* or pyelonephriti*).tw,kf.
15. (UTI or UTIs).tw,kf.
16. or/1-15 [Combined MeSH & text words for bacteriuria]
17. Antibody-Coated Bacteria Test, Urinary/
18. *Bacteriuria/di, pc, mi, ur
19. exp *Cystitis/di, pc, mi, ur
20. Mass Screening/
21. Microbial Sensitivity Tests/
22. Microscopy/
23. Predictive Value of Tests/
24. *Pyelonephritis/di, pc, mi, ur
25. Reagent Kits, Diagnostic/
26. Reagent Strips/
27. "Sensitivity and Specificity"/
28. Urinalysis/
29. *Urinary Tract Infections/di, pc, mi, ur
30. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw,kf.
31. diagnostic accurac*.tw,kf.
32. culture*.tw,kf.
33. (detect* or predict* or screen*).tw,kf.
34. (dip slide* or dipslide* or dip stick* or dipstick*).tw,kf.
35. (micro-scopy or microscopy).tw,kf.
36. (microb* adj2 test*).tw,kf.
37. ((re-agent* or reagent) adj3 (strip* or test*)).tw,kf.
38. strip* test*.tw,kf.
39. urine test*.tw,kf.

40. (urinalys* or urine analys*).tw,kf.
41. uriscreen.tw,kf.
42. or/17-41 [Combined MeSH & text words for screening]
43. exp Pregnancy/
44. Pregnancy Complications, Infectious/
45. Pregnant Women/
46. Prenatal Care/
47. Prenatal Diagnosis/
48. (antenatal* or pre-natal* or prenatal*).mp.
49. (expect* adj (female? or mother? or wom#n)).tw,kf.
50. pregnan*.mp.
51. or/43-50 [Combined MeSH & text words for pregnancy]
52. and/16,42,51 [Combined searches for bacteriuria, screening & pregnancy]
53. Male/ not (Female/ and Male/)
54. 52 not 53 [Male only records excluded]
55. exp Animals/ not (exp Animals/ and Humans/)
56. 54 not 55 [Animal only records excluded]
57. (comment or editorial or news or newspaper article).pt.
58. (letter not (letter and randomized controlled trial)).pt.
59. 56 not (57 or 58) [Opinion pieces excluded]
60. case reports.pt.
61. 59 not 60 [Case reports excluded]
62. limit 61 to (english or french)
63. remove duplicates from 62

KQ1: Screening Effectiveness
Database: Ovid Embase 1974 to 2016 Week 24
Date Searched: 13 June 2016
Records Retrieved: 1613

1. acute pyelonephritis/
2. asymptomatic bacteriuria/
3. asymptomatic infection/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
4. bacteriuria/
5. exp cystitis/
6. dysuria/
7. kidney infection/
8. pyelonephritis/
9. urinary tract infections/
10. bacilluria*.tw.
11. bacteriuria*.tw.
12. cystiti*.tw.
13. (cysto-pyeliti* or cystopyeliti*).tw.
14. dysuria*.tw.
15. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw.
16. (pyelo-cystiti* or pyelocystiti*).tw.

17. (pyelo-nephriti* or pyelonephriti*).tw.
18. (UTI or UTIs).tw.
19. or/1-18 [Combined Emtree & text words for bacteriuria]
20. *asymptomatic bacteriuria/di, pc
21. *acute pyelonephritis/di, pc
22. *bacteriuria/di, pc
23. exp *cystitis/di, pc
24. diagnostic kit/
25. fluorescent antibody technique/
26. *kidney infection/di, pc
27. mass screening/
28. microbial sensitivity test/
29. microscopy/
30. predictive value/
31. *pyelonephritis/di, pc
32. "sensitivity and specificity"/
33. screening/
34. test strip/
35. exp urinalysis/
36. *urinary tract infection/di, pc
37. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw.
38. diagnostic accurac*.tw.
39. culture*.tw.
40. (detect* or predict* or screen*).tw.
41. (dip slide* or dipslide* or dip stick* or dipstick*).tw.
42. (micro-scopy or microscopy).tw.
43. (microb* adj2 test*).tw.
44. ((re-agent* or reagent) adj3 (strip* or test*)).tw.
45. strip* test*.tw.
46. urine test*.tw.
47. (urinalys* or urine analys*).tw.
48. uriscreen.tw.
49. or/20-48 [Combined Emtree & text words for screening]
50. exp pregnancy/
51. pregnancy complication/
52. pregnant woman/
53. prenatal care/
54. prenatal diagnosis/
55. prenatal screening/
56. (antenatal* or pre-natal* or prenatal*).mp.
57. (expect* adj (female? or mother? or wom#n)).tw.
58. pregnan*.mp.
59. or/50-58 [Combined Emtree & text words for pregnancy]
60. and/19,49,59 [Combined Emtree & text words for pregnancy]
61. Male/ not (Female/ and Male/)
62. 60 not 61 [Male only records excluded]
63. animals/ not (animals/ and humans/)
64. 62 not 63 [Animal only records excluded]

65. (conference* or editorial or letter).pt.
66. 64 not 65 [Excluded publication types – RF note: will search conference proceedings separately with different strategy]
67. case report/ or case report*.ti.
68. 66 not 67 [Case reports excluded]
69. limit 68 to (english or french)
70. remove duplicates from 69

KQ1: Screening Effectiveness
Database: Wiley Cochrane Library
Date Searched: 13 June 2016
Records Retrieved: 11 in Cochrane Database of Systematic Reviews
Records Retrieved: 1 in Database of Abstracts of Reviews of Effects (DARE)
Records Retrieved: 112 in Cochrane Central Register of Controlled Trials (CENTRAL)
Records Retrieved: 1 in Health Technology Assessment Database

#1 [mh ^"Asymptomatic Infections"] and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*):ti,ab,kw
#2 [mh ^Bacteriuria]
#3 [mh Cystitis]
#4 [mh ^Dysuria]
#5 [mh ^Pyelonephritis]
#6 [mh ^"Urinary Tract Infections"]
#7 bacilluria*:ti,ab,kw
#8 bacteriuria*:ti,ab,kw
#9 cystiti*:ti,ab,kw
#10 (cysto-pyeliti* or cystopyeliti*):ti,ab,kw
#11 dysuria*:ti,ab,kw
#12 (infection* near/2 (bladder* or genitourin* or kidney* or urin* or urogenita*)):ti,ab,kw
#13 (pyelo-cystiti* or pyelocystiti*):ti,ab,kw
#14 (pyelo-nephriti* or pyelonephriti*):ti,ab,kw
#15 (UTI or UTIs):ti,ab,kw
#16 {or #1-#15}
#17 [mh ^"Antibody-Coated Bacteria Test, Urinary"]
#18 [mh ^Bacteriuria [mj]/DI,PC,MI,UR]
#19 [mh Cystitis [mj]/DI,PC,MI,UR]
#20 [mh ^"Mass Screening"]
#21 [mh ^"Microbial Sensitivity Tests"]
#22 [mh ^Microscopy]
#23 [mh ^"Predictive Value of Tests"]
#24 [mh ^Pyelonephritis [mj]/DI,PC,MI,UR]
#25 [mh "Reagent Kits, Diagnostic"]
#26 [mh "Reagent Strips"]
#27 [mh ^"Sensitivity and Specificity"]
#28 [mh ^Urinalysis]
#29 [mh ^"Urinary Tract Infections" [mj]/DI,PC,MI,UR]

#30 ((accurac* or diagnostic) near/5 (algorithm* or test*)):ti,ab,kw
#31 "diagnostic accurac*":ti,ab,kw
#32 culture*:ti,ab,kw
#33 (detect* or predict* or screen*):ti,ab,kw
#34 ("dip slide*" or dipslide* or "dip stick*" or dipstick*):ti,ab,kw
#35 (micro-scopy or microscopy):ti,ab,kw
#36 (microb* near/2 test*):ti,ab,kw
#37 ((re-agent* or reagent) near/3 (strip* or test*)):ti,ab,kw
#38 "strip* test*":ti,ab,kw
#39 "urine test*":ti,ab,kw
#40 (urinalys* or "urine analys*"):ti,ab,kw
#41 uriscreen:ti,ab,kw
#42 {or #17-#41}
#43 [mh Pregnancy]
#44 [mh ^"Pregnancy Complications, Infectious"]
#45 [mh ^"Pregnant Women"]
#46 [mh ^"Prenatal Care"]
#47 [mh ^"Prenatal Diagnosis"]
#48 (antenatal* or pre-natal* or prenatal*):ti,ab,kw
#49 (expect* near/1 (female* or mother* or wom?n)):ti,ab,kw
#50 pregnan*:ti,ab,kw
#51 {or #43-#50}
#52 {and #16, #42, #51}

KQ1: Screening Effectiveness
Database: CINAHL Plus with Full Text (1937 to the present) via EBSCOhost
Date Searched: 13 June 2016
Records Retrieved: 249

S1. (MH "Bacteriuria")
S2. (MH "Cystitis+")
S3. (MH "Dysuria")
S4. (MH "Pyelonephritis")
S5. (MH "Urinary Tract Infections")
S6. bacilluria*
S7. bacteriuria*
S8. cystiti*
S9. "cysto-pyeliti*" or cystopyeliti*
S10. dysuria*
S11. (infection* N2 (bladder* or genitourin* or kidney* or urin* or urogenita*))
S12. "pyelo-cystiti*" or pyelocystiti*
S13. "pyelo-nephriti*" or pyelonephriti*
S14. UTI or UTIs
S15. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16. (MM "Bacteriuria/DI/PC/MI/UR")
S17. (MM "Cystitis+/DI/MI/PC/UR")
S18. (MH "Fluorescent Antibody Technique")

S19. (MH "Health Screening")
S20. (MH "Microbial Culture and Sensitivity Tests")
S21. (MH "Microscopy")
S22. (MH "Predictive Value of Tests")
S23. (MM "Pyelonephritis/DI/PC/MI/UR")
S24. (MH "Reagent Kits, Diagnostic+")
S25. (MH "Sensitivity and Specificity")
S26. (MH "Urinalysis")
S27. (MM "Urinary Tract Infections/DI/PC/MI/UR")
S28. (accurac* or diagnostic) N5 (algorithm* or test*)
S29. "diagnostic accurac*"
S30. culture*
S31. detect* or predict* or screen*
S32. "dip slide*" or dipslide* or "dip stick*" or dipstick*
S33. "micro-scopy" or microscopy
S34. microb* N2 test*
S35. ("re-agent*" or reagent) N3 (strip* or test*)
S36. "strip* test*"
S37. "urine test*"
S38. urinalys* or "urine analys*"
S39. uriscreen
S40. S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S41. (MH "Expectant Mothers")
S42. (MH "Pregnancy+")
S43. (MH "Pregnancy Complications, Infectious")
S44. (MH "Prenatal Care")
S45. (MH "Prenatal Diagnosis")
S46. antenatal* or "pre-natal*" or prenatal*
S47. expect* N1 (female? or mother? or wom?n)
S48. pregnan*
S49. S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48
S50. S15 AND S40 AND S49
S51. MH "Male" NOT ((MH "Female") AND (MH "Male"))
S52. S50 NOT S51
S53. ((MH "Vertebrates+") NOT MH Human)
S54. S52 NOT S53
S55. Limiters - Publication Type: Anecdote, Case Study, Commentary, Editorial, Letter
S56. S54 NOT S55
S57. S56 Narrow by Language: - english [RF: No French records in results to include]

KQ1: Screening Effectiveness
Database: PubMed via NCBI Entrez (1946 to Present)
Date Searched: 14 June 2016
Records Retrieved: 1246

(((((("asymptomatic infections"[mh] AND (("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields]) OR ("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields] OR "bacteriurias"[All Fields]) OR ("urinary bladder"[MeSH Terms] OR ("urinary"[All Fields] AND "bladder"[All Fields]) OR "urinary bladder"[All Fields] OR "bladder"[All Fields]) OR ("cystitis"[MeSH Terms] OR "cystitis"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields]) OR ("pyelocystitis"[MeSH Terms] OR "pyelocystitis"[All Fields]) OR ("pyelonephritis"[MeSH Terms] OR "pyelonephritis"[All Fields]) OR ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields] OR "urinary"[All Fields]) OR ("urine"[Subheading] OR "urine"[All Fields] OR "urine"[MeSH Terms]) OR UTI[all] OR ("urinary tract infections"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "urinary tract infections"[All Fields] OR "utis"[All Fields]))) OR "bacteriuria"[MeSH Terms:noexp] OR "cystitis"[MeSH Terms] OR "dysuria"[MeSH Terms:noexp] OR "pyelonephritis"[MeSH Terms:noexp] OR "Urinary Tract Infections"[mh:noexp] OR bacilluria[tiab] OR bacteriuria[tiab] OR bacteriurias[tiab] OR "bladder infection"[tiab] OR "bladder infections"[tiab] OR cystitis[tiab] OR cystopyelitis[tiab] OR dysuria[tiab] OR "genito-urinary infection"[tiab] OR "genitourinary infection"[tiab] OR "genito-urinary infections"[tiab] OR "genitourinary infections"[tiab] OR "kidney infection"[tiab] OR "kidney infections"[tiab] OR "pyelo-nephritis"[tiab] OR pyelocystitis[tiab] OR pyelonephritis[tiab] OR "urinary infection"[tiab] OR "urinary infections"[tiab] OR "urogenital infection"[tiab] OR "urogenital infections"[tiab] OR UTI[tiab] OR UTIs[tiab]) AND ("Antibody-Coated Bacteria Test, Urinary"[mh] OR "Bacteriuria/diagnosis"[Majr] OR "Bacteriuria/prevention and control"[Majr] OR ("bacteriuria/microbiology"[Mesh Terms] AND Majr[All Fields]) OR "Bacteriuria/urine"[Majr] OR "Cystitis/diagnosis"[Majr] OR "Cystitis/prevention and control"[Majr] OR "Cystitis/microbiology"[Majr] OR "Cystitis/urine"[Majr] OR "Mass Screening"[mh:noexp] OR "Microbial Sensitivity Tests"[mh:noexp] OR "Microscopy"[mh:noexp] OR "Predictive Value of Tests"[mh:noexp] OR "Pyelonephritis/diagnosis"[Majr] OR "Pyelonephritis/prevention and control"[Majr] OR "Pyelonephritis/microbiology"[Majr] OR "Pyelonephritis/urine"[Majr] OR "Reagent Kits, Diagnostic"[mh:noexp] OR "Reagent Strips"[mh:noexp] OR "Sensitivity and Specificity"[mh:noexp] OR "Urinalysis"[mh:noexp] OR "Urinary Tract Infections/diagnosis"[Majr] OR "Urinary Tract Infections/prevention and control"[Majr] OR "Urinary Tract Infections/microbiology"[Majr] OR "Urinary Tract Infections/urine"[Majr] OR detect[tiab] OR detected[tiab] OR detection[tiab] OR detecting[tiab] OR detects[tiab] OR "diagnostic accuracy"[tiab] OR "diagnostic algorithm"[tiab] OR "dip slide"[tiab] OR "dip slides"[tiab] OR "dip stick"[tiab] OR "dip sticks"[tiab] OR dipslide[tiab] OR dipslides[tiab] OR dipstick[tiab] OR dipsticks[tiab] OR culture[tiab] OR cultures[tiab] OR "diagnostic test"[tiab] OR "diagnostic tests"[tiab] OR "microbial test"[tiab] OR "microbial tests"[tiab] OR microscopy[tiab] OR predict[tiab] OR predicted[tiab] OR prediction[tiab] OR predicting[tiab] OR predicts[tiab] OR "reagent strip"[tiab] OR "reagent strips"[tiab] OR "reagent test"[tiab] OR "reagent testing"[tiab] OR "reagent tests"[tiab] OR screen[tiab] OR screened[tiab] OR screening[tiab] OR screens[tiab] OR "strip test"[tiab] OR "strip tests"[tiab] OR "strip testing"[tiab] OR "test accuracy"[tiab] OR urinalyses[tiab] OR urinalysis[tiab] OR "urine analyses"[tiab] OR "urine analysis"[tiab] OR "urine test"[tiab] OR "urine tested"[tiab] OR "urine testing"[tiab] OR "urine tests"[tiab] OR uriscreen[tiab]) AND ("Pregnancy"[mh] OR "Pregnancy Complications, Infectious"[mh:noexp] OR "Pregnant Women"[mh:noexp] OR "Prenatal Care"[mh:noexp] OR "Prenatal Diagnosis"[mh:noexp] OR antenatal[tiab] OR "pre-natal"[tiab] OR prenatal[tiab] OR "expectant mother"[tiab] OR "expectant mothers"[tiab] OR "expecting mothers"[tiab] OR "expecting mothers"[tiab] OR "expectant woman"[tiab] OR "expectant women"[tiab] OR "expecting women"[tiab] OR pregnancies[tiab] OR pregnancy[tiab] OR pregnant[tiab])) NOT ("Male"[mh] NOT ("Female"[mh] AND "Male"[mh]))) NOT (((Animals[MESH] OR Animal Experimentation[MESH] OR "Models, Animal"[MESH] OR Vertebrates[MESH]) NOT (Humans[MESH] OR Human

experimentation[MESH])) OR (((animals[tiab] OR animal model[tiab] OR rat[tiab] OR rats[tiab] OR mouse[tiab] OR mice[tiab] OR rabbit[tiab] OR rabbits[tiab] OR pig[tiab] OR pigs[tiab] OR porcine[tiab] OR swine[tiab] OR dog[tiab] OR dogs[tiab] OR hamster[tiab] OR hamsters[tiab] OR chicken[tiab] OR chickens[tiab] OR sheep[tiab]) AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])) NOT (human[ti] OR humans[ti] OR people[ti] OR children[ti] OR adults[ti] OR seniors[ti] OR patient[ti] OR patients[ti]))))) NOT (case reports[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR newspaper article[pt])
> limit to English or French

KQ2: Women's Outcome Valuation
Database: Ovid Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Date Searched: 4 July 2016
Records Retrieved: 2965

1. Asymptomatic Infections/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
2. Bacteriuria/
3. exp Cystitis/
4. Dysuria/
5. Pyelonephritis/
6. Urinary Tract Infections/
7. bacilluria*.tw,kf.
8. bacteriuria*.tw,kf.
9. cystiti*.tw,kf.
10. (cysto-pyeliti* or cystopyeliti*).tw,kf.
11. dysuria*.tw,kf.
12. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw,kf.
13. (pyelo-cystiti* or pyelocystiti*).tw,kf.
14. (pyelo-nephriti* or pyelonephriti*).tw,kf.
15. (UTI or UTIs).tw,kf.
16. or/1-15 [Combined MeSH & text words for bacteriuria]
17. Antibody-Coated Bacteria Test, Urinary/
18. *Bacteriuria/di, pc, mi, ur
19. exp *Cystitis/di, pc, mi, ur
20. Mass Screening/
21. Microbial Sensitivity Tests/
22. Microscopy/
23. Predictive Value of Tests/
24. *Pyelonephritis/di, pc, mi, ur
25. Reagent Kits, Diagnostic/
26. Reagent Strips/
27. "Sensitivity and Specificity"/
28. Urinalysis/
29. *Urinary Tract Infections/di, pc, mi, ur
30. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw,kf.
31. diagnostic accurac*.tw,kf.

32. culture*.tw,kf.
33. (detect* or predict* or screen*).tw,kf.
34. (dip slide* or dipslide* or dip stick* or dipstick*).tw,kf.
35. (micro-scopy or microscopy).tw,kf.
36. (microb* adj2 test*).tw,kf.
37. ((re-agent* or reagent) adj3 (strip* or test*)).tw,kf.
38. strip* test*.tw,kf.
39. urine test*.tw,kf.
40. (urinalys* or urine analys*).tw,kf.
41. uriscreen.tw,kf.
42. or/17-41 [Combined MeSH & text words for screening]
43. and/16,42 [Combined searches for ASB and screening]
44. Anti-Bacterial Agents/
45. Antibiotic Prophylaxis/
46. Anti-Infective Agents, Urinary/
47. Asymptomatic Infections/dt, th
48. *Bacteriuria/dt, th
49. Drug Therapy, Combination/
50. Norfloxacin/
51. exp Penicillins/
52. exp Sulfonamides/
53. *Urinary Tract Infections/dt, th
54. amoxicillin*.mp.
55. ampicillin*.mp.
56. (anti-bacteria* or antibacteria*).tw,kf.
57. (anti-biotic* or antibiotic*).tw,kf.
58. aztreonam*.mp.
59. cefadroxil*.mp.
60. cefepime*.mp.
61. ceftibuten*.mp.
62. ceftri?xone*.mp.
63. cefuroxime*.mp.
64. cephalexin*.mp.
65. cephalosporin*.mp.
66. cephradine*.mp.
67. clindamycin*.mp.
68. (co-trimoxazole* or cotrimoxazole*).mp.
69. cycloserine*.mp.
70. fosfomycin*.mp.
71. gentam#cin*.mp.
72. nalidixic acid*.mp.
73. nitrofurantoin*.mp.
74. penicillin*.mp.
75. piperacillin*.mp.
76. pivampicillin*.mp.
77. pivmecillinam*.mp.
78. sulfadimethoxine*.mp.
79. sulfadiazine*.mp.

80. sulfamethizole*.mp.
81. sulfamethoxazole*.mp.
82. sulfamethoxypyridazine*.mp.
83. sulfonamide*.mp.
84. sulphadimidine*.mp.
85. sulphonamide*.mp.
86. tetracycline*.mp.
87. vancomycin*.mp.
88. or/44-87 [Combined MeSH & text words for antibiotic treatment]
89. exp Pregnancy/
90. Pregnancy Complications, Infectious/
91. Pregnant Women/
92. Prenatal Care/
93. Prenatal Diagnosis/
94. (antenatal* or pre-natal* or prenatal*).mp.
95. (expect* adj (female? or mother? or wom#n)).tw,kf.
96. pregnan*.mp.
97. or/89-96 [Combined MeSH & text words for pregnancy]
98. and/88,97 [Combined searches for antibiotic treatment and pregnancy]
99. Choice Behavior/
100. *Consumer Behavior/
101. exp Consumer Participation/
102. Cooperative Behavior/
103. exp Decision Making/
104. Focus Groups/
105. Health Care Surveys/
106. exp Informed Consent/
107. Interviews as Topic/
108. Patient Acceptance of Health Care/
109. exp Patient Education as Topic/
110. Patient Participation/
111. Patient Preference/
112. Social Values/
113. "Surveys and Questionnaires"/
114. Treatment Refusal/
115. (15D* and (HRQoL or QoL or "quality of life")).mp.
116. ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or refus* or respons* or valuation or value? or valuing or view*) adj3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom#n)).tw,kf.
117. ((analys#s or valuation? or value? or valuing) adj3 (conjoint or contingent)).tw,kf.
118. (choice? adj2 (behavio?r* or discrete or experiment*)).tw,kf.
119. ((choice? or choos* or consent* or decision*) adj1 informed).tw,kf.
120. ((choice? or choos* or decision*) adj2 (made or make or makes or making or shar* or support*)).tw,kf.
121. (EQ 5D or EQ5D or EuroQoL 5D or EuroQoL5D).mp.
122. (focus group? or interview* or questionnaire? or survey*).tw,kf.
123. gambl*.tw,kf.

124. health utilit*.tw,kf.
125. HUI.tw,kf.
126. (multi?attribute or multi?criteria).tw,kf.
127. (preference? adj1 (elicit* or scor* or state*)).tw,kf.
128. prospect theor*.tw,kf.
129. (SF 12 or SF 36 or SF 6D or SF12 or SF36 or SF6D).mp.
130. (trade off? or tradeoff?).tw,kf.
131. (willing* adj2 pay*).tw,kf.
132. or/99-131 [Combined MeSH & text words for patient preferences & values]
133. and/43,132 [Combined searches for patient preferences & ASB screening]
134. and/98,132 [Combined searches for patient preferences & antibiotic treatment and pregnancy]
135. or/133-134 [Combined sets of patient preferences for ASB screening & patient preferences for antibiotic treatment in pregnancy]
136. Male/ not Female/
137. 135 not 136 [Male only records excluded]
138. exp Animals/ not (exp Animals/ and Humans/)
139. 137 not 138 [Animal only records excluded]
140. (comment or editorial or news or newspaper article).pt.
141. (letter not (letter and randomized controlled trial)).pt.
142. 139 not (140 or 141) [Opinion pieces excluded]
143. case reports.pt.
144. 142 not 143 [Case reports excluded]
145. limit 144 to (english or french)
146. remove duplicates from 145

KQ2: Women's Outcome Valuation
Database: Ovid Embase 1974 to 2016 Week 27
Date Searched: 4 July 2016
Records Retrieved: 3922

1. acute pyelonephritis/
2. asymptomatic bacteriuria/
3. asymptomatic infection/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
4. bacteriuria/
5. exp cystitis/
6. dysuria/
7. kidney infection/
8. pyelonephritis/
9. urinary tract infections/
10. bacilluria*.tw.
11. bacteriuria*.tw.
12. cystiti*.tw.
13. (cysto-pyeliti* or cystopyeliti*).tw.
14. dysuria*.tw.
15. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw.
16. (pyelo-cystiti* or pyelocystiti*).tw.

17. (pyelo-nephriti* or pyelonephriti*).tw.
18. (UTI or UTIs).tw.
19. or/1-18 [Combined Emtree & text words for bacteriuria]
20. *asymptomatic bacteriuria/di, pc
21. *acute pyelonephritis/di, pc
22. *bacteriuria/di, pc
23. exp *cystitis/di, pc
24. diagnostic kit/
25. fluorescent antibody technique/
26. *kidney infection/di, pc
27. mass screening/
28. microbial sensitivity test/
29. microscopy/
30. predictive value/
31. *pyelonephritis/di, pc
32. "sensitivity and specificity"/
33. screening/
34. test strip/
35. exp urinalysis/
36. *urinary tract infection/di, pc
37. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw.
38. culture*.tw.
39. (detect* or predict* or screen*).tw.
40. diagnostic accurac*.tw.
41. (dip slide* or dipslide* or dip stick* or dipstick*).tw.
42. (micro-scopy or microscopy).tw.
43. (microb* adj2 test*).tw.
44. ((re-agent* or reagent) adj3 (strip* or test*)).tw.
45. strip* test*.tw.
46. urine test*.tw.
47. (urinalys* or urine analys*).tw.
48. uriscreen.tw.
49. or/20-48 [Combined Emtree & text words for screening]
50. and/19,49 [Combined searches for ASB and screening]
51. antibiotic agent/
52. antibiotic prophylaxis/
53. antiinfective agent/
54. *asymptomatic bacteriuria/dt, th
55. *asymptomatic infection/dt, th
56. *bacteriuria/dt, th
57. exp *cystitis/dt, th
58. drug combination/
59. *kidney infection/dt, th
60. norfloxacin/
61. penicillin derivative/
62. *pyelonephritis/dt, th
63. sulfonamide/
64. urinary tract antiinfective agent/

65. *urinary tract infection/dt, th
66. amoxicillin*.mp.
67. ampicillin*.mp.
68. (anti-bacteria* or antibacteria*).tw.
69. (anti-biotic* or antibiotic*).tw.
70. aztreonam*.mp.
71. cefadroxil*.mp.
72. cefepime*.mp.
73. ceftibuten*.mp.
74. ceftri?xone*.mp.
75. cefuroxime*.mp.
76. cephalexin*.mp.
77. cephalosporin*.mp.
78. cephradine*.mp.
79. clindamycin*.mp.
80. (co-trimoxazole* or cotrimoxazole*).mp.
81. cycloserine*.mp.
82. fosfomycin*.mp.
83. gentam#cin*.mp.
84. nalidixic acid*.mp.
85. nitrofurantoin*.mp.
86. penicillin*.mp.
87. piperacillin*.mp.
88. pivampicillin*.mp.
89. pivmecillinam*.mp.
90. sulfadimethoxine*.mp.
91. sulfadiazine*.mp.
92. sulfamethizole*.mp.
93. sulfamethoxazole*.mp.
94. sulfamethoxypyridazine*.mp.
95. sulfonamide*.mp.
96. sulphadimidine*.mp.
97. sulphonamide*.mp.
98. tetracycline*.mp.
99. vancomycin*.mp.
100. or/51-99 [Combined Emtree & text words for antibiotic treatment]
101. exp pregnancy/
102. pregnancy complication/
103. pregnant woman/
104. prenatal care/
105. prenatal diagnosis/
106. prenatal screening/
107. (antenatal* or pre-natal* or prenatal*).mp.
108. (expect* adj (female? or mother? or wom#n)).tw.
109. pregnan*.mp.
110. or/101-109 [Combined Emtree & text words for pregnancy]
111. and/100,110 [Combined searches for antibiotic treatment and pregnancy]
112. cooperation/

113. *consumer attitude/
114. exp decision making/
115. health care survey/
116. informed consent/
117. exp interview/
118. exp patient attitude/
119. patient education/
120. exp questionnaire/
121. social psychology/
122. treatment refusal/
123. (15D* and (HRQoL or QoL or "quality of life")).mp.
124. ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or refus* or respons* or valuation or value? or valuing or view*) adj3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom#n)).tw,kw.
125. (choice? adj2 (behavio?r* or discrete or experiment*)).tw,kw.
126. ((choice? or choos* or consent* or decision*) adj1 informed).tw,kw.
127. ((choice? or choos* or decision*) adj2 (made or make or makes or making or shar* or support*)).tw,kw.
128. (EQ 5D or EQ5D or EuroQoL 5D or EuroQoL5D).mp.
129. (focus group? or interview* or questionnaire? or survey*).tw,kw.
130. gambl*.tw,kw.
131. health utilit*.tw,kw.
132. HUI.tw,kw.
133. (multi?attribute or multi?criteria).tw,kw.
134. (preference? adj1 (elicit* or scor* or state*)).tw,kw.
135. prospect theor*.tw,kw.
136. (SF 12 or SF 36 or SF 6D or SF12 or SF36 or SF6D).mp.
137. (trade off? or tradeoff?).tw,kw.
138. (willing* adj2 pay*).tw,kw.
139. or/112-138 [Combined Emtree & text words for patient preferences & values]
140. and/50,139 [Combined searches for patient preferences & ASB screening]
141. and/111,139 [Combined searches for patient preferences & antibiotic treatment and pregnancy]
142. or/140-141 [Combined sets of patient preferences for ASB screening & patient preferences for antibiotic treatment in pregnancy]
143. Male/ not (Female/ and Male/)
144. 142 not 143 [Male only records excluded]
145. animals/ not (animals/ and humans/)
146. 144 not 145 [Animal only records excluded]
147. (conference* or editorial or letter).pt.
148. 146 not 147 [Excluded publication types – RF note: will search conference proceedings separately with different strategy]
149. case report/ or case report*.ti.
150. 148 not 149 [Case reports excluded]
151. limit 150 to (english or french)
152. remove duplicates from 151

KQ2: Women's Outcome Valuation
Database: Wiley Cochrane Library
Date Searched: 5 July 2016
Records Retrieved: 45 in Cochrane Database of Systematic Reviews
Records Retrieved: 1 in Database of Abstracts of Reviews of Effects (DARE)
Records Retrieved: 321 in Cochrane Central Register of Controlled Trials (CENTRAL)
Records Retrieved: 4 in Cochrane Methodology Register
Records Retrieved: 14 in Economic Evaluations Database

#1 [mh ^"Asymptomatic Infections"] and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*):ti,ab,kw
#2 [mh ^Bacteriuria]
#3 [mh Cystitis]
#4 [mh ^Dysuria]
#5 [mh ^Pyelonephritis]
#6 [mh ^"Urinary Tract Infections"]
#7 bacilluria*:ti,ab,kw
#8 bacteriuria*:ti,ab,kw
#9 cystiti*:ti,ab,kw
#10 (cysto-pyeliti* or cystopyeliti*):ti,ab,kw
#11 dysuria*:ti,ab,kw
#12 (infection* near/2 (bladder* or genitourin* or kidney* or urin* or urogenita*)):ti,ab,kw
#13 (pyelo-cystiti* or pyelocystiti*):ti,ab,kw
#14 (pyelo-nephriti* or pyelonephriti*):ti,ab,kw
#15 (UTI or UTIs):ti,ab,kw
#16 {or #1-#15}
#17 [mh ^"Antibody-Coated Bacteria Test, Urinary"]
#18 [mh ^Bacteriuria [mj]/DI,PC,MI,UR]
#19 [mh Cystitis [mj]/DI,PC,MI,UR]
#20 [mh ^"Mass Screening"]
#21 [mh ^"Microbial Sensitivity Tests"]
#22 [mh ^Microscopy]
#23 [mh ^"Predictive Value of Tests"]
#24 [mh ^Pyelonephritis [mj]/DI,PC,MI,UR]
#25 [mh "Reagent Kits, Diagnostic"]
#26 [mh "Reagent Strips"]
#27 [mh ^"Sensitivity and Specificity"]
#28 [mh ^Urinalysis]
#29 [mh ^"Urinary Tract Infections" [mj]/DI,PC,MI,UR]
#30 ((accurac* or diagnostic) near/5 (algorithm* or test*)):ti,ab,kw
#31 "diagnostic accurac*":ti,ab,kw
#32 culture*:ti,ab,kw
#33 (detect* or predict* or screen*):ti,ab,kw
#34 ("dip slide*" or dipslide* or "dip stick*" or dipstick*):ti,ab,kw
#35 (micro-scopy or microscopy):ti,ab,kw
#36 (microb* near/2 test*):ti,ab,kw
#37 ((re-agent* or reagent) near/3 (strip* or test*)):ti,ab,kw

#38 "strip* test*":ti,ab,kw
#39 "urine test*":ti,ab,kw
#40 (urinalys* or "urine analys*"):ti,ab,kw
#41 uriscreen:ti,ab,kw
#42 {or #17-#41}
#43 #16 and #42
#44 [mh ^"Anti-Bacterial Agents"]
#45 [mh ^"Antibiotic Prophylaxis"]
#46 [mh ^"Anti-Infective Agents, Urinary"]
#47 [mh ^"Asymptomatic Infections"/DT,TH]
#48 [mh ^Bacteriuria [mj]/DT,TH]
#49 [mh ^"Drug Therapy, Combination"]
#50 [mh ^Norfloxacin]
#51 [mh Penicillins]
#52 [mh Sulfonamides]
#53 [mh ^"Urinary Tract Infections" [mj]/DT,TH]
#54 amoxicillin*:ti,ab,kw
#55 ampicillin*:ti,ab,kw
#56 ("anti-bacteria*" or antibacteria*):ti,ab,kw
#57 ("anti-biotic*" or antibiotic*):ti,ab,kw
#58 aztreonam*:ti,ab,kw
#59 cefadroxil*:ti,ab,kw
#60 cefepime*:ti,ab,kw
#61 ceftibuten*:ti,ab,kw
#62 ceftri?xone*:ti,ab,kw
#63 cefuroxime*:ti,ab,kw
#64 cephalexin*:ti,ab,kw
#65 cephalosporin*:ti,ab,kw
#66 cephradine*:ti,ab,kw
#67 clindamycin*:ti,ab,kw
#68 ("co-trimoxazole*" or cotrimoxazole*):ti,ab,kw
#69 cycloserine*:ti,ab,kw
#70 fosfomycin*:ti,ab,kw
#71 gentam?cin*:ti,ab,kw
#72 "nalidixic acid*":ti,ab,kw
#73 nitrofurantoin*:ti,ab,kw
#74 penicillin*:ti,ab,kw
#75 piperacillin*:ti,ab,kw
#76 pivampicillin*:ti,ab,kw
#77 pivmecillinam*:ti,ab,kw
#78 sulfadimethoxine*:ti,ab,kw
#79 sulfadiazine*:ti,ab,kw
#80 sulfamethizole*:ti,ab,kw
#81 sulfamethoxazole*:ti,ab,kw
#82 sulfamethoxypyridazine*:ti,ab,kw
#83 sulfonamide*:ti,ab,kw
#84 sulphadimidine*:ti,ab,kw
#85 sulphonamide*:ti,ab,kw

#86 tetracycline*:ti,ab,kw
#87 vancomycin*:ti,ab,kw
#88 {or #44-#87}
#89 [mh Pregnancy]
#90 [mh ^"Pregnancy Complications, Infectious"]
#91 [mh ^"Pregnant Women"]
#92 [mh ^"Prenatal Care"]
#93 [mh ^"Prenatal Diagnosis"]
#94 (antenatal* or "pre-natal*" or prenatal*):ti,ab,kw
#95 (expect* near/1 (female* or mother* or wom?n)):ti,ab,kw
#96 pregnan*:ti,ab,kw
#97 {or #89-#96}
#98 #88 and #97
#99 [mh ^"Choice Behavior"]
#100 [mh ^"Consumer Behavior" [mj]]
#101 [mh "Consumer Participation"]
#102 [mh ^"Cooperative Behavior"]
#103 [mh "Decision Making"]
#104 [mh ^"Focus Groups"]
#105 [mh ^"Health Care Surveys"]
#106 [mh "Informed Consent"]
#107 [mh ^"Interviews as Topic"]
#108 [mh ^"Patient Acceptance of Health Care"]
#109 [mh "Patient Education as Topic"]
#110 [mh ^"Patient Participation"]
#111 [mh ^"Patient Preference"]
#112 [mh ^"Social Values"]
#113 [mh ^"Surveys and Questionnaires"]
#114 [mh ^"Treatment Refusal"]
#115 (15D* and (HRQoL or QoL or "quality of life")):ti,ab,kw
#116 ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or refus* or respons* or valuation or value? or valuing or view*) near/3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom?n)):ti,ab,kw
#117 ((analys?s or valuation? or value? or valuing) near/3 (conjoint or contingent)):ti,ab,kw
#118 (choice? near/2 (behavio?r* or discrete or experiment*)):ti,ab,kw
#119 ((choice? or choos* or consent* or decision*) near/1 informed):ti,ab,kw
#120 ((choice? or choos* or decision*) near/2 (made or make or makes or making or shar* or support*)):ti,ab,kw
#121 ("EQ 5D" or EQ5D or "EuroQoL 5D" or EuroQoL5D):ti,ab,kw
#122 ("focus group?" or interview* or questionnaire? or survey*):ti,ab,kw
#123 gambl*:ti,ab,kw
#124 "health utilit*":ti,ab,kw
#125 HUI:ti,ab,kw
#126 ("multi-attribute" or "multi-criteria" or multiattribute or multicriteria):ti,ab,kw
#127 (preference? near/1 (elicit* or scor* or state*)):ti,ab,kw
#128 "prospect theor*":ti,ab,kw
#129 ("SF 12" or "SF 36" or "SF 6D" or SF12 or SF36 or SF6D):ti,ab,kw

#130 ("trade off?" or tradeoff?):ti,ab,kw
#131 (willing* near/2 pay*):ti,ab,kw
#132 {or #99-#131}
#133 #43 and #132
#134 #98 and #132
#135 #133 or #134

KQ2: Women's Outcome Valuation
Database: Ovid PsycINFO 1806 to June Week 5 2016
Date Searched: 5 July 2016
Records Retrieved: 113

1. Bacterial Disorders/ and (bladder* or genitourin* or kidney* or urin* or urogenita*).mp.
2. Infectious Disorders/ and (bladder* or genitourin* or kidney* or urin* or urogenita*).mp.
3. Urinary Function Disorders/ and infection*.mp.
4. Urogenital Disorders/ and infection*.mp.
5. bacilluria*.mp.
6. bacteriuria*.mp.
7. cystiti*.mp.
8. (cysto-pyeliti* or cystopyeliti*).mp.
9. dysuria*.mp.
10. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).mp.
11. (pyelo-cystiti* or pyelocystiti*).mp.
12. (pyelo-nephriti* or pyelonephriti*).mp.
13. (UTI or UTIs).mp.
14. or/1-13 [Combined subject headings & text words for bacteriuria]
15. Health Screening/
16. Screening/
17. Screening Tests/
18. Test Reliability/
19. exp Test Validity/
20. Urinalysis/
21. ((accurac* or diagnostic) adj5 (algorithm* or test*)).ti,ab.
22. diagnostic accurac*.ti,ab.
23. culture*.ti,ab.
24. (detect* or predict* or screen*).ti,ab.
25. (dip slide* or dipslide* or dip stick* or dipstick*).ti,ab.
26. (micro-scopy or microscopy).ti,ab.
27. (microb* adj2 test*).ti,ab.
28. ((re-agent* or reagent) adj3 (strip* or test*)).ti,ab.
29. strip* test*.ti,ab.
30. urine test*.ti,ab.
31. (urinalys* or urine analys*).ti,ab.
32. uriscreen.ti,ab.
33. or/15-32 [Combined subject headings & text words for screening]
34. and/14,33 [Combined searches for ASB and screening]
35. antibiotics/

36. penicillins/
37. amoxicillin*.mp.
38. ampicillin*.mp.
39. (anti-bacteria* or antibacteria*).mp.
40. (anti-biotic* or antibiotic*).mp.
41. aztreonam*.mp.
42. cefadroxil*.mp.
43. cefepime*.mp.
44. ceftibuten*.mp.
45. ceftri?xone*.mp.
46. cefuroxime*.mp.
47. cephalexin*.mp.
48. cephalosporin*.mp.
49. cephradine*.mp.
50. clindamycin*.mp.
51. (co-trimoxazole* or cotrimoxazole*).mp.
52. cycloserine*.mp.
53. fosfomycin*.mp.
54. gentam#cin*.mp.
55. nalidixic acid*.mp.
56. nitrofurantoin*.mp.
57. penicillin*.mp.
58. piperacillin*.mp.
59. pivampicillin*.mp.
60. pivmecillinam*.mp.
61. sulfadimethoxine*.mp.
62. sulfadiazine*.mp.
63. sulfamethizole*.mp.
64. sulfamethoxazole*.mp.
65. sulfamethoxypyridazine*.mp.
66. sulfonamide*.mp.
67. sulphadimidine*.mp.
68. sulphonamide*.mp.
69. tetracycline*.mp.
70. vancomycin*.mp.
71. or/35-70 [Combined subject headings & text words for antibiotic treatment]
72. adolescent pregnancy/
73. pregnancy/
74. prenatal care/
75. (antenatal* or pre-natal* or prenatal*).ti,ab.
76. (expect* adj (female? or mother? or wom#n)).ti,ab.
77. pregnan*.mp.
78. or/72-77 [Combined subject headings & text words for pregnancy]
79. and/71,78 [Combined searches for antibiotic treatment and pregnancy]
80. Choice Behavior/
81. Client Attitudes/
82. Client Participation/
83. Client Rights/

84. Cooperation/
85. Decision Making/
86. *Consumer Behavior/
87. Informed Consent/
88. Interviews/
89. Preferences/
90. Questionnaires/
91. Social Values/
92. Surveys/
93. Treatment Barriers/
94. Treatment Refusal/
95. (15D* and (HRQoL or QoL or "quality of life")).mp.
96. ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or respons* or valuation or value? or valuing or view*) adj3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom#n)).ti,ab.
97. ((analys#s or valuation? or value? or valuing) adj3 (conjoint or contingent)).ti,ab.
98. (choice? adj2 (behavio?r* or discrete or experiment*)).mp.
99. ((choice? or choos* or consent* or decision*) adj1 informed).ti,ab.
100. ((choice? or choos* or decision*) adj2 (made or make or makes or making or shar* or support*)).ti,ab.
101. (EQ 5D or EQ5D or EuroQoL 5D or EuroQoL5D).mp.
102. (focus group? or interview* or questionnaire? or survey*).ti,ab.
103. gambl*.ti,ab.
104. health utilit*.ti,ab.
105. HUI.mp.
106. (multi?attribute or multi?criteria).mp.
107. (preference? adj1 (elicit* or scor* or state*)).mp.
108. prospect theor*.ti,ab.
109. (SF 12 or SF 36 or SF 6D or SF12 or SF36 or SF6D).mp.
110. (trade off? or tradeoff?).ti,ab.
111. (willing* adj2 pay*).ti,ab.
112. or/80-111 [Combined subject & text words for patient preferences & values]
113. and/34,112 [Combined searches for patient preferences & ASB screening]
114. and/79,112 [Combined searches for patient preferences & antibiotic treatment and pregnancy]
115. or/113-114 [Combined sets of patient preferences for ASB screening & patient preferences for antibiotic treatment in pregnancy]
116. (boy* or male* or men).ti.
117. 115 not 116 [Male records excluded]
118. (case report* or comment* or editorial or letter).ti.
119. 117 not 118 [Opinion pieces & case reports excluded]
120. limit 119 to (english or french)
121. remove duplicates from 120

KQ2: Women's Outcome Valuation
Database: CINAHL Plus with Full Text (1937 to the present) via EBSCOhost
Date Searched: 5 July 2016

Records Retrieved: 872

S1. (MH "Bacteriuria")
S2. (MH "Cystitis+")
S3. (MH "Dysuria")
S4. (MH "Pyelonephritis")
S5. (MH "Urinary Tract Infections")
S6. bacilluria*
S7. bacteriuria*
S8. cystiti*
S9. "cysto-pyeliti*" or cystopyeliti*
S10. dysuria*
S11. (infection* N2 (bladder* or genitourin* or kidney* or urin* or urogenita*))
S12. "pyelo-cystiti*" or pyelocystiti*
S13. "pyelo-nephriti*" or pyelonephriti*
S14. UTI or UTIs
S15. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16. (MM "Bacteriuria/DI/PC/MI/UR")
S17. (MM "Cystitis+/DI/MI/PC/UR")
S18. (MH "Fluorescent Antibody Technique")
S19. (MH "Health Screening")
S20. (MH "Microbial Culture and Sensitivity Tests")
S21. (MH "Microscopy")
S22. (MH "Predictive Value of Tests")
S23. (MM "Pyelonephritis/DI/PC/MI/UR")
S24. (MH "Reagent Kits, Diagnostic+")
S25. (MH "Sensitivity and Specificity")
S26. (MH "Urinalysis")
S27. (MM "Urinary Tract Infections/DI/PC/MI/UR")
S28. (accurac* or diagnostic) N5 (algorithm* or test*)
S29. "diagnostic accurac*"
S30. culture*
S31. detect* or predict* or screen*
S32. "dip slide*" or dipslide* or "dip stick*" or dipstick*
S33. "micro-scopy" or microscopy
S34. microb* N2 test*
S35. ("re-agent*" or reagent) N3 (strip* or test*)
S36. "strip* test*"
S37. "urine test*"
S38. urinalys* or "urine analys*"
S39. uriscreen
S40. S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S41. S15 AND S40 [Combined searches for ASB and screening]
S42. (MH "Antibiotic Prophylaxis")
S43. (MH "Antibiotics")
S44. (MH "Antibiotics, Combined")
S45. (MH "Antiinfective Agents, Urinary+")

S46. (MM "Bacteriuria/DT/TH")
S47. (MH "Penicillins")
S48. (MH "Sulfonamides")
S49. (MM "Urinary Tract Infections/DT/TH")
S50. amoxicillin*
S51. ampicillin*
S52. ("anti-bacteria*" or antibacteria*)
S53. ("anti-biotic*" or antibiotic*)
S54. aztreonam*
S55. cefadroxil*
S56. cefepime*
S57. ceftibuten*
S58. ceftri?xone*
S59. cefuroxime*
S60. cephalexin*
S61. cephalosporin*
S62. cephradine*
S63. clindamycin*
S64. ("co-trimoxazole*" or cotrimoxazole*)
S65. cycloserine*
S66. fosfomycin*
S67. gentam?cin*
S68. "nalidixic acid*"
S69. nitrofurantoin*
S70. penicillin*
S71. piperacillin*
S72. pivampicillin*
S73. pivmecillinam*
S74. sulfadimethoxine*
S75. sulfadiazine*
S76. sulfamethizole*
S77. sulfamethoxazole*
S78. sulfamethoxypyridazine*
S79. sulfonamide*
S80. sulphadimidine*
S81. sulphonamide*
S82. tetracycline*
S83. vancomycin*
S84. S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83
S85. (MH "Expectant Mothers")
S86. (MH "Pregnancy+")
S87. (MH "Pregnancy Complications, Infectious")
S88. (MH "Prenatal Care")
S89. (MH "Prenatal Diagnosis")
S90. antenatal* or "pre-natal*" or prenatal*

S91. expect* N1 (female? or mother? or wom?n)
S92. pregnan*
S93. S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92
S94. S84 AND S93
S95. (MH "Consumer Participation")
S96. (MH "Consensus")
S97. (MH "Consent+")
S98. (MH "Cooperative Behavior")
S99. (MH "Decision Making")
S100. (MH "Decision Making, Patient")
S101. (MH "Dissent and Disputes+")
S102. (MH "Focus Groups")
S103. (MH "Interviews+")
S104. (MH "Patient Education")
S105. (MH "Quality of Health Care")
S106. (MH "Questionnaires+")
S107. (MH "Self Report")
S108. (MH "Social Values+")
S109. (MH "Surveys")
S110. (MH "Treatment Refusal")
S111. (15D* and (HRQoL or QoL or "quality of life"))
S112. ((accept* or consider* or choice* or choos* or chose* or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective* or prefer* or refus* or respons* or valuation or value* or valuing or view*) N3 (citizen* or client* or consumer* or female* or male* or men or patient* or public or "stake-holder*" or stakeholder* or user* or wom?n))
S113. ((analys?s or valuation* or value* or valuing) N3 (conjoint or contingent))
S114. (choice* N2 (behavio* or discrete or experiment*))
S115. ((choice* or choos* or consent* or decision*) N1 informed)
S116. ((choice* or choos* or decision*) N2 (made or make or makes or making or shar* or support*))
S117. ("EQ 5D" or EQ5D or "EuroQoL 5D" or EuroQoL5D)
S118. ("focus group*" or interview* or questionnaire* or survey*)
S119. gambl*
S120. "health utilit*"
S121. HUI
S122. ("multi-attribute" or "multi-criteria" or multiattribute or multicriteria)
S123. (preference* N1 (elicit* or scor* or state*))
S124. "prospect theor*"
S125. ("SF 12" or "SF 36" or "SF 6D" or SF12 or SF36 or SF6D)
S126. ("trade off*" or tradeoff*)
S127. (willing* N2 pay*)
S128. S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127
S129. S41 AND S128
S130. S94 AND S128
S131. S129 OR S130
S132. MH "Male" NOT ((MH "Female") AND (MH "Male"))
S133. S131 NOT S132

S134. ((MH "Vertebrates+") NOT MH Human)
S135. S133 NOT S134
S136. Limiters - Publication Type: Anecdote, Case Study, Commentary, Editorial, Letter
S137. S135 NOT S136
S138. S135 NOT S136 Narrow by Language: - english [RF: No French records in results to include]

KQ2: Women's Outcome Valuation
Database: PubMed via NCBI Entrez (1946 to Present)
Date Searched: 5 July 2016
Records Retrieved: 65

((((((("asymptomatic infections"[mh] AND (("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields]) OR ("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields] OR "bacteriurias"[All Fields]) OR ("urinary bladder"[MeSH Terms] OR ("urinary"[All Fields] AND "bladder"[All Fields]) OR "urinary bladder"[All Fields] OR "bladder"[All Fields]) OR ("cystitis"[MeSH Terms] OR "cystitis"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields]) OR ("pyelocystitis"[MeSH Terms] OR "pyelocystitis"[All Fields]) OR ("pyelonephritis"[MeSH Terms] OR "pyelonephritis"[All Fields]) OR ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields] OR "urinary"[All Fields]) OR ("urine"[Subheading] OR "urine"[All Fields] OR "urine"[MeSH Terms]) OR UTI[all] OR ("urinary tract infections"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "urinary tract infections"[All Fields] OR "utis"[All Fields]))) OR "bacteriuria"[MeSH Terms:noexp] OR "cystitis"[MeSH Terms] OR "dysuria"[MeSH Terms:noexp] OR "pyelonephritis"[MeSH Terms:noexp] OR "Urinary Tract Infections"[mh:noexp] OR bacilluria[tiab] OR bacteriuria[tiab] OR bacteriurias[tiab] OR "bladder infection"[tiab] OR "bladder infections"[tiab] OR cystitis[tiab] OR cystopyelitis[tiab] OR dysuria[tiab] OR "genito-urinary infection"[tiab] OR "genitourinary infection"[tiab] OR "genito-urinary infections"[tiab] OR "genitourinary infections"[tiab] OR "kidney infection"[tiab] OR "kidney infections"[tiab] OR "pyelo-nephritis"[tiab] OR pyelocystitis[tiab] OR pyelonephritis[tiab] OR "urinary infection"[tiab] OR "urinary infections"[tiab] OR "urogenital infection"[tiab] OR "urogenital infections"[tiab] OR UTI[tiab] OR UTIs[tiab]) AND ("Antibody-Coated Bacteria Test, Urinary"[mh] OR "Bacteriuria/diagnosis"[Majr] OR "Bacteriuria/prevention and control"[Majr] OR ("bacteriuria/microbiology"[Mesh Terms] AND Majr[All Fields]) OR "Bacteriuria/urine"[Majr] OR "Cystitis/diagnosis"[Majr] OR "Cystitis/prevention and control"[Majr] OR "Cystitis/microbiology"[Majr] OR "Cystitis/urine"[Majr] OR "Mass Screening"[mh:noexp] OR "Microbial Sensitivity Tests"[mh:noexp] OR "Microscopy"[mh:noexp] OR "Predictive Value of Tests"[mh:noexp] OR "Pyelonephritis/diagnosis"[Majr] OR "Pyelonephritis/prevention and control"[Majr] OR "Pyelonephritis/microbiology"[Majr] OR "Pyelonephritis/urine"[Majr] OR "Reagent Kits, Diagnostic"[mh:noexp] OR "Reagent Strips"[mh:noexp] OR "Sensitivity and Specificity"[mh:noexp] OR "Urinalysis"[mh:noexp] OR "Urinary Tract Infections/diagnosis"[Majr] OR "Urinary Tract Infections/prevention and control"[Majr] OR "Urinary Tract Infections/microbiology"[Majr] OR "Urinary Tract Infections/urine"[Majr] OR detect[tiab] OR detected[tiab] OR detection[tiab] OR detecting[tiab] OR detects[tiab] OR "diagnostic accuracy"[tiab] OR "diagnostic algorithm"[tiab] OR "dip slide"[tiab] OR "dip slides"[tiab] OR "dip stick"[tiab] OR "dip sticks"[tiab] OR dipslide[tiab] OR dipslides[tiab] OR dipstick[tiab] OR dipsticks[tiab] OR culture[tiab] OR cultures[tiab] OR "diagnostic test"[tiab] OR "diagnostic tests"[tiab] OR "microbial test"[tiab] OR "microbial tests"[tiab] OR microscopy[tiab] OR predict[tiab] OR predicted[tiab] OR prediction[tiab] OR predicting[tiab] OR predicts[tiab] OR "reagent strip"[tiab] OR "reagent strips"[tiab] OR "reagent

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amoxicillins[tiab] OR ampicillin[tiab] OR ampicillins[tiab] OR "anti-bacteria"[tiab] OR "anti-bacterial"[tiab] OR "anti-bacterials"[tiab] AND "anti-biotic"[tiab] OR "anti-biotics"[tiab] OR antibacteria[tiab] OR antibacterial[tiab] OR antibacterials[tiab] OR antibiotic[tiab] OR antibiotics[tiab] OR aztreonam[tiab] OR cefadroxil[tiab] OR cefepime[tiab] OR ceftibuten[tiab] OR ceftriaxone[tiab] OR cefuroxime[tiab] OR cephalexin[tiab] OR cephalosporin[tiab] OR cephalosporins[tiab] OR cephradine[tiab] OR clindamycin[tiab] OR "co-trimoxazole"[tiab] OR cotrimoxazole[tiab] OR cycloserine[tiab] OR cycloserines[tiab] OR fosfomycin[tiab] OR gentamicin[tiab] OR gentamycin[tiab] OR "nalidixic acid"[tiab] OR nitrofurantoin[tiab] OR penicillin[tiab] OR penicillins[tiab] OR piperacillin[tiab] OR pivampicillin[tiab] OR pivmecillinam[tiab] OR sulfadimethoxine[tiab] OR sulfadiazine[tiab] OR sulfamethizole[tiab] OR sulfamethoxazole[tiab] OR sulfamethoxypyridazine[tiab] OR sulfonamide[tiab] OR sulfonamides[tiab] OR sulphadimidine[tiab] OR sulphonamide[tiab] OR tetracycline[tiab] OR tetracyclines[tiab] OR vancomycin[tiab]) AND ("Pregnancy"[mh] OR "Pregnancy Complications, Infectious"[mh:noexp] OR "Pregnant Women"[mh:noexp] OR "Prenatal Care"[mh:noexp] OR "Prenatal Diagnosis"[mh:noexp] OR antenatal[tiab] OR "pre-natal"[tiab] OR prenatal[tiab] OR "expectant mother"[tiab] OR "expectant mothers"[tiab] OR "expecting mothers"[tiab] OR "expecting mothers"[tiab] OR "expectant woman"[tiab] OR "expectant women"[tiab] OR "expecting women"[tiab] OR pregnancies[tiab] OR pregnancy[tiab] OR pregnant[tiab])) AND ("Choice Behavior"[mh:noexp] OR "Consumer Behavior"[majr:noexp] OR "Consumer Participation"[mh] OR "Cooperative Behavior"[mh:noexp] OR "Decision Making"[mh] OR "Focus Groups"[mh:noexp] OR "Health Care Surveys"[mh:noexp] OR "Informed Consent"[mh] OR "Interviews as Topic"[mh:noexp] OR "Patient Acceptance of Health Care"[mh:noexp] OR "Patient Education as Topic"[mh] OR "Patient Participation"[mh] OR "Patient Preference"[mh:noexp] OR "Social Values"[mh:noexp] OR "Surveys and Questionnaires"[mh:noexp] OR "Treatment Refusal"[mh:noexp] OR (15D[tiab] AND (HRQoL[tiab] OR QoL[tiab] OR "quality of life"[tiab])) OR ((accept[tiab] OR accepted[tiab] OR accepting[tiab] OR accepts[tiab] OR consider[tiab] OR consideration[tiab] OR considerations[tiab] OR considered[tiab] OR considering[tiab] OR considers[tiab] OR choice[tiab] OR choices[tiab] OR choose[tiab] OR chooses[tiab] OR choosing[tiab] OR chose[tiab] OR chosen[tiab] OR decide[tiab] OR decided[tiab] OR deciding[tiab] OR decides[tiab] OR decision[tiab] OR decisionmaker[tiab] OR decisionmaking[tiab] OR decisions[tiab] OR decisive[tiab] OR input[tiab] OR involve[tiab] OR involved[tiab] OR involving[tiab] OR involvement[tiab] OR involves[tiab] OR opinion[tiab] OR opinionated[tiab] OR opinions[tiab] OR participate[tiab] OR participated[tiab] OR participating[tiab] OR participation[tiab] OR participates[tiab] OR perceive[tiab] OR perceived[tiab] OR perceiving[tiab] OR perceives[tiab] OR perception[tiab] OR perceptions[tiab] OR perceptive[tiab] OR perspective[tiab] OR perspectives[tiab] OR prefer[tiab] OR preference[tiab] OR preferences[tiab] OR preferred[tiab] OR preferring[tiab] OR refusal[tiab] OR refuse[tiab] OR refused[tiab] OR refusing[tiab] OR refuses[tiab] OR response[tiab] OR responses[tiab] OR valuation[tiab] OR value[tiab] OR valued[tiab] OR values[tiab] OR valuing[tiab] OR view[tiab] OR viewed[tiab] OR viewing[tiab] OR viewpoint[tiab] OR viewpoints[tiab] OR views[tiab]) AND (citizen[tiab] OR citizens[tiab] OR client[tiab] OR clients[tiab] OR consumer[tiab] OR consumers[tiab] OR female[tiab] OR females[tiab] OR male[tiab] OR males[tiab] OR men[tiab] OR patient[tiab] OR patients[tiab] OR public[tiab] OR "stake-holder"[tiab] OR "stake-holders"[tiab] OR stakeholder[tiab] OR stakeholders[tiab] OR user[tiab] OR users[tiab] OR woman[tiab] OR women[tiab])) OR ((analyses[tiab] OR analysis[tiab] OR valuation[tiab] OR valuations[tiab] OR value[tiab] OR values[tiab] OR valuing[tiab]) AND (conjoint[tiab] OR contingent[tiab])) OR "choice behavior"[tiab] OR "choice behaviour"[tiab] OR "choice experiment"[tiab] OR "choice experiments"[tiab] OR "discrete choice"[tiab] OR "EQ 5D"[tiab] OR EQ5D[tiab] OR "EuroQoL 5D"[tiab] OR EuroQoL5D[tiab] OR "focus group"[tiab] OR "focus groups"[tiab] OR gamble[tiab] OR gambled[tiab] OR gambling[tiab] OR gambles[tiab] OR "health utilities"[tiab] OR "health utility"[tiab]

OR HUI[tiab] OR "informed choice"[tiab] OR "informed choices"[tiab] OR "informed consent"[tiab] OR "informed decision"[tiab] OR interview[tiab] OR interviewed[tiab] OR interviewing[tiab] OR interviews[tiab] OR "multi-attribute"[tiab] OR "multi-criteria"[tiab] OR multiattribute[tiab] OR multicriteria[tiab] OR "preference score"[tiab] OR "preference scores"[tiab] OR "preference scoring"[tiab] OR "prospect theory"[tiab] OR questionnaire[tiab] OR questionnaires[tiab] OR "SF 12"[tiab] OR "SF 36"[tiab] OR "SF 6D"[tiab] OR SF12[tiab] OR SF36[tiab] OR SF6D[tiab] OR "stated preference"[tiab] OR survey[tiab] OR surveyed[tiab] OR surveys[tiab] OR "trade off"[tiab] OR "trade offs"[tiab] OR tradeoff[tiab] OR tradeoffs[tiab] OR "willing to pay"[tiab] OR "willingness to pay"[tiab]))) NOT ("Male"[mh] NOT ("Female"[mh] AND "Male"[mh]))) NOT (((Animals[MESH] OR Animal Experimentation[MESH] OR "Models, Animal"[MESH] OR Vertebrates[MESH]) NOT (Humans[MESH] OR Human experimentation[MESH])) OR (((animals[tiab] OR animal model[tiab] OR rat[tiab] OR rats[tiab] OR mouse[tiab] OR mice[tiab] OR rabbit[tiab] OR rabbits[tiab] OR pig[tiab] OR pigs[tiab] OR porcine[tiab] OR swine[tiab] OR dog[tiab] OR dogs[tiab] OR hamster[tiab] OR hamsters[tiab] OR chicken[tiab] OR chickens[tiab] OR sheep[tiab]) AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])) NOT (human[ti] OR humans[ti] OR people[ti] OR children[ti] OR adults[ti] OR seniors[ti] OR patient[ti] OR patients[ti])))) NOT (case reports[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR newspaper article[pt])) AND ((publisher[sb] NOT pubstatusnihms NOT pubstatuspmcsd NOT pmcbook) OR (pubstatusaheadofprint))
> limit to English or French

KQs4,5: Systematic Review & HTA Search
Database: PubMed via NCBI Entrez (1946 to Present)
Date Searched: 14 October 2016
Records Retrieved: 104

(((((((("asymptomatic infections"[mh] AND (("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields]) OR ("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields] OR "bacteriurias"[All Fields]) OR ("urinary bladder"[MeSH Terms] OR ("urinary"[All Fields] AND "bladder"[All Fields]) OR "urinary bladder"[All Fields] OR "bladder"[All Fields]) OR ("cystitis"[MeSH Terms] OR "cystitis"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields]) OR ("pyelocystitis"[MeSH Terms] OR "pyelocystitis"[All Fields]) OR ("pyelonephritis"[MeSH Terms] OR "pyelonephritis"[All Fields]) OR ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields] OR "urinary"[All Fields]) OR ("urine"[Subheading] OR "urine"[All Fields] OR "urine"[MeSH Terms]) OR UTI[all] OR ("urinary tract infections"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "urinary tract infections"[All Fields] OR "utis"[All Fields]))) OR "bacteriuria"[MeSH Terms:noexp] OR "cystitis"[MeSH Terms] OR "dysuria"[MeSH Terms:noexp] OR "pyelonephritis"[MeSH Terms:noexp] OR "Urinary Tract Infections"[mh:noexp] OR bacilluria[tiab] OR bacteriuria[tiab] OR bacteriurias[tiab] OR "bladder infection"[tiab] OR "bladder infections"[tiab] OR cystitis[tiab] OR cystopyelitis[tiab] OR dysuria[tiab] OR "genito-urinary infection"[tiab] OR "genitourinary infection"[tiab] OR "genito-urinary infections"[tiab] OR "genitourinary infections"[tiab] OR "kidney infection"[tiab] OR "kidney infections"[tiab] OR "pyelo-nephritis"[tiab] OR pyelocystitis[tiab] OR pyelonephritis[tiab] OR "urinary infection"[tiab] OR "urinary infections"[tiab] OR "urogenital infection"[tiab] OR "urogenital infections"[tiab] OR UTI[tiab] OR UTIs[tiab]) AND (("Antibody-Coated Bacteria Test, Urinary"[mh] OR "Bacteriuria/diagnosis"[Majr] OR "Bacteriuria/prevention and control"[Majr] OR ("bacteriuria/microbiology"[Mesh Terms] AND Majr[All Fields]) OR "Bacteriuria/urine"[Majr] OR "Cystitis/diagnosis"[Majr] OR "Cystitis/prevention and control"[Majr] OR

"Cystitis/microbiology"[Majr] OR "Cystitis/urine"[Majr] OR "Mass Screening"[mh:noexp] OR "Microbial Sensitivity Tests"[mh:noexp] OR "Microscopy"[mh:noexp] OR "Predictive Value of Tests"[mh:noexp] OR "Pyelonephritis/diagnosis"[Majr] OR "Pyelonephritis/prevention and control"[Majr] OR "Pyelonephritis/microbiology"[Majr] OR "Pyelonephritis/urine"[Majr] OR "Reagent Kits, Diagnostic"[mh:noexp] OR "Reagent Strips"[mh:noexp] OR "Sensitivity and Specificity"[mh:noexp] OR "Urinalysis"[mh:noexp] OR "Urinary Tract Infections/diagnosis"[Majr] OR "Urinary Tract Infections/prevention and control"[Majr] OR "Urinary Tract Infections/microbiology"[Majr] OR "Urinary Tract Infections/urine"[Majr] OR detect[tiab] OR detected[tiab] OR detection[tiab] OR detecting[tiab] OR detects[tiab] OR "diagnostic accuracy"[tiab] OR "diagnostic algorithm"[tiab] OR "dip slide"[tiab] OR "dip slides"[tiab] OR "dip stick"[tiab] OR "dip sticks"[tiab] OR dipslide[tiab] OR dipslides[tiab] OR dipstick[tiab] OR dipsticks[tiab] OR culture[tiab] OR cultures[tiab] OR "diagnostic test"[tiab] OR "diagnostic tests"[tiab] OR "microbial test"[tiab] OR "microbial tests"[tiab] OR microscopy[tiab] OR predict[tiab] OR predicted[tiab] OR prediction[tiab] OR predicting[tiab] OR predicts[tiab] OR "reagent strip"[tiab] OR "reagent strips"[tiab] OR "reagent test"[tiab] OR "reagent testing"[tiab] OR "reagent tests"[tiab] OR screen[tiab] OR screened[tiab] OR screening[tiab] OR screens[tiab] OR "strip test"[tiab] OR "strip tests"[tiab] OR "strip testing"[tiab] OR "test accuracy"[tiab] OR urinalyses[tiab] OR urinalysis[tiab] OR "urine analyses"[tiab] OR "urine analysis"[tiab] OR "urine test"[tiab] OR "urine tested"[tiab] OR "urine testing"[tiab] OR "urine tests"[tiab] OR uriscreen[tiab]) OR ("Anti-Bacterial Agents"[mh:noexp] OR "Antibiotic Prophylaxis"[mh:noexp] OR "Anti-Infective Agents, Urinary"[mh] OR "Asymptomatic Infections/therapy"[mh] OR "Bacteriuria/drug therapy"[Majr] OR "Bacteriuria/therapy"[Majr] OR "Drug Therapy, Combination"[mh:noexp] OR "Norfloxacin"[mh:noexp] OR "Penicillins"[mh] OR "Sulfonamides"[mh] OR "Urinary Tract Infections/drug therapy"[Majr] OR "Urinary Tract Infections/therapy"[Majr] OR amoxicillin[tiab] OR amoxicillins[tiab] OR ampicillin[tiab] OR ampicillins[tiab] OR "anti-bacteria"[tiab] OR "anti-bacterial"[tiab] OR "anti-bacterials"[tiab] AND "anti-biotic"[tiab] OR "anti-biotics"[tiab] OR antibacteria[tiab] OR antibacterial[tiab] OR antibacterials[tiab] OR antibiotic[tiab] OR antibiotics[tiab] OR aztreonam[tiab] OR cefadroxil[tiab] OR cefepime[tiab] OR ceftibuten[tiab] OR ceftriaxone[tiab] OR cefuroxime[tiab] OR cephalexin[tiab] OR cephalosporin[tiab] OR cephalosporins[tiab] OR cephradine[tiab] OR clindamycin[tiab] OR "co-trimoxazole"[tiab] OR cotrimoxazole[tiab] OR cycloserine[tiab] OR cycloserines[tiab] OR fosfomycin[tiab] OR gentamicin[tiab] OR gentamycin[tiab] OR "nalidixic acid"[tiab] OR nitrofurantoin[tiab] OR penicillin[tiab] OR penicillins[tiab] OR piperacillin[tiab] OR pivampicillin[tiab] OR pivmecillinam[tiab] OR sulfadimethoxine[tiab] OR sulfadiazine[tiab] OR sulfamethizole[tiab] OR sulfamethoxazole[tiab] OR sulfamethoxypyridazine[tiab] OR sulfonamide[tiab] OR sulfonamides[tiab] OR sulphadimidine[tiab] OR sulphonamide[tiab] OR tetracycline[tiab] OR tetracyclines[tiab] OR vancomycin[tiab]))) AND ("Pregnancy"[mh] OR "Pregnancy Complications, Infectious"[mh:noexp] OR "Pregnant Women"[mh:noexp] OR "Prenatal Care"[mh:noexp] OR "Prenatal Diagnosis"[mh:noexp] OR antenatal[tiab] OR "pre-natal"[tiab] OR prenatal[tiab] OR "expectant mother"[tiab] OR "expectant mothers"[tiab] OR "expecting mothers"[tiab] OR "expecting mothers"[tiab] OR "expectant woman"[tiab] OR "expectant women"[tiab] OR "expecting women"[tiab] OR pregnancies[tiab] OR pregnancy[tiab] OR pregnant[tiab])) AND (systematic[sb] OR meta-analysis[pt] OR meta-analysis as topic[mh] OR meta-analysis[mh] OR meta analy*[tw] OR metanaly*[tw] OR metaanaly*[tw] OR met analy*[tw] OR integrative research[tiab] OR integrative review*[tiab] OR integrative overview*[tiab] OR research integration*[tiab] OR research overview*[tiab] OR collaborative review*[tiab] OR collaborative overview*[tiab] OR systematic review*[tiab] OR technology assessment*[tiab] OR technology overview*[tiab] OR "Technology Assessment, Biomedical"[mh] OR HTA[tiab] OR HTAs[tiab] OR comparative efficacy[tiab] OR comparative effectiveness[tiab] OR outcomes research[tiab] OR indirect comparison*[tiab] OR ((indirect treatment[tiab] OR mixed-treatment[tiab])

AND comparison*[tiab]) OR Embase*[tiab] OR Cinahl*[tiab] OR systematic overview*[tiab] OR methodological overview*[tiab] OR methodologic overview*[tiab] OR methodological review*[tiab] OR methodologic review*[tiab] OR quantitative review*[tiab] OR quantitative overview*[tiab] OR quantitative synthes*[tiab] OR pooled analy*[tiab] OR Cochrane[tiab] OR Medline[tiab] OR Pubmed[tiab] OR Medlars[tiab] OR handsearch*[tiab] OR hand search*[tiab] OR meta-regression*[tiab] OR metaregression*[tiab] OR data synthes*[tiab] OR data extraction[tiab] OR data abstraction*[tiab] OR mantel haenszel[tiab] OR peto[tiab] OR der-simonian[tiab] OR dersimonian[tiab] OR fixed effect*[tiab] OR "Cochrane Database Syst Rev"[Journal] OR "health technology assessment winchester, england"[Journal] OR "Evid Rep Technol Assess (Full Rep)"[Journal] OR "Evid Rep Technol Assess (Summ)"[Journal] OR "Int J Technol Assess Health Care"[Journal] OR "GMS Health Technol Assess"[Journal] OR "Health Technol Assess (Rockv)"[Journal] OR "Health Technol Assess Rep"[Journal])) NOT ("Male"[mh] NOT ("Female"[mh] AND "Male"[mh]))) NOT (((Animals[MESH] OR Animal Experimentation[MESH] OR "Models, Animal"[MESH] OR Vertebrates[MESH]) NOT (Humans[MESH] OR Human experimentation[MESH])) OR (((animals[tiab] OR animal model[tiab] OR rat[tiab] OR rats[tiab] OR mouse[tiab] OR mice[tiab] OR rabbit[tiab] OR rabbits[tiab] OR pig[tiab] OR pigs[tiab] OR porcine[tiab] OR swine[tiab] OR dog[tiab] OR dogs[tiab] OR hamster[tiab] OR hamsters[tiab] OR chicken[tiab] OR chickens[tiab] OR sheep[tiab]) AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])) NOT (human[ti] OR humans[ti] OR people[ti] OR children[ti] OR adults[ti] OR seniors[ti] OR patient[ti] OR patients[ti]))))) NOT (case reports[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR newspaper article[pt])

KQs4,5: Systematic Review & HTA Search
Database: Wiley Cochrane Library
Date Searched: 14 October 2016
Records Retrieved: 19 in Cochrane Database of Systematic Reviews
Records Retrieved: 4 in Database of Abstracts of Reviews of Effects (DARE)
Records Retrieved: 1 in Health Technology Assessment Database
Records Retrieved: 3 in Economic Evaluations Database

#1 [mh ^"Asymptomatic Infections"] and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*):ti,ab,kw
#2 [mh ^Bacteriuria]
#3 [mh Cystitis]
#4 [mh ^Dysuria]
#5 [mh ^Pyelonephritis]
#6 [mh ^"Urinary Tract Infections"]
#7 bacilluria*:ti,ab,kw
#8 bacteriuria*:ti,ab,kw
#9 cystiti*:ti,ab,kw
#10 (cysto-pyeliti* or cystopyeliti*):ti,ab,kw
#11 dysuria*:ti,ab,kw
#12 (infection* near/2 (bladder* or genitourin* or kidney* or urin* or urogenita*)):ti,ab,kw
#13 (pyelo-cystiti* or pyelocystiti*):ti,ab,kw
#14 (pyelo-nephriti* or pyelonephriti*):ti,ab,kw
#15 (UTI or UTIs):ti,ab,kw
#16 {or #1-#15}

#17 [mh ^"Antibody-Coated Bacteria Test, Urinary"]
#18 [mh ^Bacteriuria [mj]/DI,PC,MI,UR]
#19 [mh Cystitis [mj]/DI,PC,MI,UR]
#20 [mh ^"Mass Screening"]
#21 [mh ^"Microbial Sensitivity Tests"]
#22 [mh ^Microscopy]
#23 [mh ^"Predictive Value of Tests"]
#24 [mh ^Pyelonephritis [mj]/DI,PC,MI,UR]
#25 [mh "Reagent Kits, Diagnostic"]
#26 [mh "Reagent Strips"]
#27 [mh ^"Sensitivity and Specificity"]
#28 [mh ^Urinalysis]
#29 [mh ^"Urinary Tract Infections" [mj]/DI,PC,MI,UR]
#30 ((accurac* or diagnostic) near/5 (algorithm* or test*)):ti,ab,kw
#31 "diagnostic accurac*":ti,ab,kw
#32 culture*:ti,ab,kw
#33 (detect* or predict* or screen*):ti,ab,kw
#34 ("dip slide*" or dipslide* or "dip stick*" or dipstick*):ti,ab,kw
#35 (micro-scopy or microscopy):ti,ab,kw
#36 (microb* near/2 test*):ti,ab,kw
#37 ((re-agent* or reagent) near/3 (strip* or test*)):ti,ab,kw
#38 "strip* test*":ti,ab,kw
#39 "urine test*":ti,ab,kw
#40 (urinalys* or "urine analys*"):ti,ab,kw
#41 uriscreen:ti,ab,kw
#42 {or #17-#41}
#43 [mh ^"Anti-Bacterial Agents"]
#44 [mh ^"Antibiotic Prophylaxis"]
#45 [mh ^"Anti-Infective Agents, Urinary"]
#46 [mh ^"Asymptomatic Infections"/DT,TH]
#47 [mh ^Bacteriuria [mj]/DT,TH]
#48 [mh ^"Drug Therapy, Combination"]
#49 [mh ^Norfloxacin]
#50 [mh Penicillins]
#51 [mh Sulfonamides]
#52 [mh ^"Urinary Tract Infections" [mj]/DT,TH]
#53 amoxicillin*:ti,ab,kw
#54 ampicillin*:ti,ab,kw
#55 ("anti-bacteria*" or antibacteria*):ti,ab,kw
#56 ("anti-biotic*" or antibiotic*):ti,ab,kw
#57 aztreonam*:ti,ab,kw
#58 cefadroxil*:ti,ab,kw
#59 cefepime*:ti,ab,kw
#60 ceftibuten*:ti,ab,kw
#61 ceftri?xone*:ti,ab,kw
#62 cefuroxime*:ti,ab,kw
#63 cephalexin*:ti,ab,kw
#64 cephalosporin*:ti,ab,kw

#65	cephradine*:ti,ab,kw
#66	clindamycin*:ti,ab,kw
#67	("co-trimoxazole*" or cotrimoxazole*):ti,ab,kw
#68	cycloserine*:ti,ab,kw
#69	fosfomycin*:ti,ab,kw
#70	gentam?cin*:ti,ab,kw
#71	"nalidixic acid*":ti,ab,kw
#72	nitrofurantoin*:ti,ab,kw
#73	penicillin*:ti,ab,kw
#74	piperacillin*:ti,ab,kw
#75	pivampicillin*:ti,ab,kw
#76	pivmecillinam*:ti,ab,kw
#77	sulfadimethoxine*:ti,ab,kw
#78	sulfadiazine*:ti,ab,kw
#79	sulfamethizole*:ti,ab,kw
#80	sulfamethoxazole*:ti,ab,kw
#81	sulfamethoxypyridazine*:ti,ab,kw
#82	sulfonamide*:ti,ab,kw
#83	sulphadimidine*:ti,ab,kw
#84	sulphonamide*:ti,ab,kw
#85	tetracycline*:ti,ab,kw
#86	vancomycin*:ti,ab,kw
#87	{or #43-#86}
#88	#16 and (#42 or #87)
#89	[mh Pregnancy]
#90	[mh ^"Pregnancy Complications, Infectious"]
#91	[mh ^"Pregnant Women"]
#92	[mh ^"Prenatal Care"]
#93	[mh ^"Prenatal Diagnosis"]
#94	(antenatal* or "pre-natal*" or prenatal*):ti,ab,kw
#95	(expect* near/1 (female* or mother* or wom?n)):ti,ab,kw
#96	pregnan*:ti,ab,kw
#97	{or #89-#96}
#98	#88 and #97

Supplement 3. Eligibility criteria for screening effectiveness, women's outcome valuation, and treatment effectiveness

Question	PICOTS	Study designs; Language
Benefits and harms of screening	**P:** Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria **I:** Any screening program, whereby there is an intent (i.e., clinical algorithm) for all pregnant women to receive a screening test with follow-up of screen-positive cases **C:** No screening program (but may include indicated testing and/or treatment upon development of symptoms), or a different screening test or algorithm **O*:** Maternal mortality (9), maternal sepsis (8), pyelonephritis (7), perinatal mortality ≥20 weeks' gestation (9), spontaneous abortion/pregnancy loss before 20 weeks' gestation (8), neonatal sepsis (8), preterm delivery <37 weeks' gestation (7), low birth weight <2500g (6), serious maternal and neonatal harms (7) **T:** Any timing **S:** Any primary care or clinical setting providing antenatal care to pregnant women	RCTs, CCTs, controlled observational designs (i.e., prospective and retrospective cohort, case-control, controlled before-after) English and French
Outcome valuation	**P:** Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria; will also accept asymptomatic women who are not pregnant if necessary **I:** Any screening program or test, and any antibiotic; will accept studies on treatment for any bacterial condition in pregnancy **C:** Not applicable **O:** Several possible outcomes (e.g., relative weight/utilities of benefits and harms; willingness to be screened based on relative value placed on benefits and harms of screening programs or treatment) **T:** Any timing **S:** Any primary care or clinical setting providing antenatal care to pregnant women	Qualitative, mixed methods, surveys/cross-sectional designs English and French
Benefits and harms of treatment	**P:** Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria **I:** Any antibiotic **C:** No treatment or placebo **O*:** Maternal mortality (9), maternal sepsis (8), pyelonephritis (7), perinatal mortality ≥20 weeks' gestation (9), spontaneous abortion/pregnancy loss before 20 weeks' gestation (8), neonatal sepsis (8), preterm delivery <37 weeks' gestation (7), low birth weight <2500g (6), serious maternal and neonatal harms (7)	RCTs (or systematic review(s)) English and French

	T: Any timing **S:** Any primary care or clinical setting providing antenatal care to pregnant women	

CCT: controlled clinical trial; g: grams: PICOTS: populations, interventions, comparators, outcomes, timing, and setting; RCT: randomized clinical trial

* Outcomes ratings included in brackets; these were rated as critical/important for decision-making by CTFPHC members and by women recruited for patient engagement

Supplement 4. Characteristics of included studies on screening effectiveness, outcome valuation, and treatment effectiveness

Characteristics of included studies on screening effectiveness

Gérard, Blazquez & Mounac, 1983	
Objective	To determine if a routine screening program for ASB can reduce the incidence of pyelonephritis and other adverse pregnancy outcomes, and if such a program would be economically feasible
Methods	Design: Non-concurrent cohort Inclusion criteria: All pregnant women followed at the Centre Hospitalier de Corbeil-Essonnes (prospective). Controls were all women who were not involved in the screening program (retrospective). Exclusion criteria: NR
Participants	Setting: Centre Hospitalier de Corbeil-Essonnes (a Hospital) Study period: January-October 1979 (and 10 previous months for the control group) Sample: n=370 pregnant women; n=170 in study group; n=200 in control group Mean age, y (SD): NR Risk factors: NR Length of follow-up: until delivery, and for 3-6 months after in those with ≥2 instances of ASB; loss to follow-up: n=0.
Interventions	Implementation of a routine screening and treatment program for ASB: 1) Screening of all women at 3, 5, 7 and 9 months of pregnancy, and treatment of those diagnosed with ASB 2) Controls only screened after presenting with clinical signs Urine testing characteristics: Urine collection: Midstream urine sample with cleansing of the vulva before micturition Urine testing: Microscopy, urine culture and Gram staining Criteria for positive test: $\geq 10^5$ CFU/mL Gestational age (weeks) at first prenatal visit: ~3 months for the treatment group; NR for the control group Number of prenatal visits: at least 4 (every 2 months) for the treatment group; NR for control group Treatment: Treatment based on antibiotic sensitivity and at the discretion of the prescribing physician
Outcomes	Acute pyelonephritis: Clinical signs (fever, lumbar pain, dysuria, pollakiuria (urinary frequency)) and positive urine culture of 10^5 CFU/mL Spontaneous abortion: ≤28 wks GA Preterm delivery: Delivery at <37 wks GA Birth weight: Reported means for ASB vs. non-ASB in study group; symptomatic + positive culture vs. asymptomatic in controls Perinatal mortality: “stillbirth” as either death in utero or during delivery, all ≥31 wks GA

	Adverse event(s): NR
Notes	Study is descriptive, no between-group associations tested

ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millilitre; GA: gestational age; n: number; NR: not reported; SD: standard deviation; wks: weeks; y: year

Gratacós et al., 1994	
Objective	To determine the incidence of pyelonephritis in pregnant women before and after the introduction of a screening program for ASB
Methods	Design: Non-concurrent cohort Inclusion criteria: Study group were women who were seen at the clinic at <25 wks GA who subsequently delivered January 1991-December 1992. Controls were women who were seen at the clinic at <25 wks GA and delivered January 1987-December 1990. Exclusion criteria: NR
Participants	Setting: An obstetrics clinic in Barcelona, Spain Study period: January 1987-December 1992 (study group: January 1991-December 1992; controls: January 1987-December 1990) Sample: n=4,917 pregnant women; n=1,652 in study group, n=3,265 in control group Mean age, y (SD): NR Risk factors: NR Length of follow-up: until delivery; loss to follow-up: n=10
Interventions	Implementation of a routine screening and treatment program for ASB: 1) Screening of all women <25 wks pregnant and treatment of those diagnosed with ASB 2) Controls: no routine screening Urine testing characteristics: Urine collection: Midstream morning urine sample. Women with positive culture returned within 1-2 wks for a second midstream urine culture, after stressing the importance of cleansing the vulva before micturition. Urine testing: Urine culture following the guidelines of the National Committee for Clinical Laboratory Standards Criteria for positive test: Two consecutive positive urine cultures (number of organisms NR) with growth of the same species Gestational age (wks), at first prenatal visit: <25 Number of prenatal visits: study group: NR; controls: NR Treatment: 7-day course of antibiotics based on antibiotic sensitivity testing, started 1-2 wks after the second culture. At 1-4 wks after treatment and at least once more before delivery, additional midstream urine samples were obtained. If repeat cultures were positive, antibacterial therapy was repeated until cultures were negative for ASB.
Outcomes	Pyelonephritis: fever, flank pain, tenderness in costovertebral angle, ≥1 positive culture

	Adverse event(s): NR
Notes	Also investigated prevalence of ASB and response to treatment in the study group, but this was not compared to the controls who did not receive routine screening

ASB: asymptomatic bacteriuria; n: number; ND: not defined; NR: not reported; SD: standard deviation; wks: weeks; y: year(s)

Rhode, 2007	
Objective	To determine if urinary tract infection, high blood pressure, and gestational diabetes mellitus are underdiagnosed when prenatal urine testing is done on a clinically indicated basis versus a routine basis
Methods	Design: Non-concurrent cohort Inclusion criteria: Routine screening group were all pregnant women who enrolled for care and delivered before August 15, 2002. Indicated screening group were all women who enrolled for care and delivered after August 15, 2002. Exclusion criteria: Women who were in the transitional urine screening group (enrollment prior to and delivery after August 15, 2002), who received both screening techniques (n=570)
Participants	Setting: Hospital-based nurse-midwifery practice, Aurora, Colorado; provides care to predominantly medically underserved and Hispanic women Study period: Charts of patients enrolled for care and delivered November 2000-March 2004 Sample: n= 1,952 pregnant women; n=933 in routine screening group; n=1019 in indicated screening group Mean age, y (SD): Routine screening= 24.4 (5.6); Indicated screening= 24.9 (5.1) Risk factors: Gestational diabetes: routine screening=81 (9.3%), indicated screening=42 (4.2%) Race (ethnicity): Hispanic; routine screening=669 (72.1%), indicated screening=783 (76.9%) Length of follow-up: until delivery or patient left the practice; loss to follow-up (n=112; 4.6%); total ineligible=459 (19%), due to: spontaneous abortion (n=58), transfer of care (n=218), transfer to high risk care (n=71)
Interventions	Routine urine screening (enrollment and delivery before August 15, 2002): first visit with chemical reagent strips, lab urinalysis and culture; subsequent visits with chemical reagent strips, culture or urinalysis as indicated[1] Indicated urine screening (enrollment on and delivery after August 15, 2002): first visit with chemical reagent strips, lab urinalysis and culture; subsequent visits with chemical reagent strip only if one of the criteria was present (risk factors for UTI, GDM). Follow-up of culture or lab urinalysis as indicated[1] Urine testing characteristics: Urine collection: midstream morning urine sample, first visit Urine testing: chemical reagent strip test, lab urinalysis and culture;

	Mean number of strip tests performed (SD): Routine screening= 7.8 (3.4), range 0-19; Indicated screening= 1.4 (1.3), range 0-16 Criteria for positive test: NR Gestational age (wks) at start of care (SD): Routine screening= 20.5 (9.4); Indicated screening= 20.3 (8.9) Number of prenatal visits: NR Treatment: NR
Outcomes	Pyelonephritis: ND; however, clearly differentiated from ASB, cystitis and undetermined UTI Preterm delivery: <37 wks GA[2] Adverse event(s): NR
Notes	Authors compared eligible participants to those who became ineligible during the study period. In the routine screening group, eligible and ineligible women differed in terms of marital status, race, payment source, # preterm deliveries, and # weeks gestation at start of care. In the indicated screening group, eligible and ineligible women differed in terms of race, # of abortions, and # weeks of gestation at start of care.

ASB: asymptomatic bacteriuria; n: number; ND: not defined; NR: not reported; SD: standard deviation; UTI: urinary tract infection; GDM: gestational diabetes mellitus; wks: weeks; y: year(s)

[1] lab urinalysis may be used instead of culture due to presence of blood in urine; culture typically done to confirm reagent strip, unless reagent strip was used to test for elevated blood pressure (information provided by study author)

[2] Criteria for outcomes were confirmed by study author(s)

Uncu, 2001	
Objective	To determine the incidence of asymptomatic bacteriuria during pregnancy and its relation to pregnancy complications
Methods	Design: Non-concurrent cohort Inclusion criteria: Screened group were pregnant women ≤32 wks GA seen at the antenatal outpatient clinic. Controls were women who delivered in clinic before study and were not screened for ASB; formed in retrospective manner from first day of study Exclusion criteria: Patients who were followed-up at clinic due to prior renal disease, positive for ASB or were taking antibiotics
Participants	Setting: Antenatal outpatient clinic, Uludag University Faculty of Medicine, Department of Obstetrics and Gynecology, Turkey Study period: June 1998-January 1999 Sample: Screened= 186; Controls= 186 Mean age, y (SD): Screened= 27.7 (5.1); Controls= 27.7 (4.6) Risk factors: Gestational diabetes mellitus: Screened=7 (3.8%); Controls= 5 (2.7%) Socioeconomic status: lower SES correlated with high prevalence of ASB* Length of follow-up: NR; loss to follow-up: NR

Interventions	Determine incidence of asymptomatic bacteriuria during pregnancy and relation to pregnancy complications: 1) Screening group: All pregnant women routinely screened at first visit with whole blood count, total urine analysis and urine culture. 2) Controls: Formed in a retrospective manner from the first day of the study with pregnant women who delivered in the clinic and who were not routinely screened. Urine testing characteristics: Urine collection: midstream morning urine sample, first visit Urine testing: whole blood count, total urine analysis, and urine culture Criteria for positive test: $>10^5$ CFU/mL of the same organism Gestational age (wks), at time of urine culture: beginning of pregnancy Number of prenatal visits: NR Treatment: n=23 [7-10 days of antibiotics, Follow-up 7-days of antibiotics for recurrent ASB (n=5)]; ASB recurrence 5/23 (21.7%)
Outcomes	Pyelonephritis: ND Intrauterine death[2]: no fetal cardiac activity by USG, after 20 weeks' gestation Prematurity[2]: <37 wks of gestation Adverse event(s): NR Fetal abnormalities: ND
Notes	Total screened for ASB=270→ with urine cultures=247→ sufficient delivery records=186 (61 excluded)

*statistically significant; ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millitre; GA: gestational age; ND: not defined; NR: not reported; SD: standard deviation; SES: socioeconomic status; USG: ultrasonography; wks: weeks; y: year(s)

[2] Criteria for outcomes were confirmed by study author(s)

Characteristics of included studies on women's outcome valuation

Butters, 1990	
Objective	To determine the level of knowledge of the effects of commonly used drugs on a fetus
Methods	Design: Cross-sectional (self-completed questionnaire) Recruitment: Participants were recruited from postnatal wards of the hospitals on a weekly basis
Participants	Setting: Two maternity hospitals: one serves a white urban and semirural population, the other serves a wider population mix from rural to urban and includes ethnic minorities. Both are located in Glasgow, Scotland. Inclusion criteria: Postnatal women who were still in hospital after delivering. They had to be given the questionnaire in person (i.e. they were either in their bed or in the sitting room when the questionnaire was distributed). Exclusion criteria: Women who had vaginal delivery on the day of the study, women one or two days post-delivery by caesarean section, and women who were unable to read English. Study period: October 1, 1987 and March 31, 1988. Sample: n=514 Age range: 15 to 40 years; 66 (13%) between 15 and 20 years, 141 (27%) between 21 and 25 years, 176 (34%) between 26 and 30 years, and 127 (25%) aged over 30 years. Gestational age: NA Parity: First pregnancy (53%) Race/ethnicity: Multiple ethnicities, mainly Scottish. Education level: NR
Interventions	Anonymous short questionnaire with mostly tick boxes.
Outcomes	-254 (49%) said they would take an antibiotic prescribed by their doctor, 246 (48%) said they would not, and 14 (3%) did not respond. -The responses were similar for all ages and social class groups. -There was a strong relationship between the women that would avoid taking an analgesic (n=80, 74%)) and those that would avoid taking an antibiotic (187, 45%), p<0.0001.

NA: not applicable; NR: not reported

Kazemier, 2015	
Objective	To investigate the consequences of treated and untreated ASB in pregnancy

Methods	Design: Prospective cohort (screening vs. no screening) with embedded RCT (decision on entry into the study considered cross-sectional) Recruitment: Pregnant women attending antenatal clinics offering screening (not routinely available)
Participants	Setting: 8 hospitals and 5 ultrasound centres, the Netherlands Inclusion criteria: Pregnant women aged ≥18 years with a singleton pregnancy who were between 16 and 22 wks GA, tested positive for ASB, and did not have symptoms of UTI. Exclusion criteria: History of preterm delivery <34 wks GA, warning signs of imminent preterm delivery, fetal congenital malformations, antibiotic use within 2 weeks of screening, known glucose-6-phosphate dehydrogenase deficiency, hypersensitivity to nitrofurantoin, risk factors for complicated UTI (e.g., pre-gestational DM, use of immunosuppressive medication or functional or structural abnormalities of the urinary tract). Study period: October 11, 2011-August 22, 2014 Sample: n=248 Mean age (SE), years: treated=29 (0.74), placebo or untreated=31 (0.33) Gestational age (wks + days at screening (SE)): treated=20+2 (19+6 to 20+5), placebo or untreated=20+0 (19+3 to 20+3) Parity (% nulliparous): treated=50%, placebo or untreated=42% Ethnicity (non-white): treated n=3 (8%), placebo or untreated n=36 (17%) Low education (≤pre-vocational level): treated n=6 (15%), placebo or untreated n=21 (10%)
Interventions	Women who were positive for ASB were invited to participate in a treatment RCT. Reasons for declining participation were recorded.
Outcomes	Most women (155/163 positive for ASB, 94%) who did not want to participate made this choice because they did not want to receive antibiotics during pregnancy for an asymptomatic condition.

ASB: asymptomatic bacteriuria; DM: diabetes mellitus; GA: gestational age; NA: not applicable; NR: not reported; RCT: randomized controlled trial; SE: standard error; UTI: urinary tract infection; wks: weeks

Lupattelli, 2014	
Objective	To investigate the association between health literacy and perception of medication risk, beliefs about medications, use and non-adherence to prescribed pharmacotherapy during pregnancy.
Methods	Design: Cross-sectional internet-based questionnaire Recruitment: Banners announcing the study were placed on one to four websites per country and/or social networks commonly visited by pregnant women that had a high number of daily users.

Participants	Setting: Anonymous internet questionnaire with participants from 18 countries: Australia, Austria, Canada, Croatia, Finland, France, Iceland, Italy, The Netherlands, Norway, Poland, Russia, Serbia, Slovenia, Sweden, Switzerland, United Kingdom and United Sates as well as some South American countries. Inclusion criteria: Pregnant women at any stage of gestation. Exclusion criteria: Women who were not currently pregnant. Study period: October 1 2011 to February 29, 2012 Sample: n=4999 Mean age (SD): NR overall Gestational age in weeks, mean (SD): 22.4 (10.3) Race/ethnicity: Multinational
Interventions	Health literacy was measured using a self-assessment scale of 0 to 4 for three questions. Perceived risk of medications was measured using 13 agents on a scale of 0 to 10. Beliefs about medications were measured using a 5-point agreement scale for three questions. Participants were asked standardized questions about medication use for specific illnesses, non-adherence and over-the-counter medication use with free text entry.
Outcomes	-96.2% of participants felt penicillin antibiotics posed a teratogenic risk.

NR: not reported; SD: standard deviation

Mashayekhi, 2009	
Objective	To examine the awareness of pregnant women about the effects of drugs in pregnancy
Methods	Design: Cross sectional, questionnaire Recruitment: Women in the postnatal and prenatal wards were invited.
Participants	Setting: Pre and Post-natal wards of two maternity hospitals in Iran, one private and one public. Inclusion criteria: Antenatal and postnatal women. Exclusion criteria: Women who had a complicated labor. Study period: August 2006 and May 2007 Sample: n=400 Median age (SD or SE), range: 26 (4.90), 15 to 44 years Gestational age: NA Gravidity: None – 183 (45.8%), one – 118 (29.5%), two – 69 (17.3%), more than two – 30 (7.5%)

	Parity: None – 200 (50.0%), one – 127 (31.8%), two (54, 13.5%), more than two – 19 (4.8%) Race/ethnicity: Iranian Education level: High school or lower – 184 (46.0%), diploma – 147 (36.8%), University education – 69 (17.3%)
Interventions	Face-to-face questionnaire divided into three sections: demographic information, drug use before and during pregnancy including drug safety, source of information regarding drugs safety during pregnancy. Majority of response options were tick boxes.
Outcomes	-Specific antibiotics the women felt were safe: penicillin – 51 (12.8%), ampicillin – 36 (9.0%), amoxicillin – 66 (16.5%), metronidazole - 20 (5.0%), cephalosporin - 10 (2.5%), other antibiotics - 6 (1.5%). -For penicillin use none felt it was unsafe for the mother, 143 (35.8%) felt it was unsafe for the fetus, 40 (10.0%) felt it was unsafe for both. -For ampicillin use 4 (1.0%) felt it was unsafe for the mother, 145 (36.3%) felt it was unsafe for the fetus, 28 (7.0%) felt it was unsafe for both. -For amoxicillin use 5 (1.3%) felt it was unsafe for the mother, 147 (36.8%) felt it was unsafe for the fetus, 18 (4.5%) felt it was unsafe for both. -For metronidazole use none felt it was unsafe for the mother, 129 (32.3%) felt it was unsafe for the fetus, 21 (5.3%) felt it was unsafe for both. -For cephalosporin use none felt it was unsafe for the mother, 127 (31.8%) felt it was unsafe for the fetus, 18 (4.5%) felt it was unsafe for both. -For other antibiotic use none felt it was unsafe for the mother, 125 (31.3%) felt it was unsafe for the fetus, 28 (7.0%) felt it was unsafe for both.

NA: not applicable; SE: standard error; SD: standard deviation

Nordeng, 2010	
Objective	To evaluate the perception of risk of drugs during pregnancy and sources of drug exposure information most commonly used
Methods	Design: Retrospective web-based questionnaire Recruitment: Invitation to participate in the questionnaire was posted to four webpages commonly used by pregnant women and mothers.
Participants	Setting: Internet Inclusion criteria: Pregnant woman or a mother of a child less than 5 years old. Exclusion criteria: NR Study period: September 16, 2008 to October 25, 2008 Sample: n=1793; 866 (48.3%) pregnant, 927 (51.7%) mothers Mean age (median, range): 30, 17 to 45 years Gestational age: NR Parity: primiparous – 689 (38.4%), one or more previous children – 1104 (61.6%)

	Race/ethnicity: Norwegian Education level: Basic school level – 88 (4.9%), upper secondary education – 390 (21.8%), tertiary education (<4 years) – 810 (45.2%), tertiary education (>4 years) – 421 (23.5%), other education – 84 (4.7%)
Interventions	Questionnaire consisted of open-ended questions and numeric rating scales from 0 to 10 relating to teratogenic risk of 17 drugs, foods, chemicals and radiation.
Outcomes	-There was a significant difference in mean risk perception scores between non-users of the indicated drugs and users of 4.3 vs. 3.0 (p<0.001) with a ratio between non-users/users of 1.4.

NR: not reported

Sanz, 2001	
Objective	To assess the perception of the teratogenic risk of common medication by professionals and the public
Methods	Design: Cross-sectional Recruitment: Pregnant women attending a regular obstetric follow up in an out-patient clinic at a University hospital; non-pregnant women from an obstetric and gynecological out-patient clinic in the hospital and in a randomized manner from four different neighborhoods. Medical staff (general physicians, gynecologists and medical students were also recruited and interviewed, their data are not included here).
Participants	Setting: Outpatient clinic at a University hospital, home setting Inclusion criteria: Currently pregnant for the pregnant women group, not pregnant for the comparison group Exclusion criteria: NR Study period: NR Sample: n=81 pregnant women, n=63 non-pregnant women Median age: NR Gestational age: NR Gravidity: NR Parity: NR Race/ethnicity: Spanish Education level: NR
Interventions	A visual analogue scale with a 10 cm horizontal line with a short vertical line at each end, with a scale of 0 to 100%. Participants were asked to mark on the scale what they thought was the potential risk for fetal malformations and malformations in non-pregnant women given exposure to a particular drug.

Outcomes	-The mean value of the perceived teratogenic risk by non-pregnant women was higher than that perceived by pregnant women for erythromycin (55.6 vs. 38.7) but not amoxicillin (49.3 vs. 40.4) (Mann-Whitney U Test). -The median value of the perceived teratogenic risk by non-pregnant women was higher than that perceived by pregnant women for erythromycin (50.0 vs. 30.0) but not amoxicillin (50.5 vs. 34.0) (Mann-Whitney U Test). -In comparison to the "true" limits, risk from antibiotics was rated higher by pregnant women (erythromycin chi-square: 3.99, p=0.045; amoxicillin chi-square: 17.21, p=0.0001).

cm: centimeter(s); NR: not reported

Sharma, 2006	
Objective	To evaluate the drug utilization pattern in pregnant women and the effect of education and economic status.
Methods	Design: Retrospective cross-sectional study Recruitment: Medical students interviewed pregnant women visiting the antenatal clinic.
Participants	Setting: Antenatal clinic of a medical college in North India Inclusion criteria: Pregnant women Exclusion criteria: NR Study period: June 2005 to December 2005 Sample: n=405 Age range: Less than 20 years – 25 (6.17%), 20 to 35 years – 240 (59.26%), more than 35 years – 90 (22.22%) Gestational age: First trimester – 30 (7.40%), second trimester – 100 (24.69%), third trimester – 275 (67.90%) Gravidity: 243 primigravida; 152 multigravida Race/ethnicity: Indian Education level: Undergraduates – 220 (54.32%), graduates - 185 (45.68%)
Interventions	98 medical students trained in pharmacokinetic and pharmacodynamic changes in pregnancy completed a written questionnaire after interviewing each participant. The participants' statements were confirmed by their records if available.
Outcomes	-190 (46.91%) believed antibiotics should not be used in pregnancy while 25 (6.17%) felt they should be used.

NR: not reported

Twigg, 2016	
Objective	To describe beliefs and risk perception associated with medicines for treatment of common acute conditions.
Methods	Design: Cross-sectional internet-based questionnaire

	Recruitment: Advertisements announcing the study were placed on two commonly visited by pregnant women or new mothers
Participants	Setting: Anonymous internet questionnaire with participants from across the United Kingdom (England, Scotland, Wales and Northern Ireland). Inclusion criteria: Women who were pregnant or within one year of giving birth. Exclusion criteria: NR Study period: November 15, 2011 to January 15, 2012 Sample: n=1120 Mean age (SD): 30.5 (5.2) years Gestational age: 442 (39.5%) were currently pregnant Parity (95% CI): No previous children – 48.0% (45.1-50.9%) Race/ethnicity: NR Education level (95% CI): Less than high school – 0.6% (0.14-1.05), high school – 27.9% (25.3-30.5), more than high school – 52.1% (49.2 – 55.0), other – 19.3% (17.0-21.6).
Interventions	Health literacy was measured using a self-assessment scale of 0 to 4 for three questions. General beliefs about medicine were obtained using the validated Beliefs about Medicines Questionnaire (BMQ-General) with an additional four questions regarding the benefit of medications on a scale of 1 to 5.
Outcomes	-Women with a UTI using medication for treatment had lower mean risk perception scores relating to the overuse and harm of medication and a higher mean risk score relating to the benefits of medication compared to women with a UTI who did not undergo treatment with medication. Overuse [mean(SD)]: 11.5 (2.8) vs. 12.6 (2.7), p=0.006 Harm [mean(SD)]: 9.3 (2.7) vs. 10.4 (2.9), p=0.014 Benefit [mean(SD)]: 16.3 (2.2) vs. 14.9 (2.3), p<0.001
Notes	Sub-study of the Multinational Medication Use in Pregnancy Study which was reported by Lupattelli et al. and another paper from that study is included in this review.

CI: confidence interval; NR: not reported; SD: standard deviation; UK: United Kingdom; UTI: urinary tract infection

Characteristics of included studies on treatment effectiveness

Brumfitt, 1975	
Objective	To assess the impact of screening and treatment for ASB on maternal and fetal health
Methods	Design: RCT (randomization ND); placebo controlled Recruitment: Pregnant women attending one of three antenatal clinics for the first time Inclusion criteria: Pregnant women who were screened and found to be positive for 'significant bacteriuria' at their first antenatal visit and 7-10 days later Exclusion criteria: Home delivery, abortions, treatment before confirmation of bacteriuria and other complicating factors
Participants	Setting: Birmingham (1 clinic) and London (2 clinics), UK; urban Study period: NR; ~1967-1968 Sample: n=426; treated (n=235), placebo (n=179) Mean age (SD), years: Treated=26.5 (6.8); Placebo=26.2 (6.9) Risk factors: Ethnicity (Asian and West Indian): Treated n=49 (20.8%); Placebo n=35 (14.1%) Length of follow-up: until delivery and the postpartum period for perinatal mortality Loss to follow-up: NR; outcome of pyelonephritis reported only for a subset (n=173); n=413 for outcome of low birth weight.
Interventions	Screening characteristics: Timing: First antenatal visit Urine collection: Clean-catch urine sample Urine testing method: Urine culture Criteria for positive test: Two positive tests; women with one positive test were recalled for a second test 7-10 days later and 'detailed documentation'. Microbiological criteria NR. Treatment characteristics (Williams, 1968): Type of antibiotic and length of treatment: 2g sulphonamide in a single dose; additional courses of treatment for persistent bacteriuria Control group: Received placebo under 'double-blind conditions' Follow-up testing: Subset of treated women (n=87) retested after 1 and 2 courses of treatment (as applicable)
Outcomes	Benefits: Pyelonephritis: Presence of loin pain and tenderness together with a temperature of ≥100◦F and $>10^5$ CFU/mL (Condie, 1968) Low birth weight (reported as prematurity): ≤2500g Harms: NR
Notes	Study also included a non-bacteriuric control group. There are two preliminary reports associated with this study (Condie, 1968; Williams, 1968). Brumfitt, 1975 reported outcome of pyelonephritis for the placebo group only (55/179), comparison between groups only

	available for a subset of treatment group (Condie, 1968). No explanation for variation in number of participants across reports for this study, nor for the various outcomes.

ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millilitre; F: Fahrenheit; g: gram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; UK: United Kingdom

Elder, 1966	
Objective	To evaluate the effectiveness of sulfasymazine for the treatment of ASB in pregnant women
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women registering for prenatal care Inclusion criteria: Pregnant women ≤32 wks GA with bacteriuria at registration confirmed in two additional samples Exclusion criteria: >32 wks GA, included in other bacteriuria studies, given treatment in error, moved away
Participants	Setting: Boston City Hospital, Boston, US; urban Study period: June 9, 1965-March 9, 1966 Sample: n=106; treated (n=54); placebo (n=52) Mean age (SD): NR Risk factors: NR Length of follow-up: Until delivery Loss to follow-up: 5 (5%) lost; 2(4%) treated patients left the community, 3 (6%) placebo-treated patients dropped out of the study
Interventions	Screening characteristics: Timing: At registration for prenatal care Urine collection: Clean-voided urine sample Urine testing method: Urine culture Criteria for a positive test: Three uncontaminated urine specimens containing the same species of bacteria with $\geq 10^4$ CFU/mL in one and $\geq 10^5$ CFU/mL in the other two. Treatment characteristics Type of antibiotic and length of treatment: 0.5g sulfasymazine once daily until delivery; if there was evidence of persistent bacteriuria, another treatment was given according to clinical judgment (usually nitrofurantoin) Control group: Received placebo Follow-up testing: Retested after one week of treatment, and at each clinic visit (at least weekly for the first 3 wks, then at least biweekly until 36 wks GA, then weekly until delivery)
Outcomes	Benefits: NR Harms: NR

Notes	There are no relevant results reported in this study. Study also included non-bacteriuric control patients. 7/52 (13%) of women in the placebo group developed 'asymptomatic pyelonephritis', but not information provided for the treated group.

ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millilitre; g: gram(s); GA: gestational age; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; US: United States; wks: weeks

Elder, 1971	
Objective	To assess the effect of treatment of ASB on pregnancy outcomes
Methods	Design: Quasi-RCT; placebo-controlled Recruitment: Patients registering for prenatal care Inclusion criteria: Pregnant women ≤32 wks GA, with confirmed bacteriuria at the first prenatal visit Exclusion criteria: Treated for UTI during the current pregnancy and before the first obstetric appointment, >32 wks GA, delivered or had aborted before the first obstetric visit, went elsewhere for prenatal care, delivered twins
Participants	Setting: Boston City Hospital, Boston, US; urban Study period: January 28, 1963-July 2, 1965 Sample: n=281; treated (n=133), placebo (n=148) Mean age (SE), years: Treated=24.8 (0.60); Placebo=25.3 (0.46) Risk factors: Ethnicity (non-white): Treated=66.2%; Placebo=54.7% Previous UTI: Treated=35.9%; Placebo=40.1% Length of follow-up: Until delivery, and postpartum (time frame ND) for complications Loss to follow-up: Of original n=289, 8 (3%) were excluded because they moved away. No loss to follow-up for pyelonephritis; 3 (1%) patients in the placebo group lost for low birthweight because they were treated for reasons other than UTI; 8 (3%) lost for perinatal mortality, 11 (4%) for neonatal sepsis, and 16 (6%) fetal abnormalities and hemolytic anemia, reasons NR.
Interventions	Screening characteristics: Timing: Upon registration at the clinic Urine collection: Clean-voided urine sample Urine testing method: Urine culture Criteria for a positive test: Three samples (two at registration and one at the first obstetric visit); colony count from 2 of 3 specimens $\geq 10^5$ CFU/mL and no specimens with $<10^4$ CFU/mL, with the same species predominating in all 3 specimens Treatment characteristics: Type of antibiotic and length of treatment: 250mg tetracycline, 4 times daily for 6 wks; if infection did not clear in 2 wks, another antibiotic (usually nitrofurantoin) was given until it cleared Control group: Given identically appearing placebo to be taken similarly

	Follow-up testing: Retested at each clinic visit until delivery (includes recurrence and excludes those who became symptomatic); colony count $<10^3$ CFU/mL on two successive cultures considered cleared
Outcomes	Benefits: Pyelonephritis: Temperature of ≥100◦F with signs and symptoms localized to the urinary tract and not otherwise explained Perinatal mortality: Stillbirth or neonatal death prior to hospital discharge Respiratory distress: Respiratory distress syndrome and other causes of 'respiratory embarrassment' Low birth weight (defined as prematurity): ≤2500g Harms: Serious adverse events: Congenital malformations of bone, genitourinary system, other; hemolytic anemia (erythroblastosis fetalis)
Notes	Study also included a non-bacteriuric control group. Some patients may have participated more than once if they had more than one pregnancy during the study period (treatment assigned by alternation regardless of assignment for previous pregnancy). Outcomes of low birth weight, fetal abnormalities and hemolytic anemia reported for live births only. 4 bacteriuric women delivered twins and are not included.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; ◦F: degrees Fahrenheit; g: gram(s); GA: gestational age; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SE: standard error; US: United States; UTI: urinary tract infection; wks: weeks

Foley, 1987	
Objective	Test of treatment vs. non-treatment of ASB for the prevention of symptomatic UTI in pregnancy
Methods	Design: RCT Recruitment: Pregnant women attending an antenatal clinic for the first time Inclusion criteria: Pregnant women with bacteriuria at the first prenatal visit Exclusion criteria: NR
Participants	Setting: National Maternity Hospital, Dublin, Ireland; urban Study period: 1985 Sample: n=220; treated (n=100); not treated (n=120) Mean age (SD), years: NR Risk factors: NR Length of follow-up: Until delivery (patients interviewed post-delivery) Loss to follow-up: Reported follow-up rate of 81%, unclear if these were from treatment or control groups (total n used in analysis).
Interventions	Screening characteristics: Timing: First antenatal visit Urine collection: Midstream urine sample

	Urine testing method: NR Criteria for a positive test: One urine sample with >10^5 CFU/mL Treatment characteristics: Type of antibiotic and length of treatment: 300mg sulphamethizole or 150mg nitrofurantoin daily for 3 days, on the basis of sensitivity testing; further treatment, including maintenance treatment, provided if needed to render urine sterile Control group: Received no treatment Follow-up testing: Retested 'at follow-up'; not further defined
Outcomes	Benefits: Pyelonephritis: ND; 'admitted with pyelonephritis' Harms: NR
Notes	Reported as a letter to the editor, not a full publication.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; mg: milligram(s); ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; UTI: urinary tract infection

Furness, 1975	
Objective	To examine the effectiveness of urinary antiseptics in preventing pyelonephritis and adverse among pregnant women with ASB
Methods	Design: RCT Recruitment: Pregnant women attending their initial prenatal visit Inclusion criteria: Pregnant women with 'significant' bacteriuria at the second prenatal visit Exclusion criteria: NR
Participants	Setting: Queen Victoria Hospital, Adelaide, Australia; urban Study period: NR Sample: n=206; treated (n=139); not treated (n=67) Mean age (SD), years: NR Risk factors: NR Length of follow-up: Until 6 wks postpartum Loss to follow-up: None reported
Interventions	Screening characteristics: Timing: At the second antenatal visit Urine collection: Midstream urine sample Urine testing method: Dipslide Criteria for a positive test: One specimen with >10^5 CFU/mL or two specimens each with 10^4 to 10^5 CFU/mL Treatment characteristics

	Type of antibiotic and length of treatment: 1g methenamine mandelate 4 times daily or 1g methenamine hippurate twice daily until delivery; if pyelonephritis developed the patient was treated with the appropriate antibiotic and no further antiseptics were given Control group: Received no treatment Follow-up testing: A postnatal urine specimen was obtained at the 6-week postnatal visit from women who did not develop clinical pyelonephritis during pregnancy or the puerperium
Outcomes	Benefits: Pyelonephritis: Frequency and burning on micturition accompanied by pyrexia or loin tenderness, with presence of a significant number of bacteria in urine Spontaneous abortion: ND; 'abortions' Preterm delivery: <38 wks GA Harms: Serious adverse events: Major fetal abnormality (anencephaly)
Notes	The treatment group received one of two antiseptics, the two groups were combined for reporting of outcomes. Outcome of pyelonephritis includes both during pregnancy and the puerperium. Three intrauterine deaths reported but it is unclear which group the patients belonged to. GA at delivery reported for 118 treated and 52 placebo untreated patients with no explanation given, total n used as denominator in analysis.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; wks: weeks

Gold, 1966	
Objective	To determine whether chemotherapy for ASB, continued throughout the rest of the prenatal period, reduces the incidence of prematurity
Methods	Design: Quasi-RCT; placebo-controlled Recruitment: Pregnant women registering at a prenatal clinic Inclusion criteria: Pregnant women with two consecutive positive tests for bacteriuria at any prenatal visit Exclusion criteria: Failed to return to the clinic, aborted, delivered at other hospitals, found to not be pregnant, ectopic pregnancy, transferred to other care, delivered by a private physician
Participants	Setting: Prenatal clinic at a hospital in New York, NY, US; urban Study period: February 2, 1962-December 21, 1964 Sample: n=65; treated (n=35); placebo (n=30) Mean age (SD), years: NR Risk factors: Ethnicity: 85% non-white, 6% Puerto-Rican, 9% other white (distribution among groups NR) Length of follow-up: Until the 'postpartum period' (exact time NR) Loss to follow-up: None reported

Interventions	Screening characteristics: Timing: First prenatal visit and each visit thereafter Urine collection: Clean-voided midstream urine sample Urine testing method: Urine culture Criteria for a positive test: Two consecutive laboratory reports with $>10^5$ CFU/mL of the same species Treatment characteristics: Type of antibiotic and length of treatment: 0.5g sulfadimethoxine once per day until 36 wks GA, 1g sulfadiazine 3 times daily thereafter until delivery Control group: Received placebo tablets taken in the same manner Follow-up testing: Each patient had repeat tests at each antenatal visit until delivery (either for diagnosis or persistent bacteriuria); data presented for persistent bacteriuria at delivery.
Outcomes	Benefits: Pyelonephritis: ND Harms: NR
Notes	Also reported delivery data for non-bacteriuric patients. Only antepartum pyelonephritis included in the analysis (postpartum excluded). 'Preterm delivery' reported for 2/35 treated and 0/30 placebo patients, but this is not further defined.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; n: number; ND: not defined; NR: not reported; NY: New York; RCT: randomized controlled trial; SD: standard deviation; US: United States; wks: weeks

Kass, 1960	
Objective	To assess the effect of early detection and eradication of bacteriuria on excessive morbidity in pregnant women
Methods	Design: Quasi-RCT; placebo controlled Recruitment: Pregnant women ≤32 wks GA registering for a prenatal clinic Inclusion criteria: Pregnant women with bacteriuria at the first prenatal visit and confirmed on two repeat cultures Exclusion criteria: >32 wks GA, chronic renal insufficiency, given treatment in error, did not have further prenatal care, records were inadequate or unobtainable, urine samples were contaminated, unable to void, found to not be pregnant
Participants	Setting: Boston City Hospital, Boston, US; urban Study period: October 1956-April 1960 Sample: n=214 (n=11 recruited via renal clinic); treatment (n=93); placebo (n=98) Mean age (SD), years: NR; similar distribution between treated and placebo groups Risk factors: Ethnicity (black): Treated (~50%); placebo (slightly <50%) History of UTI: ~15% (distribution by group NR) Diabetes: n=2 (distribution by group NR)

	Uterine abnormalities: reported for n=2 bacteriuric women with cesarean section; prevalence in rest of population NR Length of follow-up: Until the post-delivery period and up to 12 months postpartum; records reviewed 3-4 years later Loss to follow-up: n=23 (11%) lost; 13 (12%) in the treatment group (7 not seen in last 4 wks before delivery, 5 delivered out of state, 1 incorrectly assigned), 10 (9%) in the placebo group (8 cleared spontaneously or false positive, 2 lost)
Interventions	Screening characteristics: Timing: At the time of registration for the clinic Urine collection: Clean-voided urine sample Urine testing method: Urine culture Criteria for a positive test: 10^3-10^5 CFU/mL at registration, then two additional cultures with >10^5 CFU/mL of the same species Treatment characteristics: Type of antibiotic and length of treatment: 0.5g sulfamethoxypyridazine daily until delivery; if infection did not clear in one week, the patient was given 100mg nitrofurantoin 3 times daily until delivery Control group: Received a placebo tablet supplied by the same manufacturer Follow-up testing: Treated patients were retested within the 4 wks preceding delivery. Data for 3-12 months postpartum bacteriuria presented for a subset of women (n=91) (Kass, 1960).
Outcomes	Benefits: Pyelonephritis: dysuria, frequency, and flank pain or other localizing evidence of inflammation, with either documented temperature of 100◦F or above or a history of chills and fever. When patients were seen outside the clinic (e.g., accident floor or emergency department), it was not always clear that patients were indeed febrile. Perinatal mortality: ND; 'perinatal death' and fetal loss >20 wks GA Low birth weight (defined as prematurity): <2500g Harms: NR
Notes	Kass, 1960 is a preliminary report, updated and more complete data retrieved from Savage, 1967 are presented. The study also includes a group of non-bacteriuric women. Some patients participated for >1 pregnancy, and were reassigned to the same treatment they received in the first pregnancy. Outcome of pyelonephritis reported only for the antenatal period, postpartum excluded. Outcome of low birth weight given for the total number of deliveries (3 twin deliveries in the placebo group and none in the treated group).

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; F: Fahrenheit; g: gram(s); GA: gestational age; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; US: United States; UTI urinary tract infection; wks: weeks

Kazemier, 2015	
Objective	To investigate the consequences of treated and untreated ASB in pregnancy
Methods	Design: Prospective cohort (screening vs. no screening) with embedded RCT Recruitment: Pregnant women attending antenatal clinics offering screening (not routinely available)

	Inclusion criteria: Pregnant women aged ≥18 years with a singleton pregnancy who were between 16 and 22 wks GA, tested positive for ASB, and did not have symptoms of UTI Exclusion criteria: History of preterm delivery <34 wks, warning signs of imminent preterm delivery, fetal congenital malformations, antibiotic use within 2 wks of screening, known glucose-6-phosphate dehydrogenase deficiency, hypersensitivity to nitrofurantoin, risk factors for complicated UTI (e.g., pre-gestational DM, use of immunosuppressive medication or functional or structural abnormalities of the urinary tract)
Participants	Setting: 8 hospitals and 5 ultrasound centres, the Netherlands Study period: October 11, 2011-August 22, 2014 Sample: n=248; treated (n=40); placebo (n=45), untreated (n=163) Mean age (SE), years: treated=29 (0.74), placebo or untreated=31 (0.33) Risk factors: Ethnicity (non-white): treated n=3 (8%), placebo or untreated n=36 (17%) Low education (≤pre-vocational level): treated n=6 (15%), placebo or untreated n=21 (10%) Length of follow-up: Until 6 wks postpartum Loss to follow-up: n=12 (5%) lost, all from the untreated or placebo group; 5 women could not be contacted for outcomes because of errors in their contact information. Missing data were imputed (see notes).
Interventions	Screening characteristics: Timing, median (IQR) wks + days GA: treated=20+2 (19+6 to 20+5), placebo or untreated=20+0 (19+3 to 20+3) Urine collection: Midstream urine sample Urine testing method: Dipslide Criteria for a positive test: $\geq 10^5$ CFU/mL of a single microorganism or when two different colony types were present but one had a concentration of $\geq 10^5$ CFU/mL Treatment characteristics: Type of antibiotic and length of treatment: 100mg nitrofurantoin twice daily for 5 days; if bacteriuria did not clear the treatment was repeated for a maximum of two rounds Control group: Received identical placebo capsules on the same dose and schedule as treated patients, or no treatment Follow-up testing: All participants provided a follow-up dipslide 1 week after the end of treatment; those who remained positive were retested after each new round of treatment, for a maximum of two rounds
Outcomes	Benefits: Pyelonephritis: Hospital admission with ≥2 of the following: fever (body temperature ≥38◦C), symptoms of pyelonephritis (nausea, vomiting, chills, and costovertebral tenderness), and a positive urine culture indicating the presence of bacteria in the urine. Perinatal mortality: neonatal death before discharge from the neonatal ward Preterm delivery: spontaneous birth between 32 and 37 wks GA Low birth weight: $<10^{th}$ or 5^{th} percentile Neonatal sepsis: Confirmed with culture, includes group B streptococcal sepsis Harms: Serious adverse events: Congenital abnormalities (ND)

Notes	Cohort study addressed screening, results reported here for treatment RCT only. Study included both placebo and untreated groups who were combined in the analysis. When data were missing, these were imputed taking into account patient characteristics and outcomes. Differences in outcomes between groups were controlled for potential confounders (smoking, low education, conception through in-vitro fertilization or intracytoplasmic sperm injection, pre-existing hypertension). 5 women originally assigned to treatment group were later found to not have ASB, but remained in their assigned group (intention-to-treat analysis).

ASB: asymptomatic bacteriuria; C: Celsius; CFU/mL: colony forming units per millilitre; DM: diabetes mellitus; g: gram(s); GA: gestational age; IQR: interquartile range; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SE: standard error; UTI: urinary tract infection; wks: weeks

Kincaid-Smith, 1965	
Objective	To assess the effectiveness of antibacterial drugs for pregnant women with bacteriuria in preventing pyelonephritis, perinatal mortality, and low birth weight
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending their first antenatal visit before 26 wks GA Inclusion criteria: Pregnant women <26 wks GA with ASB at the first antenatal visit and confirmed by a subsequent positive test Exclusion criteria: NR
Participants	Setting: Queen Victoria Hospital, Melbourne, Australia; urban Study period: 1964-1965 Sample: n=145; treated (n=61), placebo (n=56) (see notes) Mean age (SD), years: NR Risk factors: (see notes) Socioeconomic status: All from lowest income category in community, but the community has a high standard of living Urogenital anomalies: At post-delivery testing, 51.4% of patients had an abnormal intravenous pyelogram and 5 patients had poorly functioning or non-functioning kidneys on one side due to ureteric obstruction. Length of follow-up: Until 6 months postpartum Loss to follow-up: Of initial 240 women with completed pregnancies, no outcomes reported for 95 women for various reasons (6 aborted before treatment, 20 developed symptoms before treatment, 22 attended infrequently, 33 failed to take tablets continuously, 14 had coagulase-negative staphylococcal bacteriuria); further information on non-compliant patients NR
Interventions	Screening characteristics: Timing: First antenatal visit Urine collection: Midstream urine sample; the second test was clean-voided (first was not) Urine testing method: Urine culture Criteria for a positive test: $>10^5$ CFU/mL on two occasions

	Treatment characteristics: Type of antibiotic and length of treatment: 0.5g sulphamexydiazine daily, changing to 1g sulphadimidine 3 times daily in the 13th week of gestation, continuing until delivery; if resistance to sulphonamides was indicated by sensitivity tests, 500mg ampicillin 3 times daily or 50mg nitrofurantoin 4 times daily was prescribed instead. Control group: Received identical placebo capsules and tablets Follow-up testing: Patients re-examined at monthly intervals, on any hospital admission, and at delivery. Retesting at 6 wks-3 months and 6 months postpartum ongoing at the time of publication. These subsequent samples involved cleansing of the periurethral area and insertion of a vaginal tampon to avoid contamination.
Outcomes	Benefits: Pyelonephritis: Loin pain and tenderness, with or without pyrexia, and rigors, with or without symptoms of dysuria and frequency Perinatal mortality: >28 wks GA Low birth weight (reported as preterm delivery): <2500g Harms: NR
Notes	Study also included a non-bacteriuric group. 29/145 (20%) patients were given treatment or placebo prior to confirmation of ASB (before the second culture was analyzed); outcomes for these patients were reported separately, leaving 116 in the current analysis. 11 fetal losses reported but group assignment NR.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; mg: milligram(s); NR: not reported; RCT: randomized controlled trial; SD: standard deviation; wks: weeks

Little, 1966	
Objective	To assess the effect of antibiotic treatment for pregnant women with ASB on incidence of pyelonephritis and adverse pregnancy outcomes
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending their first antenatal visit Inclusion criteria: Pregnant women with bacteriuria at the first antenatal visit and confirmed with a subsequent culture Exclusion criteria: NR
Participants	Setting: Charing Cross Hospital and Fulham Maternity Hospital, London, England; urban Study period: 1962-1965 Sample: n=265; treated (n=124), placebo (n=141) Mean age (SD), years: NR; 6.89% 10-20, 4.99% 21-30, 4.62% 31-40, 4.25% ≥40 Risk factors: Past history of urinary tract disease: 62 (23.4%) recalled a past episode (both groups combined) Length of follow-up: Until 6 wks postpartum

	Loss to follow-up: None reported.
Interventions	Screening characteristics: Timing: First antenatal visit, usually ~12th week of gestation Urine collection: Clean-voided midstream urine sample Urine testing method: Urine culture Criteria for a positive test: Two consecutive urine cultures with >10^5 CFU/mL Treatment characteristics: Type of antibiotic and length of treatment: At start of trial, patients were given 0.5g sulphamethoxypyridazine daily for 30 days; if bacteriuria did not clear, 1.5g ampicillin daily was given for 1 week, then a maintenance dose of 1g daily until delivery. Because treatment with ampicillin was generally not successful, later in the trial, a single dose of 100mg nitrofurantoin became the first form of treatment. Control group: Received placebo tablets Follow-up testing: Retested monthly throughout pregnancy
Outcomes	Benefits: Pyelonephritis: Loin pain and tenderness, a fever >100◦F, >10^5 CFU/mL. Usually there was also frequency and dysuria, and sometimes rigors and hematuria Perinatal mortality: ND Low birth weight (reported as prematurity): <2500g Harms: Serious adverse events: fetal abnormalities, ND
Notes	No additional notes

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; F: Fahrenheit; g: gram(s); mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation

Mulla, 1960	
Objective	To evaluate the clinical results of treatment of bacteriuria in pregnant women with long-acting sulfonamide
Methods	Design: RCT Recruitment: Pregnant women attending the obstetrical clinic Inclusion criteria: Pregnant women with ASB at their 30-32 wks GA obstetric visit Exclusion criteria: NR
Participants	Setting: St. Elizabeth Hospital, Ohio, US; urban Study period: NR Sample: n=100; treated (n=50), not treated (n=50) Mean age (SD), years: NR Risk factors: NR Length of follow-up: Until delivery and immediately after

	Loss to follow-up: None reported.
Interventions	Screening characteristics: Timing: Obstetric visit at 30-32 wks GA Urine collection: Catheter urinalysis (antimicrobial jelly used on the catheter) Urine testing method: Urine culture Criteria for a positive test: NR Treatment characteristics: Type of antibiotic and length of treatment: 250mg sulfadimethoxine twice daily for 1 week; the regimen was repeated if bacteriuria persisted Control group: Received no medication until symptoms appeared Follow-up testing: Followed at weekly intervals until delivery; were re-tested at least once, after the first course of treatment.
Outcomes	Benefits: Pyelonephritis: Clinical evidence of active infection, including acute symptoms of cystopyelitis; urine was tested at the time of the episode Harms: NR
Notes	Pyelonephritis after delivery was reported, but this was excluded from the present analysis.

ASB: asymptomatic bacteriuria; GA: gestational age; mg: milligram(s); n: number; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; US: United States; wks: weeks

Pathak, 1969	
Objective	To determine the effect of short-term antibacterial therapy on eradication of bacteriuria during pregnancy, and its effects on pregnancy outcomes
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending antenatal clinics Inclusion criteria: Pregnant women ≤24 wks GA with confirmed bacteriuria on two consecutive tests Exclusion criteria: Confirmation of bacteriuria at >24 wks GA, blood pressure >130/90mmHg at the initial antenatal visit, did not re-attend after first examination (wrong dates or could not be traced), early abortions, clinical pyelonephritis, 'mentally defective'
Participants	Setting: University College Hospital and Kingston Public Hospital, Jamaica; urban Study period: NR Sample: n=178; treated (n=76); placebo (n=76) Mean age (SD), years: NR Risk factors: Sickle-cell trait: 18/24 (21.4%) in bacteriuric patients, incidence by group NR Urogenital anomalies: 9/50 (18%) of bacteriurics had abnormalities on postpartum intravenous pyelogram (1 bilateral hydroureter with hydronephrosis, 1 localized calyceal clubbing, 1 bifid pelvis, 2 had changes consistent with papillary necrosis, 4 showed evidence of chronic pyelonephritis).

	Length of follow-up: Until delivery (all) and 3-9 months postpartum for a subset Loss to follow-up: n=26 (15%) lost; 12 (14%) treated (9 antibiotic received for positive serology, 3 defaulted from the clinic and could not be traced), 14 (16%) placebo (12 antibiotic received, 3 defaulted from the clinic)
Interventions	Screening characteristics: Timing: NR; ≤24 wks GA Urine collection: clean-voided urine sample Urine testing method: NR Criteria for a positive test: $>10^5$ CFU/mL on two consecutive specimens Treatment characteristics: Type of antibiotic and length of treatment: 100mg nitrofurantoin twice daily for 3 wks; patients who did not respond received 400mg nitrofurantoin daily for a further 4 days Control group: Received placebo identical in appearance Follow-up testing: Retested at weekly intervals during treatment (or placebo), then every 2 wks until delivery, and a subset (n=69, 24 treated and 45 placebo) at 3-9 months postpartum
Outcomes	Benefits: Pyelonephritis: ND Harms: NR
Notes	Reported preterm birth/fetal loss only by bacteriuric status, not by treatment group.

ASB: asymptomatic bacteriuria; CFU: colony forming units per millilitre; GA: gestational age; mg: milligram; mmHg: millimetre of mercury; n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; wks: weeks

Thomsen, 1987	
Objective	To assess the effect of treatment for group-B streptococcal bacteriuria in pregnant women on the incidence of preterm labour
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending Statens Seruminstitut Inclusion criteria: Pregnant women 27-31 wks GA who were positive for group-B streptococcal bacteriuria Exclusion criteria: NR; <27 or >31 wks GA
Participants	Setting: University Hospital, Denmark; urban Study period: October 1, 1984-October 1, 1986 Sample: n=69; treated (n=37), placebo (n=32) Mean age, years: 28.1, similar for both groups Risk factors: Ethnicity: All patients were white Socioeconomic status: Similar for both groups

	Length of follow-up: Until delivery (see notes) Loss to follow-up: None reported.
Interventions	Screening characteristics: Timing: NR; 27-31 wks GA Urine collection: Midstream urine sample Urine testing method: Urine culture Criteria for a positive test: 10^2-10^6 CFU/mL of group-B streptococci bacteria Treatment characteristics: Type of antibiotic and length of treatment: 10^6 IU penicillin 3 times daily for 6 days; treatment was repeated if bacteriuria persisted Control group: Received placebo tablets Follow-up testing: Retested weekly until delivery for persistent bacteriuria or recurrence
Outcomes	Benefits: Preterm delivery: <37 wks GA (mean wks GA for treated: 39.6, placebo: 36.2) Neonatal sepsis: ND Harms: NR
Notes	Patients positive for streptococci at delivery were treated with 2g ampicillin intravenously followed by 1g intravenously every 4 hours from the start of labour. Infants were given ampicillin (50mg/kg) intramuscularly every 12 hours to avoid sepsis. Umbilical cord blood was tested from group-B streptococci and babies with positive cultures were treated for 6 days. One infant tested positive for sepsis at 6 wks post-delivery.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram; GA: gestational age; IU: international unit; kg: kilogram; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; wks: weeks

Williams, 1969	
Objective	To investigate the effect of treatment of ASB in pregnancy on urine concentrating ability and the development of symptomatic UTI
Methods	Design: RCT Recruitment: Pregnant women attending their first antenatal visit Inclusion criteria: Pregnant women <30 wks GA with significant ASB at the first antenatal visit, confirmed by a second positive test within 10 days Exclusion criteria: NR
Participants	Setting: Maternity Hospital and St. David's Hospital, Cardiff, Wales, England; urban Study period: 1967 Sample: n=163; treated (n=85), untreated (n=78) Mean age (SE), years: 24.82 (0.49) for all bacteriurics, differences between groups NR Risk factors: NR

	Length of follow-up: Until 10 days postpartum Loss to follow-up: None reported
Interventions	Screening characteristics: Timing: First antenatal visit; mean (SE) 20.78 (0.45) wks GA Urine collection: Clean-voided midstream urine sample Urine testing method: Urine culture Criteria for a positive test: $>10^5$ gram-negative CFU/mL in at least two consecutive urine specimens; if the first specimen was positive, patients were recalled for a second specimen within 10 days Treatment characteristics: Type of antibiotic: 1g sulphadimidine 3 times daily for 7 days; if bacteriuria persisted, patients received 100mg nitrofurantoin twice daily for 7 days; if bacteriuria still persisted, patients received 250mg ampicillin 3 times daily for 7 days (ampicillin repeated as necessary) Control group: received no treatment until symptoms presented Follow-up testing: Retested 2-3 wks after the first course of treatment, and each subsequent course of treatment
Outcomes	Benefits: Pyelonephritis: loin pain and tenderness with or without fever (no record of fever in antenatal patients) Harms: NR
Notes	The study also included a non-bacteriuric and a non-pregnant group. Data for pyelonephritis includes postpartum infections (n=6) because group assignment NR.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; mg: milligram(s); n: number; NR: not reported; RCT: randomized controlled trial; SE: standard error; UTI: urinary tract infection; wks: weeks

Wren, 1969	
Objective	To evaluate the effect of treatment of pregnant women with ASB on the incidence of premature deliveries and other adverse pregnancy outcomes
Methods	Design: Quasi-RCT Recruitment: Pregnant women booking at an antenatal clinic Inclusion criteria: Pregnant women with ASB at their first antenatal visit Exclusion criteria: NR
Participants	Setting: Royal Hospital for Women, New South Wales, Australia; urban Study period: November 1968-December 1968 Sample: n=183; treated (n=83), untreated (n=90) Mean age (SD): NR Risk factors: NR

	Length of follow-up: Until 6 wks postpartum Loss to follow-up: Of original n=183, 10 (5%) women lost; 2 sets of twins, 4 moved away and could not be traced, 3 received antibiotics before the trial started, 1 refused to take the treatment
Interventions	Screening characteristics: Timing: First antenatal visit Urine collection: Midstream urine sample Urine testing method: NR Criteria for a positive test: NR Treatment characteristics: Type of antibiotic and length of treatment: Rotational therapy with 100mg nitrofurantoin twice daily for 2 wks, 250mg ampicillin 4 times daily for 1 week, 500mg sulphurazole 4 times daily for 4 wks, and nalidixic acid 4 times daily for 2 wks. Each new patient started with one of the four drugs, then rotated through the remaining drugs in order. Every 9 wks, patients began a new course of rotational therapy until 1-6 wks after delivery. Control group: Untreated until clinical evidence of UTI developed Follow-up testing: Patients were retested one per month when possible, until the last month of pregnancy
Outcomes	Benefits: Spontaneous abortion: ND; 'abortion' Perinatal mortality: Stillbirth and neonatal death Preterm delivery: <37 wks GA Low birth weight (reported as prematurity): <2501g Harms: NR
Notes	The study also included a control group of non-bacteriuric women.

ASB: asymptomatic bacteriuria; g: gram(s); GA: gestational age; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; UTI: urinary tract infection; wks: weeks

Supplement 5. Risk of bias (ROB) assessments for included studies

Summary of ROB for studies of screening effectiveness

First Author, Year	Selection					Comparability		Outcome				Total Score[a] (max 9)	Selective Outcome Reporting[b]
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at start of study (pyelonephritis/ other outcomes)	Total	Comparability of cohorts	Total	Assessment of outcome	Adequacy of length of follow-up	Adequacy of follow-up of cohorts	Total		
Gérard, 1983	1	1	0	0/1	3	0	0	1	1	1	3	6	Suspected[c]
Gratacós, 1994	1	1	0	0/1	3	0	0	1	1	1	3	6	Suspected[d]
Rhode, 2007	1	1	1	0/1	4	1	1	1	1	1	3	8	Suspected[e]
Uncu, 2002	1	1	1	0/1	4	0	0	1	1	0	2	6	Not suspected[f]

[a]Assessed using the Newcastle-Ottawa Quality Assessment Scale[31]

[b]Assessed due to concern regarding reporting bias in the studies, but assessment not included in the total score

[c]Did not report on fetal abnormalities

[d]Did not report on spontaneous abortion, perinatal mortality, preterm delivery or fetal abnormalities

[e]Did not report on spontaneous abortion, perinatal mortality, or fetal abnormalities

[f]Reported on all outcomes, including fetal death >20 weeks of gestation (eligible for perinatal mortality)

ROB for studies of screening effectiveness

Domain	Author's judgement	Support for judgement
Gérard, 1983 (cohort)		
Representativeness of the exposed cohort	1	Included all pregnant women who visited the clinic at <25 wks GA.
Selection of the non-exposed cohort	1	Formed retrospectively, pregnant women attending the clinic in the 10 previous months (before implementation of screening).
Ascertainment of exposure	0	Not reported.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	0	No evidence of comparability.
Assessment of outcome	1	Appear to have used a chart review.
Adequacy of length of follow-up	1	Follow-up until delivery and for 3-6 months post-partum for those with ≥2 instances of asymptomatic bacteriuria.
Adequacy of follow-up of cohorts	1	No loss to follow-up.
Selective outcome reporting[b]	suspected	Did not report on fetal abnormalities.
Total score (maximum 10)	6	
Gratacós, 1944 (cohort)		
Representativeness of the exposed cohort	1	All pregnant women presenting to the clinic at <25 wks GA between January 1991 and December 1992.
Selection of the non-exposed cohort	1	Women who visited the same clinic in years (January 1987 to December 1990) before implementation of the screening program.
Ascertainment of exposure	0	Not reported.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	0	No evidence of comparability.
Assessment of outcome	1	Used a chart review – 'was recorded for 6 years'.
Adequacy of length of follow-up	1	Followed-up until delivery.
Adequacy of follow-up of cohorts	1	10 (6.9%) lost to follow-up.
Selective outcome reporting[b]	suspected	Did not report on spontaneous abortion, perinatal mortality, preterm delivery or fetal abnormalities.
Total score (maximum 10)	6	
Rhode, 2007 (cohort)		
Representativeness of the exposed cohort	1	All pregnant women who enrolled for care and delivered after August 15, 2002.
Selection of the non-exposed cohort	1	All pregnant women who enrolled for care at the same practice and delivered before August 15, 2002.

Domain	Author's judgement	Support for judgement
Ascertainment of exposure	1	Used delivery records.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	1	Compared 10 demographic factors, showing that groups were similar.
Assessment of outcome	1	Used a chart review.
Adequacy of length of follow-up	1	Followed-up until delivery of the patient left the practice.
Adequacy of follow-up of cohorts	1	112 (4.6%) lost to follow-up.
Selective outcome reporting[b]	suspected	Did not report on spontaneous abortion, perinatal mortality or fetal abnormalities.
Total score (maximum 10)	8	
Uncu, 2002 (cohort)		
Representativeness of the exposed cohort	1	All pregnant women <32 wks GA seen at an antenatal outpatient clinic.
Selection of the non-exposed cohort	1	Women who visited the clinic prior to the start of the screening study.
Ascertainment of exposure	1	Used delivery records.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	0	No evidence of comparability.
Assessment of outcome	1	Used delivery records.
Adequacy of length of follow-up	1	Follow-up until post-delivery.
Adequacy of follow-up of cohorts	0	Not reported.
Selective outcome reporting[b]	not suspected	Reported on all outcomes, including fetal death >20 wks GA (eligible for perinatal mortality).
Total score (maximum 10)	6	

GA: gestational age; wks: weeks

[a]Assessed using the Newcastle-Ottawa Quality Assessment Scale

[b]Assessed due to concern regarding reporting bias in the studies, but assessment not included in the total score

Summary of ROB for studies of women's outcome valuation

First Author, Year	Did the study address a clearly focused question / issue?	Is the research method (study design) appropriate for answering the research question?	Is the method of selection of the subjects clearly described?	Could the way the sample was obtained introduce bias?	Was the sample of subjects representative of the population to which the findings will be referred?	Was the sample size based on pre-study considerations of [illegible]?	Was a satisfactory response rate achieved?	Are the measurements (questionnaires) likely to be valid and reliable?	Was the statistical significance assessed?	Are confidence intervals given for the main results?	Could there be confounding factors that haven't been accounted for?	Can the results be applied to your organization?
Butters, 1990	1	1	1	2	1	2	1	2	1	3	1	1
Kazemier, 2015	2	2	1	3	1	2	2	2	3	3	2	3
Lupattelli, 2014	1	1	1	1	1	2	2	2	1	1	3	1
Mashayekhi, 2009	1	1	1	1	1	2	2	2	1	3	1	1
Nordeng, 2010	1	1	1	1	1	2	2	2	1	3	2	1
Sanz, 2000	1	1	3	2	1	2	2	2	1	3	1	1
Sharma, 2006	1	1	3	2	1	2	2	1	1	3	1	1
Twigg, 2016	1	1	1	1	1	2	2	1	1	3	1	1

[a]Assessed using a tool developed by the Center for Evidence-based Management[32] for cross-sectional studies (surveys)

1=Yes, 2=Can't Tell, 3=No

ROB for studies of women's outcome valuation

Domain	Author's judgement*	Support for judgement
Butters, 1990 (cross-sectional survey)		
Clearly focused question/issue	1	Awareness of the effects of commonly used drugs, cigarettes and alcohol on the fetus
Appropriate research method (study design)	1	Cross-sectional survey of women in postnatal wards
Selection of subjects clearly described	1	Provides inclusion and exclusion criteria, outlines selection methods
Sampling method introduces bias	2	Sampling was not random, may be consecutive
Sample of subjects representative of the population	1	Included women who were recently post-partum
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	1	Response rate was 87%
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Chi-square analysis
Confidence intervals for main results	3	No confidence intervals reported
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Identifies areas for further education in this population
Kazemier, 2015 (Prospective multi-centre screening cohort with embedded treatment RCT; valuation of outcomes obtained/reported in cross-sectional manner)		
Clearly focused question/issue	2	To assess maternal and neonatal consequences of treating and not treating asymptomatic bacteriuria in pregnancy; however, no direct examination of outcome valuation set out in protocol or study methods
Appropriate research method (study design)	2	Appears to be cross-sectional for information regarding why eligible women did not consent to participate in treatment trial
Selection of subjects clearly described	1	Clear inclusion and exclusion criteria for screening cohort and treatment RCT, with study flow documented
Sampling method introduces bias	3	Various clinics, hospitals and ultrasound centres in the Netherlands
Sample of subjects representative of the population	1	Women 18 years or older with singleton pregnancy without symptoms of urinary tract infection.
Sample size based on pre-study considerations of statistical power	2	Sample size estimates reported in statistical analysis, but none specified for cross-section of women for outcome valuation
Satisfactory response rate	2	Authors did not report response rate specifically for cross-section of women who declined treatment. Of 255 ASB-positive women, 163 received no treatment (of whom 155 did not want treatment for specified reason), but authors do not report if those who participated in treatment trial were asked/provided reason(s)

Questionnaires are likely to be valid and reliable	2	Validation of reason(s) for dissenting not reported
Statistical significance assessed	3	Fisher's exact test for outcomes from screening cohort and treatment trial; no significance for outcome valuation data
Confidence intervals for main results	3	CI's reported for outcomes from screening cohort and treatment trial; no CI's for outcome valuation data
Confounding factors not accounted for	2	Assessed confounders for outcomes from screening cohort and treatment trial, but not for outcome valuation data
Applicability of the results	3	Medication avoidance for asymptomatic conditions in pregnancy among Dutch women acknowledged by study authors to align with Dutch guidelines (not routinely screening and treating women with ASB); may be more applicable for the Netherlands but not for Canada where routine screening and treatment is standing practice
Lupattelli, 2014 (cross-sectional survey)		
Clearly focused question/issue	1	Association of health literacy and risk perception
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women
Selection of subjects clearly described	1	Self-selection, voluntary internet survey
Sampling method introduces bias	1	Informal sampling method – self-selection was not random or consecutive
Sample of subjects representative of the population	1	Pregnant women with internet access
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Mann-Whitney U test, Spearman's rank correlation coefficient, logistic regression
Confidence intervals for main results	1	Reported in Table 3
Confounding factors not accounted for	3	Adjusted for confounders in statistical analysis
Applicability of the results	1	Health literacy is significantly associated with adherence to pharmacotherapy in pregnant women
Mashayekhi, 2009 (cross-sectional survey)		
Clearly focused question/issue	1	Awareness of pregnant women on the effects of drugs during pregnancy
Appropriate research method (study design)	1	Cross-sectional survey of pre and postnatal women
Selection of subjects clearly described	1	Reports selection methods
Sampling method introduces bias	1	Sampling was not random or consecutive
Sample of subjects representative of the population	1	Included pre and postnatal women in hospital wards

Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Chi-square, Student's t-test, Pearson correlations, ANOVA
Confidence intervals for main results	3	Not reported
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Identifies roles for pharmacists in education of this population
Nordeng, 2010 (cross-sectional survey)		
Clearly focused question/issue	1	Women's perception of risk during pregnancy
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women and mothers
Selection of subjects clearly described	1	Self-selection, voluntary internet survey
Sampling method introduces bias	1	Informal sampling method – self-selection was not random or consecutive
Sample of subjects representative of the population	1	Pregnant women and young mothers (child less than 5 years) with internet access
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Linear regression, ANOVA, Student's t-test
Confidence intervals for main results	3	Confidence intervals were available in graph format only
Confounding factors not accounted for	2	Addressed in limitations
Applicability of the results	1	Indicates women overestimate risks and more education in this area is needed.
Sanz, 2000 (cross-sectional)		
Clearly focused question/issue	1	Drug utilization in pregnant women
Appropriate research method (study design)	1	Cross sectional, visual analogue scale
Selection of subjects clearly described	3	Selection methods are not reported for all populations
Sampling method introduces bias	2	Not reported for all populations
Sample of subjects representative of the population	1	Pregnant women attending out-patient clinic at a hospital
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Small n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of VAS questions was not reported
Statistical significance assessed	1	Mann-Whitney U, Kruskal Wallis, Chi-squared

Confidence intervals for main results	3	Only in graph format
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Pregnant women have high perceptions of teratogenic risk
Sharma, 2006 (cross-sectional survey)		
Clearly focused question/issue	1	Drug utilization in pregnant women
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women
Selection of subjects clearly described	3	Selected from an antenatal clinic but no sampling methods
Sampling method introduces bias	2	Not reported
Sample of subjects representative of the population	1	Pregnant women
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	1	Women's statements were confirmed through medical records when available
Statistical significance assessed	1	Chi-squared test
Confidence intervals for main results provided	3	Not reported
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Education of women of child-bearing age regarding benefits and harms of drug use during pregnancy is needed
Twigg, 2016 (cross-sectional survey)		
Clearly focused question/issue	1	Risk perception of medications in pregnant women and relationship with use
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women and new mothers
Selection of subjects clearly described	1	Self-selection, voluntary internet survey
Sampling method introduces bias	1	Informal sampling method – self-selection was not random or consecutive
Sample of subjects representative of the population	1	Pregnant women or women <1 year post-natal with internet access
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	1	Used validated BMQ-General questionnaire
Statistical significance assessed	1	Chi-square, Fisher's exact test, Mann-Whitney U, Independent t-test
Confidence intervals for main results	3	No confidence intervals for the main results, descriptive statistics only
Confounding factors not accounted for	1	Adjustment for confounding not reported in design or analysis

Applicability of the results	1	Medication use by pregnant women is impacted by beliefs about risk

[a]Assessed using a tool developed by the Center for Evidence-based Management for cross-sectional studies
* 1=Yes, 2=Can't Tell, 3=No
ANOVA: analysis of variance; ASB: asymptomatic bacteriuria; BMQ: beliefs about medicine questionnaire; n: sample size; RCT:randomized clinical trial; VAS: visual analogue scale

Summary of ROB for studies of treatment effectiveness

Study	Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel[1]	Blinding of Outcome Assessors[1]	Incomplete Reporting[2]	Selective Reporting[3]	Other Bias[4]	Overall Risk of Bias*
Brumfitt 1975								
Elder 1966								
Elder 1971								
Foley 1987								
Furness 1975								
Gold 1966								
Kass 1960								
Kazemier 2015								
Kincaid-Smith 1965								
Little 1966								
Mulla 1960								
Pathak 1969								
Thomsen 1987								
Williams 1969								
Wren 1969								

[a] Assessed using the Cochrane Risk of Bias[34] tool

[1] For the blinding domains, objective outcomes were considered to be at lower ROB than subjective outcomes

[2] For the incomplete reporting domain, 10-30% loss to follow-up were considered as Unclear ROB if no apparent between groups or reasons were provided

[3] For the selective reporting domain, a default of Low ROB was used for selective reporting when this was undetected or not highly suspected

[4] Assessed as: Low risk of bias if no other sources of bias are identified, High risk of bias if other sources of bias detected such as: participant characteristics (baseline imbalances), study design characteristics (crossover, cluster-randomized, or blocked randomization in trials without blinding); Unclear risk of bias assessment not applicable for this domain.

* Assessed as: Low if all domains are assessed as low, Unclear if at least one domain is assessed as unclear and no domains are assessed as high, or High if at least one domain is assessed as high.

Legend:

- Low risk
- Unclear risk
- High risk

ROB for individual studies of treatment effectiveness

Domain	Author's judgement	Support for judgement
Brumfitt, 1975 (RCT)		
Random sequence generation	Unclear	No description of the sequence generation process, how women were assigned to treatment or placebo, unequal numbers in treatment and placebo groups.
Allocation concealment	Unclear	No information provided to judge.
Blinding of participants and personnel	Low	"…were given placebo under double-blind conditions". Method not described in sufficient detail. Objective outcomes.
Blinding of outcome assessment	Low	"…were given placebo under double-blind conditions". Method not described in sufficient detail. Objective outcomes.
Incomplete outcome data	High	Inconsistencies in total number of women not explained (number of <2500g babies provided for 413/326 bacteriuric women); results not provided for pyelonephritis for all women in treated group (only subset).
Selective reporting	High	Results not provided for pyelonephritis for all women allocated to treatment.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Elder, 1966 (RCT)		
Random sequence generation	Unclear	"…a random sequence". Insufficient information to judge.
Allocation concealment	Unclear	No information provided to judge.
Blinding of participants and personnel	Low	"…double-blind trial"; no information provided to judge. Objective outcomes.
Blinding of outcome assessment	Low	"…double-blind trial"; no information provided to judge. Objective outcomes.
Incomplete outcome data	Low	Information provided on women lost to follow-up, reasonably balanced between groups.
Selective reporting	High	Result not provided for pyelonephritis for all participants; no pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Elder, 1971 (CCT)		
Random sequence generation	High	"…alternate bacteriuric…were assigned."
Allocation concealment	High	Participants were allocated by alternation.
Blinding of participants and personnel	Unclear	"identical-appearing placebo"; insufficient information to judge.
Blinding of outcome assessment	Unclear	"identical-appearing placebo"; insufficient information to judge.
Incomplete outcome data	Unclear	Insufficient information to judge.
Selective reporting	Unclear	Unable to judge; twin deliveries were excluded.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Foley, 1987		

Domain	Author's judgement	Support for judgement
Random sequence generation	Low	Allocated to treatment or no treatment by "toss of a coin".
Allocation concealment	Unclear	No information to judge.
Blinding of participants and personnel	Unclear	No description of any attempt at blinding; not placebo-controlled. Objective outcomes.
Blinding of outcome assessment	Unclear	No description of any attempt at blinding; not placebo-controlled. Objective outcomes.
Incomplete outcome data	Unclear	Loss to follow-up: 19%; no reasons provided for missing outcome data.
Selective reporting	High	No pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Furness, 1975 (RCT)		
Random sequence generation	Unclear	"by random allocation"; no additional information to judge.
Allocation concealment	Unclear	No information to judge.
Blinding of participants and personnel	Unclear	Not placebo-controlled. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge.
Incomplete outcome data	High	20/226 women withdrawn from trial, no details provided. All women included in outcome of pyelonephritis, 17% loss to follow-up or low birthweight and GA at delivery.
Selective reporting	Unclear	Unable to separate incidence of pyelonephritis during pregnancy and puerperium; results combined.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Gold, 1966 (CCT)		
Random sequence generation	High	Women allocated to treatment based on study number: odd number treatment, even number control.
Allocation concealment	High	Allocated to treatment based on study number.
Blinding of participants and personnel	Unclear	Placebo-controlled; no further details provided. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge. Objective outcomes.
Incomplete outcome data	Low	Does not appear to be any loss to follow-up.
Selective reporting	Unclear	No definition provided for prematurity.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Kass, 1960 (CCT)		
Random sequence generation	High	"alternate women received a placebo".
Allocation concealment	High	Allocation based on alternation: "alternate women received a placebo".

Domain	Author's judgement	Support for judgement
Blinding of participants and personnel	Low	Placebo was used and "the nature of the treatment was not known to the patient or to the attending obstetrical staff".
Blinding of outcome assessment	Unclear	Although a placebo was used, no further details are provided on blinding of outcome assessment. Objective outcomes.
Incomplete outcome data	Unclear	40 (21%) women were not enrolled either because they were >32 weeks GA before treatment could be started (n=30), or already received treatment for symptomatic infection (n=10). Loss to follow-up: 23 (11%) for pyelonephritis and low birthweight, no details provided; 69 (34%) for long-term persistent bacteriuria.
Selective reporting	Unclear	3 women had subsequent pregnancy and were reassigned to their original treatment group included in the analysis. In 5 placebo patients, symptomatic disease was assumed but no symptoms were documented. Not all women in symptomatic group were confirmed to have fever. Women treated for infections other than that in the urinary tract were included in the symptomatic group if they had cleared their bacteriuria.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Kazemier, 2015 (RCT)		
Random sequence generation	Low	Random assignment in 1:1 ratio; computer-generated list with random block sizes of 2/4/6 participants.
Allocation concealment	Low	Women, treating physicians and researchers remained unaware of bacteriuria status and treatment allocation. Central allocation - unmasking of treatment allocation was possible by 24h telephone service.
Blinding of participants and personnel	Low	Double-blinded. Women, treating physicians and researchers remained unaware of bacteriuria status and treatment allocation. Objective outcomes.
Blinding of outcome assessment	Low	Outcomes recorded by participants on questionnaires, and from data provided by hospitals and midwives up to 6 weeks post-delivery.
Incomplete outcome data	Low	ITT and dropout rate <10% (12/255 ASB-positive)
Selective reporting	Low	Cost-effectiveness was outlined in protocol but not reported in final study methods or results.
Other bias	Low	No other sources of bias identified.
Overall risk of bias	Low	
Kincaid-Smith, 1965 (RCT)		
Random sequence generation	Unclear	No description of sequence generation process.
Allocation concealment	Low	"a code of instructions to the pharmacist ensured that the trial remained double-blind despite…alterations in therapeutic regimen".
Blinding of participants and personnel	Low	"a code of instructions to the pharmacist ensured that the trial remained double-blind despite…alterations in therapeutic regimen".
Blinding of outcome assessment	Low	"a code of instructions to the pharmacist ensured that the trial remained double-blind despite…alterations in therapeutic regimen".
Incomplete outcome data	Unclear	240 women initially identified as bacteriuric; no information available on 55 (23%) women randomized to treatment but not included in the analysis because of poor compliance (attended infrequently or failed to take tablets continuously).
Selective reporting	Unclear	Insufficient information to judge.

Domain	Author's judgement	Support for judgement
Other bias	Low	Insufficient information to judge.
Overall risk of bias	Unclear	
Little, 1966 (RCT)		
Random sequence generation	Unclear	No information to judge.
Allocation concealment	Unclear	Allocation to treatment or control was drawn for "a pool of sealed envelopes containing a slip of paper", but there was no information provided to ensure appropriate safeguards to prevent investigators being aware of the treatment group.
Blinding of participants and personnel	Unclear	Participants in the control group "were given placebo"; no further details provided. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge. Objective outcomes.
Incomplete outcome data	Low	No missing outcome data.
Selective reporting	Unclear	Insufficient information to judge.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	Unclear	
Mulla, 1960 (RCT)		
Random sequence generation	Unclear	No description of sequence generation process.
Allocation concealment	Unclear	Women were "randomly divided into two groups"; no other details provided
Blinding of participants and personnel	Unclear	Not placebo-controlled. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge. Objective outcomes.
Incomplete outcome data	Low	No missing outcome data.
Selective reporting	High	No definition for outcome of cystopyelitis; no pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Pathak, 1969 (RCT)		
Random sequence generation	Unclear	"on a random basis". Insufficient information provided to permit further judgement.
Allocation concealment	Unclear	Method of concealment not described.
Blinding of participants and personnel	Unclear	No information to judge.
Blinding of outcome assessment	Unclear	No information to judge.
Incomplete outcome data	Low	Missing outcome data balanced; reasons similar and unlikely to have introduced bias.
Selective reporting	High	No pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Thomsen, 1987 (RCT)		

Domain	Author's judgement	Support for judgement
Random sequence generation	Unclear	Described as "randomly allocated" but no description of the sequence generation process.
Allocation concealment	Unclear	Method of concealment of allocation not described.
Blinding of participants and personnel	Unclear	Placebo-controlled, described as "double-blinded" but no additional data. Objective outcomes.
Blinding of outcome assessment	Unclear	Described as "double-blinded" but no specific information provided to ensure outcome assessment was blinded. Objective outcomes.
Incomplete outcome data	Low	No missing outcome data.
Selective reporting	Unclear	Insufficient information to judge.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	Unclear	
Williams, 1969 (RCT)		
Random sequence generation	Unclear	"allocation at random"; no additional information to judge.
Allocation concealment	Unclear	No information to judge.
Blinding of participants and personnel	Unclear	No blinding, outcome may have been influenced by lack of blinding. No treatment group was given antibiotics to take if symptoms of infection developed. Objective outcomes.
Blinding of outcome assessment	Unclear	No blinding; assessment of outcome (pyelonephritis) may have been influenced by knowledge of treatment allocation. Objective outcomes.
Incomplete outcome data	Unclear	No explanation for unequal group sizes; no information provided on any missing data. An unknown number of women in the control group were given antibiotic treatment if they developed symptoms of UTI.
Selective reporting	High	No pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Wren, 1969 (CCT)		
Random sequence generation	High	Women "were divided into two groups, alternate patients being treated".
Allocation concealment	High	Women "were divided into two groups, alternate patients being treated".
Blinding of participants and personnel	Unclear	No blinding; knowledge of treatment group may have influenced outcome; women in untreated group who developed clinical UTI (33/90) were given antibiotics at the choice of the obstetrician, continued to delivery in 50% of cases. Objective outcomes.
Blinding of outcome assessment	Unclear	No blinding; however, outcome of birthweight unlikely to be influenced by lack of blinding.
Incomplete outcome data	Low	10 (6%) women not included in outcomes: 2 sets of twins excluded, 6 moved and 2 could not be traced, 3 delivered before antibiotics could be started, 1 refused treatment.
Selective reporting	Unclear	Insufficient information to judge; outcome of pyelonephritis not reported.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	

[a]Assessed using the Cochrane Risk of Bias tool

ASB: asymptomatic bacteriuria; g: gram(s); GA: gestational age; UTI: urinary tract infection

Supplement 6. GRADE Summary of Findings & Evidence Profiles tables & forest plots

Evidence Set 1. Table 1.1 GRADE Summary of Findings – Benefits and harms of screening compared to no screening

Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Patient or population: asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: screening

Comparison: no screening

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no screening	**Risk with screening**				
Maternal mortality	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal mortality.
Maternal sepsis	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal sepsis.
Pyelonephritis	**Median**		**RR 0.28** (0.15 to 0.54)	5659 (3 observational studies)	⨁◯◯◯ VERY LOW [1,a]	We are very uncertain about the effects of screening on pyelonephritis.
	18 per 1,000	**13 fewer per 1,000** (from 8 fewer to 16 fewer)				
Perinatal mortality	**Median**		**RR 1.21** (0.01 to 102.93)	724 (2 observational studies)	⨁◯◯◯ VERY LOW [1,b]	We are very uncertain about the effects of screening on perinatal mortality.
	19 per 1,000	**4 more per 1,000** (from 19 fewer to 1,000 more)				
Spontaneous abortion	55 per 1,000	**2 fewer per 1,000** (from 32 fewer to 70 more)	**RR 0.96** (0.41 to 2.27)	370 (1 observational study)	⨁◯◯◯ VERY LOW [1,c]	We are very uncertain about the effects of screening on spontaneous abortion.

Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Patient or population: asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: screening

Comparison: no screening

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no screening	**Risk with screening**				
Neonatal sepsis	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on neonatal sepsis.
Preterm delivery	**Median** 13 per 1,000	**102 more per 1,000** (from 9 fewer to 1,000 more)	**RR 8.70** (0.32 to 240.07)	722 (2 observational studies)	⨁◯◯◯ VERY LOW [1, d]	We are very uncertain about the effects of screening on preterm delivery.
Low birthweight	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on low birthweight.
Maternal serious harm(s)	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal serious harms.
Neonatal serious harm: fetal abnormalities	11 per 1,000	**5 more per 1,000** (from 8 fewer to 85 more)	**RR 1.50** (0.25 to 8.87)	372 (1 observational study)	⨁◯◯◯ VERY LOW [1, e]	We are very uncertain about the effects of screening on fetal abnormalities.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Patient or population: asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: screening

Comparison: no screening

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no screening	**Risk with screening**				

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

Pyelonephritis [a] → Very Low Quality Evidence: Three non-concurrent cohort studies (Gérard 1983, Gratacós 1994, Uncu 2001) reported this outcome (n=5,659). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics. The optimal information size is met (sample size >5600), therefore downgrading for **imprecision** is not warranted. There were no serious concerns to warrant downgrading for **inconsistency**, **indirectness**, or **other considerations**.

Perinatal mortality [b] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=724; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on perinatal mortality. Further downgrading is warranted for **imprecision** due to optimal information size not being met with a small sample size. There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

Spontaneous abortion [c] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Gérard 1983). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk

factors or other patient characteristics, and suspected reporting bias as two studies did not report on spontaneous abortion. Only one study provided data on spontaneous abortion, so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to low event rates (total of 20) without optimal information size. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Preterm delivery [d] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=722; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on preterm delivery. Further downgrading is warranted for **imprecision** for inadequate sample size and optimal information size not being met (total of 38 events). There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

Neonatal serious harm: fetal abnormalities (harm) [e] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Uncu 2001). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as three studies did not report on fetal abnormalities. Only one study provided data on this outcome so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to the optimal information size not being met for rare events. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Evidence Set 1. Table 1.2 GRADE Evidence Profile – Benefits and harms of screening compared to no screening

Question: Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**screening**	**no screening**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal mortality												
0									not estimable		-	CRITICAL
Maternal sepsis												
0									not estimable		-	CRITICAL
Pyelonephritis												
3	observational studies	serious	not serious	not serious	serious	none	10/2008 (0.5%)	1.8%	**RR 0.28** (0.15 to 0.54)	**13 fewer per 1,000** (from 8 fewer to 16 fewer)	⊕◯◯◯ VERY LOW [1, a]	CRITICAL
Perinatal mortality												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**screening**	**no screening**	**Relative (95% CI)**	**Absolute (95% CI)**		
2	observational studies	serious	not serious	not serious	serious	none	6/349 (1.7%)	1.9%	**RR 1.21** (0.01 to 102.93)	**4 more per 1,000** (from 19 fewer to 1,000 more)	⊕◯◯◯ VERY LOW [1, b]	CRITICAL
Spontaneous abortion												
1	observational studies	serious	serious	not serious	serious	none	9/170 (5.3%)	11/200 (5.5%)	**RR 0.96** (0.41 to 2.27)	**2 fewer per 1,000** (from 32 fewer to 70 more)	⊕◯◯◯ VERY LOW [1, c]	CRITICAL
Neonatal sepsis												
0									not estimable		-	CRITICAL
Preterm delivery												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**screening**	**no screening**	**Relative (95% CI)**	**Absolute (95% CI)**		
2	observational studies	serious	not serious	not serious	serious	none	33/347 (9.5%)	1.3%	**RR 8.70** (0.32 to 240.07)	**102 more per 1,000** (from 9 fewer to 1,000 more)	⨁◯◯◯ VERY LOW [1, d]	CRITICAL
Low birthweight												
0									not estimable		-	IMPORTANT
Maternal serious harm(s)												
0									not estimable		-	CRITICAL
Neonatal serious harm: fetal abnormalities												
1	observational studies	serious	serious	not serious	serious	none	3/186 (1.6%)	2/186 (1.1%)	**RR 1.50** (0.25 to 8.87)	**5 more per 1,000** (from 8 fewer to 85 more)	⨁◯◯◯ VERY LOW [1, e]	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

Pyelonephritis [a] → Very Low Quality Evidence: Three non-concurrent cohort studies (Gérard 1983, Gratacós 1994, Uncu 2001) reported this outcome (n=5,659). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics. The optimal information size is met (sample size >5600), therefore downgrading for **imprecision** is not warranted. There were no serious concerns to warrant downgrading for **inconsistency**, **indirectness**, or **other considerations**.

Perinatal mortality [b] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=724; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on perinatal mortality. Further downgrading is warranted for **imprecision** due to optimal information size not being met with a small sample size. There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

Spontaneous abortion [c] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Gérard 1983). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on spontaneous abortion. Only one study provided data on spontaneous abortion, so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to low event rates (total of 20) without optimal information size. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Preterm delivery [d] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=722; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on preterm delivery. Further downgrading is warranted for **imprecision** for inadequate sample size and optimal information size not being met (total of 38 events). There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

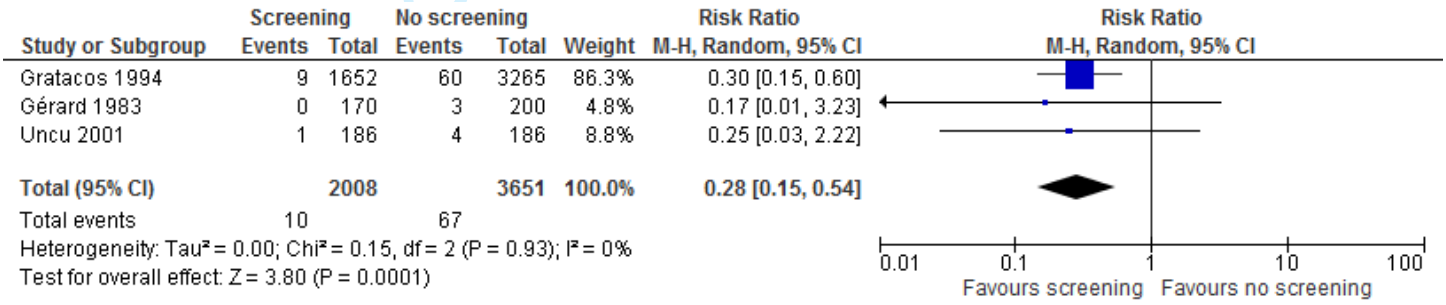
Neonatal serious harm: fetal abnormalities [e] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Uncu 2001). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as three studies did not report on fetal abnormalities. Only one study provided data on this outcome so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to the optimal information size not being met for rare events. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Evidence Set 1. Forest Plots 1.1-1.5 – Benefits and harms of screening compared to no screening

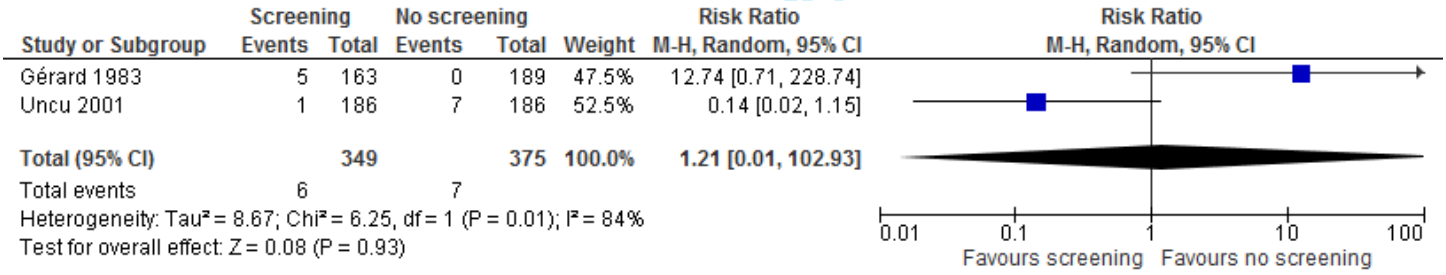
Outcome	No. of studies	No. of participants	Effect size (Risk Ratio; M-H, Random, 95%CI)
1.1 Pyelonephritis	3	5659	0.28 [0.15, 0.54]
1.2 Perinatal mortality >=20 wks GA note: Gérard >=31 wks; Uncu >20 wks	2	724	1.21 [0.01, 102.93]
1.3 Spontaneous abortion <20 wks GA note: 1 study <=28 wks (all occurred 7-21 wks)	1	370	0.96 [0.41, 2.27]
1.4 Preterm delivery <37 wks GA	2	722	8.70 [0.32, 240.07]
1.5 Neonatal serious harm: fetal abnormalities	1	372	1.50 [0.25, 8.87]

CI: confidence interval; GA: gestational age; M-H: Mantel-Haenszel; No.: number; wks: weeks

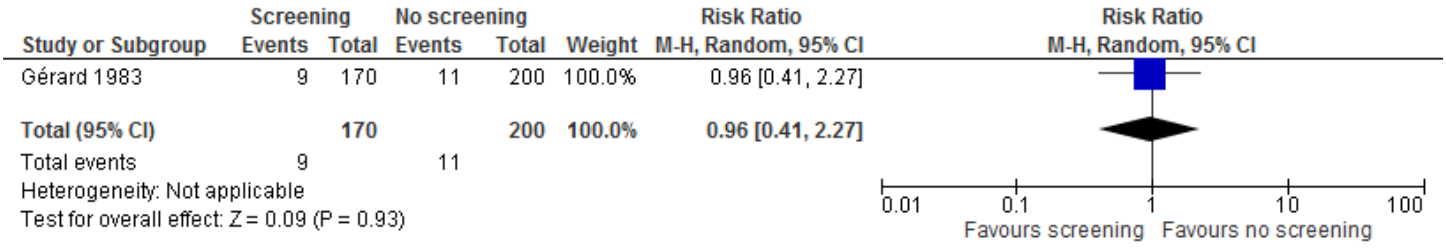
1.1 Pyelonephritis



1.2 Perinatal mortality (>=20 wks GA)



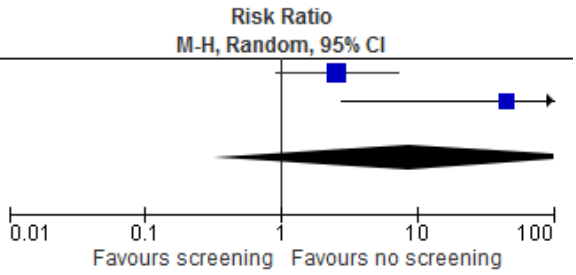
1.3 Spontaneous abortion (<20 wks GA)



1.4 Preterm delivery (<37 wks GA)

Study or Subgroup	Screening Events	Screening Total	No screening Events	No screening Total	Weight	Risk Ratio M-H, Random, 95% CI
Gérard 1983	11	161	5	189	57.5%	2.58 [0.92, 7.28]
Uncu 2001	22	186	0	186	42.5%	45.00 [2.75, 736.39]
Total (95% CI)		**347**		**375**	**100.0%**	**8.70 [0.32, 240.07]**
Total events	33		5			

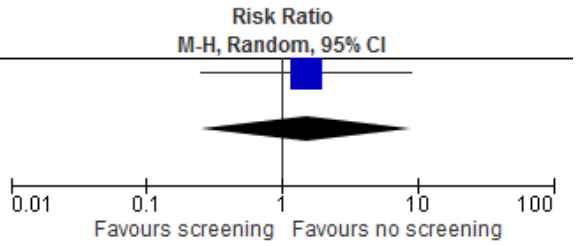
Heterogeneity: Tau² = 4.70; Chi² = 5.07, df = 1 (P = 0.02); I² = 80%
Test for overall effect: Z = 1.28 (P = 0.20)



1.5 Neonatal serious harm: fetal abnormalities

Study or Subgroup	Screening Events	Screening Total	No screening Events	No screening Total	Weight	Risk Ratio M-H, Random, 95% CI
Uncu 2001	3	186	2	186	100.0%	1.50 [0.25, 8.87]
Total (95% CI)		**186**		**186**	**100.0%**	**1.50 [0.25, 8.87]**
Total events	3		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.45 (P = 0.65)



Evidence Set 2. Table 2.1 GRADE Summary of Findings - Benefits and harms of frequent screening compared to one-time screening

Frequent screening compared to one-time screening for asymptomatic bacteriuria						
Patient or population: asymptomatic bacteriuria **Setting**: Any primary clinical care setting providing care to pregnant women **Intervention**: frequent screening **Comparison**: one-time screening						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with one-time screening	**Risk difference with frequent screening**				
Pyelonephritis	4 per 1,000	**0 fewer per 1,000** (from 3 fewer to 13 more)	**RR 1.09** (0.27 to 4.35)	1952 (1 observational study)	⨁◯◯◯ VERY LOW [1, a]	We are very uncertain about the effects of frequent screening compared to one-time screening on pyelonephritis.
Preterm delivery	49 per 1,000	**28 more per 1,000** (from 5 more to 60 more)	**RR 1.57** (1.11 to 2.23)	1952 (1 observational study)	⨁◯◯◯ VERY LOW [1, b]	We are very uncertain about the effects of frequent screening compared to one-time screening on preterm delivery.
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio						
GRADE Working Group grades of evidence **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect						

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when

optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

CI: Confidence interval; **RR:** Risk ratio

Pyelonephritis [a] → Very Low Quality Evidence: One non-concurrent cohort study (n=1952; Rhode 2007) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** associated with: 1) no demonstration that pyelonephritis was not present at start of study, 2) no demonstration of comparability between frequent and one-time screening groups, and 3) no adjustment to analyses to account for risk factors or other patient characteristics. Only one study provided data for this outcome so downgrading is warranted for **inconsistency**. Further downgrading is warranted for **indirectness** as the women are predominantly medically underserved, Hispanic and receiving care from a midwifery clinic, with a high rate of gestational diabetes (9%). The optimal information size is not met (8 events) with sample size (n=1952), therefore this warrants downgrading for **imprecision**. There were no serious concerns to warrant downgrading for **other considerations**.

Preterm delivery [b] → Very Low Quality Evidence: One non-concurrent cohort study (n=1952; Rhode 2007) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to very serious **risk of bias** associated with: 1) no demonstration of comparability between frequent and one-time screening groups, 2) no adjustment to analyses to account for risk factors or other patient characteristics, and 3) suspected reporting bias among outcomes reported by studies (did not report on spontaneous abortion, perinatal mortality or fetal abnormalities). Only one study provided data for this outcome so downgrading is warranted for **inconsistency**. Further downgrading is warranted for **indirectness** as the women are predominantly medically underserved, Hispanic and receiving care from a midwifery clinic, with a high rate of gestational diabetes (9%). The event rate is low (122 events) without meeting optimal information size, so this is downgraded for **imprecision**. There were no serious concerns to warrant downgrading for **other considerations**.

Evidence Set 3. Table 3.1 GRADE Summary of Findings – Benefits and harms of treatment compared to no treatment

Treatment compared to no treatment for asymptomatic bacteriuria

Patient or population: asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: treatment

Comparison: no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with treatment**				
Maternal mortality	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal mortality.
Maternal sepsis	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal sepsis.
Pyelonephritis	**Median**		**RR 0.24** (0.13 to 0.41)	2017 (12 RCTs)	⊕⊕◯◯ LOW [1, a]	There may be a reduction in pyelonephritis from treatment.
	232 per 1,000	**176 fewer per 1,000** (from 137 fewer to 202 fewer)				
Perinatal mortality	**Median**		**RR 0.96** (0.27 to 3.39)	1104 (6 RCTs)	⊕◯◯◯ VERY LOW [1, b]	We are very uncertain about the effects of treatment on perinatal mortality.
	40 per 1,000	**2 fewer per 1,000** (from 29 fewer to 97 more)				
Spontaneous abortion	**Median**		**RR 0.60** (0.11 to 3.10)	379 (2 RCTs)	⊕◯◯◯ VERY LOW [1, c]	We are very uncertain about the effects of treatment on spontaneous abortion.
	33 per 1,000	**13 fewer per 1,000** (from 30 fewer to 70 more)				

Treatment compared to no treatment for asymptomatic bacteriuria

Patient or population: asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: treatment

Comparison: no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with treatment**				
Neonatal sepsis	**Median**		**RR 0.22** (0.01 to 4.54)	154 (2 RCTs)	⨁◯◯◯ VERY LOW [1, d]	We are very uncertain about the effects of treatment on neonatal sepsis.
	22 per 1,000	**17 fewer per 1,000** (from 22 fewer to 79 more)				
Preterm delivery	**Median**		**RR 0.57** (0.21 to 1.56)	533 (4 RCTs)	⨁◯◯◯ VERY LOW [1, e]	We are very uncertain about the effects of treatment on preterm delivery.
	158 per 1,000	**68 fewer per 1,000** (from 125 fewer to 88 more)				
Low birth weight	**Median**		**RR 0.63** (0.45 to 0.90)	1522 (7 RCTs)	⨁◯◯◯ LOW [1, f]	There may be a reduction in low birth weight from treatment.
	118 per 1,000	**44 fewer per 1,000** (from 12 fewer to 65 fewer)				
Maternal serious harm(s)	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal serious harms.
	Median					

Treatment compared to no treatment for asymptomatic bacteriuria

Patient or population: asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: treatment

Comparison: no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with treatment**				
Neonatal serious harm: fetal abnormalities	19 per 1,000	**9 fewer per 1,000** (from 15 fewer to 8 more)	**RR 0.49** (0.17 to 1.43)	821 (4 RCTs)	⨁◯◯◯ VERY LOW [1, g]	We are very uncertain about the effects of treatment on harms (fetal abnormalities).
Neonatal serious harm: hemolytic anemia	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	265 (1 RCT)	⨁◯◯◯ VERY LOW [1, h]	We are very uncertain about the effects of treatment on harms (hemolytic anemia).

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

CI: Confidence interval; **RR:** Risk ratio

Pyelonephritis, overall [a] → Low Quality Evidence: Twelve trials (Brumfitt 1975, Elder 1971, Foley 1987, Furness 1975, Gold 1966, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Mulla 1960, Pathak 1969, Williams 1969) reported this outcome (n=2,017). Quality of evidence is downgraded from high to moderate due to serious **risk of bias**

associated with use of alternation for sequence generation (Elder 1971, Gold 1966, Kass 1960), inadequate allocation concealment (Elder 1971, Gold 1966, Kass 1960), and incomplete reporting (Brumfitt 1975, Furness 1975). This body of evidence on treatment effectiveness is downgraded from moderate to low for **indirectness** due to studies that did not explicitly include asymptomatic women (only 3 studies included exclusively asymptomatic women; Kazemier 2015, Mulla 1960, and Williams 1969), and studies that included high-risk women (Elder 1971, Kincaid-Smith 1965, Little 1966, and Pathak 1969). The optimal information size criterion is met (control group event rate=20%; total number of events=253) with an adequate sample size (n=2,017), and the confidence interval (0.13 to 0.41) indicates there may be important benefit; therefore, downgrading is not warranted for **imprecision**. There were no concerns with **inconsistency** or **other considerations** to warrant further downgrading.

Perinatal mortality [b] → Very Low Quality Evidence: Six trials (n=1,104; Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Kass 1960, Wren 1969), and inadequate allocation concealment (Elder 1971, Kass 1960). This body of evidence on treatment effectiveness is downgraded for **indirectness** due to studies that did not explicitly include asymptomatic women as well as studies that included high-risk women. Further downgrading is warranted for **imprecision** due to the samples size not being met for optimal information size criterion (37 events). There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Spontaneous abortion [c]→ Very Low Quality Evidence: Two trials (n=379; Furness 1975, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969) and incomplete reporting (Furness 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size is inadequate with optimal information size not met (10 events) to warrant downgrading twice from low to very low for **imprecision**. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal sepsis [d] → Very Low Quality Evidence: Two trials (n=154; Kazemier 2015, Thomsen 1987) reported this outcome. Quality of evidence is downgraded for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size (<2000) is not met with only 2 events to warrant downgrading twice for **imprecision**. There were no concerns to warrant downgrading for **risk of bias, inconsistency** or **other considerations**.

Preterm delivery [e] → Very Low Quality Evidence: Four trials (n=533; Furness 1975, Kazemier 2015, Thomsen 1987, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969), and incomplete reporting (Furness 1975). There is substantial heterogeneity (I^2=70%) with point estimates on both sides of the line of no effect to warrant downgrading for **inconsistency**. Downgrading from moderate to low for **indirectness** is warranted due to studies that did not explicitly include exclusively asymptomatic women. There were no concerns to warrant downgrading for **imprecision or other considerations**.

Low birth weight [f] → Low Quality Evidence: Seven trials (n=1,522; Brumfitt 1975, Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Kass 1960, Wren 1969), inadequate allocation concealment (Elder 1971, Kass 1960, Wren 1969), and incomplete reporting (Brumfitt 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. The optimal information size was not quite met (<2000 patients and <200 events), but we did not think the concerns were serious enough to downgrade for this outcome for **imprecision.** There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: fetal abnormalities [g] → Very Low Quality Evidence: Four trials (n=821; Elder 1971, Furness 1975, Kazemier 2015, Little 1966) reported this outcome. Quality of evidence is downgraded from high to moderate for

serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971), inadequate allocation concealment (Elder 1971), and incomplete reporting (Furness 1975). Downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. Further downgrading from low to very low for **imprecision** is warranted due to optimal information size (sample size of 821) not being met for rare events. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: hemolytic anemia [h] → Very Low Quality Evidence: One trial (n=265; Elder 1971) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation and inadequate allocation concealment. Only one study provided data for this outcome so downgrading from moderate to low for **inconsistency** is warranted. Further downgrading from low to very low is warranted for **indirectness** due the study not explicitly including exclusively asymptomatic women as well as studies that included high-risk women. Due to optimal information size (sample size of 265) not being met for rare events, downgrading twice is warranted for **imprecision**. There were no concerns to warrant downgrading for **other considerations**.

Evidence Set 3. Table 3.1 GRADE Evidence Profile – Benefits and harms of treatment compared to no treatment

Question: Treatment compared to no treatment for asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Bibliography:

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**treatment**	**no treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal mortality												
0									not estimable		-	CRITICAL
Maternal sepsis												
0									not estimable		-	CRITICAL
Pyelonephritis												
12	randomised trials	serious	not serious	serious	not serious	none	55/1023 (5.4%)	23.2%	**RR 0.24** (0.13 to 0.41)	**176 fewer per 1,000** (from 137 fewer to 202 fewer)	⨁⨁◯◯ LOW [1, a]	CRITICAL
Perinatal mortality												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision [1]	Other considerations	treatment	no treatment	Relative (95% CI)	Absolute (95% CI)		
6	randomised trials	serious	not serious	serious	serious	none	16/529 (3.0%)	4.0%	**RR 0.96** (0.27 to 3.39)	**2 fewer per 1,000** (from 29 fewer to 97 more)	⨁◯◯◯ VERY LOW [1, b]	CRITICAL
Spontaneous abortion												
2	randomised trials	serious	not serious	serious	very serious	none	4/222 (1.8%)	3.3%	**RR 0.60** (0.11 to 3.10)	**13 fewer per 1,000** (from 30 fewer to 70 more)	⨁◯◯◯ VERY LOW [1, c]	CRITICAL
Neonatal sepsis												
2	randomised trials	not serious	not serious	serious	very serious	none	0/77 (0.0%)	2.2%	**RR 0.22** (0.01 to 4.54)	**17 fewer per 1,000** (from 22 fewer to 79 more)	⨁◯◯◯ VERY LOW [1, d]	CRITICAL
Preterm delivery												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**treatment**	**no treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
4	randomised trials	serious	serious	not serious	very serious	none	34/299 (11.4%)	15.8%	**RR 0.57** (0.21 to 1.56)	**68 fewer per 1,000** (from 125 fewer to 88 more)	⊕◯◯◯ VERY LOW [1, e]	CRITICAL
Low birth weight												
7	randomised trials	serious	not serious	serious	not serious	none	64/769 (8.3%)	11.8%	**RR 0.63** (0.45 to 0.90)	**44 fewer per 1,000** (from 12 fewer to 65 fewer)	⊕⊕◯◯ LOW [1, f]	IMPORTANT
Maternal serious harm(s)												
0									not estimable		-	CRITICAL
Neonatal serious harm: fetal abnormalities												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision [1]	Other considerations	treatment	no treatment	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	serious	not serious	serious	very serious	none	4/425 (0.9%)	1.9%	**RR 0.49** (0.17 to 1.43)	**9 fewer per 1,000** (from 15 fewer to 8 more)	⨁◯◯◯ VERY LOW [1, g]	CRITICAL
Neonatal serious harm: hemolytic anemia												
1	randomised trials	serious	serious	serious	very serious	none	0/122 (0.0%)	0/143 (0.0%)	not estimable		⨁◯◯◯ VERY LOW [1, h]	CRITICAL

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

CI: Confidence interval; **RR:** Risk ratio

Pyelonephritis, overall [a] → Low Quality Evidence: Twelve trials (Brumfitt 1975, Elder 1971, Foley 1987, Furness 1975, Gold 1966, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Mulla 1960, Pathak 1969, Williams 1969) reported this outcome (n=2,017). Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Gold 1966, Kass 1960), inadequate allocation concealment (Elder 1971, Gold 1966, Kass 1960), and incomplete reporting (Brumfitt 1975, Furness 1975). This body of evidence on treatment effectiveness is downgraded from moderate to low for **indirectness** due to studies that did not explicitly include asymptomatic women (only 3 studies included exclusively asymptomatic women; Kazemier 2015, Mulla 1960, and Williams 1969), and studies that included high-risk women (Elder 1971, Kincaid-Smith 1965, Little 1966, and Pathak 1969). The optimal information size criterion is met (control group event rate=20%; total number of events=253) with an adequate sample size (n=2,017), and the confidence interval (0.13 to 0.41) indicates there may be important benefit; therefore, downgrading is not warranted for **imprecision**. There were no concerns with **inconsistency** or **other considerations** to warrant further downgrading.

Perinatal mortality [b] → Very Low Quality Evidence: Six trials (n=1,104; Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence

generation (Elder 1971, Kass 1960, Wren 1969), and inadequate allocation concealment (Elder 1971, Kass 1960). This body of evidence on treatment effectiveness is downgraded for **indirectness** due to studies that did not explicitly include asymptomatic women as well as studies that included high-risk women. Further downgrading is warranted for **imprecision** due to the samples size not being met for optimal information size criterion (37 events). There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Spontaneous abortion [c]→ Very Low Quality Evidence: Two trials (n=379; Furness 1975, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969) and incomplete reporting (Furness 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size is inadequate with optimal information size not met (10 events) to warrant downgrading twice from low to very low for **imprecision**. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal sepsis [d] → Very Low Quality Evidence: Two trials (n=154; Kazemier 2015, Thomsen 1987) reported this outcome. Quality of evidence is downgraded for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size (<2000) is not met with only 2 events to warrant downgrading twice for **imprecision**. There were no concerns to warrant downgrading for **risk of bias, inconsistency** or **other considerations**.

Preterm delivery [e] → Very Low Quality Evidence: Four trials (n=533; Furness 1975, Kazemier 2015, Thomsen 1987, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969), and incomplete reporting (Furness 1975). There is substantial heterogeneity (I^2=70%) with point estimates on both sides of the line of no effect to warrant downgrading for **inconsistency**. Downgrading from moderate to low for **indirectness** is warranted due to studies that did not explicitly include exclusively asymptomatic women. There were no concerns to warrant downgrading for **imprecision or other considerations**.

Low birth weight [f] → Low Quality Evidence: Seven trials (n=1,522; Brumfitt 1975, Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Kass 1960, Wren 1969), inadequate allocation concealment (Elder 1971, Kass 1960, Wren 1969), and incomplete reporting (Brumfitt 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. The optimal information size was not quite met (<2000 patients and <200 events), but we did not think the concerns were serious enough to downgrade for this outcome for **imprecision.** There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: fetal abnormalities [g] → Very Low Quality Evidence: Four trials (n=821; Elder 1971, Furness 1975, Kazemier 2015, Little 1966) reported this outcome. Quality of evidence is downgraded from high to moderate for serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971), inadequate allocation concealment (Elder 1971), and incomplete reporting (Furness 1975). Downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. Further downgrading from low to very low for **imprecision** is warranted due to optimal information size (sample size of 821) not being met for rare events. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: hemolytic anemia [h] → Very Low Quality Evidence: One trial (n=265; Elder 1971) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation and inadequate allocation concealment. Only one study provided data for this outcome so downgrading from moderate to low for **inconsistency** is warranted. Further downgrading from low to very low is warranted for **indirectness** due the study not explicitly including exclusively asymptomatic women as well as studies that included high-risk women. Due to

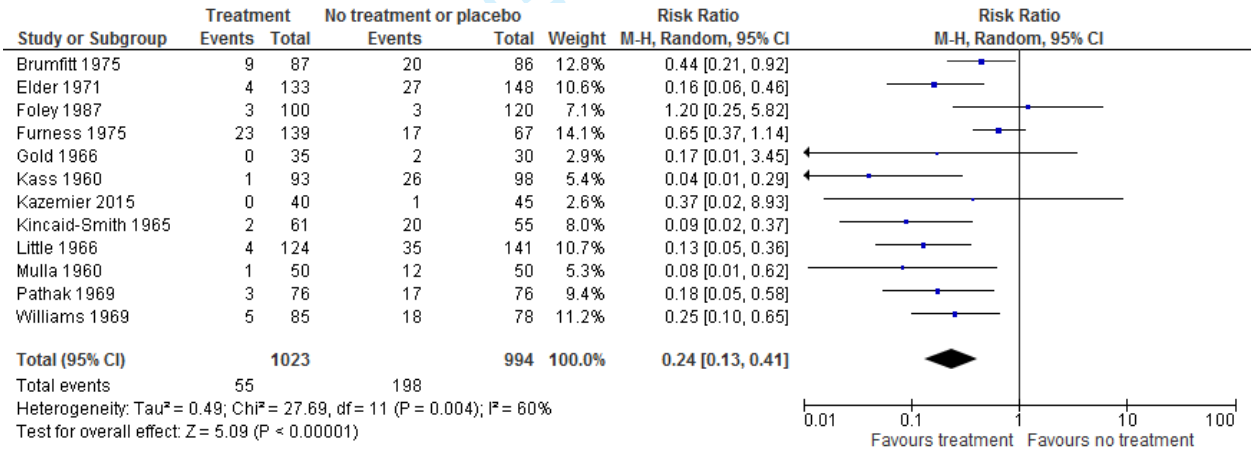
optimal information size (sample size of 265) not being met for rare events, downgrading twice is warranted for **imprecision**. There were no concerns to warrant downgrading for **other considerations**.

Evidence Set 3: Forest Plots 3.1-3.8 - KQ4: Benefits and harms of treatment compared to no treatment

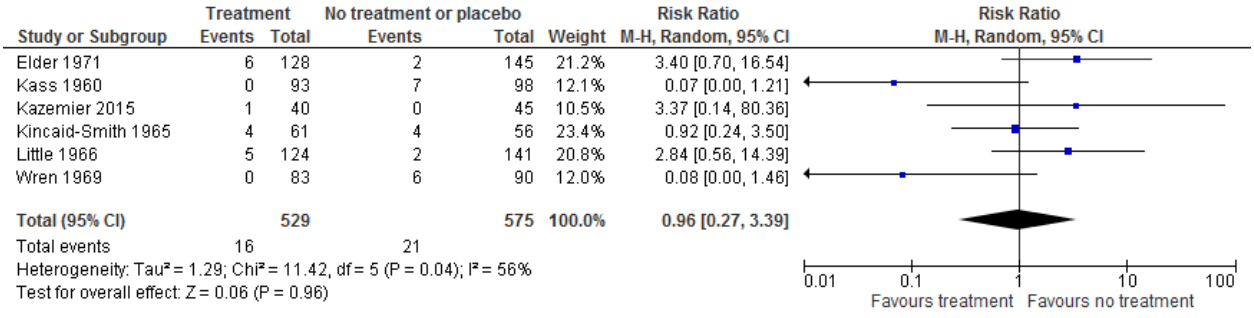
Outcome	No. of studies	No. of participants	Effect size (Risk Ratio; M-H, Random, 95%CI)
3.1 Pyelonephritis	12	2017	0.24 [0.13, 0.41]
3.2 Perinatal mortality (≥20 wks, including intrauterine demise, stillbirth, early neonatal death)	6	1104	0.96 [0.27, 3.39]
3.3 Spontaneous abortion (<20 wks)	2	379	0.60 [0.11, 3.10]
3.4 Neonatal sepsis	2	154	0.22 [0.01, 4.54]
3.5 Preterm delivery (<38 wks)	4	533	0.57 [0.21, 1.56]
3.6 Low birth weight (≤2500g; SGA <10th percentile & <5th percentile)	7	1522	0.63 [0.45, 0.90]
3.7 Neonatal serious harm: fetal abnormalities	4	821	0.49 [0.17, 1.43]
3.8 Neonatal serious harm: hemolytic anemia	1	265	Not estimable

CI: confidence interval; g: grams; M-H: Mantel-Haenszel; No.: number; SGA: small for gestational age; wks: weeks

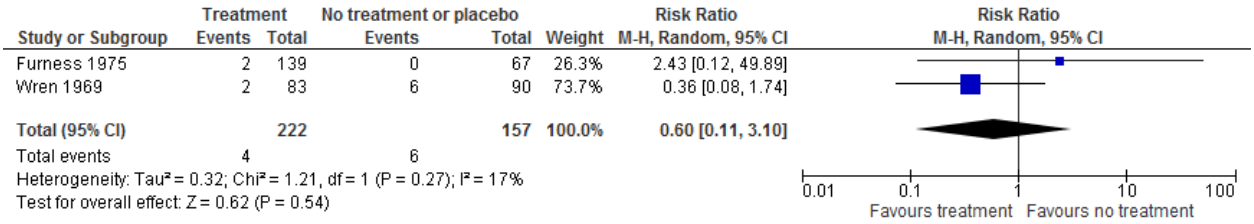
3.1 Pyelonephritis



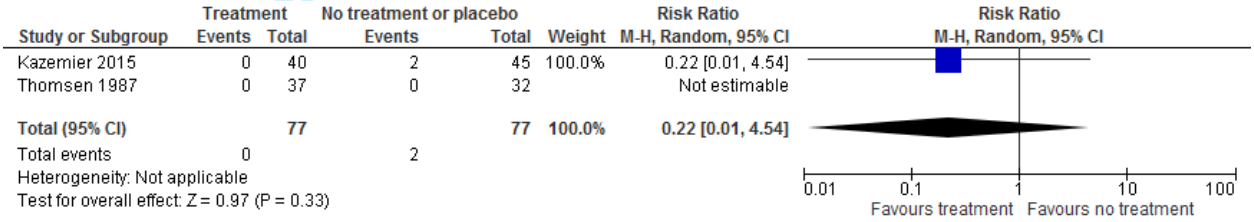
3.2 Perinatal mortality



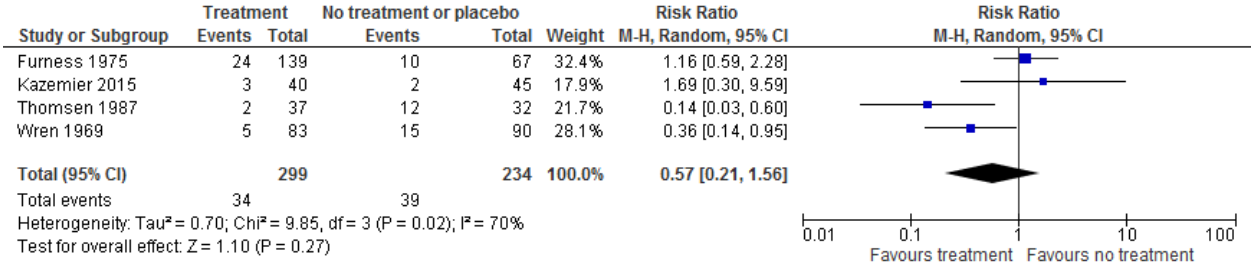
3.3 Spontaneous abortion



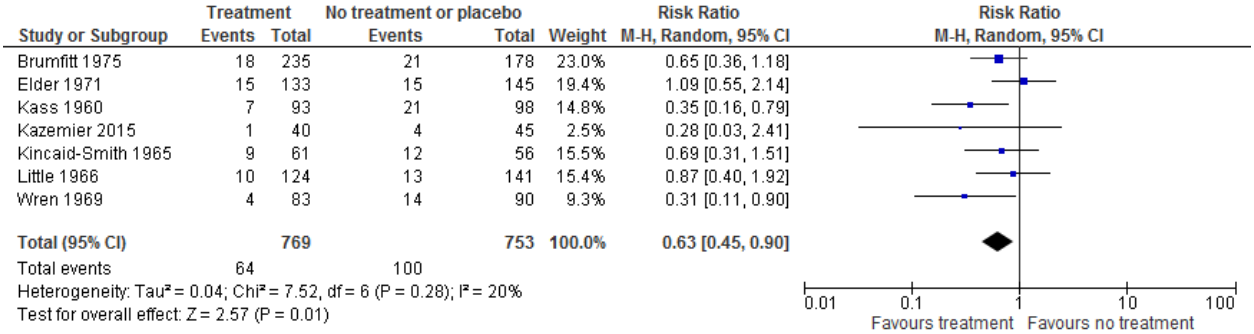
3.4 Neonatal sepsis



3.5 Preterm delivery



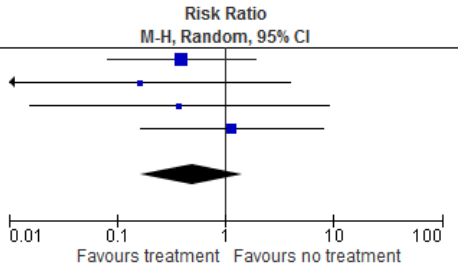
3.6 Low birthweight



3.7 Neonatal serious harm: fetal abnormalities

Study or Subgroup	Treatment Events	Total	No treatment or placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Elder 1971	2	122	6	143	46.4%	0.39 [0.08, 1.90]
Furness 1975	0	139	1	67	11.4%	0.16 [0.01, 3.92]
Kazemier 2015	0	40	1	45	11.5%	0.37 [0.02, 8.93]
Little 1966	2	124	2	141	30.7%	1.14 [0.16, 7.95]
Total (95% CI)		**425**		**396**	**100.0%**	**0.49 [0.17, 1.43]**
Total events	4		10			

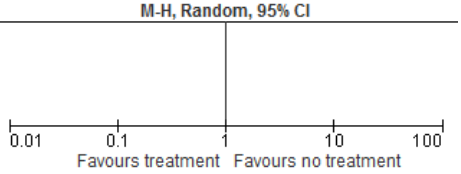
Heterogeneity: Tau² = 0.00; Chi² = 1.29, df = 3 (P = 0.73); I² = 0%
Test for overall effect: Z = 1.31 (P = 0.19)



3.8 Neonatal serious harm: hemolytic anemia

Study or Subgroup	Treatment Events	Total	No treatment or placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Elder 1971	0	122	0	143		Not estimable
Total (95% CI)		**122**		**143**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

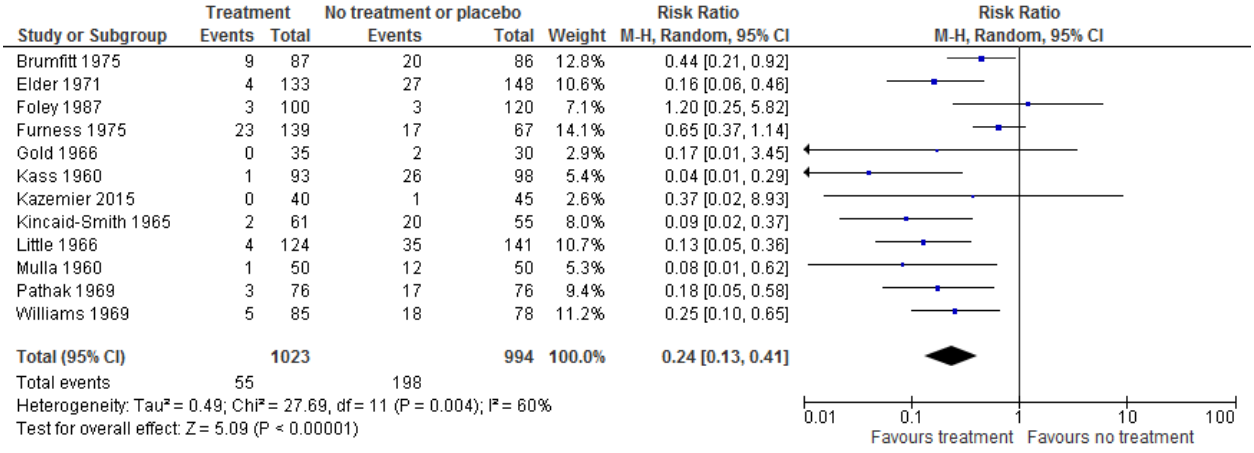


Evidence Set 3. Forest Plots for Subgroup Analyses 3.1.1-3.1.4 – KQ4: Benefits and harms of treatment compared to no treatment

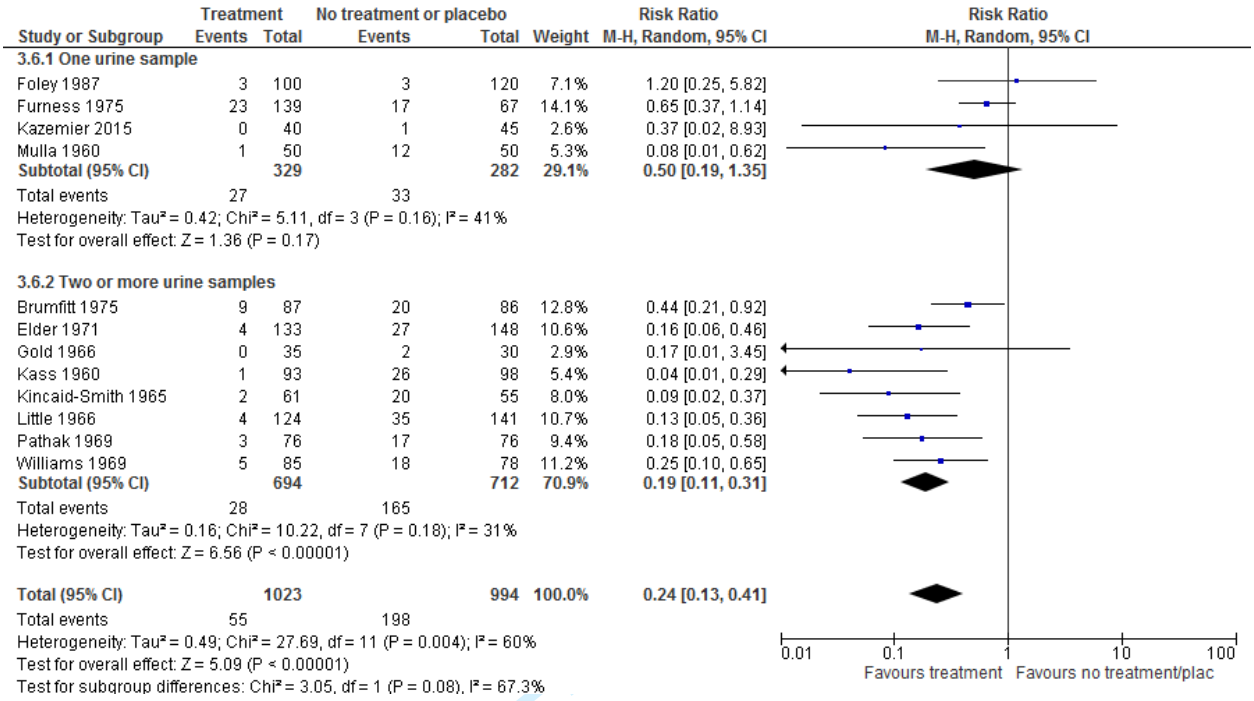
Outcome	No. of studies	No. of participants	Effect size (Risk Ratio; M-H, Random, 95%CI)
3.1 Pyelonephritis (overall)	**12**	**2017**	**0.24 [0.13, 0.41]**
3.1.1 Subgroup analysis: no. of urine samples before confirming bacteriuria and giving treatment			
One urine sample	4	611	0.50 [0.19, 1.35]
Two or more urine samples	8	1406	0.19 [0.11, 0.31]
3.1.2 Subgroup analysis: testing for persistent bacteriuria			
Tested for persistent bacteriuria during pregnancy	8	1352	0.26 [0.15, 0.45]
Testing for persistent bacteriuria post-delivery only	1	206	0.65 [0.37, 1.14]
Testing for persistent bacteriuria during pregnancy and post-delivery	3	459	0.11 [0.05, 0.25]
3.1.3 Subgroup analysis: follow-up			
Follow-up until delivery or puerperium (≤6 wks post-delivery)	9	1558	0.31 [0.18, 0.54]
Follow-up until >6 wks post-delivery	3	459	0.11 [0.05, 0.25]

CI: confidence interval; M-H: Mantel-Haenszel; No.: number; wks: weeks

3.1 Pyelonephritis (overall)

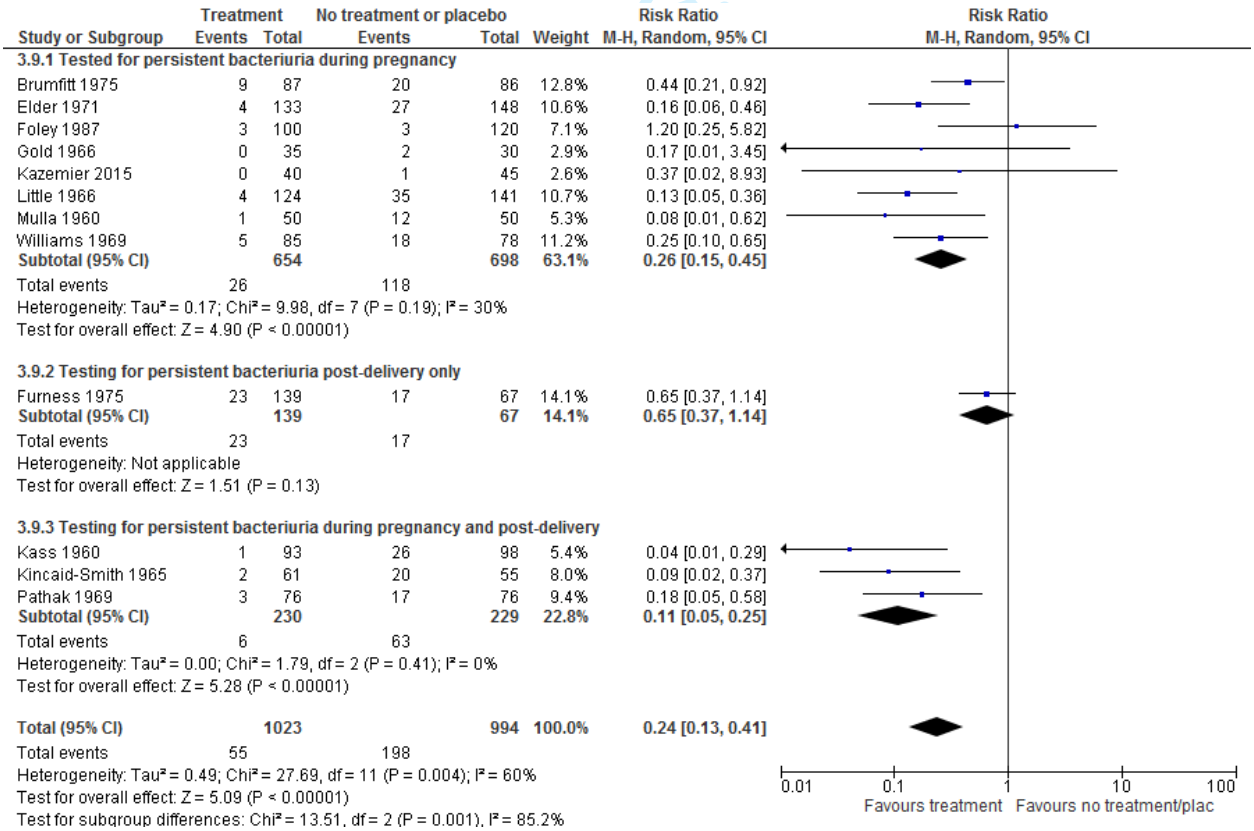


3.1.1 Pyelonephritis subgroup: number of urine samples at each screening visit*

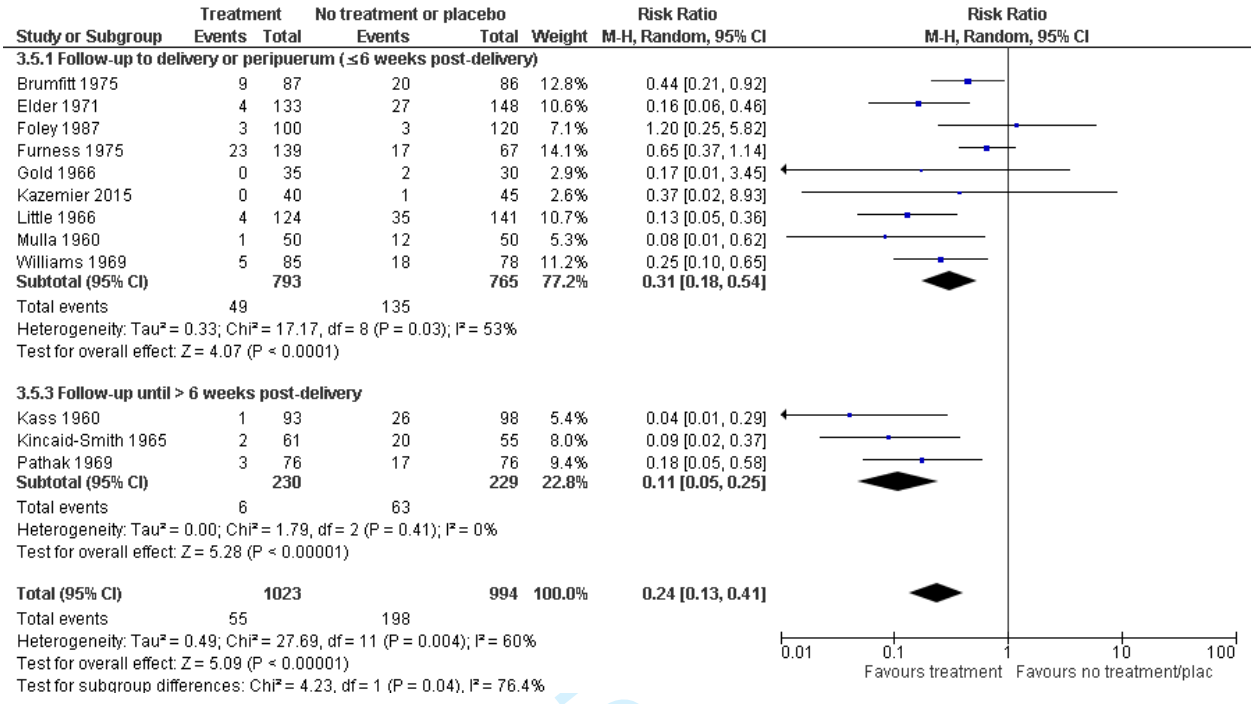


*The additional culture(s) was used to confirm levels of bacteriuria.

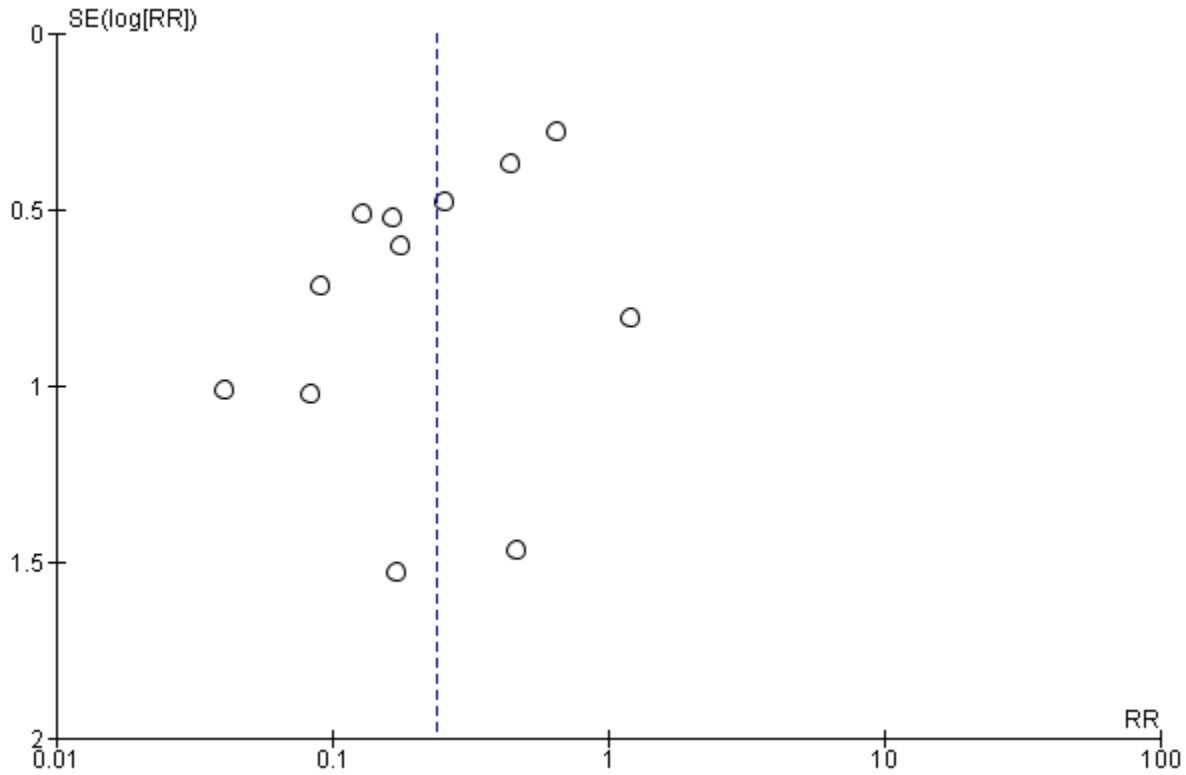
3.1.2 Pyelonephritis subgroup: timing of testing for persistent bacteriuria



3.1.3 Pyelonephritis subgroup: duration of follow-up



Supplement 7. Funnel Plot Asymmetry Test for outcome of pyelonephritis for treatment effectiveness



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	p. 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	p. 3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	p. 3 & 4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Abstract; p. 3; Supplement 1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	p. 4; Supplement 3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	p. 3-4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	p. 4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	p. 4-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	p. 4-5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	p. 4-5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	p. 5

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	p. 5

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	p. 4-5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	p. 5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	p. 5-7; Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	p. 5-7; Table 1; Supplement 4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	p. 8-10; Supplement 5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	p. 8-10; Table 2; Supplement 4 & 6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	p. 9-13; Table 2; Supplement 6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	p.10-13; Supplement 5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	p. 10-12 Supplement 6
DISCUSSION			

PRISMA 2009 Checklist

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	p. 12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	p. 12; Box
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	p. 12-13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	p.14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Asymptomatic Bacteriuria in Pregnancy: Systematic Reviews of Screening and Treatment Effectiveness and Patient Preferences

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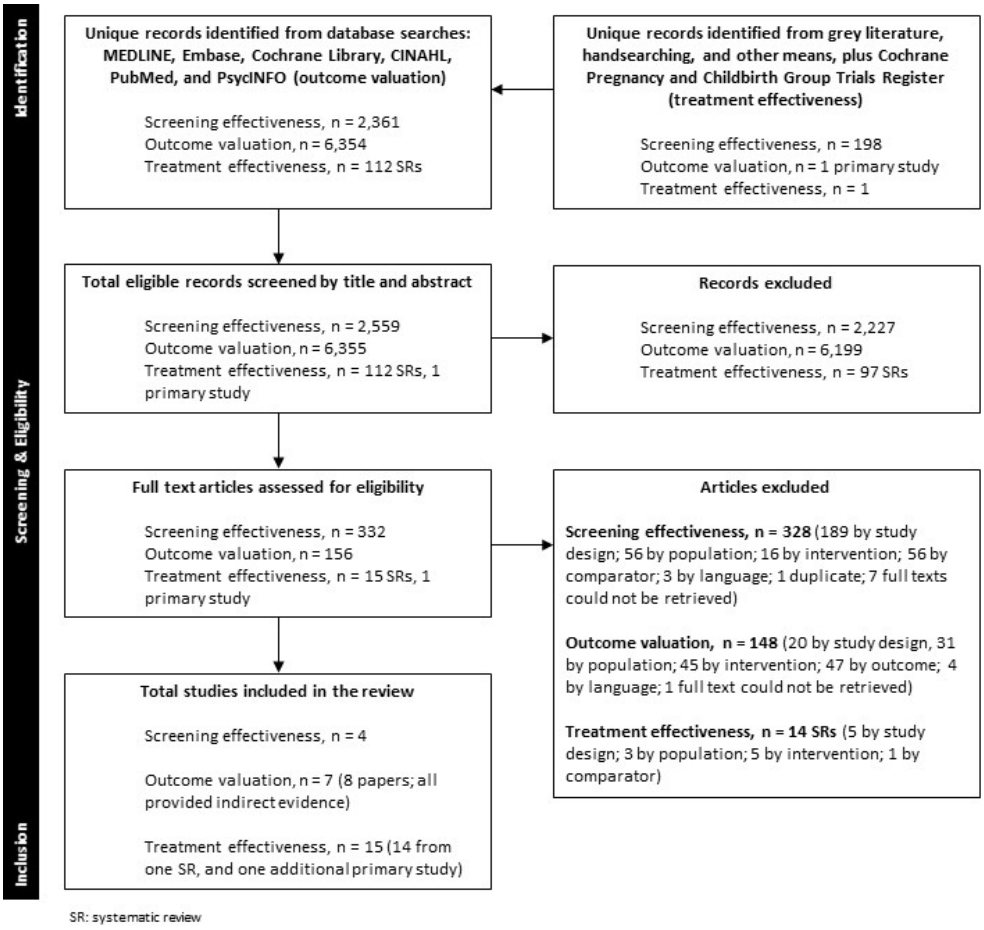
Date Submitted by the Author:	16-Aug-2018
Complete List of Authors:	Wingert, Aireen; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave.,, Pediatrics Pillay, Jennifer; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave., Pediatrics Sebastianski, Meghan; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave., Pediatrics Gates, Michelle; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave., Pediatrics Featherstone, Robin; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave., Pediatrics Shave, Kassi; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave., Pediatrics Vandermeer, Ben; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave., Pediatrics Hartling, Lisa; University of Alberta, Alberta Research Centre for Health Evidence (ARCHE), Edmonton Clinic Health Academy, 11405-87 Ave., Pediatrics
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Evidence based practice
Keywords:	asymptomatic infections, bacteriuria, pregnancy, mass screening, anti-bacterial agents, systematic review
Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.	
Screening for ASB in Pregnancy-Manuscript-clean.docx	



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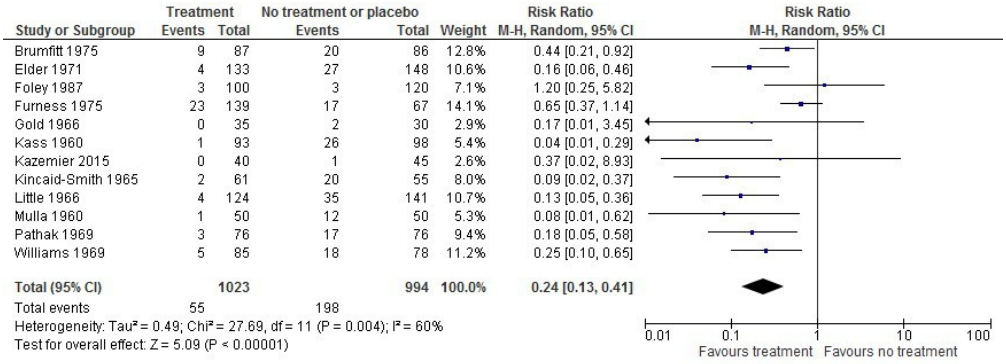

Figure 2. Forest plot of the effect of antibiotic treatment on incidence of pyelonephritis

73x27mm (300 x 300 DPI)

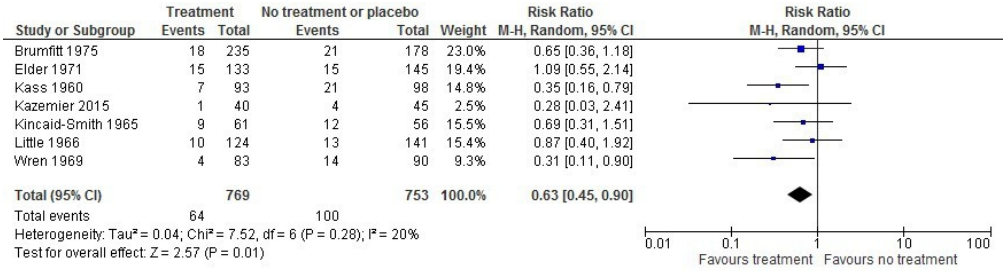

Figure 3. Forest plot of the effect of antibiotic treatment on incidence of babies born at low birth weight

73x20mm (300 x 300 DPI)

Supplement 1. Protocol: Screening for asymptomatic bacteriuria in pregnancy

December 1, 2016

ERSC Project Lead Investigator: Lisa Hartling
ERSC Project Staff: Aireen Wingert, Jennifer Pillay, Robin Featherstone (MLIS), and Ben Vandermeer (Statistician)

Suggested citation: Wingert A, Pillay J, Featherstone R, Vandermeer B, and Hartling L. Screening for asymptomatic bacteriuria in pregnancy: protocol for evidence review. Edmonton, AB; Evidence Review Synthesis Centre. Available at: http://canadiantaskforce.ca/ctfphc-guidelines/overview/

Author Contributions

AW and JP drafted the protocol and RF developed the search strategy and provided text for the protocol. AW, JP, and LH contributed to discussions with the CTFPHC and PHAC on the scope for this work. LH and BV critically reviewed the protocol. All of the authors approved the final version of this protocol.

Acknowledgements

We would like to acknowledge the contribution of the following individuals for their clinical and methodological input and/or their review of the protocol:

CTFPHC Asymptomatic Bacteriuria Working Group: Ainsley Moore (Chair), Roland Grad, Stéphane Groulx, Kevin Pottie, Brett Thombs, and Marcello Tonelli

PHAC Global Health & Guidance Division Staff: Marion Doull, Alejandra Jaramillo Garcia, Susan Courage, Nicki Sims-Jones

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Section I. Background and Purpose

Asymptomatic Bacteriuria in Pregnancy

Asymptomatic bacteriuria (ASB) - synonymous with asymptomatic urinary tract infection (UTI) - signifies a significant quantitative count of bacteria in the urine without symptoms of a lower (acute cystitis) or upper urinary tract (acute pyelonephritis) infection (1, 2). There is a 2-10% prevalence of ASB in premenopausal, ambulatory women (1), but due to anatomical and physiological changes (e.g., urinary stasis - difficulty emptying the bladder due to extended accumulation of urine) to the urinary tract in pregnancy there are theoretical reasons to suspect a greater chance of progression to symptomatic UTI and other pregnancy complications (e.g., maternal kidney infection, preterm delivery) (1, 3). Numerous risk factors for ASB in pregnancy have been identified, with low socioeconomic status, parity, a history of recurrent UTI, diabetes, and anatomical abnormalities of the urinary tract most cited (1, 2, 4).

Consequences of Untreated Bacteriuria in Pregnancy and Rationale for Review of Screening

There is a potentially greater risk in pregnant women compared to other populations for ASB developing into pyelonephritis (upper urinary tract infection) (3) with its associated inflammation of the renal parenchyma, calices and pelvis (5), although controversy exists. There is significant heterogeneity in reports of the incidence of pyelonephritis in untreated ASB during pregnancy. Some reports suggest low incidences of 1% or less after the introduction of screening and treatment for ASB and 4% or higher before the era of screening and treatment of ASB in pregnancy. Historical reports prior to 1966 indicated up to 40% of pregnant women with ASB developed pyelonephritis. These higher rates were before modern obstetrical care; however, these numbers continue to be cited in current systematic reviews (4) and guidelines (6) of ASB in pregnancy (1, 7). Furthermore, whether there is evidence to support a causal link between ASB and pyelonephritis in contemporary practice is uncertain.

There is an association between clinical signs of pyelonephritis and maternal respiratory insufficiency, septicemia, renal dysfunction and anemia, as well as evidence of a 20 to 50% higher incidence of preterm birth and low birth weight (4, 8). However, controversy exists over the direct link between ASB, pyelonephritis, and adverse perinatal outcomes (e.g., whether ASB affects pregnancy and neonatal outcomes solely through pyelonephritis or also other mechanisms) (2, 4), and also about whether treatment of ASB will reduce the risk of such adverse outcomes. A 2015 Cochrane review (4) found that antibiotic treatment for ASB in pregnancy may greatly reduce the incidence of pyelonephritis, preterm birth, and low birth weight babies. However, the authors' confidence in the findings were low due to poor quality evidence. A preliminary search identified a recent cohort study (9) with an embedded RCT, which found no statistically significant difference between ASB-positive women who were untreated or placebo-treated compared to ASB-negative women in terms of both pyelonephritis and preterm birth (6/208 [2.9%] vs 77/4035 [1.9%]; adjusted odds ratio [OR] 1.5, 95% CI 0.6–3.5).

Although the direct link between pyelonephritis and adverse perinatal outcomes may not be easily resolved (4), some main issues to examine include: 1) which, if any, screening tests and methods (e.g., collection methods, timing) are most accurate, and; 2) whether screening of all pregnant women and treatment for positive cases is effective (9). The effectiveness of screening for reducing risk of pyelonephritis and neonatal and maternal complications need to be examined in an era of modern obstetrical care.

Issues to Consider for Screening Tests

Significant bacteriuria is usually defined by the presence of at least 10^5 colony-forming units (CFU) per mL of urine of a single uropathogen, in two consecutive clean-catch specimens (4, 7). Acceptable thresholds and repetitions considered positive for bacteriuria in pregnancy may vary in practice. The quantitative urine culture is considered to be the gold standard for accurate detection of ASB. However, it is costlier, more labor intensive and more time-consuming compared with other rapid urine screening tests (urinalysis, dipstick nitrite tests) which reportedly have lower sensitivity[1] (1, 2). A preliminary search for recent literature identified a systematic review of onsite tests (point-of-care tests that are widely available in resource-limited settings) compared with urine culture that concluded specificity[2] was high overall but sensitivity was low and therefore onsite tests were not reliable in detecting pregnant women with ASB (10). There is no consistent recommendation for urine specimen collection in pregnancy (clean-catch with or without perineal cleansing) or optimal timing and frequency of screening tests or follow-up cultures (2). It is unclear whether universal screening (with subsequent treatment) for ASB confers benefits, and whether available screening tests for ASB are comparable to the current gold standard (urine culture) for identifying bacteriuric patients. The standard urine culture protocol is evolving with the testing of emerging techniques that may improve the detection of uropathogens (11, 12). However, at this time, urine culture is considered the reference standard. Resource needs for screening may be an important factor to consider. For example, an economic analysis indicated that screening with a dipstick and providing screen positive women treatment with antibiotics remained cost-beneficial for reducing pyelonephritis when prevalence of ASB is <2% or when the proportion of patients with ASB who develop pyelonephritis dropped to 10%, but the cost-benefit was not seen for culture diagnostics where the absolute clinical benefit was shown to be reduced (13).

[1]Sensitivity is a diagnostic test accuracy outcome that refers to how well a test correctly identifies individuals with a disease/condition; [2]Specificity is a diagnostic test accuracy outcome that refers to how well a test correctly identifies individuals without a disease/condition.

Issues to Consider for Harms of Screening

Patients may have preferences for avoiding harms due to screening and treatment in asymptomatic conditions (e.g., test anxiety/distress). Although the harms from screening tests may be considered minimal, harms from antibiotic treatment need to be considered when making decisions about screening practices for ASB in pregnancy. Some sources have outlined concerns with incidence and reporting on adverse effects of antibiotic treatment for ASB, UTIs, or antibiotic use in general during pregnancy (2, 4, 14). Some trials evaluating treatment versus no treatment/placebo of ASB in pregnancy have been critiqued for poorly reporting harms (4), such that making judgments on the net balance of benefits and harms may be difficult. The significance of the expected side effects from a short course of antibiotics may be small although increasingly there are concerns about the effect of antibiotics on the human microbiome and the

immune system. Antimicrobial resistance has certainly made the selection of an antibiotic for an individual woman more difficult (4). Additionally, patients may have preferences for avoiding treatment harms in asymptomatic conditions that need to be considered.

The goal of this review is to determine the effectiveness of screening for ASB among pregnant women. This evidence synthesis will inform recommendations on screening for ASB made by the Canadian Task Force for Preventive Healthcare (CTFPHC). As part of the guideline development process, the CTFPHC will also engage organizational stakeholders and peer-reviewers to gather information on key implementation considerations, such as strategies to help address potential health inequities and any concerns about the acceptability and feasibility of the guideline.

Section II. Recommendations in Other Guidelines and Current Practice

Canadian Organizations

The Society of Obstetricians and Gynecologists of Canada (SOGC), concerned over maternal and perinatal risks associated with ASB, recommends to treat single-strain colony counts of 10^5 CFU/mL (or 10^8 CFU/L) or greater with appropriate antibiotics during pregnancy to prevent adverse outcomes such as pyelonephritis and preterm birth (15). They support a single quantitative culture in any trimester as sufficient and recommend re-treatment with sensitivities for women with recurrent bacteriuria although they do not make recommendations for timing or frequency of re-testing. Similar recommendations apply when group B streptococcal (GBS) bacteria is detected in the urine during screening in pregnancy; separate recommendations (not relevant for this review) are made for screening and treating GBS (at any colony counts) at time of labour or rupture of membranes for prevention of early-onset neonatal GBS disease.

Guidelines from International Organizations

The U.S. Preventive Services Task Force 2008 guideline (16) on screening of ASB in adults recommends all pregnant women be screened at 12 to 16 weeks' gestation (or first prenatal visit) for ASB using a urine culture, and that treatment with antibiotics significantly reduces the incidence of symptomatic maternal urinary tract infections. The evidence informing this reaffirmation of the original recommendation from 2004 is mainly drawn from a Cochrane review of treatment effectiveness (17). The American Academy of Family Physicians (AAFP) (18) endorses the recommendations of the USPSTF. The Infectious Diseases Society of America (6) recommends screening for bacteriuria by urine culture for pregnant women in early pregnancy, and treatment if results are positive, with periodic re-testing for recurrent bacteriuria after therapy. The American Academy of Pediatrics (AAP), jointly with the American College of Obstetricians and Gynecologists (ACOG) recommend to treat ASB and then to test for cure (19).

The UK's National Institute for Health and Care Excellence (NICE) states that women should be offered routine screening for ASB by midstream urine culture early in pregnancy to reduce the risk of developing pyelonephritis (20).

The Scottish Intercollegiate Guidelines Network (SIGN) recommends that pregnant women be tested for ASB by urine culture at the first antenatal visit and culture-positive patients be treated with an antibiotic (21).

Current Practice

Several major healthcare organizations in North America (USPSTF, IDSA, ACOG, AAP, AAFP) advocate screening of pregnant women, and nearly all recommend treating patients who have been confirmed with ASB using antibiotics. In Canada, the current usual practice is to obtain a urine sample at each prenatal visit, where testing may typically be done by culture early in pregnancy and then followed with subsequent testing if indicated. It is clear there is diversity in which of these samples are collected for the presence of significant bacteriuria, how the sample is collected, how presence of bacteriuria is determined, and when sample(s) for ASB is/are collected in pregnancy. It is unclear whether and to what degree practices use screening methods incorporating tests other than urine culture.

Section III. Review Approach and Scope

This review will be completed by the Evidence Review and Synthesis Centre (ERSC) at the University of Alberta. The review will be developed, conducted, and prepared according to the CTFPHC methods (http://canadiantaskforce.ca/methods/methods-manual/). A working group of CTFPHC members was formed for development of the topic, refinement of the key questions and scope, and rating of patient-important outcomes considered most important for creating a recommendation. The CTFPHC will not be involved in the conduct of the review including selection of studies and data analysis, but will comment on the draft report and provide input on the interpretations of findings. The Global Health and Guidelines Division science team at the Public Health Agency of Canada provided assistance and input on CTFPHC methodological considerations during the topic refinement and development of the protocol. Perspectives of patients, and members of the public have been be incorporated regarding prioritization of outcomes (benefits and harms), as well as other aspects of guideline development. A draft version of this protocol was reviewed by nine external topic experts and stakeholders and all comments were considered when finalizing this protocol. This final version of the protocol has been approved by the entire CTFPHC and will be posted on the CTFPHC website and registered with the International Prospective Registry of Systematic Reviews (PROSPERO) database.

Analytical Framework and Staged Approach

Figure 1 is an analytical framework that depicts the structure used to address the Key Questions (KQs) for evaluating the benefits and harms of screening asymptomatic women during pregnancy for bacteriuria.

A staged approach will be followed based on the availability and quality of the body of evidence. Quality of evidence (classified as high, moderate, low, very low) will be assessed using methods developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group (http://www.gradeworkinggroup.org/), whereby high quality evidence relies on precise and consistent effect estimates from studies having few limitations on internal validity (i.e., low bias) and examining directly relevant populations, interventions, comparators, and outcomes (i.e., PICOs) (see Section IV for more details). The staging approach of the

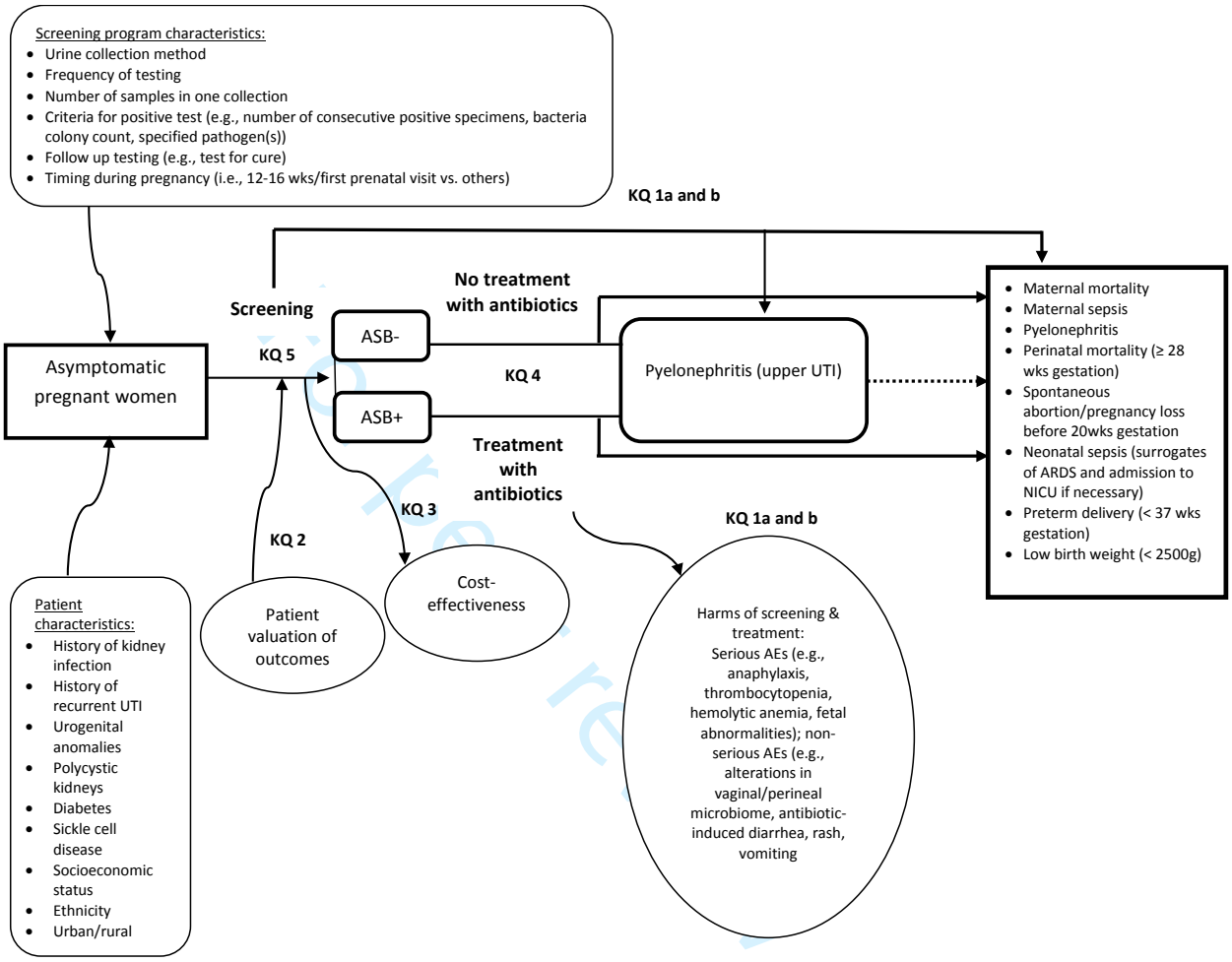
CTFPHC relies on choices made when considering, primarily, the GRADE domains of study limitations and indirectness. Moreover, decisions made during the evidence review are based on the information needs of the CTFPHC for making a screening recommendation based on the balance of critical patient-important benefits and harms.

The most direct and least biased evidence for the effectiveness of screening for ASB will be prioritized. This review will start by examining evidence from randomized-controlled trials (RCTs) on the clinical effectiveness of screening on patient-important outcomes. Staging beyond this point will require careful deliberation with documentation of rationale. If data from the initial stage is scarce for critical benefits or harms the CTFPHC will consider searching for data from (potentially) more biased study designs or indirect evidence (e.g., evidence from observational studies treatment RCTs, test accuracy studies. In cases where evidence on test accuracy and treatment effects will be used to provide indirect evidence on screening effectiveness, the limitations of such an indirect approach will be described. Examining both accuracy and treatment data may not be useful in all cases; for example, if the CTFPHC becomes confident that treatment is ineffective there would be no need to further examine test accuracy. In general, subsequent stages will only be conducted when the evidence from the previous stage(s) is non-existent or of too poor quality (e.g., very low quality based on GRADE tables) for the Task Force to make a screening recommendation based on the balance of patient-important benefits and harms.

For this review, the first stage will focus on identifying and using data from studies directly linking screening for ASB to patient-important benefits and harms (KQ1). Study designs providing the highest internal validity (e.g., RCTs) for this KQ will be preferred with a hierarchy of evidence used after this point if necessary. After RCTs we will consider controlled clinical trials (CCTs; defined for this review as *experimental trials without random allocation but where intervention(s) are introduced, standardized, and allocated objectively [e.g., by date of birth, but not using subjective means such as patient or clinician preferences] by investigators and blinding of participants is typically possible*) and then prospective and retrospective controlled observational studies. This stage will also include examination of KQ2 on women's valuation of benefit and harm outcomes of screening for ASB (and more broadly/indirectly treatment with antibiotics) in pregnancy. The cost-effectiveness of screening for ASB (KQ3) will also be considered only if there is evidence from KQ1 indicating a favorable benefit-harm ratio such that screening may be recommended.

If this first stage does not provide high enough quality of evidence for making a recommendation, the CTFPHC will carefully consider pursuing stage two with documentation of rationale before proceeding. Stage two will commence with examination of effectiveness of treatment of ASB in pregnancy (KQ4). If there is sufficient quality evidence indicating favorable treatment effectiveness from KQ4, an examination of KQ5 on diagnostic test accuracy will be considered in stage 3. Due to the indirectness of evidence provided by KQs 4 and 5 for making recommendations for the clinical effectiveness of screening, we will only seek data from study designs offering the greatest potential for high internal validity. That is, for KQ4 (treatment) we will focus on RCTs, and for KQ5 (test accuracy) we will exclude case-control designs. Where high quality systematic reviews exist examining these indirect evidence links, we will utilize these when possible.

Figure 1. Analytical Framework



AEs: adverse events; ARDS: acute respiratory distress syndrome; ASB: asymptomatic bacteriuria; d: day; g: grams; KQ: key question; NICU: neonatal intensive care unit; UTI: urinary tract infection; wks: weeks

Key Questions (KQs)*

Stage 1:

Benefits and harms of screening

KQ1a: What are the benefits and harms of screening compared with no screening for asymptomatic bacteriuria in pregnancy? Are there subgroup differences with SES or other patient characteristics?

KQ1b: What are the comparative benefits and harms of screening with different screening tests/algorithms for asymptomatic bacteriuria in pregnancy?

Outcome valuation

KQ2a: How do women weigh the benefits and harms of screening and treatment of asymptomatic bacteriuria in pregnancy?
KQ2b: How do women's valuation of benefits and harms of screening and treatment inform their decisions to undergo screening?

Resource use**

KQ3: What is the cost-effectiveness of screening for asymptomatic bacteriuria in pregnancy?

Stage 2:

Treatment

KQ4: What are the benefits and harms of antibiotic treatment compared with no treatment for asymptomatic bacteriuria in pregnancy?

Stage 3:

Diagnostic accuracy of screening tests

KQ5: What is the diagnostic accuracy of screening tests for asymptomatic bacteriuria in pregnancy?

Decision process for staging outlined in section on Analytical Framework and Staged Approach
****Conducted if benefit-harm ratio deemed beneficial based on KQ1***

Section IV. Review Methods

Literature Search

The literature search strategy will be developed and implemented by a research librarian. The search strategy will consist of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords, and will be peer-reviewed. Methodological filters will not be applied to limit retrieval by study design; study designs included for each KQ are identified in the section on inclusion and exclusion criteria. Searches will be restricted by language to include full texts published in English and French, without a publication date restriction.

We will conduct comprehensive searches in bibliographic databases most relevant for each KQ. For evidence informing stage 1 of our review we will perform comprehensive searches for studies meeting our inclusion criteria as described below. For KQ1, we will search MEDLINE (1946-) via Ovid; Embase (1974-) via Ovid; Cochrane Library; CINAHL (1937-present) via EBSCOhost; and PubMed via NCBI Entrez. The detailed search strategy for MEDLINE is reported in Appendix 1 and will be adapted to accommodate the controlled vocabularies of each database. For KQs 2 (women's outcome valuation) and 3 (cost-effectiveness of screening), we will modify the search to include relevant terms and will add suitable databases (e.g. PsycINFO for patient preferences, NHS Economic Evaluation Database [EED] for cost effectiveness). Full search strategies for all databases will be included in the final report.

For evidence used in stages 2 and 3, we are aware of at least one high-quality systematic review for KQs 4 (4) and 5 (10) which we may rely on. For KQ4 on effectiveness of antibiotic treatment compared with no treatment, we anticipate updating a recent Cochrane review of treatment for asymptomatic bacteriuria in pregnancy (4); if an update is not possible, we will follow methods adopted by the CTFPHC for integrating systematic reviews (see Appendix 2). If we update this review, the original search will be updated. For KQ5 (test accuracy), we anticipate using a recent review of screening tests for asymptomatic bacteriuria in pregnancy (10) and any additional reviews that may be identified as similar in scope. While multiple reviews may be considered for KQ5 (test accuracy) if found, we will not attempt to update the search(es) to identify more recent studies. If the scope of any review is narrower (e.g., does not include all interventions applicable to our topic), we may screen the excluded studies list(s) to identify potentially relevant studies for inclusion. To ensure we have identified all potentially relevant systematic reviews relevant to KQs 4 and 5, we will conduct a database search for systematic reviews. We will search PubMed (1946-) via NCBI Entrez, the Cochrane Database of Systematic Reviews (inception-) and the Database of Abstracts of Reviews of Effects (DARE) (inception-2013) via Wiley Cochrane Library to identify systematic reviews, meta-analyses and health technology assessments. Our PubMed search will utilize a search filter from CADTH (https://www.cadth.ca/resources/finding-evidence).

Grey literature will be searched and documented according to CTFPHC methods and will include internet-based searches (via adapted Canadian Agency for Drugs and Therapeutics in Health [CADTH] checklists; https://www.cadth.ca/resources/finding-evidence/grey-matters), electronic libraries (e.g., Health Canada Library, Canadian Electronic Library), and trial registries (ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform). Based on consultation with clinical experts, the following highly relevant conference proceedings will be hand-searched for recent studies not yet published (2014-present): Society of Obstetricians and Gynaecologists of Canada, Association of Medical Microbiology and Infectious Disease Canada, ID Week, and American Society for Microbiology meeting (ICAAC). Clinical and content experts identified by the CTFPHC will be contacted and invited to identify relevant research reports for consideration; websites of relevant Canadian stakeholder organizations will be searched.

Eligibility Criteria

Table 1 outlines the inclusion and exclusion criteria for all KQs, and details are provided below.

Population

Studies will be considered for inclusion in all KQs if they examine pregnant women at any stage of pregnancy where the population represents a “routine screening” scenario (e.g., the majority of patients do not have a degree of signs or symptoms prompting diagnostic testing and/or treatment for upper or lower UTI). It is recognized that many women experience nocturnal and increased frequency of urination, or other symptoms, which do not necessarily indicate bacteriuria or infections. We will include studies where a proportion of, but not all, women have risk factors for UTIs or other outcomes of the review. KQ2 on women’s outcome valuation, we will include studies of women of child-bearing age if no evidence is found from studies with pregnant women; studies will still be required to examine screening or antibiotic treatment during pregnancy.

We will exclude studies *exclusively* including women with conditions that place them at substantially higher than average risk for bacteriuria (i.e., kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infections [UTI], diabetes, sickle-cell disease), or with symptoms of UTI.

***Population subgroups of interest*:** history of kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection (UTI), diabetes, sickle cell disease, socioeconomic status (i.e., education, income), ethnicity (i.e., percent South Asian versus others), and urban/rural setting.

Interventions & Comparators

For clinical effectiveness of screening (KQ1), any screening test/algorithm for ASB will be eligible for inclusion and the comparator is absence of screening (1a) or a different urine test or screening algorithm (1b). Studies that compare urine cultures of differing criteria (e.g., threshold 10^3 CFU/mL versus 10^5 CFU/mL) will also be eligible for inclusion. For women's outcome valuation (KQ2), any screening test for ASB during pregnancy will be eligible for inclusion; indirect evidence about antibiotic treatment during pregnancy broadly will be used if needed. For cost-effectiveness (KQ3), any screening test compared with no screening or another screening test (i.e., urine culture) will be eligible for inclusion; costs must be compared with outcomes/effects such that studies examining costs only will be excluded. For treatment effectiveness (KQ4), any antibiotic treatment for ASB compared to no treatment or placebo will be eligible for inclusion. For diagnostic accuracy (KQ5), any index test compared with a urine culture for detecting ASB will be eligible for inclusion. For all KQs, studies that include screening or treatment for group B streptococcus (GBS) at any time of pregnancy for any of the outcomes of interest will be included.

We will exclude studies exclusively examining urine tests used for screening for other conditions (e.g., proteinuria, glycosuria), and non-urine screening tests (e.g., vaginal/rectal swab culture for GBS testing).

***Screening subgroups of interest*:** urine collection methods (e.g., clean-catch and/or midstream; excluding catheter methods/samples), frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, and timing during pregnancy.

Outcomes

As with the KQs, the outcomes for inclusion for KQ1 (screening effectiveness) and KQ4 (treatment) will be staged to some extent, if necessary. Each outcome has been rated independently by members of the CTFPHC and by women, as per the patient engagement activities of an independent group with expertise in knowledge translation from St. Michael's Hospital in Toronto, Ontario. All patient-important outcomes rated as critical (7 to 9 out of 9) or important (4 to 6 out of 9) for decision making were considered for inclusion. From these ratings, the eight outcomes were rated as critical will be included in stage 1; of three outcomes rated as important, low birth weight (but not hypertension or acute kidney injury) will be included

because in the past (i.e. older studies) this was conceptually considered the same as "pre-term birth", which both the CTFPHC members and patients rated as critical. Considering harms separately, if no evidence is found for any of the outcomes (serious adverse events [AEs]) in stage 1, there will be inclusion of the outcomes (non-serious AEs) from stage 2. This grouped and staged approach to harms will address infrequent reporting, reporting of different harms across studies, and also uncertainty regarding all the potential harms that may be reported. Non-serious AEs, particularly if frequent or severe, are considered important but not critical for decision making by the CTFPHC. This approach acknowledges guidance to limit the number of total outcomes (maximum 7) to those which can be successfully managed cognitively by guideline panels when balancing multiple benefits and harms.

Outcomes for KQs 1 and 4 with ratings:

Benefits (reduced incidence for all):

1. maternal mortality (9)
2. maternal sepsis (8)
3. pyelonephritis (7)
4. perinatal mortality (≥ 28 weeks of gestation (e.g., intrauterine demise, stillbirth, early neonatal death)) (9)
5. spontaneous abortion/pregnancy loss before 20 weeks of gestation (8)
6. neonatal sepsis (if not reported will include surrogate outcomes of acute respiratory distress syndrome [ARDS] or admission to neonatal intensive care unit [NICU]) (8)
7. preterm delivery (live fetus passed < 37 weeks of gestation) (7)
8. low birth weight (< 2500g) (6)

Harms:

1. serious adverse event(s)[a] associated with antibiotic treatment, *including but not limited to*: (7)
    a. anaphylaxis,
    b. thrombocytopenia,
    c. hemolytic anemia,
    d. fetal abnormalities; and,
2. non-serious adverse event(s) associated with treatment, *including but not limited to*: (4)
    a. alterations in vaginal/perineal microbiome (e.g., candidiasis, vaginitis),
    b. antibiotic-induced diarrhea,
    c. rash,
    d. vomiting

[a]Serious adverse event (experience) or reaction is any untoward medical occurrence that: a) results in death, b) is life-threatening, c) requires in-patient hospitalisation or prolongation of existing hospitalisation, d) results in persistent or significant disability/incapacity, or e) is a congenital anomaly/birth defect (Health Canada, 2011);

We will exclude studies that screen pregnant women for group B streptococcus near delivery or at time of rupture of membranes for the prevention or treatment of chorioamnionitis or neonatal GBS (without other outcomes of interest listed above).

Women's outcome valuation (KQ2) include several possible outcomes related to the weighing of benefits and harms of screening and treatment (KQs 1 and 4) and how this may affect their decisions to undergo screening (e.g., relative weight/utilities of benefit and harms; willingness to be screened based on relative value placed on benefits and harms of screening programs or treatment); these outcomes will be based on considerations of the possibility or perceived/expected magnitude of effects for the outcomes identified for KQs 1 and 4.

During focus groups, women identified an additional outcome - psychological distress/anxiety - and rated this as critical (7 out of 9), although it was interpreted differently by some women as either a benefit (e.g., reduction in psychological distress/anxiety by knowing the health status of themselves and their baby) or a harm (e.g., another of many tests and potential worries during pregnancy). Anxiety as a critical outcome will be sought and synthesized within findings from KQ2 on women's valuation of benefits and harms of screening and treatment, as well as within interpretation of test accuracy outcomes from KQ5 (TP, TN, FP, FN) which will be *interpreted based on the CTFPHC judgments* on the magnitude of potential consequences of each (e.g., unnecessary anxiety from high FP, loss of potential benefit in FN) as identified in the section below "Assessment of the Overall Quality of the Evidence using GRADE".

Cost-effectiveness (KQ3) outcomes include cost per quality-adjusted life year (QALYs), incremental cost-effectiveness ratios (ICERs), and net benefit (in dollars from cost-benefit studies.

Diagnostic test accuracy (KQ5) outcomes include: sensitivity, specificity, false positives, false negatives, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio.

Setting, Study Design & Timing

Studies conducted in primary care, or relevant clinical settings (e.g., prisons, remote stations, community health centers, midwifery practice) will be included. For KQ3 on cost-effectiveness we will limit studies to those conducted using data relevant to Canada, thus within countries having a very high Human Development Index (22).

For KQ1 (screening effectiveness), we will include RCTs initially and then, if needed based on the GRADE assessment of overall quality of the evidence, we will search for CCTs (defined in Section III) and then controlled observational studies (i.e., prospective and retrospective cohort, case-control, controlled before-after). For KQ2 (outcome valuation), we will include any study where women are asked to balance the benefits and harms of screening and treatment for ASB and state/choose their willingness to be screened and treated; surveys, experimental designs (e.g., contingent valuation), and qualitative research are examples. Cost-effectiveness (KQ3) will look at any study comparing effects and costs (e.g., cost-effectiveness, cost-utility, cost-benefit) and may include modelling of effects and/or costs. For KQ4 (treatment), we will rely on RCTs. For KQ5 (test accuracy), we will rely on prospective and retrospective studies where a consecutive or random sample of participants receive both the index test(s) and reference standard, or where participants are randomized to different index tests but all receive the reference standard, and

assessment in a cross-sectional manner. We will exclude case-control studies and studies with longitudinal assessment of the reference standard.

For all KQs, case reports and case series (i.e., group of patients selected based on particular outcome) will be excluded as will papers not reporting primary research (e.g. editorials, commentaries, opinion pieces). Conference abstracts will not be eligible for inclusion, but will be captured and serve to help identify full study reports and assess the quality of evidence in relation to potential publication and reporting biases. No limits will be applied to publication year.

Additional considerations

We do not have a minimum sample size for inclusion, nor do we have a minimum threshold for extent of incomplete follow-up or participant attrition; these factors will be considered during assessment of the quality of evidence (e.g., precision domain accounts for sample size across studies), and during sensitivity analyses in cases of substantial heterogeneity in findings at the data synthesis stage (see relevant sections).

Tables 1 to 5. Inclusion and Exclusion Criteria for Key Questions

Table 1. KQ1a, b: Benefits and harms of screening

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions	Any screening program or test Screening subgroups/algorithms, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for group B streptococcus (GBS) testing)
Comparator	KQ1a: No screening (but may include indicated/targeted testing and/or treatment upon development of symptoms or for high-risk groups) KQ1b: A different screening test or algorithm (see intervention subgroups)
Outcomes	*Benefits (reduced incidence for all)*: 1. maternal mortality (9) 2. maternal sepsis (8)\ 3. pyelonephritis (7) 4. perinatal mortality (≥ 28 week's gestation (e.g., intrauterine demise, stillbirth, early neonatal death)) (9) 5. spontaneous abortion/pregnancy loss before 20 week's gestation (8) 6. neonatal sepsis (if not reported will include surrogate outcomes of acute respiratory distress syndrome [ARDS] or admission to neonatal intensive care unit [NICU]) (8) 7. preterm delivery (live fetus passed < 37 week's gestation) (7) 8. low birth weight (< 2500g) (6) *Harms:* 1. serious adverse event(s)[a] associated with antibiotic treatment, *including but not limited to*: (7) a. anaphylaxis,

	b. thrombocytopenia, c. hemolytic anemia, d. fetal abnormalities; and, 2. non-serious adverse event(s) associated with treatment, *including but not limited to*: (4) a. alterations in vaginal/perineal microbiome (e.g., candidiasis, vaginitis), b. antibiotic-induced diarrhea, c. rash, d. vomiting Exclude: screening for GBS near delivery or at time of rupture of membranes for the prevention or treatment of chorioamnionitis or neonatal GBS (without other outcomes of interest in list above)
Study Designs	Staged: RCTs, CCTs, controlled observational (i.e., prospective and retrospective cohorts, case-control, controlled before-after)
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices)
Timeframe	No publication date limits

CCT: controlled clinical trial; KQ: key question; RCT: randomized controlled trial
[a]Serious adverse event (experience) or reaction is any untoward medical occurrence that: a) results in death, b) is life-threatening, c) requires in-patient hospitalisation or prolongation of existing hospitalisation, d) results in persistent or significant disability/incapacity, or e) is a congenital anomaly/birth defect (Health Canada, 2011)

Table 2. KQ2: Outcome valuation

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria; will also accept asymptomatic women who are not pregnant if necessary Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any screening program or test, and any antibiotic; will accept studies on treatment for any bacterial condition in pregnancy Screening subgroups/algorithms, including: urine collection method, frequency of testing, criteria for a positive test (including number of consecutive positive specimens, bacteria colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine *screening* is done for other conditions (e.g., proteinuria, glycosuria), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	Not applicable
Outcomes[§]	Several possible outcomes (e.g., relative weight/utilities of benefit and harms; willingness to be screened based on relative value placed on benefits and harms of screening programs or treatment)
Study Designs	Qualitative, mixed methods, surveys/cross-sectional
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices)
Time frame	No publication date limits

KQ: key question

[§]If there is a very limited quality of evidence base for KQ2 (i.e., in terms of quantity/sample size, methodological quality, inconsistency between studies, or applicability to our population or setting) we will consider including studies examining women's valuation of harms *or* benefits rather than the trade-off between the two. For example, studies examining women's acceptance of screening and/or treatment for ASB when only considering their perspectives on the potential

risks of antibiotic treatment to their baby, or the importance placed on reassurance about the potential to prevent preterm delivery et cetera, could offer some indirect evidence to help the CTFPHC in their deliberations. Likewise, the relative value placed on different benefit or harm outcomes (e.g., serious versus non-serious AEs) could be informative.

Table 3. KQ3: Cost-effectiveness of screening

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any screening program or test Screening subgroups/algorithms, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	No screening (but may include indicated/targeted testing and/or treatment upon development of symptoms or for high-risk groups), or a different screening test or algorithm (see intervention subgroups)
Outcomes	Cost per quality-adjusted life-years (cost per QALY), incremental cost-effectiveness ratio (ICER), net benefit/cost
Study Designs	Economic evaluations
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices); limited to countries rated as having very high Human Development Index (22)
Time frame	No publication date limits

KQ: key question

Table 4. KQ4: Treatment

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any antibiotic Screening subgroups/algorithms, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia,), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	No treatment or placebo
Outcomes*	*Benefits (reduced incidence for all)*: 1. maternal mortality (9)

	2. maternal sepsis (8)\ 3. pyelonephritis (7) 4. perinatal mortality (≥ 28 week's gestation (e.g., intrauterine demise, stillbirth, early neonatal death)) (9) 5. spontaneous abortion/pregnancy loss before 20 week's gestation (8) 6. neonatal sepsis (if not reported will include surrogate outcomes of acute respiratory distress syndrome [ARDS] or admission to neonatal intensive care unit [NICU]) (8) 7. preterm delivery (live fetus passed < 37 week's gestation) (7) 8. low birth weight (< 2500g) (6) *Harms:* 1. serious adverse event(s)[a] associated with antibiotic treatment, *including but not limited to*: (7) a. anaphylaxis, b. thrombocytopenia, c. hemolytic anemia, d. fetal abnormalities; and, 2. non-serious adverse event(s) associated with treatment, *including but not limited to*: (4) a. alterations in vaginal/perineal microbiome (e.g., candidiasis, vaginitis), b. antibiotic-induced diarrhea, c. rash, d. vomiting Exclude: screening for group B streptococcus near delivery or at time of rupture of membranes for the prevention or treatment of chorioamnionitis or neonatal GBS (without other outcomes of interest listed above)
Study Designs	RCTs
Language	English and French
Setting	Primary care and clinical settings (e.g., prisons, remote stations, community centers, midwifery practices)
Time frame	No publication date limits

KQ: key question; RCT: randomized controlled trial

[a]Serious adverse event (experience) or reaction is any untoward medical occurrence that: a) results in death, b) is life-threatening, c) requires in-patient hospitalisation or prolongation of existing hospitalisation, d) results in persistent or significant disability/incapacity, or e) is a congenital anomaly/birth defect (Health Canada, 2011)

Table 5. KQ5: Diagnostic accuracy of screening tests

Population	Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria. Patient subgroups: women with kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI]), diabetes, sickle cell disease, socioeconomic status, ethnicity, urban/rural Exclude: studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent urinary tract infection [UTI], diabetes, and sickle cell disease), or with symptoms of UTI
Interventions/Index Test	Any index test Screening subgroups/algorithm, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Comparator/Reference Standard	A urine culture Screening subgroups/algorithm, including: urine collection method, frequency of testing, number of samples in one collection, criteria for a positive test (including number of consecutive positive specimens, bacterial colony count, and specified pathogen(s)), follow-up testing during pregnancy, timing during pregnancy

	Exclude: urine screening is done for other conditions (e.g., proteinuria, glycosuria, Chlamydia), non-urine screening test (e.g., vaginal/rectal swab culture for GBS testing)
Outcomes	Sensitivity, specificity, false positives, true positive, false negatives, true negatives, positive and negative likelihood ratios, prevalence/pre-test probability (true positive + false positive)/total number of people)
Study Designs	Prospective and retrospective studies where a consecutive or random sample of participants receive both the index test(s) and the reference standard, or where participants are randomized to different index tests but all receive the reference standard, and assessment in a cross-sectional manner Exclude: case-control studies and studies with longitudinal assessment of the reference standard
Language	English and French

Screening and Selecting Studies for Inclusion

For the database searches, two reviewers will independently screen the titles and abstracts (when available) using broad inclusion/exclusion criteria. Citations will be classified as "include/unsure," "exclude," or "reference" (i.e., conference abstracts, protocols, and systematic reviews). One reviewer will review the "reference" group and will conduct all other searching as outlined in the above section. The full text of all studies classified as "include/unsure" or identified after reviewing the reference citations will be retrieved for full review; two reviewers will independently assess eligibility using a standard form that outlines the inclusion and exclusion criteria. Disagreements on final inclusion of all studies will be resolved through consensus or third party adjudication. For KQs 4 and 5, any existing systematic review(s) identified as relevant will be assessed for eligibility based on whether the authors: i) searched more than one database, ii) report their selection criteria, and iii) use PICOTS criteria that are a close match to that for the relevant KQ. In cases where there is more than one possible review providing results for the same intervention-outcome pair, we will choose one based on: AMSTAR (23) rating (score 8 or higher preferred), comprehensiveness of search (i.e., reports on most or more papers included by other existing reviews), closest match to our PICOTS, most recent date of study inclusion/search, and the quality and extent of reporting on individual study characteristics, data, and quality assessments. All decisions to exclude a study at full text review will be provided. The title/abstract screening and full-text selection processes will be conducted and documented in DistillerSR. The flow of literature and reasons for full text exclusions will be recorded in a PRISMA Flow Chart.

Data Extraction & Reporting

One reviewer will independently extract data from each included study or systematic review into DistillerSR; a second reviewer will verify all data. Disagreements will be resolved through discussion or third-party consultation until consensus is reached.

When using individual studies for a KQ, a narrative summary (with accompanying tables) will be provided to report on all studies by design, country of origin, sample sizes, population(s) (including subgroups), intervention(s)/index tests (including data on thresholds and for subgroup questions), comparator(s)/reference test, setting, and outcome measures, as reported by studies. When there are multiple publications associated with a study we will consider the earliest report of the main (primary) outcome data to be the primary data source. We will extract data from the primary source first and then add outcome data reported in the secondary/associated publications and data sources. We will reference the primary source throughout the evidence report; all associated literature will be tabulated for reference.

When relying on systematic reviews for KQs 4 (treatment) and 5 (test accuracy), we will extract data on the characteristics of the systematic review (PICOTS), the included studies with specifics related to the population (size and characteristics), outcomes evaluated (including definitions and timing of assessment), quality/risk of bias (by domain/construct if available), the methods of analysis (meta-analytical approach and its findings in relation to heterogeneity, if applicable), findings from their syntheses including subgroup analysis and GRADE or other quality assessments if performed across studies, and any limitations noted by the systematic review authors. For KQs 4 and 5, data verification will be completed on 5 to 10% of included studies in any existing systematic review(s), and if satisfied with concordance, we will consider incorporating the reported data on study and participant characteristics without returning to the primary studies. If additional studies are included (e.g., new studies from updated search [KQ4] or excluded studies in the identified systematic review that is subsequently included for current review to ensure coverage of scope [KQ5]), these will be clearly identified and presented.

When using individual studies, we will record intention-to-treat results, if possible. For continuous outcomes measures, we will extract (by arm) the mean baseline and endpoint or change scores, standard deviations (SD) or other measure of variability, and number analyzed. We will not include outcome data from studies that did not provide a follow up change or endpoint mean or data that could be used to calculate follow up scores. If necessary, we will approximate means by medians. If standard deviations are not given, they will be computed from p-values, 95% confidence intervals (95% CIs), standard errors, z-statistics, or t-statistics. If computation is not possible they will be estimated from upper bound p-values, ranges, inter-quartile ranges, or (as a last resort) by imputation using the largest reported SD from the other studies in the same meta-analysis. When computing SDs for change from baseline values, we will assume a correlation of 0.5, unless other information is present in the study that allows us to compute it more precisely. For dichotomous outcomes, we will report counts or proportions, and sample size, by study arm.

For dichotomous data on harms, each adverse event (AE) will be counted as if it represents a unique individual; because a single individual might experience more than one AE, this assumption may overestimate the number of people having an AE. Only numerical data for AEs will be extracted; that is, we will make no assumptions on lack or presence of an AE if this is not reported; authors that report only p-values or that one arm had fewer events than another (but where it is explicit that the outcome was captured in the study) will be contacted (3 times via email) to provide the data.

Data on within-study subgroup analysis will be collected, including: subgroups (independent variables), the type of analysis (e.g., subgroup/stratified or regression analysis), the outcomes assessed (dependent variables), and the authors' conclusions. We will collect data suitable for all patient and intervention subgroups (see Table 1) for performing our own subgroup analyses (e.g., stratified analysis, meta-regression) based on study-level data.

Risk of Bias/Methodological Quality Assessment

Two reviewers will independently assess the risk of bias (ROB) of each included study (KQs 1-3), with disagreements resolved through discussion or third-party consultation to reach consensus. The results for each study and across studies will be reported by each domain and for

the overall ROB score. The ROB for each study will be assessed on an outcome basis where needed, particularly when different outcomes are assumed to have different susceptibilities to bias; for example, subjective outcomes and expected harms are more prone to bias from non-blinding than objective outcomes and unexpected/rare harms.

RCTs and CCTs (theoretically only differing from RCTs by lack of random sequence generation and not by other ROB domains) will be appraised using the Cochrane Risk of Bias tool (24). This tool consists of six domains (sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and "other" sources of bias) and a categorization of the overall risk of bias. Blinding will be assessed separately for patients/providers and outcome assessors taking into account the type of outcome that may be affected (e.g. subjective vs. objective). To assist with outcome reporting bias assessments, we will seek study protocols and studies/data from registries. The overall assessment is based on the responses to individual domains. If one or more individual domains are assessed as having a high risk of bias, the overall score will be rated as high risk of bias. If at least one domain is assessed as unclear, and no domains are assessed as high, the overall score will be rated as unclear risk of bias. The overall risk of bias will be considered low only if all components are rated as having a low risk of bias.

Controlled observational studies will be appraised using the Newcastle-Ottawa Quality Assessment Scale (25); three domains (sample selection, comparability of cohorts, and assessment of outcomes) are evaluated. Each item that is adequately addressed is awarded one star, except for the "comparability of cohorts" item, for which a maximum of two stars can be given. The overall score is calculated by tallying the stars. We will consider a total score of 6 to 8 stars to indicate low ROB, 4 or 5 stars to indicate moderate ROB, and 3 or fewer stars to indicate high ROB.

For diagnostic accuracy studies (KQ5), we will rely on the Quality of Diagnostic Accuracy Studies (QUADAS-2) (26) used to assess ROB. This tool assesses concerns of risk of bias among four domains (patient selection, index test, reference standard, and flow and timing) and concerns of applicability across the first three domains.

If one or more systematic review(s) is used to provide evidence for KQ4 (treatment) or KQ5 (accuracy), we will assess if the review used an explicit tool (e.g., Cochrane ROB [KQ4], QUADAS [KQ5]) for assessing the main sources of potential bias. If so, we will complete assessments on 5 to 10% of included studies to establish concordance before considering the use of assessments reported by each review.

Studies answering KQ2 (outcome valuation) will be evaluated by tools appropriate to their study design: for surveys and qualitative studies we will use tools developed by the Center for Evidence-based Management (http://www.cebma.org/resources-and-tools/what-is-critical-appraisal/). The quality of economic evaluation studies (KQ3) will be assessed using Drummond's checklist for economic evaluation studies (27).

Data Analysis & Synthesis

We will provide summaries of intervention effects for each study by calculating the appropriate statistics based on types of outcomes.

Key Question 1

For pair-wise meta-analysis in KQ1 (screening effectiveness), we will employ a random effects model. For continuous outcomes, we will report a pooled mean difference (MD) when one measurement tool is used, or other options that exist for communicating results when combining two or more outcome scales measuring similar constructs (28, 29). For dichotomous outcomes, we will report relative risks (RR) and risk differences (RD) between groups with corresponding 95% CIs. For those outcomes (e.g. serious adverse events) where at least one intervention group contains zero events, only the risk difference will be used. For calculating the RD, we will use the median baseline risk for the control group in the included studies, although may perform sensitivity analysis using differing baseline risks if thought suitable (30, 31). The decision to pool studies will not be based on the statistical heterogeneity (I^2 statistic will be reported), but rather on interpretation of the clinical and methodological differences between studies. When substantial heterogeneity is suspected, we will conduct sensitivity analyses if appropriate (e.g., in the presence of studies with outlying effect sizes, for studies rated as high risk of bias in some domains such as incomplete outcome data [<80 percent] or lack of allocation concealment, parallel versus cross-over designs). Heterogeneity will also be examined during our planned subgroup analyses for important patient and intervention variables (see Table 1). Where there are at least eight studies in a meta-analysis, we will analyze publication bias both visually using the funnel plot and quantitatively using Egger's test (32). We will not combine results from RCTs with CCTs or controlled observational studies (if used via staging approach for KQ on screening); rather, the latter two will be used to support or provide context for the evidence from RCTs.

Key Questions 2 & 3

For KQs 2 (outcome valuation) and 3 (cost-effectiveness), results will be narratively described in most cases. If more than one study is identified providing numerical values for ranking benefits and/or harms (KQ2) or similar outcomes (KQ3) these will be summarized descriptively and results across studies compared. Thematic analysis may be undertaken for KQ2, including coding data (meaning and context) into descriptive themes that accurately reflect the data and then summarizing this in a narrative format.

Key Questions 4 and 5

When using systematic reviews for stages 2 and 3, any meta-analysis will be reconstructed if possible to provide graphical representation of the findings to support our interpretations. Meta-analysis may be recalculated, if possible, when new studies are found in search updates (KQ4), analysis methods are not thought appropriate (e.g., use of random rather than fixed effects models, ability but no use of HSROC models [see below]) or if further analysis (e.g. between-study stratification) may be possible for subgroups of interest. When substantial methodological heterogeneity was found, we may conduct sensitivity analyses if appropriate and able (e.g., for studies rated as high risk of bias, different study designs) or decide to not use the pooled/combined estimate. If not conducted by the authors and when there are at least eight studies in a meta-analysis, we will if possible analyze publication bias both visually using the

funnel plot and quantitatively using Egger's test (32). If meta-analysis was not performed, we will summarize the findings of the systematic review authors.

For KQ5 (diagnostic accuracy), if individual studies are incorporated we will construct 2 x 2 tables and calculate sensitivity, specificity, and positive and negative likelihood ratios (LR+, LR-). Sensitivity and specificity are measures of test accuracy. Likelihood ratios are used to estimate the increased or decreased probability of disease (i.e., ASB) for a patient and can be used to refine clinical judgement based on varying pre-test probabilities. The larger the LR+, the more accurate the test is and the greater the likelihood of disease following a positive test; the smaller the LR-, the more accurate the test is, the lesser the likelihood of disease following a negative test (33). A LR+ that is >10 indicates a large and often conclusive probability that the condition is present; a LR- that is <0.10 suggests a large and often conclusive probability that the condition is not present. A likelihood ratio of one means that a positive or negative result is equally probable in a patient with and without the disease/condition.

If there are more than three studies and they are clinically homogenous (i.e., timing in pregnancy, thresholds, diagnostic criteria), we will pool data using a hierarchical summary receiver-operator curve (HSROC) and bivariate analysis of sensitivity and specificity (34). The HSROC simultaneously compares the sensitivity and specificity (taking their correlation into account) for all studies comparing a particular screening test with ASB diagnostic criteria. We will use Review Manager Version 5.0 (The Cochrane Collaboration, Copenhagen, Denmark) to perform meta-analyses, and Stata 11.0 (metandi program; StataCorp LP, College Station, TX, USA) to fit the bivariate and HSROC models and produce the pooled estimates of sensitivity, specificity, and likelihood ratios.

The results will be organized by type of screening test. If possible, we will examine the impact of screening before and after 12-16 weeks' gestation and in relation to other intervention subgroups described in Table 5. Sensitivities, specificities, and likelihood ratios and their 95% confidence intervals (CI) will be presented in summary tables that include all screening tests and diagnostic criteria. Based on the findings for sensitivity and specificity and estimates of one or more relevant baseline prevalence, an evidence profile will be generated for the outcomes FN, FP, TN, and TP (30).

Subgroup Analyses

Our primary approach for evaluating differential effect for subgroups will be to record any within-study subgroup analyses performed by study investigators using individual patient data; these results preserve the within-study randomization. Because these results are often based on diverse methodology and may be difficult to interpret across the body of evidence, we will also perform our own subgroup analyses using study-level data, as possible, using formal statistical approaches (e.g., meta-regressions) or by stratifying the results of the pairwise meta-analyses by subgroup variables. When determining whether entire studies fall into a particular subgroup category (e.g., recurrent UTI), we will consider ≥80 percent of the study population meeting the criteria as sufficient. We will employ regression analyses when: for continuous variables (e.g., timing during pregnancy) there are at least six to ten studies reporting on the outcome within a specific subgroup, and for categorical variables (e.g., history of recurrent UTI) there are at least three studies for each category level. The number of sufficient studies serves as a rule of thumb

for the lower bound that investigators can consider for a meta-regression, but power will vary according to the size and variability of the effect. These analyses would rely on study-level data, such that the results would be considered observational in nature.

Assessment of the Overall Quality of the Evidence using GRADE

Two reviewers will independently assess the quality of the body of evidence or confidence in the effect for each outcome of interest (see Table 1) using the GRADE methodology. Discrepancies will be resolved through discussion or third-party consultation to reach consensus. Assessments will be entered into the GRADEPro software and summarized in GRADE evidence profiles, Summary of Findings tables and Evidence to Decision Tables. Footnotes to the tables will explain all decisions. The CTFPHC will then use this evidence on each outcome, to assess the net benefits and harms of each service, consider patient preferences and values, and other elements of the GRADE methodology to develop the recommendations on screening for bacteriuria (feasibility, acceptability and equity).

The general approach is outlined here although methods will align with GRADE guidance (30, 35). When using systematic reviews, GRADE assessments will be based on the individual studies and reporting by review authors (e.g., on ROB assessments and PICOTS characteristics) and upon validation of a sample by the review team. For evidence on the benefits and harms of screening (KQ1), as a starting point the quality is assigned as high for evidence from RCTs and low for evidence from observational studies, when used. For accuracy studies, cross-sectional or cohort studies in patients with diagnostic uncertainty and direct comparison of test results with an appropriate reference standard will be considered high quality. Thereafter, we will examine and potentially downgrade the quality based on five core domains: study limitations/ROB, inconsistency, indirectness, imprecision, and publication/reporting bias. For outcomes where there is evidence from observational studies and no other reason to downgrade the evidence, we will also consider the additional domains of dose-response association, plausible confounding, and strength of association (i.e., large magnitude of effect [i.e., large ≤ 0.5 or ≥ 2.0 or very large RR ≤ 0.2 or ≥ 5.0]), to potentially upgrade the quality (36).

For the *study limitations (risk of bias)* domain RCTs and CCTs may be downgraded one or two levels depending on the proportion of trials (e.g., one very large trial may outweigh two very small trials) assessed as having high ROB for the particular outcome under consideration (37). Evidence from observational studies will be downgraded when most studies have moderate or high ROB. For *inconsistency* (consistent, inconsistent) we will assess the magnitude of the effects of the included studies (e.g., inconsistent when lack of overlap in 95% CIs for some studies) (38). *Indirectness* of the evidence (direct or indirect) is based on evaluating the relevance of the study's PICOs compared to ours for our primary KQ1 (effectiveness of screening); when relying on test accuracy and treatment studies there will be downgrading by at least one level for this domain (36). We will assess *imprecision* (precise or imprecise) on the basis of clinical thresholds and Optimal Information Size (39). For outcomes where clinical thresholds are used/determined, we will typically downgrade this domain once if the entire pooled 95% CI does not cross the threshold (i.e. only one limit of the CI crosses), and downgrade twice if the 95% CI crosses the threshold and no difference (0 MD or 1.0 RR) or does not cross

the threshold at all. Thresholds may be determined a priori (prior to viewing results from studies) but may also be revised post hoc based on careful benefit-harm considerations when considering all outcomes together (e.g., lower benefit threshold in cases of few and minor harms). A precise estimate is one that allows for a clinically useful conclusion. *Reporting bias* (suspected or undetected) will be evaluated with respect to publication bias.

Interpreting these domains when relying on evidence from diagnostic test (KQ5) data has certain considerations, including how certain the CTFPHC is about the consequences of each outcome (FP, FN, TP, TN) in relation to the main outcomes of interest for KQs 1, 2 & 4 (30).

External Review

The evidence review will be peer-reviewed by external content experts (minimum 3) and invited stakeholder organizations (minimum 10), with response to all comments shared with all reviewers approximately two months after posting of the final review.

Planned Schedule and Timeline

Draft protocol approved by CTFPHC members: July 29, 2016
External peer review: August 1-10, 2016
Final protocol: November 30, 2016
Draft evidence review: January 31, 2017
Final evidence review: March 31, 2017

Conflict of Interest Statement

None of the study team members have any known actual or perceived conflicts of interest related to this review.

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Appendix 1. MEDLINE Search Strategy (KQ1 [screening effectiveness])

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Title: PHTF Bacteriuria Screening in Pregnancy

Strategy:

1. Asymptomatic Infections/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
2. Bacteriuria/
3. exp Cystitis/
4. Dysuria/
5. Pyelonephritis/
6. Urinary Tract Infections/
7. bacilluria*.tw,kf.
8. bacteriuria*.tw,kf.
9. cystiti*.tw,kf.
10. (cysto-pyeliti* or cystopyeliti*).tw,kf.
11. dysuria*.tw,kf.
12. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw,kf.
13. (pyelo-cystiti* or pyelocystiti*).tw,kf.
14. (pyelo-nephriti* or pyelonephriti*).tw,kf.
15. (UTI or UTIs).tw,kf.
16. or/1-15 [Combined MeSH & text words for bacteriuria]
17. Antibody-Coated Bacteria Test, Urinary/
18. *Bacteriuria/di, pc, mi, ur
19. exp *Cystitis/di, pc, mi, ur
20. Mass Screening/
21. Microbial Sensitivity Tests/
22. Microscopy/
23. Predictive Value of Tests/
24. *Pyelonephritis/di, pc, mi, ur
25. Reagent Kits, Diagnostic/
26. Reagent Strips/
27. "Sensitivity and Specificity"/
28. Urinalysis/
29. *Urinary Tract Infections/di, pc, mi, ur
30. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw,kf.
31. diagnostic accurac*.tw,kf.
32. culture*.tw,kf.
33. (detect* or predict* or screen*).tw,kf.
34. (dip slide* or dipslide* or dip stick* or dipstick*).tw,kf.
35. (micro-scopy or microscopy).tw,kf.
36. (microb* adj2 test*).tw,kf.
37. ((re-agent* or reagent) adj3 (strip* or test*)).tw,kf.

38. strip* test*.tw,kf.
39. urine test*.tw,kf.
40. (urinalys* or urine analys*).tw,kf.
41. uriscreen.tw,kf.
42. or/17-41 [Combined MeSH & text words for screening]
43. exp Pregnancy/
44. Pregnancy Complications, Infectious/
45. Pregnant Women/
46. Prenatal Care/
47. Prenatal Diagnosis/
48. (antenatal* or pre-natal* or prenatal*).mp.
49. (expect* adj (female? or mother? or wom#n)).tw,kf.
50. pregnan*.mp.
51. or/43-50 [Combined MeSH & text words for pregnancy]
52. and/16,42,51 [Combined searches for bacteriuria, screening & pregnancy]
53. Male/ not (Female/ and Male/)
54. 52 not 53 [Male only records excluded]
55. exp Animals/ not (exp Animals/ and Humans/)
56. 54 not 55 [Animal only records excluded]
57. (comment or editorial or news or newspaper article).pt.
58. (letter not (letter and randomized controlled trial)).pt.
59. 56 not (57 or 58) [Opinion pieces excluded]
60. case reports.pt.
61. 59 not 60 [Case reports excluded]
62. limit 61 to (english or french)
63. remove duplicates from 62

Appendix 2. Methods for Integrating Existing Systematic Reviews into New Reviews

One or more systematic reviews may exist that align with one or more key questions (KQs) of the reviews undertaken to inform CTFPHC guidelines. The CTFPHC and ERSCs have considered the manner in which new reviews conducted for CTFPHC guidelines can benefit from efficiencies by incorporating existing systematic reviews, while maintaining methodological rigor in their own systematic review conduct, closely aligning existing reviews within their review scope (i.e., inclusion/exclusion criteria), and maintaining consistency with other CTFPHC Methods. They have based their approach on work conducted by a methods working group composed of investigators from the Evidence-based Practice Center Program funded by the U.S. Agency for Healthcare Research and Quality.[1,2] A summary of the way the ERSCs will operationalize the 12 AHRQ recommendations (Box 1) to meet their needs is outlined below. This approach differs from situations when "updating" a single existing systematic review is deemed suitable, that is, in some cases a high-quality review will be used to answer one or more of the CTFPHC KQs in entirety, usually without revisions to the review's scope, search for evidence (apart from updating to present), methodological quality/risk of bias assessments, data extraction, or data analysis.

Summary of CTFPHC Approach

The recommendations developed by AHRQ (Box 1) will serve as an overall framework for ERSC reviews, although in most cases existing systematic reviews will be used to build efficiencies in discrete steps within the review process—mainly search and selection of literature, and data extraction—which will not generally include refinement of the scope or data analysis and interpretation. Moreover, we will not in most circumstances include a systematic review itself as a study design for inclusion (unless the intention is to specifically conduct an overview of reviews). The ability to use any given systematic review will largely depend on how it aligns with the CTFPHC review's scope (PICOTS). A further primary consideration will be the comprehensiveness of its search strategy and reporting of literature flow. It is important to note that some CTFPHC reviews need to be complex with multiple stages (e.g., a review of screening effectiveness for patient-important benefits and harms may require including evidence on indirect evidence of test accuracy and treatment) such that existing systematic reviews may exist for one or more discrete stages but not for others. Some key points on the operationalization, and minor revision, by the ERSCs of these recommendations are provided below.

1. **Choosing systematic reviews**: Following the identification of relevant reviews (a search for systematic reviews may be undertaken for some topics), the evidence for each will be mapped to the PICOTS elements and the quality of the review will be assessed (e.g., using the AMSTAR tool which has been evaluated and found effective to discriminate reviews with high and low quality of methods and reporting).[3] Some of the CTFPHC KQs may only have a single existing systematic review for possible incorporation, while others may have more than one; if suitable, a decision between systematic reviews will be based on methodological quality, comprehensiveness and quality of its literature search and reporting (e.g., assessed using PRESS checklist), comprehensiveness of reporting on included studies, and the best fit within the CTFPHC scope and methods. In some cases two or more reviews may be integrated because, together, they capture the full scope of the CTFPHC KQ(s). Rationale will be provided for choices made.

Note: If no review is deemed a good fit for purpose for integration (i.e., de novo process all together appears to be best option) we will at minimum examine available reviews for their search strategies (to ensure that our search strategies are comprehensive) and review their reference lists for identification of studies.

2. **Searching**: Various strategies will be considered. If one or more reviews are fit for purpose (but do not meet criteria for classification as a systematic review update) and cover a scope that is *very similar or broader* than the CTFPHC topic, we may update the search(es) if the last search date was prior to 6 months before commencing our review. When there are multiple reviews being considered, updating the literature to present may involve a new comprehensive search strategy to identify studies published after the date of the earliest existing review; this may reduce complexities when trying to implement, document, and remove duplicates from multiple searches. Alternatively, if the scope of the existing review(s) is *narrower* (e.g., missing an element in PICOTS) or the search *deemed sub-optimal in some manner* (e.g., missing key terms, additional database viewed as highly relevant) we may re-run the existing review's search concurrent with an original (e.g., broader) search and remove the citations previously screened for the other review. If more appropriate, we may update the other review's search and use a new search for the missing PICO element(s) (e.g., one additional intervention) for a longer time period to meet our timeframe. In cases where we feel screening excluded studies lists is appropriate we will also undertake this. Careful consideration will be used to ensure a comprehensive search is conducted regardless of approach taken; moreover, the ERSC librarians will help determine on a case-by-case basis what approach would be feasible for implementation to ensure aims of building efficiencies are possible.
3. **Screening and selection**: We will assess articles included in all relevant reviews (based on full text if necessary) to determine if they meet our inclusion criteria.
4. **Data extraction and methodological quality assessments**: We will consider incorporating the data on study and participant characteristics rather than extracting these data anew; we may also use the review author's risk of bias assessments if the tools/methods are consistent with CTFPHC methods. These steps will create efficiencies but because they are dependent on the quality of the systematic review and extent of reporting, the ERSC staff will verify the data on at least 5 to 10% of studies.[1]
5. **Data analysis**: We will consider using quantitative outcome data from reviews (with verification), but will not typically use meta-analyses or quality (GRADE) assessments of existing reviews.
6. **Reporting**: Transparent reporting of all integration steps used will be included in the evidence review report.

Box 1. Recommendations developed by AHRQ EPCs*[1,2]

*Strength of evidence refers to AHRQ's slightly modified approach to the GRADE quality of evidence approach

1. Existing reviews should be confirmed as systematic reviews through the application of a minimum set of eligibility criteria. We propose that the minimum eligibility criteria for systematic reviews include an explicit and adequate search, application of predefined eligibility criteria to select studies, risk of bias assessment for included studies, and synthesis of results.
2. Criteria to assess the relevance, in terms of question elements and currency, and quality of existing systematic reviews under consideration for inclusion in reviews should be predefined.
3. The quality of relevant existing systematic reviews should be assessed in an explicit manner with a minimum set of quality criteria that include search of multiple sources, use of a generally accepted tool for risk of bias assessment, and sufficient information to assess the strength of the body of evidence that includes the major domains of risk of bias, directness, consistency, precision, and reporting bias.
4. The risk of bias assessments from the existing systematic review may be used when the review described an explicit process, including the use of a tool or method that is compatible with the approach of the current review and that assessed the key sources of potential bias.
5. We suggest that risk of bias assessment be repeated in a sample of studies from an existing review under consideration for inclusion in a new review to confirm concordance with current review team approach.
6. We recommend that at a minimum, reviews should narratively describe findings of the prior review(s), including the number and types of studies included, and the overall findings.
7. We recommend that newly identified studies be clearly distinguished from studies in the existing review(s) when presented in the narrative and any tables (eg, separate tables).
8. Summary tables should include sufficient information to support ratings for overall strength of evidence, including ratings for individual strength of evidence domains (study limitations, consistency, precision, directness, reporting bias). The strength of evidence ratings should be based on the underlying primary evidence, not the number or quality of existing systematic reviews.
9. Using strength of evidence domains as a framework (study limitations, consistency, precision, directness, and reporting bias), review authors should consider how new evidence would change estimates of effect or ratings for strength of evidence. A new quantitative synthesis (ie, pooled estimate) is needed if new studies would change conclusions or strength of evidence judgements, or to obtain a more precise or more up-to-date estimate.
10. In cases where the existing systematic review(s) did not complete strength of evidence grading for a comparison and outcome of interest, the strength of evidence should be assessed for the body of evidence, considering primary studies from prior review(s) and any new studies identified.
11. In cases where no new studies are added to the body of evidence, the strength of evidence assessment from the existing systematic review may be used if conducted using an acceptable grading approach consistent with current review context. In these cases, we suggest that the overall strength of evidence assessment be reviewed, considering the strength of evidence domains, to confirm consistency with current review team assessments.
12. In cases where new studies are added to the body of evidence, the strength of evidence may need to be reassessed on the basis of all studies/evidence.

Appendix 2 References

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2. Robinson KA, Chou R, Berkman ND, et al. Twelve recommendations for integrating existing systematic reviews into new reviews: EPC guidance. J Clin Epidemiol. 2016 Feb;70:38-44. PMID: 26261004.

3. Foisy M, Hartling L. Challenges and considerations involved in using AMSTAR in overviews of reviews. 22nd Cochrane Colloquium. Hyderabad (India); 2014 Sept 21-26.

Supplement 2. Search Strategy

KQ1: Screening Effectiveness
Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Date Searched: 13 June 2016
Date Updated: 6 September 2017
Records Retrieved: 1437

1. Asymptomatic Infections/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
2. Bacteriuria/
3. exp Cystitis/
4. Dysuria/
5. Pyelonephritis/
6. Urinary Tract Infections/
7. bacilluria*.tw,kf.
8. bacteriuria*.tw,kf.
9. cystiti*.tw,kf.
10. (cysto-pyeliti* or cystopyeliti*).tw,kf.
11. dysuria*.tw,kf.
12. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw,kf.
13. (pyelo-cystiti* or pyelocystiti*).tw,kf.
14. (pyelo-nephriti* or pyelonephriti*).tw,kf.
15. (UTI or UTIs).tw,kf.
16. or/1-15 [Combined MeSH & text words for bacteriuria]
17. Antibody-Coated Bacteria Test, Urinary/
18. *Bacteriuria/di, pc, mi, ur
19. exp *Cystitis/di, pc, mi, ur
20. Mass Screening/
21. Microbial Sensitivity Tests/
22. Microscopy/
23. Predictive Value of Tests/
24. *Pyelonephritis/di, pc, mi, ur
25. Reagent Kits, Diagnostic/
26. Reagent Strips/
27. "Sensitivity and Specificity"/
28. Urinalysis/
29. *Urinary Tract Infections/di, pc, mi, ur
30. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw,kf.
31. diagnostic accurac*.tw,kf.
32. culture*.tw,kf.
33. (detect* or predict* or screen*).tw,kf.
34. (dip slide* or dipslide* or dip stick* or dipstick*).tw,kf.
35. (micro-scopy or microscopy).tw,kf.
36. (microb* adj2 test*).tw,kf.
37. ((re-agent* or reagent) adj3 (strip* or test*)).tw,kf.
38. strip* test*.tw,kf.

39. urine test*.tw,kf.
40. (urinalys* or urine analys*).tw,kf.
41. uriscreen.tw,kf.
42. or/17-41 [Combined MeSH & text words for screening]
43. exp Pregnancy/
44. Pregnancy Complications, Infectious/
45. Pregnant Women/
46. Prenatal Care/
47. Prenatal Diagnosis/
48. (antenatal* or pre-natal* or prenatal*).mp.
49. (expect* adj (female? or mother? or wom#n)).tw,kf.
50. pregnan*.mp.
51. or/43-50 [Combined MeSH & text words for pregnancy]
52. and/16,42,51 [Combined searches for bacteriuria, screening & pregnancy]
53. Male/ not (Female/ and Male/)
54. 52 not 53 [Male only records excluded]
55. exp Animals/ not (exp Animals/ and Humans/)
56. 54 not 55 [Animal only records excluded]
57. (comment or editorial or news or newspaper article).pt.
58. (letter not (letter and randomized controlled trial)).pt.
59. 56 not (57 or 58) [Opinion pieces excluded]
60. case reports.pt.
61. 59 not 60 [Case reports excluded]
62. limit 61 to (english or french)
63. remove duplicates from 62

KQ1: Screening Effectiveness
Database: Ovid Embase 1974 to 2016 Week 24
Date Searched: 13 June 2016
Date Updated: 6 September 2017
Records Retrieved: 1613

1. acute pyelonephritis/
2. asymptomatic bacteriuria/
3. asymptomatic infection/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
4. bacteriuria/
5. exp cystitis/
6. dysuria/
7. kidney infection/
8. pyelonephritis/
9. urinary tract infections/
10. bacilluria*.tw.
11. bacteriuria*.tw.
12. cystiti*.tw.
13. (cysto-pyeliti* or cystopyeliti*).tw.
14. dysuria*.tw.

15. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw.
16. (pyelo-cystiti* or pyelocystiti*).tw.
17. (pyelo-nephriti* or pyelonephriti*).tw.
18. (UTI or UTIs).tw.
19. or/1-18 [Combined Emtree & text words for bacteriuria]
20. *asymptomatic bacteriuria/di, pc
21. *acute pyelonephritis/di, pc
22. *bacteriuria/di, pc
23. exp *cystitis/di, pc
24. diagnostic kit/
25. fluorescent antibody technique/
26. *kidney infection/di, pc
27. mass screening/
28. microbial sensitivity test/
29. microscopy/
30. predictive value/
31. *pyelonephritis/di, pc
32. "sensitivity and specificity"/
33. screening/
34. test strip/
35. exp urinalysis/
36. *urinary tract infection/di, pc
37. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw.
38. diagnostic accurac*.tw.
39. culture*.tw.
40. (detect* or predict* or screen*).tw.
41. (dip slide* or dipslide* or dip stick* or dipstick*).tw.
42. (micro-scopy or microscopy).tw.
43. (microb* adj2 test*).tw.
44. ((re-agent* or reagent) adj3 (strip* or test*)).tw.
45. strip* test*.tw.
46. urine test*.tw.
47. (urinalys* or urine analys*).tw.
48. uriscreen.tw.
49. or/20-48 [Combined Emtree & text words for screening]
50. exp pregnancy/
51. pregnancy complication/
52. pregnant woman/
53. prenatal care/
54. prenatal diagnosis/
55. prenatal screening/
56. (antenatal* or pre-natal* or prenatal*).mp.
57. (expect* adj (female? or mother? or wom#n)).tw.
58. pregnan*.mp.
59. or/50-58 [Combined Emtree & text words for pregnancy]
60. and/19,49,59 [Combined Emtree & text words for pregnancy]
61. Male/ not (Female/ and Male/)
62. 60 not 61 [Male only records excluded]

63. animals/ not (animals/ and humans/)
64. 62 not 63 [Animal only records excluded]
65. (conference* or editorial or letter).pt.
66. 64 not 65 [Excluded publication types – RF note: will search conference proceedings separately with different strategy]
67. case report/ or case report*.ti.
68. 66 not 67 [Case reports excluded]
69. limit 68 to (english or french)
70. remove duplicates from 69

KQ1: Screening Effectiveness
Database: Wiley Cochrane Library
Date Searched: 13 June 2016
Date Update: 6 September 2017
Records Retrieved: 11 in Cochrane Database of Systematic Reviews
Records Retrieved: 1 in Database of Abstracts of Reviews of Effects (DARE)
Records Retrieved: 112 in Cochrane Central Register of Controlled Trials (CENTRAL)
Records Retrieved: 1 in Health Technology Assessment Database

#1 [mh ^"Asymptomatic Infections"] and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*):ti,ab,kw
#2 [mh ^Bacteriuria]
#3 [mh Cystitis]
#4 [mh ^Dysuria]
#5 [mh ^Pyelonephritis]
#6 [mh ^"Urinary Tract Infections"]
#7 bacilluria*:ti,ab,kw
#8 bacteriuria*:ti,ab,kw
#9 cystiti*:ti,ab,kw
#10 (cysto-pyeliti* or cystopyeliti*):ti,ab,kw
#11 dysuria*:ti,ab,kw
#12 (infection* near/2 (bladder* or genitourin* or kidney* or urin* or urogenita*)):ti,ab,kw
#13 (pyelo-cystiti* or pyelocystiti*):ti,ab,kw
#14 (pyelo-nephriti* or pyelonephriti*):ti,ab,kw
#15 (UTI or UTIs):ti,ab,kw
#16 {or #1-#15}
#17 [mh ^"Antibody-Coated Bacteria Test, Urinary"]
#18 [mh ^Bacteriuria [mj]/DI,PC,MI,UR]
#19 [mh Cystitis [mj]/DI,PC,MI,UR]
#20 [mh ^"Mass Screening"]
#21 [mh ^"Microbial Sensitivity Tests"]
#22 [mh ^Microscopy]
#23 [mh ^"Predictive Value of Tests"]
#24 [mh ^Pyelonephritis [mj]/DI,PC,MI,UR]
#25 [mh "Reagent Kits, Diagnostic"]
#26 [mh "Reagent Strips"]

#27 [mh ^"Sensitivity and Specificity"]
#28 [mh ^Urinalysis]
#29 [mh ^"Urinary Tract Infections" [mj]/DI,PC,MI,UR]
#30 ((accurac* or diagnostic) near/5 (algorithm* or test*)):ti,ab,kw
#31 "diagnostic accurac*":ti,ab,kw
#32 culture*:ti,ab,kw
#33 (detect* or predict* or screen*):ti,ab,kw
#34 ("dip slide*" or dipslide* or "dip stick*" or dipstick*):ti,ab,kw
#35 (micro-scopy or microscopy):ti,ab,kw
#36 (microb* near/2 test*):ti,ab,kw
#37 ((re-agent* or reagent) near/3 (strip* or test*)):ti,ab,kw
#38 "strip* test*":ti,ab,kw
#39 "urine test*":ti,ab,kw
#40 (urinalys* or "urine analys*"):ti,ab,kw
#41 uriscreen:ti,ab,kw
#42 {or #17-#41}
#43 [mh Pregnancy]
#44 [mh ^"Pregnancy Complications, Infectious"]
#45 [mh ^"Pregnant Women"]
#46 [mh ^"Prenatal Care"]
#47 [mh ^"Prenatal Diagnosis"]
#48 (antenatal* or pre-natal* or prenatal*):ti,ab,kw
#49 (expect* near/1 (female* or mother* or wom?n)):ti,ab,kw
#50 pregnan*:ti,ab,kw
#51 {or #43-#50}
#52 {and #16, #42, #51}

KQ1: Screening Effectiveness
Database: CINAHL Plus with Full Text (1937 to the present) via EBSCOhost
Date Searched: 13 June 2016
Date Updated: 6 September 2017
Records Retrieved: 249

S1. (MH "Bacteriuria")
S2. (MH "Cystitis+")
S3. (MH "Dysuria")
S4. (MH "Pyelonephritis")
S5. (MH "Urinary Tract Infections")
S6. bacilluria*
S7. bacteriuria*
S8. cystiti*
S9. "cysto-pyeliti*" or cystopyeliti*
S10. dysuria*
S11. (infection* N2 (bladder* or genitourin* or kidney* or urin* or urogenita*))
S12. "pyelo-cystiti*" or pyelocystiti*
S13. "pyelo-nephriti*" or pyelonephriti*
S14. UTI or UTIs

S15. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16. (MM "Bacteriuria/DI/PC/MI/UR")
S17. (MM "Cystitis+/DI/MI/PC/UR")
S18. (MH "Fluorescent Antibody Technique")
S19. (MH "Health Screening")
S20. (MH "Microbial Culture and Sensitivity Tests")
S21. (MH "Microscopy")
S22. (MH "Predictive Value of Tests")
S23. (MM "Pyelonephritis/DI/PC/MI/UR")
S24. (MH "Reagent Kits, Diagnostic+")
S25. (MH "Sensitivity and Specificity")
S26. (MH "Urinalysis")
S27. (MM "Urinary Tract Infections/DI/PC/MI/UR")
S28. (accurac* or diagnostic) N5 (algorithm* or test*)
S29. "diagnostic accurac*"
S30. culture*
S31. detect* or predict* or screen*
S32. "dip slide*" or dipslide* or "dip stick*" or dipstick*
S33. "micro-scopy" or microscopy
S34. microb* N2 test*
S35. ("re-agent*" or reagent) N3 (strip* or test*)
S36. "strip* test*"
S37. "urine test*"
S38. urinalys* or "urine analys*"
S39. uriscreen
S40. S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S41. (MH "Expectant Mothers")
S42. (MH "Pregnancy+")
S43. (MH "Pregnancy Complications, Infectious")
S44. (MH "Prenatal Care")
S45. (MH "Prenatal Diagnosis")
S46. antenatal* or "pre-natal*" or prenatal*
S47. expect* N1 (female? or mother? or wom?n)
S48. pregnan*
S49. S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48
S50. S15 AND S40 AND S49
S51. MH "Male" NOT ((MH "Female") AND (MH "Male"))
S52. S50 NOT S51
S53. ((MH "Vertebrates+") NOT MH Human)
S54. S52 NOT S53
S55. Limiters - Publication Type: Anecdote, Case Study, Commentary, Editorial, Letter
S56. S54 NOT S55
S57. S56 Narrow by Language: - english [RF: No French records in results to include]

KQ1: Screening Effectiveness
Database: PubMed via NCBI Entrez (1946 to Present)

Date Searched: 14 June 2016
Records Retrieved: 1246

(((((("asymptomatic infections"[mh] AND (("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields]) OR ("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields] OR "bacteriurias"[All Fields]) OR ("urinary bladder"[MeSH Terms] OR ("urinary"[All Fields] AND "bladder"[All Fields]) OR "urinary bladder"[All Fields] OR "bladder"[All Fields]) OR ("cystitis"[MeSH Terms] OR "cystitis"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields]) OR ("pyelocystitis"[MeSH Terms] OR "pyelocystitis"[All Fields]) OR ("pyelonephritis"[MeSH Terms] OR "pyelonephritis"[All Fields]) OR ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields] OR "urinary"[All Fields]) OR ("urine"[Subheading] OR "urine"[All Fields] OR "urine"[MeSH Terms]) OR UTI[all] OR ("urinary tract infections"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "urinary tract infections"[All Fields] OR "utis"[All Fields]))) OR "bacteriuria"[MeSH Terms:noexp] OR "cystitis"[MeSH Terms] OR "dysuria"[MeSH Terms:noexp] OR "pyelonephritis"[MeSH Terms:noexp] OR "Urinary Tract Infections"[mh:noexp] OR bacilluria[tiab] OR bacteriuria[tiab] OR bacteriurias[tiab] OR "bladder infection"[tiab] OR "bladder infections"[tiab] OR cystitis[tiab] OR cystopyelitis[tiab] OR dysuria[tiab] OR "genito-urinary infection"[tiab] OR "genitourinary infection"[tiab] OR "genito-urinary infections"[tiab] OR "genitourinary infections"[tiab] OR "kidney infection"[tiab] OR "kidney infections"[tiab] OR "pyelo-nephritis"[tiab] OR pyelocystitis[tiab] OR pyelonephritis[tiab] OR "urinary infection"[tiab] OR "urinary infections"[tiab] OR "urogenital infection"[tiab] OR "urogenital infections"[tiab] OR UTI[tiab] OR UTIs[tiab]) AND ("Antibody-Coated Bacteria Test, Urinary"[mh] OR "Bacteriuria/diagnosis"[Majr] OR "Bacteriuria/prevention and control"[Majr] OR ("bacteriuria/microbiology"[Mesh Terms] AND Majr[All Fields]) OR "Bacteriuria/urine"[Majr] OR "Cystitis/diagnosis"[Majr] OR "Cystitis/prevention and control"[Majr] OR "Cystitis/microbiology"[Majr] OR "Cystitis/urine"[Majr] OR "Mass Screening"[mh:noexp] OR "Microbial Sensitivity Tests"[mh:noexp] OR "Microscopy"[mh:noexp] OR "Predictive Value of Tests"[mh:noexp] OR "Pyelonephritis/diagnosis"[Majr] OR "Pyelonephritis/prevention and control"[Majr] OR "Pyelonephritis/microbiology"[Majr] OR "Pyelonephritis/urine"[Majr] OR "Reagent Kits, Diagnostic"[mh:noexp] OR "Reagent Strips"[mh:noexp] OR "Sensitivity and Specificity"[mh:noexp] OR "Urinalysis"[mh:noexp] OR "Urinary Tract Infections/diagnosis"[Majr] OR "Urinary Tract Infections/prevention and control"[Majr] OR "Urinary Tract Infections/microbiology"[Majr] OR "Urinary Tract Infections/urine"[Majr] OR detect[tiab] OR detected[tiab] OR detection[tiab] OR detecting[tiab] OR detects[tiab] OR "diagnostic accuracy"[tiab] OR "diagnostic algorithm"[tiab] OR "dip slide"[tiab] OR "dip slides"[tiab] OR "dip stick"[tiab] OR "dip sticks"[tiab] OR dipslide[tiab] OR dipslides[tiab] OR dipstick[tiab] OR dipsticks[tiab] OR culture[tiab] OR cultures[tiab] OR "diagnostic test"[tiab] OR "diagnostic tests"[tiab] OR "microbial test"[tiab] OR "microbial tests"[tiab] OR microscopy[tiab] OR predict[tiab] OR predicted[tiab] OR prediction[tiab] OR predicting[tiab] OR predicts[tiab] OR "reagent strip"[tiab] OR "reagent strips"[tiab] OR "reagent test"[tiab] OR "reagent testing"[tiab] OR "reagent tests"[tiab] OR screen[tiab] OR screened[tiab] OR screening[tiab] OR screens[tiab] OR "strip test"[tiab] OR "strip tests"[tiab] OR "strip testing"[tiab] OR "test accuracy"[tiab] OR urinalyses[tiab] OR urinalysis[tiab] OR "urine analyses"[tiab] OR "urine analysis"[tiab] OR "urine test"[tiab] OR "urine tested"[tiab] OR "urine testing"[tiab] OR "urine tests"[tiab] OR uriscreen[tiab]) AND ("Pregnancy"[mh] OR "Pregnancy Complications, Infectious"[mh:noexp] OR "Pregnant Women"[mh:noexp] OR "Prenatal Care"[mh:noexp] OR "Prenatal Diagnosis"[mh:noexp] OR antenatal[tiab] OR "pre-natal"[tiab] OR prenatal[tiab] OR "expectant mother"[tiab] OR "expectant mothers"[tiab] OR "expecting mothers"[tiab] OR "expecting mothers"[tiab] OR "expectant woman"[tiab] OR "expectant women"[tiab] OR "expecting

women"[tiab] OR pregnancies[tiab] OR pregnancy[tiab] OR pregnant[tiab])) NOT ("Male"[mh] NOT ("Female"[mh] AND "Male"[mh]))) NOT (((Animals[MESH] OR Animal Experimentation[MESH] OR "Models, Animal"[MESH] OR Vertebrates[MESH]) NOT (Humans[MESH] OR Human experimentation[MESH])) OR (((animals[tiab] OR animal model[tiab] OR rat[tiab] OR rats[tiab] OR mouse[tiab] OR mice[tiab] OR rabbit[tiab] OR rabbits[tiab] OR pig[tiab] OR pigs[tiab] OR porcine[tiab] OR swine[tiab] OR dog[tiab] OR dogs[tiab] OR hamster[tiab] OR hamsters[tiab] OR chicken[tiab] OR chickens[tiab] OR sheep[tiab]) AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])) NOT (human[ti] OR humans[ti] OR people[ti] OR children[ti] OR adults[ti] OR seniors[ti] OR patient[ti] OR patients[ti]))))) NOT (case reports[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR newspaper article[pt])
> limit to English or French

KQ2: Women's Outcome Valuation
Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Date Searched: 4 July 2016
Date Updated: 5 September 2017
Records Retrieved: 2965

1. Asymptomatic Infections/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
2. Bacteriuria/
3. exp Cystitis/
4. Dysuria/
5. Pyelonephritis/
6. Urinary Tract Infections/
7. bacilluria*.tw,kf.
8. bacteriuria*.tw,kf.
9. cystiti*.tw,kf.
10. (cysto-pyeliti* or cystopyeliti*).tw,kf.
11. dysuria*.tw,kf.
12. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw,kf.
13. (pyelo-cystiti* or pyelocystiti*).tw,kf.
14. (pyelo-nephriti* or pyelonephriti*).tw,kf.
15. (UTI or UTIs).tw,kf.
16. or/1-15 [Combined MeSH & text words for bacteriuria]
17. Antibody-Coated Bacteria Test, Urinary/
18. *Bacteriuria/di, pc, mi, ur
19. exp *Cystitis/di, pc, mi, ur
20. Mass Screening/
21. Microbial Sensitivity Tests/
22. Microscopy/
23. Predictive Value of Tests/
24. *Pyelonephritis/di, pc, mi, ur
25. Reagent Kits, Diagnostic/
26. Reagent Strips/
27. "Sensitivity and Specificity"/

28. Urinalysis/
29. *Urinary Tract Infections/di, pc, mi, ur
30. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw,kf.
31. diagnostic accurac*.tw,kf.
32. culture*.tw,kf.
33. (detect* or predict* or screen*).tw,kf.
34. (dip slide* or dipslide* or dip stick* or dipstick*).tw,kf.
35. (micro-scopy or microscopy).tw,kf.
36. (microb* adj2 test*).tw,kf.
37. ((re-agent* or reagent) adj3 (strip* or test*)).tw,kf.
38. strip* test*.tw,kf.
39. urine test*.tw,kf.
40. (urinalys* or urine analys*).tw,kf.
41. uriscreen.tw,kf.
42. or/17-41 [Combined MeSH & text words for screening]
43. and/16,42 [Combined searches for ASB and screening]
44. Anti-Bacterial Agents/
45. Antibiotic Prophylaxis/
46. Anti-Infective Agents, Urinary/
47. Asymptomatic Infections/dt, th
48. *Bacteriuria/dt, th
49. Drug Therapy, Combination/
50. Norfloxacin/
51. exp Penicillins/
52. exp Sulfonamides/
53. *Urinary Tract Infections/dt, th
54. amoxicillin*.mp.
55. ampicillin*.mp.
56. (anti-bacteria* or antibacteria*).tw,kf.
57. (anti-biotic* or antibiotic*).tw,kf.
58. aztreonam*.mp.
59. cefadroxil*.mp.
60. cefepime*.mp.
61. ceftibuten*.mp.
62. ceftri?xone*.mp.
63. cefuroxime*.mp.
64. cephalexin*.mp.
65. cephalosporin*.mp.
66. cephradine*.mp.
67. clindamycin*.mp.
68. (co-trimoxazole* or cotrimoxazole*).mp.
69. cycloserine*.mp.
70. fosfomycin*.mp.
71. gentam#cin*.mp.
72. nalidixic acid*.mp.
73. nitrofurantoin*.mp.
74. penicillin*.mp.
75. piperacillin*.mp.

76. pivampicillin*.mp.
77. pivmecillinam*.mp.
78. sulfadimethoxine*.mp.
79. sulfadiazine*.mp.
80. sulfamethizole*.mp.
81. sulfamethoxazole*.mp.
82. sulfamethoxypyridazine*.mp.
83. sulfonamide*.mp.
84. sulphadimidine*.mp.
85. sulphonamide*.mp.
86. tetracycline*.mp.
87. vancomycin*.mp.
88. or/44-87 [Combined MeSH & text words for antibiotic treatment]
89. exp Pregnancy/
90. Pregnancy Complications, Infectious/
91. Pregnant Women/
92. Prenatal Care/
93. Prenatal Diagnosis/
94. (antenatal* or pre-natal* or prenatal*).mp.
95. (expect* adj (female? or mother? or wom#n)).tw,kf.
96. pregnan*.mp.
97. or/89-96 [Combined MeSH & text words for pregnancy]
98. and/88,97 [Combined searches for antibiotic treatment and pregnancy]
99. Choice Behavior/
100. *Consumer Behavior/
101. exp Consumer Participation/
102. Cooperative Behavior/
103. exp Decision Making/
104. Focus Groups/
105. Health Care Surveys/
106. exp Informed Consent/
107. Interviews as Topic/
108. Patient Acceptance of Health Care/
109. exp Patient Education as Topic/
110. Patient Participation/
111. Patient Preference/
112. Social Values/
113. "Surveys and Questionnaires"/
114. Treatment Refusal/
115. (15D* and (HRQoL or QoL or "quality of life")).mp.
116. ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or refus* or respons* or valuation or value? or valuing or view*) adj3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom#n)).tw,kf.
117. ((analys#s or valuation? or value? or valuing) adj3 (conjoint or contingent)).tw,kf.
118. (choice? adj2 (behavio?r* or discrete or experiment*)).tw,kf.
119. ((choice? or choos* or consent* or decision*) adj1 informed).tw,kf.

120. ((choice? or choos* or decision*) adj2 (made or make or makes or making or shar* or support*)).tw,kf.
121. (EQ 5D or EQ5D or EuroQoL 5D or EuroQoL5D).mp.
122. (focus group? or interview* or questionnaire? or survey*).tw,kf.
123. gambl*.tw,kf.
124. health utilit*.tw,kf.
125. HUI.tw,kf.
126. (multi?attribute or multi?criteria).tw,kf.
127. (preference? adj1 (elicit* or scor* or state*)).tw,kf.
128. prospect theor*.tw,kf.
129. (SF 12 or SF 36 or SF 6D or SF12 or SF36 or SF6D).mp.
130. (trade off? or tradeoff?).tw,kf.
131. (willing* adj2 pay*).tw,kf.
132. or/99-131 [Combined MeSH & text words for patient preferences & values]
133. and/43,132 [Combined searches for patient preferences & ASB screening]
134. and/98,132 [Combined searches for patient preferences & antibiotic treatment and pregnancy]
135. or/133-134 [Combined sets of patient preferences for ASB screening & patient preferences for antibiotic treatment in pregnancy]
136. Male/ not Female/
137. 135 not 136 [Male only records excluded]
138. exp Animals/ not (exp Animals/ and Humans/)
139. 137 not 138 [Animal only records excluded]
140. (comment or editorial or news or newspaper article).pt.
141. (letter not (letter and randomized controlled trial)).pt.
142. 139 not (140 or 141) [Opinion pieces excluded]
143. case reports.pt.
144. 142 not 143 [Case reports excluded]
145. limit 144 to (english or french)
146. remove duplicates from 145

KQ2: Women's Outcome Valuation
Database: Ovid Embase 1974 to 2016 Week 27
Date Searched: 4 July 2016
Date Updated: 5 September 2017
Records Retrieved: 3922

1. acute pyelonephritis/
2. asymptomatic bacteriuria/
3. asymptomatic infection/ and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*).mp.
4. bacteriuria/
5. exp cystitis/
6. dysuria/
7. kidney infection/
8. pyelonephritis/
9. urinary tract infections/
10. bacilluria*.tw.

11. bacteriuria*.tw.
12. cystiti*.tw.
13. (cysto-pyeliti* or cystopyeliti*).tw.
14. dysuria*.tw.
15. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).tw.
16. (pyelo-cystiti* or pyelocystiti*).tw.
17. (pyelo-nephriti* or pyelonephriti*).tw.
18. (UTI or UTIs).tw.
19. or/1-18 [Combined Emtree & text words for bacteriuria]
20. *asymptomatic bacteriuria/di, pc
21. *acute pyelonephritis/di, pc
22. *bacteriuria/di, pc
23. exp *cystitis/di, pc
24. diagnostic kit/
25. fluorescent antibody technique/
26. *kidney infection/di, pc
27. mass screening/
28. microbial sensitivity test/
29. microscopy/
30. predictive value/
31. *pyelonephritis/di, pc
32. "sensitivity and specificity"/
33. screening/
34. test strip/
35. exp urinalysis/
36. *urinary tract infection/di, pc
37. ((accurac* or diagnostic) adj5 (algorithm* or test*)).tw.
38. culture*.tw.
39. (detect* or predict* or screen*).tw.
40. diagnostic accurac*.tw.
41. (dip slide* or dipslide* or dip stick* or dipstick*).tw.
42. (micro-scopy or microscopy).tw.
43. (microb* adj2 test*).tw.
44. ((re-agent* or reagent) adj3 (strip* or test*)).tw.
45. strip* test*.tw.
46. urine test*.tw.
47. (urinalys* or urine analys*).tw.
48. uriscreen.tw.
49. or/20-48 [Combined Emtree & text words for screening]
50. and/19,49 [Combined searches for ASB and screening]
51. antibiotic agent/
52. antibiotic prophylaxis/
53. antiinfective agent/
54. *asymptomatic bacteriuria/dt, th
55. *asymptomatic infection/dt, th
56. *bacteriuria/dt, th
57. exp *cystitis/dt, th
58. drug combination/

59. *kidney infection/dt, th
60. norfloxacin/
61. penicillin derivative/
62. *pyelonephritis/dt, th
63. sulfonamide/
64. urinary tract antiinfective agent/
65. *urinary tract infection/dt, th
66. amoxicillin*.mp.
67. ampicillin*.mp.
68. (anti-bacteria* or antibacteria*).tw.
69. (anti-biotic* or antibiotic*).tw.
70. aztreonam*.mp.
71. cefadroxil*.mp.
72. cefepime*.mp.
73. ceftibuten*.mp.
74. ceftri?xone*.mp.
75. cefuroxime*.mp.
76. cephalexin*.mp.
77. cephalosporin*.mp.
78. cephradine*.mp.
79. clindamycin*.mp.
80. (co-trimoxazole* or cotrimoxazole*).mp.
81. cycloserine*.mp.
82. fosfomycin*.mp.
83. gentam#cin*.mp.
84. nalidixic acid*.mp.
85. nitrofurantoin*.mp.
86. penicillin*.mp.
87. piperacillin*.mp.
88. pivampicillin*.mp.
89. pivmecillinam*.mp.
90. sulfadimethoxine*.mp.
91. sulfadiazine*.mp.
92. sulfamethizole*.mp.
93. sulfamethoxazole*.mp.
94. sulfamethoxypyridazine*.mp.
95. sulfonamide*.mp.
96. sulphadimidine*.mp.
97. sulphonamide*.mp.
98. tetracycline*.mp.
99. vancomycin*.mp.
100. or/51-99 [Combined Emtree & text words for antibiotic treatment]
101. exp pregnancy/
102. pregnancy complication/
103. pregnant woman/
104. prenatal care/
105. prenatal diagnosis/
106. prenatal screening/

107. (antenatal* or pre-natal* or prenatal*).mp.
108. (expect* adj (female? or mother? or wom#n)).tw.
109. pregnan*.mp.
110. or/101-109 [Combined Emtree & text words for pregnancy]
111. and/100,110 [Combined searches for antibiotic treatment and pregnancy]
112. cooperation/
113. *consumer attitude/
114. exp decision making/
115. health care survey/
116. informed consent/
117. exp interview/
118. exp patient attitude/
119. patient education/
120. exp questionnaire/
121. social psychology/
122. treatment refusal/
123. (15D* and (HRQoL or QoL or "quality of life")).mp.
124. ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or refus* or respons* or valuation or value? or valuing or view*) adj3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom#n)).tw,kw.
125. (choice? adj2 (behavio?r* or discrete or experiment*)).tw,kw.
126. ((choice? or choos* or consent* or decision*) adj1 informed).tw,kw.
127. ((choice? or choos* or decision*) adj2 (made or make or makes or making or shar* or support*)).tw,kw.
128. (EQ 5D or EQ5D or EuroQoL 5D or EuroQoL5D).mp.
129. (focus group? or interview* or questionnaire? or survey*).tw,kw.
130. gambl*.tw,kw.
131. health utilit*.tw,kw.
132. HUI.tw,kw.
133. (multi?attribute or multi?criteria).tw,kw.
134. (preference? adj1 (elicit* or scor* or state*)).tw,kw.
135. prospect theor*.tw,kw.
136. (SF 12 or SF 36 or SF 6D or SF12 or SF36 or SF6D).mp.
137. (trade off? or tradeoff?).tw,kw.
138. (willing* adj2 pay*).tw,kw.
139. or/112-138 [Combined Emtree & text words for patient preferences & values]
140. and/50,139 [Combined searches for patient preferences & ASB screening]
141. and/111,139 [Combined searches for patient preferences & antibiotic treatment and pregnancy]
142. or/140-141 [Combined sets of patient preferences for ASB screening & patient preferences for antibiotic treatment in pregnancy]
143. Male/ not (Female/ and Male/)
144. 142 not 143 [Male only records excluded]
145. animals/ not (animals/ and humans/)
146. 144 not 145 [Animal only records excluded]
147. (conference* or editorial or letter).pt.
148. 146 not 147 [Excluded publication types – RF note: will search conference proceedings separately with different strategy]

149. case report/ or case report*.ti.
150. 148 not 149 [Case reports excluded]
151. limit 150 to (english or french)
152. remove duplicates from 151

KQ2: Women's Outcome Valuation
Database: Wiley Cochrane Library
Date Searched: 5 July 2016
Date Updated: 5 September 2017
Records Retrieved: 45 in Cochrane Database of Systematic Reviews
Records Retrieved: 1 in Database of Abstracts of Reviews of Effects (DARE)
Records Retrieved: 321 in Cochrane Central Register of Controlled Trials (CENTRAL)
Records Retrieved: 4 in Cochrane Methodology Register
Records Retrieved: 14 in Economic Evaluations Database

#1 [mh ^"Asymptomatic Infections"] and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*):ti,ab,kw
#2 [mh ^Bacteriuria]
#3 [mh Cystitis]
#4 [mh ^Dysuria]
#5 [mh ^Pyelonephritis]
#6 [mh ^"Urinary Tract Infections"]
#7 bacilluria*:ti,ab,kw
#8 bacteriuria*:ti,ab,kw
#9 cystiti*:ti,ab,kw
#10 (cysto-pyeliti* or cystopyeliti*):ti,ab,kw
#11 dysuria*:ti,ab,kw
#12 (infection* near/2 (bladder* or genitourin* or kidney* or urin* or urogenita*)):ti,ab,kw
#13 (pyelo-cystiti* or pyelocystiti*):ti,ab,kw
#14 (pyelo-nephriti* or pyelonephriti*):ti,ab,kw
#15 (UTI or UTIs):ti,ab,kw
#16 {or #1-#15}
#17 [mh ^"Antibody-Coated Bacteria Test, Urinary"]
#18 [mh ^Bacteriuria [mj]/DI,PC,MI,UR]
#19 [mh Cystitis [mj]/DI,PC,MI,UR]
#20 [mh ^"Mass Screening"]
#21 [mh ^"Microbial Sensitivity Tests"]
#22 [mh ^Microscopy]
#23 [mh ^"Predictive Value of Tests"]
#24 [mh ^Pyelonephritis [mj]/DI,PC,MI,UR]
#25 [mh "Reagent Kits, Diagnostic"]
#26 [mh "Reagent Strips"]
#27 [mh ^"Sensitivity and Specificity"]
#28 [mh ^Urinalysis]
#29 [mh ^"Urinary Tract Infections" [mj]/DI,PC,MI,UR]
#30 ((accurac* or diagnostic) near/5 (algorithm* or test*)):ti,ab,kw

#31 "diagnostic accurac*":ti,ab,kw
#32 culture*:ti,ab,kw
#33 (detect* or predict* or screen*):ti,ab,kw
#34 ("dip slide*" or dipslide* or "dip stick*" or dipstick*):ti,ab,kw
#35 (micro-scopy or microscopy):ti,ab,kw
#36 (microb* near/2 test*):ti,ab,kw
#37 ((re-agent* or reagent) near/3 (strip* or test*)):ti,ab,kw
#38 "strip* test*":ti,ab,kw
#39 "urine test*":ti,ab,kw
#40 (urinalys* or "urine analys*"):ti,ab,kw
#41 uriscreen:ti,ab,kw
#42 {or #17-#41}
#43 #16 and #42
#44 [mh ^"Anti-Bacterial Agents"]
#45 [mh ^"Antibiotic Prophylaxis"]
#46 [mh ^"Anti-Infective Agents, Urinary"]
#47 [mh ^"Asymptomatic Infections"/DT,TH]
#48 [mh ^Bacteriuria [mj]/DT,TH]
#49 [mh ^"Drug Therapy, Combination"]
#50 [mh ^Norfloxacin]
#51 [mh Penicillins]
#52 [mh Sulfonamides]
#53 [mh ^"Urinary Tract Infections" [mj]/DT,TH]
#54 amoxicillin*:ti,ab,kw
#55 ampicillin*:ti,ab,kw
#56 ("anti-bacteria*" or antibacteria*):ti,ab,kw
#57 ("anti-biotic*" or antibiotic*):ti,ab,kw
#58 aztreonam*:ti,ab,kw
#59 cefadroxil*:ti,ab,kw
#60 cefepime*:ti,ab,kw
#61 ceftibuten*:ti,ab,kw
#62 ceftri?xone*:ti,ab,kw
#63 cefuroxime*:ti,ab,kw
#64 cephalexin*:ti,ab,kw
#65 cephalosporin*:ti,ab,kw
#66 cephradine*:ti,ab,kw
#67 clindamycin*:ti,ab,kw
#68 ("co-trimoxazole*" or cotrimoxazole*):ti,ab,kw
#69 cycloserine*:ti,ab,kw
#70 fosfomycin*:ti,ab,kw
#71 gentam?cin*:ti,ab,kw
#72 "nalidixic acid*":ti,ab,kw
#73 nitrofurantoin*:ti,ab,kw
#74 penicillin*:ti,ab,kw
#75 piperacillin*:ti,ab,kw
#76 pivampicillin*:ti,ab,kw
#77 pivmecillinam*:ti,ab,kw
#78 sulfadimethoxine*:ti,ab,kw

#79 sulfadiazine*:ti,ab,kw
#80 sulfamethizole*:ti,ab,kw
#81 sulfamethoxazole*:ti,ab,kw
#82 sulfamethoxypyridazine*:ti,ab,kw
#83 sulfonamide*:ti,ab,kw
#84 sulphadimidine*:ti,ab,kw
#85 sulphonamide*:ti,ab,kw
#86 tetracycline*:ti,ab,kw
#87 vancomycin*:ti,ab,kw
#88 {or #44-#87}
#89 [mh Pregnancy]
#90 [mh ^"Pregnancy Complications, Infectious"]
#91 [mh ^"Pregnant Women"]
#92 [mh ^"Prenatal Care"]
#93 [mh ^"Prenatal Diagnosis"]
#94 (antenatal* or "pre-natal*" or prenatal*):ti,ab,kw
#95 (expect* near/1 (female* or mother* or wom?n)):ti,ab,kw
#96 pregnan*:ti,ab,kw
#97 {or #89-#96}
#98 #88 and #97
#99 [mh ^"Choice Behavior"]
#100 [mh ^"Consumer Behavior" [mj]]
#101 [mh "Consumer Participation"]
#102 [mh ^"Cooperative Behavior"]
#103 [mh "Decision Making"]
#104 [mh ^"Focus Groups"]
#105 [mh ^"Health Care Surveys"]
#106 [mh "Informed Consent"]
#107 [mh ^"Interviews as Topic"]
#108 [mh ^"Patient Acceptance of Health Care"]
#109 [mh "Patient Education as Topic"]
#110 [mh ^"Patient Participation"]
#111 [mh ^"Patient Preference"]
#112 [mh ^"Social Values"]
#113 [mh ^"Surveys and Questionnaires"]
#114 [mh ^"Treatment Refusal"]
#115 (15D* and (HRQoL or QoL or "quality of life")):ti,ab,kw
#116 ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or refus* or respons* or valuation or value? or valuing or view*) near/3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom?n)):ti,ab,kw
#117 ((analys?s or valuation? or value? or valuing) near/3 (conjoint or contingent)):ti,ab,kw
#118 (choice? near/2 (behavio?r* or discrete or experiment*)):ti,ab,kw
#119 ((choice? or choos* or consent* or decision*) near/1 informed):ti,ab,kw
#120 ((choice? or choos* or decision*) near/2 (made or make or makes or making or shar* or support*)):ti,ab,kw
#121 ("EQ 5D" or EQ5D or "EuroQoL 5D" or EuroQoL5D):ti,ab,kw
#122 ("focus group?" or interview* or questionnaire? or survey*):ti,ab,kw

#123 gambl*:ti,ab,kw
#124 "health utilit*":ti,ab,kw
#125 HUI:ti,ab,kw
#126 ("multi-attribute" or "multi-criteria" or multiattribute or multicriteria):ti,ab,kw
#127 (preference? near/1 (elicit* or scor* or state*)):ti,ab,kw
#128 "prospect theor*":ti,ab,kw
#129 ("SF 12" or "SF 36" or "SF 6D" or SF12 or SF36 or SF6D):ti,ab,kw
#130 ("trade off?" or tradeoff?):ti,ab,kw
#131 (willing* near/2 pay*):ti,ab,kw
#132 {or #99-#131}
#133 #43 and #132
#134 #98 and #132
#135 #133 or #134

KQ2: Women's Outcome Valuation
Database: Ovid PsycINFO 1806 to June Week 5 2016
Date Searched: 5 July 2016
Date Updated: 5 September 2017
Records Retrieved: 113

1. Bacterial Disorders/ and (bladder* or genitourin* or kidney* or urin* or urogenita*).mp.
2. Infectious Disorders/ and (bladder* or genitourin* or kidney* or urin* or urogenita*).mp.
3. Urinary Function Disorders/ and infection*.mp.
4. Urogenital Disorders/ and infection*.mp.
5. bacilluria*.mp.
6. bacteriuria*.mp.
7. cystiti*.mp.
8. (cysto-pyeliti* or cystopyeliti*).mp.
9. dysuria*.mp.
10. (infection* adj2 (bladder* or genitourin* or kidney* or urin* or urogenita*)).mp.
11. (pyelo-cystiti* or pyelocystiti*).mp.
12. (pyelo-nephriti* or pyelonephriti*).mp.
13. (UTI or UTIs).mp.
14. or/1-13 [Combined subject headings & text words for bacteriuria]
15. Health Screening/
16. Screening/
17. Screening Tests/
18. Test Reliability/
19. exp Test Validity/
20. Urinalysis/
21. ((accurac* or diagnostic) adj5 (algorithm* or test*)).ti,ab.
22. diagnostic accurac*.ti,ab.
23. culture*.ti,ab.
24. (detect* or predict* or screen*).ti,ab.
25. (dip slide* or dipslide* or dip stick* or dipstick*).ti,ab.
26. (micro-scopy or microscopy).ti,ab.
27. (microb* adj2 test*).ti,ab.

28. ((re-agent* or reagent) adj3 (strip* or test*)).ti,ab.
29. strip* test*.ti,ab.
30. urine test*.ti,ab.
31. (urinalys* or urine analys*).ti,ab.
32. uriscreen.ti,ab.
33. or/15-32 [Combined subject headings & text words for screening]
34. and/14,33 [Combined searches for ASB and screening]
35. antibiotics/
36. penicillins/
37. amoxicillin*.mp.
38. ampicillin*.mp.
39. (anti-bacteria* or antibacteria*).mp.
40. (anti-biotic* or antibiotic*).mp.
41. aztreonam*.mp.
42. cefadroxil*.mp.
43. cefepime*.mp.
44. ceftibuten*.mp.
45. ceftri?xone*.mp.
46. cefuroxime*.mp.
47. cephalexin*.mp.
48. cephalosporin*.mp.
49. cephradine*.mp.
50. clindamycin*.mp.
51. (co-trimoxazole* or cotrimoxazole*).mp.
52. cycloserine*.mp.
53. fosfomycin*.mp.
54. gentam#cin*.mp.
55. nalidixic acid*.mp.
56. nitrofurantoin*.mp.
57. penicillin*.mp.
58. piperacillin*.mp.
59. pivampicillin*.mp.
60. pivmecillinam*.mp.
61. sulfadimethoxine*.mp.
62. sulfadiazine*.mp.
63. sulfamethizole*.mp.
64. sulfamethoxazole*.mp.
65. sulfamethoxypyridazine*.mp.
66. sulfonamide*.mp.
67. sulphadimidine*.mp.
68. sulphonamide*.mp.
69. tetracycline*.mp.
70. vancomycin*.mp.
71. or/35-70 [Combined subject headings & text words for antibiotic treatment]
72. adolescent pregnancy/
73. pregnancy/
74. prenatal care/
75. (antenatal* or pre-natal* or prenatal*).ti,ab.

76. (expect* adj (female? or mother? or wom#n)).ti,ab.
77. pregnan*.mp.
78. or/72-77 [Combined subject headings & text words for pregnancy]
79. and/71,78 [Combined searches for antibiotic treatment and pregnancy]
80. Choice Behavior/
81. Client Attitudes/
82. Client Participation/
83. Client Rights/
84. Cooperation/
85. Decision Making/
86. *Consumer Behavior/
87. Informed Consent/
88. Interviews/
89. Preferences/
90. Questionnaires/
91. Social Values/
92. Surveys/
93. Treatment Barriers/
94. Treatment Refusal/
95. (15D* and (HRQoL or QoL or "quality of life")).mp.
96. ((accept* or consider* or choice? or choos* or chose? or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective? or prefer* or respons* or valuation or value? or valuing or view*) adj3 (citizen? or client? or consumer? or female? or male? or men or patient? or public or stake?holder* or user? or wom#n)).ti,ab.
97. ((analys#s or valuation? or value? or valuing) adj3 (conjoint or contingent)).ti,ab.
98. (choice? adj2 (behavio?r* or discrete or experiment*)).mp.
99. ((choice? or choos* or consent* or decision*) adj1 informed).ti,ab.
100. ((choice? or choos* or decision*) adj2 (made or make or makes or making or shar* or support*)).ti,ab.
101. (EQ 5D or EQ5D or EuroQoL 5D or EuroQoL5D).mp.
102. (focus group? or interview* or questionnaire? or survey*).ti,ab.
103. gambl*.ti,ab.
104. health utilit*.ti,ab.
105. HUI.mp.
106. (multi?attribute or multi?criteria).mp.
107. (preference? adj1 (elicit* or scor* or state*)).mp.
108. prospect theor*.ti,ab.
109. (SF 12 or SF 36 or SF 6D or SF12 or SF36 or SF6D).mp.
110. (trade off? or tradeoff?).ti,ab.
111. (willing* adj2 pay*).ti,ab.
112. or/80-111 [Combined subject & text words for patient preferences & values]
113. and/34,112 [Combined searches for patient preferences & ASB screening]
114. and/79,112 [Combined searches for patient preferences & antibiotic treatment and pregnancy]
115. or/113-114 [Combined sets of patient preferences for ASB screening & patient preferences for antibiotic treatment in pregnancy]
116. (boy* or male* or men).ti.
117. 115 not 116 [Male records excluded]
118. (case report* or comment* or editorial or letter).ti.

119. 117 not 118 [Opinion pieces & case reports excluded]
120. limit 119 to (english or french)
121. remove duplicates from 120

KQ2: Women's Outcome Valuation
Database: CINAHL Plus with Full Text (1937 to the present) via EBSCOhost
Date Searched: 5 July 2016
Date Updated: 5 September 2017
Records Retrieved: 872

S1. (MH "Bacteriuria")
S2. (MH "Cystitis+")
S3. (MH "Dysuria")
S4. (MH "Pyelonephritis")
S5. (MH "Urinary Tract Infections")
S6. bacilluria*
S7. bacteriuria*
S8. cystiti*
S9. "cysto-pyeliti*" or cystopyeliti*
S10. dysuria*
S11. (infection* N2 (bladder* or genitourin* or kidney* or urin* or urogenita*))
S12. "pyelo-cystiti*" or pyelocystiti*
S13. "pyelo-nephriti*" or pyelonephriti*
S14. UTI or UTIs
S15. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16. (MM "Bacteriuria/DI/PC/MI/UR")
S17. (MM "Cystitis+/DI/MI/PC/UR")
S18. (MH "Fluorescent Antibody Technique")
S19. (MH "Health Screening")
S20. (MH "Microbial Culture and Sensitivity Tests")
S21. (MH "Microscopy")
S22. (MH "Predictive Value of Tests")
S23. (MM "Pyelonephritis/DI/PC/MI/UR")
S24. (MH "Reagent Kits, Diagnostic+")
S25. (MH "Sensitivity and Specificity")
S26. (MH "Urinalysis")
S27. (MM "Urinary Tract Infections/DI/PC/MI/UR")
S28. (accurac* or diagnostic) N5 (algorithm* or test*)
S29. "diagnostic accurac*"
S30. culture*
S31. detect* or predict* or screen*
S32. "dip slide*" or dipslide* or "dip stick*" or dipstick*
S33. "micro-scopy" or microscopy
S34. microb* N2 test*
S35. ("re-agent*" or reagent) N3 (strip* or test*)
S36. "strip* test*"
S37. "urine test*"

S38. urinalys* or "urine analys*"
S39. uriscreen
S40. S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S41. S15 AND S40 [Combined searches for ASB and screening]
S42. (MH "Antibiotic Prophylaxis")
S43. (MH "Antibiotics")
S44. (MH "Antibiotics, Combined")
S45. (MH "Antiinfective Agents, Urinary+")
S46. (MM "Bacteriuria/DT/TH")
S47. (MH "Penicillins")
S48. (MH "Sulfonamides")
S49. (MM "Urinary Tract Infections/DT/TH")
S50. amoxicillin*
S51. ampicillin*
S52. ("anti-bacteria*" or antibacteria*)
S53. ("anti-biotic*" or antibiotic*)
S54. aztreonam*
S55. cefadroxil*
S56. cefepime*
S57. ceftibuten*
S58. ceftri?xone*
S59. cefuroxime*
S60. cephalexin*
S61. cephalosporin*
S62. cephradine*
S63. clindamycin*
S64. ("co-trimoxazole*" or cotrimoxazole*)
S65. cycloserine*
S66. fosfomycin*
S67. gentam?cin*
S68. "nalidixic acid*"
S69. nitrofurantoin*
S70. penicillin*
S71. piperacillin*
S72. pivampicillin*
S73. pivmecillinam*
S74. sulfadimethoxine*
S75. sulfadiazine*
S76. sulfamethizole*
S77. sulfamethoxazole*
S78. sulfamethoxypyridazine*
S79. sulfonamide*
S80. sulphadimidine*
S81. sulphonamide*
S82. tetracycline*
S83. vancomycin*

S84. S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83
S85. (MH "Expectant Mothers")
S86. (MH "Pregnancy+")
S87. (MH "Pregnancy Complications, Infectious")
S88. (MH "Prenatal Care")
S89. (MH "Prenatal Diagnosis")
S90. antenatal* or "pre-natal*" or prenatal*
S91. expect* N1 (female? or mother? or wom?n)
S92. pregnan*
S93. S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92
S94. S84 AND S93
S95. (MH "Consumer Participation")
S96. (MH "Consensus")
S97. (MH "Consent+")
S98. (MH "Cooperative Behavior")
S99. (MH "Decision Making")
S100. (MH "Decision Making, Patient")
S101. (MH "Dissent and Disputes+")
S102. (MH "Focus Groups")
S103. (MH "Interviews+")
S104. (MH "Patient Education")
S105. (MH "Quality of Health Care")
S106. (MH "Questionnaires+")
S107. (MH "Self Report")
S108. (MH "Social Values+")
S109. (MH "Surveys")
S110. (MH "Treatment Refusal")
S111. (15D* and (HRQoL or QoL or "quality of life"))
S112. ((accept* or consider* or choice* or choos* or chose* or decid* or decis* or input* or involv* or opinion* or participat* or perceiv* or percepti* or perspective* or prefer* or refus* or respons* or valuation or value* or valuing or view*) N3 (citizen* or client* or consumer* or female* or male* or men or patient* or public or "stake-holder*" or stakeholder* or user* or wom?n))
S113. ((analys?s or valuation* or value* or valuing) N3 (conjoint or contingent))
S114. (choice* N2 (behavio* or discrete or experiment*))
S115. ((choice* or choos* or consent* or decision*) N1 informed)
S116. ((choice* or choos* or decision*) N2 (made or make or makes or making or shar* or support*))
S117. ("EQ 5D" or EQ5D or "EuroQoL 5D" or EuroQoL5D)
S118. ("focus group*" or interview* or questionnaire* or survey*)
S119. gambl*
S120. "health utilit*"
S121. HUI
S122. ("multi-attribute" or "multi-criteria" or multiattribute or multicriteria)
S123. (preference* N1 (elicit* or scor* or state*))
S124. "prospect theor*"
S125. ("SF 12" or "SF 36" or "SF 6D" or SF12 or SF36 or SF6D)

S126. ("trade off*" or tradeoff*)
S127. (willing* N2 pay*)
S128. S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127
S129. S41 AND S128
S130. S94 AND S128
S131. S129 OR S130
S132. MH "Male" NOT ((MH "Female") AND (MH "Male"))
S133. S131 NOT S132
S134. ((MH "Vertebrates+") NOT MH Human)
S135. S133 NOT S134
S136. Limiters - Publication Type: Anecdote, Case Study, Commentary, Editorial, Letter
S137. S135 NOT S136
S138. S135 NOT S136 Narrow by Language: - english [RF: No French records in results to include]

KQ2: Women's Outcome Valuation
Database: PubMed via NCBI Entrez (1946 to Present)
Date Searched: 5 July 2016
Records Retrieved: 65

((((((("asymptomatic infections"[mh] AND (("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields]) OR ("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields] OR "bacteriurias"[All Fields]) OR ("urinary bladder"[MeSH Terms] OR ("urinary"[All Fields] AND "bladder"[All Fields]) OR "urinary bladder"[All Fields] OR "bladder"[All Fields]) OR ("cystitis"[MeSH Terms] OR "cystitis"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields]) OR ("pyelocystitis"[MeSH Terms] OR "pyelocystitis"[All Fields]) OR ("pyelonephritis"[MeSH Terms] OR "pyelonephritis"[All Fields]) OR ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields] OR "urinary"[All Fields]) OR ("urine"[Subheading] OR "urine"[All Fields] OR "urine"[MeSH Terms]) OR UTI[all] OR ("urinary tract infections"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "urinary tract infections"[All Fields] OR "utis"[All Fields]))) OR "bacteriuria"[MeSH Terms:noexp] OR "cystitis"[MeSH Terms] OR "dysuria"[MeSH Terms:noexp] OR "pyelonephritis"[MeSH Terms:noexp] OR "Urinary Tract Infections"[mh:noexp] OR bacilluria[tiab] OR bacteriuria[tiab] OR bacteriurias[tiab] OR "bladder infection"[tiab] OR "bladder infections"[tiab] OR cystitis[tiab] OR cystopyelitis[tiab] OR dysuria[tiab] OR "genito-urinary infection"[tiab] OR "genitourinary infection"[tiab] OR "genito-urinary infections"[tiab] OR "genitourinary infections"[tiab] OR "kidney infection"[tiab] OR "kidney infections"[tiab] OR "pyelo-nephritis"[tiab] OR pyelocystitis[tiab] OR pyelonephritis[tiab] OR "urinary infection"[tiab] OR "urinary infections"[tiab] OR "urogenital infection"[tiab] OR "urogenital infections"[tiab] OR UTI[tiab] OR UTIs[tiab]) AND ("Antibody-Coated Bacteria Test, Urinary"[mh] OR "Bacteriuria/diagnosis"[Majr] OR "Bacteriuria/prevention and control"[Majr] OR ("bacteriuria/microbiology"[Mesh Terms] AND Majr[All Fields]) OR "Bacteriuria/urine"[Majr] OR "Cystitis/diagnosis"[Majr] OR "Cystitis/prevention and control"[Majr] OR "Cystitis/microbiology"[Majr] OR "Cystitis/urine"[Majr] OR "Mass Screening"[mh:noexp] OR "Microbial Sensitivity Tests"[mh:noexp] OR "Microscopy"[mh:noexp] OR "Predictive Value of Tests"[mh:noexp] OR "Pyelonephritis/diagnosis"[Majr] OR "Pyelonephritis/prevention and control"[Majr] OR "Pyelonephritis/microbiology"[Majr] OR "Pyelonephritis/urine"[Majr] OR "Reagent

Kits, Diagnostic"[mh:noexp] OR "Reagent Strips"[mh:noexp] OR "Sensitivity and Specificity"[mh:noexp] OR "Urinalysis"[mh:noexp] OR "Urinary Tract Infections/diagnosis"[Majr] OR "Urinary Tract Infections/prevention and control"[Majr] OR "Urinary Tract Infections/microbiology"[Majr] OR "Urinary Tract Infections/urine"[Majr] OR detect[tiab] OR detected[tiab] OR detection[tiab] OR detecting[tiab] OR detects[tiab] OR "diagnostic accuracy"[tiab] OR "diagnostic algorithm"[tiab] OR "dip slide"[tiab] OR "dip slides"[tiab] OR "dip stick"[tiab] OR "dip sticks"[tiab] OR dipslide[tiab] OR dipslides[tiab] OR dipstick[tiab] OR dipsticks[tiab] OR culture[tiab] OR cultures[tiab] OR "diagnostic test"[tiab] OR "diagnostic tests"[tiab] OR "microbial test"[tiab] OR "microbial tests"[tiab] OR microscopy[tiab] OR predict[tiab] OR predicted[tiab] OR prediction[tiab] OR predicting[tiab] OR predicts[tiab] OR "reagent strip"[tiab] OR "reagent strips"[tiab] OR "reagent test"[tiab] OR "reagent testing"[tiab] OR "reagent tests"[tiab] OR screen[tiab] OR screened[tiab] OR screening[tiab] OR screens[tiab] OR "strip test"[tiab] OR "strip tests"[tiab] OR "strip testing"[tiab] OR "test accuracy"[tiab] OR urinalyses[tiab] OR urinalysis[tiab] OR "urine analyses"[tiab] OR "urine analysis"[tiab] OR "urine test"[tiab] OR "urine tested"[tiab] OR "urine testing"[tiab] OR "urine tests"[tiab] OR uriscreen[tiab])) AND ("Choice Behavior"[mh:noexp] OR "Consumer Behavior"[majr:noexp] OR "Consumer Participation"[mh] OR "Cooperative Behavior"[mh:noexp] OR "Decision Making"[mh] OR "Focus Groups"[mh:noexp] OR "Health Care Surveys"[mh:noexp] OR "Informed Consent"[mh] OR "Interviews as Topic"[mh:noexp] OR "Patient Acceptance of Health Care"[mh:noexp] OR "Patient Education as Topic"[mh] OR "Patient Participation"[mh] OR "Patient Preference"[mh:noexp] OR "Social Values"[mh:noexp] OR "Surveys and Questionnaires"[mh:noexp] OR "Treatment Refusal"[mh:noexp] OR (15D[tiab] AND (HRQoL[tiab] OR QoL[tiab] OR "quality of life"[tiab])) OR ((accept[tiab] OR accepted[tiab] OR accepting[tiab] OR accepts[tiab] OR consider[tiab] OR consideration[tiab] OR considerations[tiab] OR considered[tiab] OR considering[tiab] OR considers[tiab] OR choice[tiab] OR choices[tiab] OR choose[tiab] OR chooses[tiab] OR choosing[tiab] OR chose[tiab] OR chosen[tiab] OR decide[tiab] OR decided[tiab] OR deciding[tiab] OR decides[tiab] OR decision[tiab] OR decisionmaker[tiab] OR decisionmaking[tiab] OR decisions[tiab] OR decisive[tiab] OR input[tiab] OR involve[tiab] OR involved[tiab] OR involving[tiab] OR involvement[tiab] OR involves[tiab] OR opinion[tiab] OR opinionated[tiab] OR opinions[tiab] OR participate[tiab] OR participated[tiab] OR participating[tiab] OR participation[tiab] OR participates[tiab] OR perceive[tiab] OR perceived[tiab] OR perceiving[tiab] OR perceives[tiab] OR perception[tiab] OR perceptions[tiab] OR perceptive[tiab] OR perspective[tiab] OR perspectives[tiab] OR prefer[tiab] OR preference[tiab] OR preferences[tiab] OR preferred[tiab] OR preferring[tiab] OR refusal[tiab] OR refuse[tiab] OR refused[tiab] OR refusing[tiab] OR refuses[tiab] OR response[tiab] OR responses[tiab] OR valuation[tiab] OR value[tiab] OR valued[tiab] OR values[tiab] OR valuing[tiab] OR view[tiab] OR viewed[tiab] OR viewing[tiab] OR viewpoint[tiab] OR viewpoints[tiab] OR views[tiab]) AND (citizen[tiab] OR citizens[tiab] OR client[tiab] OR clients[tiab] OR consumer[tiab] OR consumers[tiab] OR female[tiab] OR females[tiab] OR male[tiab] OR males[tiab] OR men[tiab] OR patient[tiab] OR patients[tiab] OR public[tiab] OR "stake-holder"[tiab] OR "stake-holders"[tiab] OR stakeholder[tiab] OR stakeholders[tiab] OR user[tiab] OR users[tiab] OR woman[tiab] OR women[tiab])) OR ((analyses[tiab] OR analysis[tiab] OR valuation[tiab] OR valuations[tiab] OR value[tiab] OR values[tiab] OR valuing[tiab]) AND (conjoint[tiab] OR contingent[tiab])) OR "choice behavior"[tiab] OR "choice behaviour"[tiab] OR "choice experiment"[tiab] OR "choice experiments"[tiab] OR "discrete choice"[tiab] OR "EQ 5D"[tiab] OR EQ5D[tiab] OR "EuroQoL 5D"[tiab] OR EuroQoL5D[tiab] OR "focus group"[tiab] OR "focus groups"[tiab] OR gamble[tiab] OR gambled[tiab] OR gambling[tiab] OR gambles[tiab] OR "health utilities"[tiab] OR "health utility"[tiab] OR HUI[tiab] OR "informed choice"[tiab] OR "informed choices"[tiab] OR "informed consent"[tiab] OR "informed decision"[tiab] OR interview[tiab] OR interviewed[tiab] OR interviewing[tiab] OR interviews[tiab] OR "multi-attribute"[tiab] OR "multi-criteria"[tiab] OR multiattribute[tiab] OR

multicriteria[tiab] OR "preference score"[tiab] OR "preference scores"[tiab] OR "preference scoring"[tiab] OR "prospect theory"[tiab] OR questionnaire[tiab] OR questionnaires[tiab] OR "SF 12"[tiab] OR "SF 36"[tiab] OR "SF 6D"[tiab] OR SF12[tiab] OR SF36[tiab] OR SF6D[tiab] OR "stated preference"[tiab] OR survey[tiab] OR surveyed[tiab] OR surveys[tiab] OR "trade off"[tiab] OR "trade offs"[tiab] OR tradeoff[tiab] OR tradeoffs[tiab] OR "willing to pay"[tiab] OR "willingness to pay"[tiab])) OR ((("Anti-Bacterial Agents"[mh:noexp] OR "Antibiotic Prophylaxis"[mh:noexp] OR "Anti-Infective Agents, Urinary"[mh] OR "Asymptomatic Infections/therapy"[mh] OR "Bacteriuria/drug therapy"[Majr] OR "Bacteriuria/therapy"[Majr] OR "Drug Therapy, Combination"[mh:noexp] OR "Norfloxacin"[mh:noexp] OR "Penicillins"[mh] OR "Sulfonamides"[mh] OR "Urinary Tract Infections/drug therapy"[Majr] OR "Urinary Tract Infections/therapy"[Majr] OR amoxicillin[tiab] OR amoxicillins[tiab] OR ampicillin[tiab] OR ampicillins[tiab] OR "anti-bacteria"[tiab] OR "anti-bacterial"[tiab] OR "anti-bacterials"[tiab] AND "anti-biotic"[tiab] OR "anti-biotics"[tiab] OR antibacteria[tiab] OR antibacterial[tiab] OR antibacterials[tiab] OR antibiotic[tiab] OR antibiotics[tiab] OR aztreonam[tiab] OR cefadroxil[tiab] OR cefepime[tiab] OR ceftibuten[tiab] OR ceftriaxone[tiab] OR cefuroxime[tiab] OR cephalexin[tiab] OR cephalosporin[tiab] OR cephalosporins[tiab] OR cephradine[tiab] OR clindamycin[tiab] OR "co-trimoxazole"[tiab] OR cotrimoxazole[tiab] OR cycloserine[tiab] OR cycloserines[tiab] OR fosfomycin[tiab] OR gentamicin[tiab] OR gentamycin[tiab] OR "nalidixic acid"[tiab] OR nitrofurantoin[tiab] OR penicillin[tiab] OR penicillins[tiab] OR piperacillin[tiab] OR pivampicillin[tiab] OR pivmecillinam[tiab] OR sulfadimethoxine[tiab] OR sulfadiazine[tiab] OR sulfamethizole[tiab] OR sulfamethoxazole[tiab] OR sulfamethoxypyridazine[tiab] OR sulfonamide[tiab] OR sulfonamides[tiab] OR sulphadimidine[tiab] OR sulphonamide[tiab] OR tetracycline[tiab] OR tetracyclines[tiab] OR vancomycin[tiab]) AND ("Pregnancy"[mh] OR "Pregnancy Complications, Infectious"[mh:noexp] OR "Pregnant Women"[mh:noexp] OR "Prenatal Care"[mh:noexp] OR "Prenatal Diagnosis"[mh:noexp] OR antenatal[tiab] OR "pre-natal"[tiab] OR prenatal[tiab] OR "expectant mother"[tiab] OR "expectant mothers"[tiab] OR "expecting mothers"[tiab] OR "expecting mothers"[tiab] OR "expectant woman"[tiab] OR "expectant women"[tiab] OR "expecting women"[tiab] OR pregnancies[tiab] OR pregnancy[tiab] OR pregnant[tiab])) AND ("Choice Behavior"[mh:noexp] OR "Consumer Behavior"[majr:noexp] OR "Consumer Participation"[mh] OR "Cooperative Behavior"[mh:noexp] OR "Decision Making"[mh] OR "Focus Groups"[mh:noexp] OR "Health Care Surveys"[mh:noexp] OR "Informed Consent"[mh] OR "Interviews as Topic"[mh:noexp] OR "Patient Acceptance of Health Care"[mh:noexp] OR "Patient Education as Topic"[mh] OR "Patient Participation"[mh] OR "Patient Preference"[mh:noexp] OR "Social Values"[mh:noexp] OR "Surveys and Questionnaires"[mh:noexp] OR "Treatment Refusal"[mh:noexp] OR (15D[tiab] AND (HRQoL[tiab] OR QoL[tiab] OR "quality of life"[tiab])) OR ((accept[tiab] OR accepted[tiab] OR accepting[tiab] OR accepts[tiab] OR consider[tiab] OR consideration[tiab] OR considerations[tiab] OR considered[tiab] OR considering[tiab] OR considers[tiab] OR choice[tiab] OR choices[tiab] OR choose[tiab] OR chooses[tiab] OR choosing[tiab] OR chose[tiab] OR chosen[tiab] OR decide[tiab] OR decided[tiab] OR deciding[tiab] OR decides[tiab] OR decision[tiab] OR decisionmaker[tiab] OR decisionmaking[tiab] OR decisions[tiab] OR decisive[tiab] OR input[tiab] OR involve[tiab] OR involved[tiab] OR involving[tiab] OR involvement[tiab] OR involves[tiab] OR opinion[tiab] OR opinionated[tiab] OR opinions[tiab] OR participate[tiab] OR participated[tiab] OR participating[tiab] OR participation[tiab] OR participates[tiab] OR perceive[tiab] OR perceived[tiab] OR perceiving[tiab] OR perceives[tiab] OR perception[tiab] OR perceptions[tiab] OR perceptive[tiab] OR perspective[tiab] OR perspectives[tiab] OR prefer[tiab] OR preference[tiab] OR preferences[tiab] OR preferred[tiab] OR preferring[tiab] OR refusal[tiab] OR refuse[tiab] OR refused[tiab] OR refusing[tiab] OR refuses[tiab] OR response[tiab] OR responses[tiab] OR valuation[tiab] OR value[tiab] OR valued[tiab] OR values[tiab] OR valuing[tiab] OR view[tiab] OR viewed[tiab] OR viewing[tiab] OR viewpoint[tiab] OR viewpoints[tiab] OR views[tiab])

AND (citizen[tiab] OR citizens[tiab] OR client[tiab] OR clients[tiab] OR consumer[tiab] OR consumers[tiab] OR female[tiab] OR females[tiab] OR male[tiab] OR males[tiab] OR men[tiab] OR patient[tiab] OR patients[tiab] OR public[tiab] OR "stake-holder"[tiab] OR "stake-holders"[tiab] OR stakeholder[tiab] OR stakeholders[tiab] OR user[tiab] OR users[tiab] OR woman[tiab] OR women[tiab])) OR ((analyses[tiab] OR analysis[tiab] OR valuation[tiab] OR valuations[tiab] OR value[tiab] OR values[tiab] OR valuing[tiab]) AND (conjoint[tiab] OR contingent[tiab])) OR "choice behavior"[tiab] OR "choice behaviour"[tiab] OR "choice experiment"[tiab] OR "choice experiments"[tiab] OR "discrete choice"[tiab] OR "EQ 5D"[tiab] OR EQ5D[tiab] OR "EuroQoL 5D"[tiab] OR EuroQoL5D[tiab] OR "focus group"[tiab] OR "focus groups"[tiab] OR gamble[tiab] OR gambled[tiab] OR gambling[tiab] OR gambles[tiab] OR "health utilities"[tiab] OR "health utility"[tiab] OR HUI[tiab] OR "informed choice"[tiab] OR "informed choices"[tiab] OR "informed consent"[tiab] OR "informed decision"[tiab] OR interview[tiab] OR interviewed[tiab] OR interviewing[tiab] OR interviews[tiab] OR "multi-attribute"[tiab] OR "multi-criteria"[tiab] OR multiattribute[tiab] OR multicriteria[tiab] OR "preference score"[tiab] OR "preference scores"[tiab] OR "preference scoring"[tiab] OR "prospect theory"[tiab] OR questionnaire[tiab] OR questionnaires[tiab] OR "SF 12"[tiab] OR "SF 36"[tiab] OR "SF 6D"[tiab] OR SF12[tiab] OR SF36[tiab] OR SF6D[tiab] OR "stated preference"[tiab] OR survey[tiab] OR surveyed[tiab] OR surveys[tiab] OR "trade off"[tiab] OR "trade offs"[tiab] OR tradeoff[tiab] OR tradeoffs[tiab] OR "willing to pay"[tiab] OR "willingness to pay"[tiab]))) NOT ("Male"[mh] NOT ("Female"[mh] AND "Male"[mh]))) NOT (((Animals[MESH] OR Animal Experimentation[MESH] OR "Models, Animal"[MESH] OR Vertebrates[MESH]) NOT (Humans[MESH] OR Human experimentation[MESH])) OR (((animals[tiab] OR animal model[tiab] OR rat[tiab] OR rats[tiab] OR mouse[tiab] OR mice[tiab] OR rabbit[tiab] OR rabbits[tiab] OR pig[tiab] OR pigs[tiab] OR porcine[tiab] OR swine[tiab] OR dog[tiab] OR dogs[tiab] OR hamster[tiab] OR hamsters[tiab] OR chicken[tiab] OR chickens[tiab] OR sheep[tiab]) AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])) NOT (human[ti] OR humans[ti] OR people[ti] OR children[ti] OR adults[ti] OR seniors[ti] OR patient[ti] OR patients[ti]))))) NOT (case reports[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR newspaper article[pt])) AND ((publisher[sb] NOT pubstatusnihms NOT pubstatuspmcsd NOT pmcbook) OR (pubstatusaheadofprint))
> limit to English or French

KQs4,5: Systematic Review & HTA Search
Database: PubMed via NCBI Entrez (1946 to Present)
Date Searched: 14 October 2016
Records Retrieved: 104

(((((("asymptomatic infections"[mh] AND (("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields]) OR ("bacteriuria"[MeSH Terms] OR "bacteriuria"[All Fields] OR "bacteriurias"[All Fields]) OR ("urinary bladder"[MeSH Terms] OR ("urinary"[All Fields] AND "bladder"[All Fields]) OR "urinary bladder"[All Fields] OR "bladder"[All Fields]) OR ("cystitis"[MeSH Terms] OR "cystitis"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields]) OR ("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields]) OR ("pyelocystitis"[MeSH Terms] OR "pyelocystitis"[All Fields]) OR ("pyelonephritis"[MeSH Terms] OR "pyelonephritis"[All Fields]) OR ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields] OR "urinary"[All Fields]) OR ("urine"[Subheading] OR "urine"[All Fields] OR "urine"[MeSH Terms]) OR UTI[all] OR ("urinary tract infections"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "urinary tract infections"[All Fields] OR "utis"[All Fields]))) OR "bacteriuria"[MeSH Terms:noexp] OR "cystitis"[MeSH Terms] OR "dysuria"[MeSH Terms:noexp] OR "pyelonephritis"[MeSH

Terms:noexp] OR "Urinary Tract Infections"[mh:noexp] OR bacilluria[tiab] OR bacteriuria[tiab] OR bacteriurias[tiab] OR "bladder infection"[tiab] OR "bladder infections"[tiab] OR cystitis[tiab] OR cystopyelitis[tiab] OR dysuria[tiab] OR "genito-urinary infection"[tiab] OR "genitourinary infection"[tiab] OR "genito-urinary infections"[tiab] OR "genitourinary infections"[tiab] OR "kidney infection"[tiab] OR "kidney infections"[tiab] OR "pyelo-nephritis"[tiab] OR pyelocystitis[tiab] OR pyelonephritis[tiab] OR "urinary infection"[tiab] OR "urinary infections"[tiab] OR "urogenital infection"[tiab] OR "urogenital infections"[tiab] OR UTI[tiab] OR UTIs[tiab]) AND (("Antibody-Coated Bacteria Test, Urinary"[mh] OR "Bacteriuria/diagnosis"[Majr] OR "Bacteriuria/prevention and control"[Majr] OR ("bacteriuria/microbiology"[Mesh Terms] AND Majr[All Fields]) OR "Bacteriuria/urine"[Majr] OR "Cystitis/diagnosis"[Majr] OR "Cystitis/prevention and control"[Majr] OR "Cystitis/microbiology"[Majr] OR "Cystitis/urine"[Majr] OR "Mass Screening"[mh:noexp] OR "Microbial Sensitivity Tests"[mh:noexp] OR "Microscopy"[mh:noexp] OR "Predictive Value of Tests"[mh:noexp] OR "Pyelonephritis/diagnosis"[Majr] OR "Pyelonephritis/prevention and control"[Majr] OR "Pyelonephritis/microbiology"[Majr] OR "Pyelonephritis/urine"[Majr] OR "Reagent Kits, Diagnostic"[mh:noexp] OR "Reagent Strips"[mh:noexp] OR "Sensitivity and Specificity"[mh:noexp] OR "Urinalysis"[mh:noexp] OR "Urinary Tract Infections/diagnosis"[Majr] OR "Urinary Tract Infections/prevention and control"[Majr] OR "Urinary Tract Infections/microbiology"[Majr] OR "Urinary Tract Infections/urine"[Majr] OR detect[tiab] OR detected[tiab] OR detection[tiab] OR detecting[tiab] OR detects[tiab] OR "diagnostic accuracy"[tiab] OR "diagnostic algorithm"[tiab] OR "dip slide"[tiab] OR "dip slides"[tiab] OR "dip stick"[tiab] OR "dip sticks"[tiab] OR dipslide[tiab] OR dipslides[tiab] OR dipstick[tiab] OR dipsticks[tiab] OR culture[tiab] OR cultures[tiab] OR "diagnostic test"[tiab] OR "diagnostic tests"[tiab] OR "microbial test"[tiab] OR "microbial tests"[tiab] OR microscopy[tiab] OR predict[tiab] OR predicted[tiab] OR prediction[tiab] OR predicting[tiab] OR predicts[tiab] OR "reagent strip"[tiab] OR "reagent strips"[tiab] OR "reagent test"[tiab] OR "reagent testing"[tiab] OR "reagent tests"[tiab] OR screen[tiab] OR screened[tiab] OR screening[tiab] OR screens[tiab] OR "strip test"[tiab] OR "strip tests"[tiab] OR "strip testing"[tiab] OR "test accuracy"[tiab] OR urinalyses[tiab] OR urinalysis[tiab] OR "urine analyses"[tiab] OR "urine analysis"[tiab] OR "urine test"[tiab] OR "urine tested"[tiab] OR "urine testing"[tiab] OR "urine tests"[tiab] OR uriscreen[tiab]) OR ("Anti-Bacterial Agents"[mh:noexp] OR "Antibiotic Prophylaxis"[mh:noexp] OR "Anti-Infective Agents, Urinary"[mh] OR "Asymptomatic Infections/therapy"[mh] OR "Bacteriuria/drug therapy"[Majr] OR "Bacteriuria/therapy"[Majr] OR "Drug Therapy, Combination"[mh:noexp] OR "Norfloxacin"[mh:noexp] OR "Penicillins"[mh] OR "Sulfonamides"[mh] OR "Urinary Tract Infections/drug therapy"[Majr] OR "Urinary Tract Infections/therapy"[Majr] OR amoxicillin[tiab] OR amoxicillins[tiab] OR ampicillin[tiab] OR ampicillins[tiab] OR "anti-bacteria"[tiab] OR "anti-bacterial"[tiab] OR "anti-bacterials"[tiab] AND "anti-biotic"[tiab] OR "anti-biotics"[tiab] OR antibacteria[tiab] OR antibacterial[tiab] OR antibacterials[tiab] OR antibiotic[tiab] OR antibiotics[tiab] OR aztreonam[tiab] OR cefadroxil[tiab] OR cefepime[tiab] OR ceftibuten[tiab] OR ceftriaxone[tiab] OR cefuroxime[tiab] OR cephalexin[tiab] OR cephalosporin[tiab] OR cephalosporins[tiab] OR cephradine[tiab] OR clindamycin[tiab] OR "co-trimoxazole"[tiab] OR cotrimoxazole[tiab] OR cycloserine[tiab] OR cycloserines[tiab] OR fosfomycin[tiab] OR gentamicin[tiab] OR gentamycin[tiab] OR "nalidixic acid"[tiab] OR nitrofurantoin[tiab] OR penicillin[tiab] OR penicillins[tiab] OR piperacillin[tiab] OR pivampicillin[tiab] OR pivmecillinam[tiab] OR sulfadimethoxine[tiab] OR sulfadiazine[tiab] OR sulfamethizole[tiab] OR sulfamethoxazole[tiab] OR sulfamethoxypyridazine[tiab] OR sulfonamide[tiab] OR sulfonamides[tiab] OR sulphadimidine[tiab] OR sulphonamide[tiab] OR tetracycline[tiab] OR tetracyclines[tiab] OR vancomycin[tiab]))) AND ("Pregnancy"[mh] OR "Pregnancy Complications, Infectious"[mh:noexp] OR "Pregnant Women"[mh:noexp] OR "Prenatal Care"[mh:noexp] OR "Prenatal Diagnosis"[mh:noexp] OR antenatal[tiab] OR "pre-natal"[tiab] OR prenatal[tiab] OR "expectant mother"[tiab] OR "expectant

mothers"[tiab] OR "expecting mothers"[tiab] OR "expecting mothers"[tiab] OR "expectant woman"[tiab] OR "expectant women"[tiab] OR "expecting women"[tiab] OR pregnancies[tiab] OR pregnancy[tiab] OR pregnant[tiab])) AND (systematic[sb] OR meta-analysis[pt] OR meta-analysis as topic[mh] OR meta-analysis[mh] OR meta analy*[tw] OR metanaly*[tw] OR metaanaly*[tw] OR met analy*[tw] OR integrative research[tiab] OR integrative review*[tiab] OR integrative overview*[tiab] OR research integration*[tiab] OR research overview*[tiab] OR collaborative review*[tiab] OR collaborative overview*[tiab] OR systematic review*[tiab] OR technology assessment*[tiab] OR technology overview*[tiab] OR "Technology Assessment, Biomedical"[mh] OR HTA[tiab] OR HTAs[tiab] OR comparative efficacy[tiab] OR comparative effectiveness[tiab] OR outcomes research[tiab] OR indirect comparison*[tiab] OR ((indirect treatment[tiab] OR mixed-treatment[tiab]) AND comparison*[tiab]) OR Embase*[tiab] OR Cinahl*[tiab] OR systematic overview*[tiab] OR methodological overview*[tiab] OR methodologic overview*[tiab] OR methodological review*[tiab] OR methodologic review*[tiab] OR quantitative review*[tiab] OR quantitative overview*[tiab] OR quantitative synthes*[tiab] OR pooled analy*[tiab] OR Cochrane[tiab] OR Medline[tiab] OR Pubmed[tiab] OR Medlars[tiab] OR handsearch*[tiab] OR hand search*[tiab] OR meta-regression*[tiab] OR metaregression*[tiab] OR data synthes*[tiab] OR data extraction[tiab] OR data abstraction*[tiab] OR mantel haenszel[tiab] OR peto[tiab] OR der-simonian[tiab] OR dersimonian[tiab] OR fixed effect*[tiab] OR "Cochrane Database Syst Rev"[Journal] OR "health technology assessment winchester, england"[Journal] OR "Evid Rep Technol Assess (Full Rep)"[Journal] OR "Evid Rep Technol Assess (Summ)"[Journal] OR "Int J Technol Assess Health Care"[Journal] OR "GMS Health Technol Assess"[Journal] OR "Health Technol Assess (Rockv)"[Journal] OR "Health Technol Assess Rep"[Journal])) NOT ("Male"[mh] NOT ("Female"[mh] AND "Male"[mh]))) NOT (((Animals[MESH] OR Animal Experimentation[MESH] OR "Models, Animal"[MESH] OR Vertebrates[MESH]) NOT (Humans[MESH] OR Human experimentation[MESH])) OR (((animals[tiab] OR animal model[tiab] OR rat[tiab] OR rats[tiab] OR mouse[tiab] OR mice[tiab] OR rabbit[tiab] OR rabbits[tiab] OR pig[tiab] OR pigs[tiab] OR porcine[tiab] OR swine[tiab] OR dog[tiab] OR dogs[tiab] OR hamster[tiab] OR hamsters[tiab] OR chicken[tiab] OR chickens[tiab] OR sheep[tiab]) AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])) NOT (human[ti] OR humans[ti] OR people[ti] OR children[ti] OR adults[ti] OR seniors[ti] OR patient[ti] OR patients[ti]))))) NOT (case reports[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR newspaper article[pt])

KQs4,5: Systematic Review & HTA Search

Database: Wiley Cochrane Library

Date Searched: 14 October 2016

Records Retrieved: 19 in Cochrane Database of Systematic Reviews

Records Retrieved: 4 in Database of Abstracts of Reviews of Effects (DARE)

Records Retrieved: 1 in Health Technology Assessment Database

Records Retrieved: 3 in Economic Evaluations Database

#1 [mh ^"Asymptomatic Infections"] and (bacteriuria* or bladder* or cystitis* or kidney* or pyelo-cystiti* or pyelocystiti* or pyelo-nephriti* or pyelonephriti* or urin* or UTI*):ti,ab,kw

#2 [mh ^Bacteriuria]

#3 [mh Cystitis]

#4 [mh ^Dysuria]

#5 [mh ^Pyelonephritis]

#6 [mh ^"Urinary Tract Infections"]

#7 bacilluria*:ti,ab,kw
#8 bacteriuria*:ti,ab,kw
#9 cystiti*:ti,ab,kw
#10 (cysto-pyeliti* or cystopyeliti*):ti,ab,kw
#11 dysuria*:ti,ab,kw
#12 (infection* near/2 (bladder* or genitourin* or kidney* or urin* or urogenita*)):ti,ab,kw
#13 (pyelo-cystiti* or pyelocystiti*):ti,ab,kw
#14 (pyelo-nephriti* or pyelonephriti*):ti,ab,kw
#15 (UTI or UTIs):ti,ab,kw
#16 {or #1-#15}
#17 [mh ^"Antibody-Coated Bacteria Test, Urinary"]
#18 [mh ^Bacteriuria [mj]/DI,PC,MI,UR]
#19 [mh Cystitis [mj]/DI,PC,MI,UR]
#20 [mh ^"Mass Screening"]
#21 [mh ^"Microbial Sensitivity Tests"]
#22 [mh ^Microscopy]
#23 [mh ^"Predictive Value of Tests"]
#24 [mh ^Pyelonephritis [mj]/DI,PC,MI,UR]
#25 [mh "Reagent Kits, Diagnostic"]
#26 [mh "Reagent Strips"]
#27 [mh ^"Sensitivity and Specificity"]
#28 [mh ^Urinalysis]
#29 [mh ^"Urinary Tract Infections" [mj]/DI,PC,MI,UR]
#30 ((accurac* or diagnostic) near/5 (algorithm* or test*)):ti,ab,kw
#31 "diagnostic accurac*":ti,ab,kw
#32 culture*:ti,ab,kw
#33 (detect* or predict* or screen*):ti,ab,kw
#34 ("dip slide*" or dipslide* or "dip stick*" or dipstick*):ti,ab,kw
#35 (micro-scopy or microscopy):ti,ab,kw
#36 (microb* near/2 test*):ti,ab,kw
#37 ((re-agent* or reagent) near/3 (strip* or test*)):ti,ab,kw
#38 "strip* test*":ti,ab,kw
#39 "urine test*":ti,ab,kw
#40 (urinalys* or "urine analys*"):ti,ab,kw
#41 uriscreen:ti,ab,kw
#42 {or #17-#41}
#43 [mh ^"Anti-Bacterial Agents"]
#44 [mh ^"Antibiotic Prophylaxis"]
#45 [mh ^"Anti-Infective Agents, Urinary"]
#46 [mh ^"Asymptomatic Infections"/DT,TH]
#47 [mh ^Bacteriuria [mj]/DT,TH]
#48 [mh ^"Drug Therapy, Combination"]
#49 [mh ^Norfloxacin]
#50 [mh Penicillins]
#51 [mh Sulfonamides]
#52 [mh ^"Urinary Tract Infections" [mj]/DT,TH]
#53 amoxicillin*:ti,ab,kw
#54 ampicillin*:ti,ab,kw

#55 ("anti-bacteria*" or antibacteria*):ti,ab,kw
#56 ("anti-biotic*" or antibiotic*):ti,ab,kw
#57 aztreonam*:ti,ab,kw
#58 cefadroxil*:ti,ab,kw
#59 cefepime*:ti,ab,kw
#60 ceftibuten*:ti,ab,kw
#61 ceftri?xone*:ti,ab,kw
#62 cefuroxime*:ti,ab,kw
#63 cephalexin*:ti,ab,kw
#64 cephalosporin*:ti,ab,kw
#65 cephradine*:ti,ab,kw
#66 clindamycin*:ti,ab,kw
#67 ("co-trimoxazole*" or cotrimoxazole*):ti,ab,kw
#68 cycloserine*:ti,ab,kw
#69 fosfomycin*:ti,ab,kw
#70 gentam?cin*:ti,ab,kw
#71 "nalidixic acid*":ti,ab,kw
#72 nitrofurantoin*:ti,ab,kw
#73 penicillin*:ti,ab,kw
#74 piperacillin*:ti,ab,kw
#75 pivampicillin*:ti,ab,kw
#76 pivmecillinam*:ti,ab,kw
#77 sulfadimethoxine*:ti,ab,kw
#78 sulfadiazine*:ti,ab,kw
#79 sulfamethizole*:ti,ab,kw
#80 sulfamethoxazole*:ti,ab,kw
#81 sulfamethoxypyridazine*:ti,ab,kw
#82 sulfonamide*:ti,ab,kw
#83 sulphadimidine*:ti,ab,kw
#84 sulphonamide*:ti,ab,kw
#85 tetracycline*:ti,ab,kw
#86 vancomycin*:ti,ab,kw
#87 {or #43-#86}
#88 #16 and (#42 or #87)
#89 [mh Pregnancy]
#90 [mh ^"Pregnancy Complications, Infectious"]
#91 [mh ^"Pregnant Women"]
#92 [mh ^"Prenatal Care"]
#93 [mh ^"Prenatal Diagnosis"]
#94 (antenatal* or "pre-natal*" or prenatal*):ti,ab,kw
#95 (expect* near/1 (female* or mother* or wom?n)):ti,ab,kw
#96 pregnan*:ti,ab,kw
#97 {or #89-#96}
#98 #88 and #97

Additional Search Sources
Database: ProQuest Dissertations & Theses Global (1861 to current)
Date Searched: 10 August 2016
Records Retrieved: 135

(((TI,AB(bacilluria* OR bacteriuria* OR cystiti* OR cystopyeliti* OR dysuria* OR (infection* NEAR/2 (bladder* OR genitourin* OR kidney* OR urin* OR urogenita*)) OR pyelocystiti* OR pyelonephriti* OR UTI OR UTIs) AND (su.Exact("prenatal care" OR "pregnancy") OR TI,AB(prenatal* OR (expect* NEAR/1 (female* OR mother* OR wom?n)) OR pregnan*)) AND ((su.Exact("urinalysis" OR "medical screening" OR "sensitivity analysis" OR "microscopy") OR TI,AB(((accurac* OR diagnostic) NEAR/5 (algorithm* OR test*)) OR "diagnostic accurac*" OR culture* OR detect* OR "dip slide*" OR dipslide* OR "dip stick*" OR dipstick* OR microscopy OR (microb* NEAR/2 test*) OR predict* OR ((re-agent* OR reagent*) NEAR/3 (strip* OR test*)) OR screen* OR "strip* test*" OR "urine test*" OR urinalys* OR "urine analys*" OR uriscreen)) OR (su.Exact("antibiotics") OR TI,AB(amoxicillin* OR ampicillin* OR anti-bacteria* OR antibacteria* OR anti-biotic* OR antibiotic* OR aztreonam* OR cefadroxil* OR cefepime* OR ceftibuten* OR ceftri*xone* OR cefuroxime* OR cephalexin* OR cephalosporin* OR cephradine* OR clindamycin* OR co-trimoxazole* OR cotrimoxazole* OR cycloserine* OR fosfomycin* OR gentam?cin* OR "nalidixic acid*" OR nitrofurantoin* OR penicillin* OR piperacillin* OR pivampicillin* OR pivmecillinam* OR sulfadimethoxine* OR sulfadiazine* OR sulfamethizole* OR sulfamethoxazole* OR sulfamethoxypyridazine* OR sulfonamide* sulphadimidine* OR sulphonamide* OR tetracycline* OR vancomycin*)))) OR ((su.Exact("prenatal care" OR "pregnancy") OR TI,AB(prenatal* OR (expect* NEAR/1 (female* OR mother* OR wom?n)) OR pregnan*)) AND (su.Exact("antibiotics") OR TI,AB(amoxicillin* OR ampicillin* OR anti-bacteria* OR antibacteria* OR anti-biotic* OR antibiotic* OR aztreonam* OR cefadroxil* OR cefepime* OR ceftibuten* OR ceftri*xone* OR cefuroxime* OR cephalexin* OR cephalosporin* OR cephradine* OR clindamycin* OR co-trimoxazole* OR cotrimoxazole* OR cycloserine* OR fosfomycin* OR gentam?cin* OR "nalidixic acid*" OR nitrofurantoin* OR penicillin* OR piperacillin* OR pivampicillin* OR pivmecillinam* OR sulfadimethoxine* OR sulfadiazine* OR sulfamethizole* OR sulfamethoxazole* OR sulfamethoxypyridazine* OR sulfonamide* sulphadimidine* OR sulphonamide* OR tetracycline* OR vancomycin*)))) NOT (su.Exact("laboratory animals") OR TI(animal OR animal-model* OR animals OR canine* OR cat OR cats OR dog OR dogs OR feline OR felines OR hamster OR hamsters OR mice OR monkey OR monkeys OR mouse OR pig OR piglet OR piglets OR pigs OR porcine OR primate* OR rabbit OR rabbits OR rat OR rats OR rodent OR rodents OR sheep OR swine OR swines))) AND la("ENG" OR "FRE")

Additional Search Sources
Registry: ClinicalTrials.gov
URL: https://clinicaltrials.gov/
Date Searched: 10 August 2016
Records Retrieved: 48

S1. Advanced search:
Search Terms: pregnancy OR pregnant OR prenatal
AND
Conditions: "Bacteriuria" OR "Cystitis" OR "Dysuria" OR "Urinary Tract Infections"
Limit to studies with female participants
Retrieved: 15

S2. Advanced search:
Search Terms: pregnancy OR pregnant OR prenatal
AND
Interventions: amoxicillin OR ampicillin OR antibiotic OR antibiotics OR "antibacterial agent" OR "antibacterial agents" OR antibacterials OR cephalosporin OR clindamycin OR cotrimoxazole OR fosfomycin OR nitrofurantoin OR penicillin OR sulphonamide OR tetracycline OR vancomycin
Retrieved: 162

S3. Advanced search:
Search Terms: pregnancy OR pregnant OR prenatal
AND
Condition: "Infections"
Interventions: "urine culture" OR "urine test" OR "urine tests" OR "urinary screening" OR urinalysis
Limit to studies with female participants
Retrieved: 4 [RF Note: Removed 4 duplicates in EndNote, and 133 pre-2014 records]

Additional Search Sources
Registry: World Health Organization's International Clinical Trial Registry Platform (ICTRP)
URL: http://apps.who.int/trialsearch/
Records Retrieved: 11

S1. Advanced search:
Title Search Terms: antenatal OR pregnancy OR pregnant OR prenatal
AND
Conditions: bacteriuria OR cystitis OR dysuria OR urinary tract infection OR urinary tract infections OR UTI OR UTIs
Recruitment status is: All
Date of registration is between: 01/01/2014 and 10/08/2016
Retrieved: 5

S2. Advanced search:
Title Search Terms: antenatal OR pregnancy OR pregnant OR prenatal
AND
Interventions: antibiotic OR antibiotics OR antibacterial agent OR antibacterial agents
Recruitment status is: All
Date of registration is between: 01/01/2014 and 10/08/2016
Retrieved: 6

S3. Advanced search:
Title Search Terms: antenatal OR pregnancy OR pregnant OR prenatal
AND
Interventions: urine culture OR urine test OR urine tests OR urine screening OR urinary screening OR urinalysis
Recruitment status is: All
Date of registration is between: 01/01/2014 and 10/08/2016
Retrieved: 0

Additional Search Sources
Database: University of York, Centre for Reviews and Dissemination – Health Technology Assessment (HTA) Database
Date Searched: 10 August 2016
Records Retrieved: 1

S1. Search HTA Database
Any field: bacteriuria
AND
Any field: antenatal OR pregnan* OR prenatal
Retrieved: 1

S2. Search HTA Database
Any field: urin*
AND
Any field: antenatal OR pregnan* OR prenatal
Retrieved: 14 (retained 0 ; 1 duplicate)

S3. Search HTA Database
Any field: antibiotic* OR antibacterial
AND
Any field: antenatal OR pregnan* OR prenatal
Retrieved: 10 (retained 0)

Additional Search Sources
Database: TRIP Database
URL: https://www.tripdatabase.com/
Date Searched: 11 August 2016
Records Retrieved: 9

S1. TRIP Search
Simple search field: bacteriuria* AND (antenatal OR pregnan* OR prenatal)
Retrieved: 84 results in All Secondary Evidence (retained 8)

S2. TRIP Search
Simple search field: ("urine test" OR "urine testing" OR "urine tests" OR "urine screening") AND (antenatal OR pregnan* OR prenatal) AND infect*
Retrieved: 131 results in All Secondary Evidence (retained 0 – 8 duplicates from search 1)

S3. TRIP Search
Simple search field: (antibiotic* OR antibacterial) AND (antenatal OR pregnan* OR prenatal) AND prefer*
Retrieved: 372 results in All Secondary Evidence (retained 1)

Additional Search Sources
Website: Health Quality Ontario Publications and OHTAC Recommendations
URL: http://www.hqontario.ca/Evidence-to-Improve-Care/Recommendations-and-Reports
Date Searched: 11 August 2016
Records Retrieved: 0

S1. Search box search: bacteriuria
Retrieved: 4 results (retained 0)

S2. Search box search: (antenatal OR pregnancy OR pregnant OR prenatal) AND (urinalysis OR urine)
Retrieved: 20 results (retained 0)

S3. Search box search: (antenatal OR pregnancy OR pregnant OR prenatal) AND (antibiotic OR antibiotics OR antibacterial)
Retrieved: 23 results (retained 0)

S4. Browsed recommendations documents from 2011- 2016 (retained 0)

S5. Browsed clinical handbooks for quality based procedures (retained 0)

S6. Browsed Choosing Wisely Canada (retained 0)

S7. Browsed Special Reports from 2005 – 2016 (retained 0)

Additional Search Sources
Website: L'Institut national d'excellence en santé et en services sociaux (INESSS)
URL: http://www.inesss.qc.ca
Date Searched: 11 August 2016
Records Retrieved: 0

S1. Search box search: bacteriuria
Retrieved: 0 results (retained 0)

S2. Search box search: (antenatal OR pregnancy OR pregnant OR prenatal) AND (urinalysis OR urine)
Retrieved: 2 results (retained 0)

S3. Search box search: (antenatal OR pregnancy OR pregnant OR prenatal) AND (antibiotic OR antibiotics OR antibacterial)
Retrieved: 6 results (retained 0)

S4. Browsed all publications
Retrieved: 240 (retained 0)

Additional Search Sources
Website: CADTH
URL: https://www.cadth.ca/

Date Searched: 11 August 2016
Records Retrieved: 0

S1. Search box search: bacteriuria
Retrieved: 17 results (retained 0)

S2. Search box search: antenatal OR pregnancy OR pregnant OR prenatal
Retrieved: 13 results (retained 0)

S3. Search box search: antibiotic OR antibiotics OR antibacterial
Retrieved: 25 results (retained 0)
S4. Search box search: urine test pregnancy
Retrieved 67 results (retained 0)

S5. Browsed laboratory test publications
Retrieved: 46 (retained 0)

S6. Browsed Kidney/Urologic publications
Retrieved: 90 (retained 0)

Supplement 3. Eligibility criteria for screening effectiveness, women's outcome valuation, and treatment effectiveness

Question	PICOTS	Study designs; Language
Benefits and harms of screening	**P:** Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria **I:** Any screening program, whereby there is an intent (i.e., clinical algorithm) for all pregnant women to receive a screening test with follow-up of screen-positive cases **C:** No screening program (but may include indicated testing and/or treatment upon development of symptoms), or a different screening test or algorithm **O*:** Maternal mortality (9), maternal sepsis (8), pyelonephritis (7), perinatal mortality ≥20 weeks' gestation (9), spontaneous abortion/pregnancy loss before 20 weeks' gestation (8), neonatal sepsis (8), preterm delivery <37 weeks' gestation (7), low birth weight <2500g (6), serious maternal and neonatal harms (7) **T:** Any timing **S:** Any primary care or clinical setting providing antenatal care to pregnant women	RCTs, CCTs, controlled observational designs (i.e., prospective and retrospective cohort, case-control, controlled before-after) English and French
Outcome valuation	**P:** Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria; will also accept asymptomatic women who are not pregnant if necessary **I:** Any screening program or test, and any antibiotic; will accept studies on treatment for any bacterial condition in pregnancy **C:** Not applicable **O:** Several possible outcomes (e.g., relative weight/utilities of benefits and harms; willingness to be screened based on relative value placed on benefits and harms of screening programs or treatment) **T:** Any timing **S:** Any primary care or clinical setting providing antenatal care to pregnant women	Qualitative, mixed methods, surveys/cross-sectional designs English and French
Benefits and harms of treatment	**P:** Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria **I:** Any antibiotic **C:** No treatment or placebo **O*:** Maternal mortality (9), maternal sepsis (8), pyelonephritis (7), perinatal mortality ≥20 weeks' gestation (9), spontaneous abortion/pregnancy loss before 20 weeks' gestation (8), neonatal sepsis (8), preterm delivery <37 weeks' gestation (7), low birth weight <2500g (6), serious maternal and neonatal harms (7)	RCTs (or systematic review(s)) English and French

	T: Any timing **S:** Any primary care or clinical setting providing antenatal care to pregnant women	

CCT: controlled clinical trial; g: grams: PICOTS: populations, interventions, comparators, outcomes, timing, and setting; RCT: randomized clinical trial

* Outcomes ratings included in brackets; these were rated as critical/important for decision-making by CTFPHC members and by women recruited for patient engagement

Supplement 4. Characteristics of included studies on screening effectiveness, outcome valuation, and treatment effectiveness

Characteristics of included studies on screening effectiveness

Gérard, Blazquez & Mounac, 1983	
Objective	To determine if a routine screening program for ASB can reduce the incidence of pyelonephritis and other adverse pregnancy outcomes, and if such a program would be economically feasible
Methods	Design: Non-concurrent cohort Inclusion criteria: All pregnant women followed at the Centre Hospitalier de Corbeil-Essonnes (prospective). Controls were all women who were not involved in the screening program (retrospective). Exclusion criteria: NR
Participants	Setting: Centre Hospitalier de Corbeil-Essonnes (a Hospital) Study period: January-October 1979 (and 10 previous months for the control group) Sample: n=370 pregnant women; n=170 in study group; n=200 in control group Mean age, y (SD): NR Risk factors: NR Length of follow-up: until delivery, and for 3-6 months after in those with ≥2 instances of ASB; loss to follow-up: n=0.
Interventions	Implementation of a routine screening and treatment program for ASB: 1) Screening of all women at 3, 5, 7 and 9 months of pregnancy, and treatment of those diagnosed with ASB 2) Controls only screened after presenting with clinical signs Urine testing characteristics: Urine collection: Midstream urine sample with cleansing of the vulva before micturition Urine testing: Microscopy, urine culture and Gram staining Criteria for positive test: $\geq 10^5$ CFU/mL Gestational age (weeks) at first prenatal visit: ~3 months for the treatment group; NR for the control group Number of prenatal visits: at least 4 (every 2 months) for the treatment group; NR for control group Treatment: Treatment based on antibiotic sensitivity and at the discretion of the prescribing physician
Outcomes	Acute pyelonephritis: Clinical signs (fever, lumbar pain, dysuria, pollakiuria (urinary frequency)) and positive urine culture of 10^5 CFU/mL Spontaneous abortion: ≤28 wks GA Preterm delivery: Delivery at <37 wks GA Birth weight: Reported means for ASB vs. non-ASB in study group; symptomatic + positive culture vs. asymptomatic in controls Perinatal mortality: “stillbirth” as either death in utero or during delivery, all ≥31 wks GA

	Adverse event(s): NR
Notes	Study is descriptive, no between-group associations tested

ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millilitre; GA: gestational age; n: number; NR: not reported; SD: standard deviation; wks: weeks; y: year

Gratacós et al., 1994	
Objective	To determine the incidence of pyelonephritis in pregnant women before and after the introduction of a screening program for ASB
Methods	Design: Non-concurrent cohort Inclusion criteria: Study group were women who were seen at the clinic at <25 wks GA who subsequently delivered January 1991-December 1992. Controls were women who were seen at the clinic at <25 wks GA and delivered January 1987-December 1990. Exclusion criteria: NR
Participants	Setting: An obstetrics clinic in Barcelona, Spain Study period: January 1987-December 1992 (study group: January 1991-December 1992; controls: January 1987-December 1990) Sample: n=4,917 pregnant women; n=1,652 in study group, n=3,265 in control group Mean age, y (SD): NR Risk factors: NR Length of follow-up: until delivery; loss to follow-up: n=10
Interventions	Implementation of a routine screening and treatment program for ASB: 1) Screening of all women <25 wks pregnant and treatment of those diagnosed with ASB 2) Controls: no routine screening Urine testing characteristics: Urine collection: Midstream morning urine sample. Women with positive culture returned within 1-2 wks for a second midstream urine culture, after stressing the importance of cleansing the vulva before micturition. Urine testing: Urine culture following the guidelines of the National Committee for Clinical Laboratory Standards Criteria for positive test: Two consecutive positive urine cultures (number of organisms NR) with growth of the same species Gestational age (wks), at first prenatal visit: <25 Number of prenatal visits: study group: NR; controls: NR Treatment: 7-day course of antibiotics based on antibiotic sensitivity testing, started 1-2 wks after the second culture. At 1-4 wks after treatment and at least once more before delivery, additional midstream urine samples were obtained. If repeat cultures were positive, antibacterial therapy was repeated until cultures were negative for ASB.
Outcomes	Pyelonephritis: fever, flank pain, tenderness in costovertebral angle, ≥1 positive culture

	Adverse event(s): NR
Notes	Also investigated prevalence of ASB and response to treatment in the study group, but this was not compared to the controls who did not receive routine screening

ASB: asymptomatic bacteriuria; n: number; ND: not defined; NR: not reported; SD: standard deviation; wks: weeks; y: year(s)

Rhode, 2007	
Objective	To determine if urinary tract infection, high blood pressure, and gestational diabetes mellitus are underdiagnosed when prenatal urine testing is done on a clinically indicated basis versus a routine basis
Methods	Design: Non-concurrent cohort Inclusion criteria: Routine screening group were all pregnant women who enrolled for care and delivered before August 15, 2002. Indicated screening group were all women who enrolled for care and delivered after August 15, 2002. Exclusion criteria: Women who were in the transitional urine screening group (enrollment prior to and delivery after August 15, 2002), who received both screening techniques (n=570)
Participants	Setting: Hospital-based nurse-midwifery practice, Aurora, Colorado; provides care to predominantly medically underserved and Hispanic women Study period: Charts of patients enrolled for care and delivered November 2000-March 2004 Sample: n= 1,952 pregnant women; n=933 in routine screening group; n=1019 in indicated screening group Mean age, y (SD): Routine screening= 24.4 (5.6); Indicated screening= 24.9 (5.1) Risk factors: Gestational diabetes: routine screening=81 (9.3%), indicated screening=42 (4.2%) Race (ethnicity): Hispanic; routine screening=669 (72.1%), indicated screening=783 (76.9%) Length of follow-up: until delivery or patient left the practice; loss to follow-up (n=112; 4.6%); total ineligible=459 (19%), due to: spontaneous abortion (n=58), transfer of care (n=218), transfer to high risk care (n=71)
Interventions	Routine urine screening (enrollment and delivery before August 15, 2002): first visit with chemical reagent strips, lab urinalysis and culture; subsequent visits with chemical reagent strips, culture or urinalysis as indicated[1] Indicated urine screening (enrollment on and delivery after August 15, 2002): first visit with chemical reagent strips, lab urinalysis and culture; subsequent visits with chemical reagent strip only if one of the criteria was present (risk factors for UTI, GDM). Follow-up of culture or lab urinalysis as indicated[1] Urine testing characteristics: Urine collection: midstream morning urine sample, first visit Urine testing: chemical reagent strip test, lab urinalysis and culture;

	Mean number of strip tests performed (SD): Routine screening= 7.8 (3.4), range 0-19; Indicated screening= 1.4 (1.3), range 0-16 Criteria for positive test: NR Gestational age (wks) at start of care (SD): Routine screening= 20.5 (9.4); Indicated screening= 20.3 (8.9) Number of prenatal visits: NR Treatment: NR
Outcomes	Pyelonephritis: ND; however, clearly differentiated from ASB, cystitis and undetermined UTI Preterm delivery: <37 wks GA[2] Adverse event(s): NR
Notes	Authors compared eligible participants to those who became ineligible during the study period. In the routine screening group, eligible and ineligible women differed in terms of marital status, race, payment source, # preterm deliveries, and # weeks gestation at start of care. In the indicated screening group, eligible and ineligible women differed in terms of race, # of abortions, and # weeks of gestation at start of care.

ASB: asymptomatic bacteriuria; n: number; ND: not defined; NR: not reported; SD: standard deviation; UTI: urinary tract infection; GDM: gestational diabetes mellitus; wks: weeks; y: year(s)

[1] lab urinalysis may be used instead of culture due to presence of blood in urine; culture typically done to confirm reagent strip, unless reagent strip was used to test for elevated blood pressure (information provided by study author)

[2] Criteria for outcomes were confirmed by study author(s)

Uncu, 2001	
Objective	To determine the incidence of asymptomatic bacteriuria during pregnancy and its relation to pregnancy complications
Methods	Design: Non-concurrent cohort Inclusion criteria: Screened group were pregnant women ≤32 wks GA seen at the antenatal outpatient clinic. Controls were women who delivered in clinic before study and were not screened for ASB; formed in retrospective manner from first day of study Exclusion criteria: Patients who were followed-up at clinic due to prior renal disease, positive for ASB or were taking antibiotics
Participants	Setting: Antenatal outpatient clinic, Uludag University Faculty of Medicine, Department of Obstetrics and Gynecology, Turkey Study period: June 1998-January 1999 Sample: Screened= 186; Controls= 186 Mean age, y (SD): Screened= 27.7 (5.1); Controls= 27.7 (4.6) Risk factors: Gestational diabetes mellitus: Screened=7 (3.8%); Controls= 5 (2.7%) Socioeconomic status: lower SES correlated with high prevalence of ASB* Length of follow-up: NR; loss to follow-up: NR

Interventions	Determine incidence of asymptomatic bacteriuria during pregnancy and relation to pregnancy complications: 1) Screening group: All pregnant women routinely screened at first visit with whole blood count, total urine analysis and urine culture. 2) Controls: Formed in a retrospective manner from the first day of the study with pregnant women who delivered in the clinic and who were not routinely screened. Urine testing characteristics: Urine collection: midstream morning urine sample, first visit Urine testing: whole blood count, total urine analysis, and urine culture Criteria for positive test: $>10^5$ CFU/mL of the same organism Gestational age (wks), at time of urine culture: beginning of pregnancy Number of prenatal visits: NR Treatment: n=23 [7-10 days of antibiotics based on sensitivity testing, Follow-up 7-days of antibiotics for recurrent ASB (n=5)]; ASB recurrence 5/23 (21.7%)
Outcomes	Pyelonephritis: ND Intrauterine death[2]: no fetal cardiac activity by USG, after 20 weeks' gestation Prematurity[2]: <37 wks of gestation Adverse event(s): NR Fetal abnormalities: ND
Notes	Total screened for ASB=270→ with urine cultures=247→ sufficient delivery records=186 (61 excluded)

*statistically significant; ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millitre; GA: gestational age; ND: not defined; NR: not reported; SD: standard deviation; SES: socioeconomic status; USG: ultrasonography; wks: weeks; y: year(s)

[2] Criteria for outcomes were confirmed by study author(s)

Characteristics of included studies on women's outcome valuation

Butters, 1990	
Objective	To determine the level of knowledge of the effects of commonly used drugs on a fetus
Methods	Design: Cross-sectional (self-completed questionnaire) Recruitment: Participants were recruited from postnatal wards of the hospitals on a weekly basis
Participants	Setting: Two maternity hospitals: one serves a white urban and semirural population, the other serves a wider population mix from rural to urban and includes ethnic minorities. Both are located in Glasgow, Scotland. Inclusion criteria: Postnatal women who were still in hospital after delivering. They had to be given the questionnaire in person (i.e. they were either in their bed or in the sitting room when the questionnaire was distributed). Exclusion criteria: Women who had vaginal delivery on the day of the study, women one or two days post-delivery by caesarean section, and women who were unable to read English. Study period: October 1, 1987 and March 31, 1988. Sample: n=514 Age range: 15 to 40 years; 66 (13%) between 15 and 20 years, 141 (27%) between 21 and 25 years, 176 (34%) between 26 and 30 years, and 127 (25%) aged over 30 years. Gestational age: NA Parity: First pregnancy (53%) Race/ethnicity: Multiple ethnicities, mainly Scottish. Education level: NR
Interventions	Anonymous short questionnaire with mostly tick boxes.
Outcomes	-254 (49%) said they would take an antibiotic prescribed by their doctor, 246 (48%) said they would not, and 14 (3%) did not respond. -The responses were similar for all ages and social class groups. -There was a strong relationship between the women that would avoid taking an analgesic (n=80, 74%)) and those that would avoid taking an antibiotic (187, 45%), p<0.0001.

NA: not applicable; NR: not reported

Kazemier, 2015	
Objective	To investigate the consequences of treated and untreated ASB in pregnancy

Methods	Design: Prospective cohort (screening vs. no screening) with embedded RCT (decision on entry into the study considered cross-sectional) Recruitment: Pregnant women attending antenatal clinics offering screening (not routinely available)
Participants	Setting: 8 hospitals and 5 ultrasound centres, the Netherlands Inclusion criteria: Pregnant women aged ≥18 years with a singleton pregnancy who were between 16 and 22 wks GA, tested positive for ASB, and did not have symptoms of UTI. Exclusion criteria: History of preterm delivery <34 wks GA, warning signs of imminent preterm delivery, fetal congenital malformations, antibiotic use within 2 weeks of screening, known glucose-6-phosphate dehydrogenase deficiency, hypersensitivity to nitrofurantoin, risk factors for complicated UTI (e.g., pre-gestational DM, use of immunosuppressive medication or functional or structural abnormalities of the urinary tract). Study period: October 11, 2011-August 22, 2014 Sample: n=248 Mean age (SE), years: treated=29 (0.74), placebo or untreated=31 (0.33) Median gestational age (wks + days at screening (IQR)): treated=20+2 (19+6 to 20+5), placebo or untreated=20+0 (19+3 to 20+3) Parity (% nulliparous): treated=50%, placebo or untreated=42% Ethnicity (non-white): treated n=3 (8%), placebo or untreated n=36 (17%) Low education (≤pre-vocational level): treated n=6 (15%), placebo or untreated n=21 (10%)
Interventions	Women who were positive for ASB were invited to participate in a treatment RCT. Reasons for declining participation were recorded.
Outcomes	Most women (155/163 positive for ASB, 94%) who did not want to participate made this choice because they did not want to receive antibiotics during pregnancy for an asymptomatic condition.

ASB: asymptomatic bacteriuria; DM: diabetes mellitus; GA: gestational age; NA: not applicable; NR: not reported; RCT: randomized controlled trial; SE: standard error; UTI: urinary tract infection; wks: weeks

Lupattelli, 2014	
Objective	To investigate the association between health literacy and perception of medication risk, beliefs about medications, use and non-adherence to prescribed pharmacotherapy during pregnancy.
Methods	Design: Cross-sectional internet-based questionnaire Recruitment: Banners announcing the study were placed on one to four websites per country and/or social networks commonly visited by pregnant women that had a high number of daily users.

Participants	Setting: Anonymous internet questionnaire with participants from 18 countries: Australia, Austria, Canada, Croatia, Finland, France, Iceland, Italy, The Netherlands, Norway, Poland, Russia, Serbia, Slovenia, Sweden, Switzerland, United Kingdom and United Sates as well as some South American countries. Inclusion criteria: Pregnant women at any stage of gestation. Exclusion criteria: Women who were not currently pregnant. Study period: October 1 2011 to February 29, 2012 Sample: n=4999 Mean age (SD): NR overall Gestational age in weeks, mean (SD): 22.4 (10.3) Race/ethnicity: Multinational
Interventions	Health literacy was measured using a self-assessment scale of 0 to 4 for three questions. Perceived risk of medications was measured using 13 agents on a scale of 0 to 10. Beliefs about medications were measured using a 5-point agreement scale for three questions. Participants were asked standardized questions about medication use for specific illnesses, non-adherence and over-the-counter medication use with free text entry.
Outcomes	-96.2% of participants felt penicillin antibiotics posed a teratogenic risk.

NR: not reported; SD: standard deviation

Mashayekhi, 2009	
Objective	To examine the awareness of pregnant women about the effects of drugs in pregnancy
Methods	Design: Cross sectional, questionnaire Recruitment: Women in the postnatal and prenatal wards were invited.
Participants	Setting: Pre and Post-natal wards of two maternity hospitals in Iran, one private and one public. Inclusion criteria: Antenatal and postnatal women. Exclusion criteria: Women who had a complicated labor. Study period: August 2006 and May 2007 Sample: n=400 Median age (SD or SE), range: 26 (4.90), 15 to 44 years Gestational age: NA Gravidity: None – 183 (45.8%), one – 118 (29.5%), two – 69 (17.3%), more than two – 30 (7.5%)

	Parity: None – 200 (50.0%), one – 127 (31.8%), two (54, 13.5%), more than two – 19 (4.8%) Race/ethnicity: Iranian Education level: High school or lower – 184 (46.0%), diploma – 147 (36.8%), University education – 69 (17.3%)
Interventions	Face-to-face questionnaire divided into three sections: demographic information, drug use before and during pregnancy including drug safety, source of information regarding drugs safety during pregnancy. Majority of response options were tick boxes.
Outcomes	-Specific antibiotics the women felt were safe: penicillin – 51 (12.8%), ampicillin – 36 (9.0%), amoxicillin – 66 (16.5%), metronidazole - 20 (5.0%), cephalosporin - 10 (2.5%), other antibiotics - 6 (1.5%). -For penicillin use none felt it was unsafe for the mother, 143 (35.8%) felt it was unsafe for the fetus, 40 (10.0%) felt it was unsafe for both. -For ampicillin use 4 (1.0%) felt it was unsafe for the mother, 145 (36.3%) felt it was unsafe for the fetus, 28 (7.0%) felt it was unsafe for both. -For amoxicillin use 5 (1.3%) felt it was unsafe for the mother, 147 (36.8%) felt it was unsafe for the fetus, 18 (4.5%) felt it was unsafe for both. -For metronidazole use none felt it was unsafe for the mother, 129 (32.3%) felt it was unsafe for the fetus, 21 (5.3%) felt it was unsafe for both. -For cephalosporin use none felt it was unsafe for the mother, 127 (31.8%) felt it was unsafe for the fetus, 18 (4.5%) felt it was unsafe for both. -For other antibiotic use none felt it was unsafe for the mother, 125 (31.3%) felt it was unsafe for the fetus, 28 (7.0%) felt it was unsafe for both.

NA: not applicable; SE: standard error; SD: standard deviation

Nordeng, 2010	
Objective	To evaluate the perception of risk of drugs during pregnancy and sources of drug exposure information most commonly used
Methods	Design: Retrospective web-based questionnaire Recruitment: Invitation to participate in the questionnaire was posted to four webpages commonly used by pregnant women and mothers.
Participants	Setting: Internet Inclusion criteria: Pregnant woman or a mother of a child less than 5 years old. Exclusion criteria: NR Study period: September 16, 2008 to October 25, 2008 Sample: n=1793; 866 (48.3%) pregnant, 927 (51.7%) mothers Mean age (median, range): 30, 17 to 45 years Gestational age: NR Parity: primiparous – 689 (38.4%), one or more previous children – 1104 (61.6%)

	Race/ethnicity: Norwegian Education level: Basic school level – 88 (4.9%), upper secondary education – 390 (21.8%), tertiary education (<4 years) – 810 (45.2%), tertiary education (>4 years) – 421 (23.5%), other education – 84 (4.7%)
Interventions	Questionnaire consisted of open-ended questions and numeric rating scales from 0 to 10 relating to teratogenic risk of 17 drugs, foods, chemicals and radiation.
Outcomes	-There was a significant difference in mean risk perception scores between non-users of the indicated drugs and users of 4.3 vs. 3.0 ($p<0.001$) with a ratio between non-users/users of 1.4.

NR: not reported

Sanz, 2001	
Objective	To assess the perception of the teratogenic risk of common medication by professionals and the public
Methods	Design: Cross-sectional Recruitment: Pregnant women attending a regular obstetric follow up in an out-patient clinic at a University hospital; non-pregnant women from an obstetric and gynecological out-patient clinic in the hospital and in a randomized manner from four different neighborhoods. Medical staff (general physicians, gynecologists and medical students were also recruited and interviewed, their data are not included here).
Participants	Setting: Outpatient clinic at a University hospital, home setting Inclusion criteria: Currently pregnant for the pregnant women group, not pregnant for the comparison group Exclusion criteria: NR Study period: NR Sample: n=81 pregnant women, n=63 non-pregnant women Median age: NR Gestational age: NR Gravidity: NR Parity: NR Race/ethnicity: Spanish Education level: NR
Interventions	A visual analogue scale with a 10 cm horizontal line with a short vertical line at each end, with a scale of 0 to 100%. Participants were asked to mark on the scale what they thought was the potential risk for fetal malformations and malformations in non-pregnant women given exposure to a particular drug.

Outcomes	-The mean value of the perceived teratogenic risk by non-pregnant women was higher than that perceived by pregnant women for erythromycin (55.6 vs. 38.7) and amoxicillin (49.3 vs. 40.4). -The median value of the perceived teratogenic risk by non-pregnant women was higher than that perceived by pregnant women for erythromycin (50.0 vs. 30.0) and amoxicillin (50.5 vs. 34.0). -The Mann-Whitney U test showed a significant difference between groups for erythromycin and amoxicillin, respectively ($p<0.05$ vs. $p<0.001$, non-pregnant vs. pregnant women). -In comparison to the "true" limits, risk from antibiotics was rated higher by pregnant women (erythromycin chi-square: 3.99, p=0.045; amoxicillin chi-square: 17.21, p=0.0001).

cm: centimeter(s); NR: not reported

Sharma, 2006	
Objective	To evaluate the drug utilization pattern in pregnant women and the effect of education and economic status.
Methods	Design: Retrospective cross-sectional study Recruitment: Medical students interviewed pregnant women visiting the antenatal clinic.
Participants	Setting: Antenatal clinic of a medical college in North India Inclusion criteria: Pregnant women Exclusion criteria: NR Study period: June 2005 to December 2005 Sample: n=405 Age range: Less than 20 years – 25 (6.17%), 20 to 35 years – 240 (59.26%), more than 35 years – 90 (22.22%) Gestational age: First trimester – 30 (7.40%), second trimester – 100 (24.69%), third trimester – 275 (67.90%) Gravidity: 243 primigravida; 152 multigravida Race/ethnicity: Indian Education level: Undergraduates – 220 (54.32%), graduates - 185 (45.68%)
Interventions	98 medical students trained in pharmacokinetic and pharmacodynamic changes in pregnancy completed a written questionnaire after interviewing each participant. The participants' statements were confirmed by their records if available.
Outcomes	-190 (46.91%) believed antibiotics should not be used in pregnancy while 25 (6.17%) felt they should be used.

NR: not reported

Twigg, 2016	
Objective	To describe beliefs and risk perception associated with medicines for treatment of common acute conditions.

Methods	Design: Cross-sectional internet-based questionnaire Recruitment: Advertisements announcing the study were placed on two commonly visited by pregnant women or new mothers
Participants	Setting: Anonymous internet questionnaire with participants from across the United Kingdom (England, Scotland, Wales and Northern Ireland). Inclusion criteria: Women who were pregnant or within one year of giving birth. Exclusion criteria: NR Study period: November 15, 2011 to January 15, 2012 Sample: n=1120 Mean age (SD): 30.5 (5.2) years Gestational age: 442 (39.5%) were currently pregnant Parity (95% CI): No previous children – 48.0% (45.1-50.9%) Race/ethnicity: NR Education level (95% CI): Less than high school – 0.6% (0.14-1.05), high school – 27.9% (25.3-30.5), more than high school – 52.1% (49.2 – 55.0), other – 19.3% (17.0-21.6).
Interventions	Health literacy was measured using a self-assessment scale of 0 to 4 for three questions. General beliefs about medicine were obtained using the validated Beliefs about Medicines Questionnaire (BMQ-General) with an additional four questions regarding the benefit of medications on a scale of 1 to 5.
Outcomes	-Women with a UTI using medication for treatment had lower mean risk perception scores relating to the overuse and harm of medication and a higher mean risk score relating to the benefits of medication compared to women with a UTI who did not undergo treatment with medication. Overuse [mean(SD)]: 11.5 (2.8) vs. 12.6 (2.7), p=0.006 Harm [mean(SD)]: 9.3 (2.7) vs. 10.4 (2.9), p=0.014 Benefit [mean(SD)]: 16.3 (2.2) vs. 14.9 (2.3), p<0.001
Notes	Sub-study of the Multinational Medication Use in Pregnancy Study which was reported by Lupattelli et al. and another paper from that study is included in this review.

CI: confidence interval; NR: not reported; SD: standard deviation; UK: United Kingdom; UTI: urinary tract infection

Characteristics of included studies on treatment effectiveness

Brumfitt, 1975	
Objective	To assess the impact of screening and treatment for ASB on maternal and fetal health
Methods	Design: RCT (randomization ND); placebo controlled Recruitment: Pregnant women attending one of three antenatal clinics for the first time Inclusion criteria: Pregnant women who were screened and found to be positive for 'significant bacteriuria' at their first antenatal visit and 7-10 days later Exclusion criteria: Home delivery, abortions, treatment before confirmation of bacteriuria and other complicating factors
Participants	Setting: Birmingham (1 clinic) and London (2 clinics), UK; urban Study period: NR; ~1967-1968 Sample: n=426; treated (n=235), placebo (n=179) Mean age (SD), years: Treated=26.5 (6.8); Placebo=26.2 (6.9) Risk factors: Ethnicity (Asian and West Indian): Treated n=49 (20.8%); Placebo n=35 (14.1%) Length of follow-up: until delivery and the postpartum period for perinatal mortality Loss to follow-up: NR; outcome of pyelonephritis reported only for a subset (n=173); n=413 for outcome of low birth weight.
Interventions	Screening characteristics: Timing: First antenatal visit Urine collection: Clean-catch urine sample Urine testing method: Urine culture Criteria for positive test: Two positive tests; women with one positive test were recalled for a second test 7-10 days later and 'detailed documentation'. Microbiological criteria NR. Treatment characteristics (Williams, 1968): Type of antibiotic and length of treatment: 2g sulphonamide in a single dose; additional courses of treatment for persistent bacteriuria Control group: Received placebo under 'double-blind conditions' Follow-up testing: Subset of treated women (n=87) retested after 1 and 2 courses of treatment (as applicable)
Outcomes	Benefits: Pyelonephritis: Presence of loin pain and tenderness together with a temperature of ≥100◦F and $>10^5$ CFU/mL (Condie, 1968) Low birth weight (reported as prematurity): ≤2500g Harms: NR
Notes	Study also included a non-bacteriuric control group. There are two preliminary reports associated with this study (Condie, 1968; Williams, 1968). Brumfitt, 1975 reported outcome of pyelonephritis for the placebo group only (55/179), comparison between groups only

	available for a subset of treatment group (Condie, 1968). No explanation for variation in number of participants across reports for this study, nor for the various outcomes.

ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millilitre; F: Fahrenheit; g: gram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; UK: United Kingdom

Elder, 1966	
Objective	To evaluate the effectiveness of sulfasymazine for the treatment of ASB in pregnant women
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women registering for prenatal care Inclusion criteria: Pregnant women ≤32 wks GA with bacteriuria at registration confirmed in two additional samples Exclusion criteria: >32 wks GA, included in other bacteriuria studies, given treatment in error, moved away
Participants	Setting: Boston City Hospital, Boston, US; urban Study period: June 9, 1965-March 9, 1966 Sample: n=106; treated (n=54); placebo (n=52) Mean age (SD): NR Risk factors: NR Length of follow-up: Until delivery Loss to follow-up: 5 (5%) lost; 2(4%) treated patients left the community, 3 (6%) placebo-treated patients dropped out of the study
Interventions	Screening characteristics: Timing: At registration for prenatal care Urine collection: Clean-voided urine sample Urine testing method: Urine culture Criteria for a positive test: Three uncontaminated urine specimens containing the same species of bacteria with ≥10^4 CFU/mL in one and ≥10^5 CFU/mL in the other two. Treatment characteristics Type of antibiotic and length of treatment: 0.5g sulfasymazine once daily until delivery; if there was evidence of persistent bacteriuria, another treatment was given according to clinical judgment (usually nitrofurantoin) Control group: Received placebo Follow-up testing: Retested after one week of treatment, and at each clinic visit (at least weekly for the first 3 wks, then at least biweekly until 36 wks GA, then weekly until delivery)
Outcomes	Benefits: NR Harms: NR

Notes	There are no relevant results reported in this study. Study also included non-bacteriuric control patients. 7/52 (13%) of women in the placebo group developed 'asymptomatic pyelonephritis', but not information provided for the treated group.

ASB: asymptomatic bacteriuria; CFU/mL: colony-forming units per millilitre; g: gram(s); GA: gestational age; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; US: United States; wks: weeks

Elder, 1971	
Objective	To assess the effect of treatment of ASB on pregnancy outcomes
Methods	Design: Quasi-RCT; placebo-controlled Recruitment: Patients registering for prenatal care Inclusion criteria: Pregnant women ≤32 wks GA, with confirmed bacteriuria at the first prenatal visit Exclusion criteria: Treated for UTI during the current pregnancy and before the first obstetric appointment, >32 wks GA, delivered or had aborted before the first obstetric visit, went elsewhere for prenatal care, delivered twins
Participants	Setting: Boston City Hospital, Boston, US; urban Study period: January 28, 1963-July 2, 1965 Sample: n=281; treated (n=133), placebo (n=148) Mean age (SE), years: Treated=24.8 (0.60); Placebo=25.3 (0.46) Risk factors: Ethnicity (non-white): Treated=66.2%; Placebo=54.7% Previous UTI: Treated=35.9%; Placebo=40.1% Length of follow-up: Until delivery, and postpartum (time frame ND) for complications Loss to follow-up: Of original n=289, 8 (3%) were excluded because they moved away. No loss to follow-up for pyelonephritis; 3 (1%) patients in the placebo group lost for low birthweight because they were treated for reasons other than UTI; 8 (3%) lost for perinatal mortality, 11 (4%) for neonatal sepsis, and 16 (6%) fetal abnormalities and hemolytic anemia, reasons NR.
Interventions	Screening characteristics: Timing: Upon registration at the clinic Urine collection: Clean-voided urine sample Urine testing method: Urine culture Criteria for a positive test: Three samples (two at registration and one at the first obstetric visit); colony count from 2 of 3 specimens $\geq 10^5$ CFU/mL and no specimens with $<10^4$ CFU/mL, with the same species predominating in all 3 specimens Treatment characteristics: Type of antibiotic and length of treatment: 250mg tetracycline, 4 times daily for 6 wks; if infection did not clear in 2 wks, another antibiotic (usually nitrofurantoin) was given until it cleared Control group: Given identically appearing placebo to be taken similarly

	Follow-up testing: Retested at each clinic visit until delivery (includes recurrence and excludes those who became symptomatic); colony count $<10^3$ CFU/mL on two successive cultures considered cleared
Outcomes	Benefits: Pyelonephritis: Temperature of ≥100◦F with signs and symptoms localized to the urinary tract and not otherwise explained Perinatal mortality: Stillbirth or neonatal death prior to hospital discharge Respiratory distress: Respiratory distress syndrome and other causes of 'respiratory embarrassment' Low birth weight (defined as prematurity): ≤2500g Harms: Serious adverse events: Congenital malformations of bone, genitourinary system, other; hemolytic anemia (erythroblastosis fetalis)
Notes	Study also included a non-bacteriuric control group. Some patients may have participated more than once if they had more than one pregnancy during the study period (treatment assigned by alternation regardless of assignment for previous pregnancy). Outcomes of low birth weight, fetal abnormalities and hemolytic anemia reported for live births only. 4 bacteriuric women delivered twins and are not included.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; ◦F: degrees Fahrenheit; g: gram(s); GA: gestational age; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SE: standard error; US: United States; UTI: urinary tract infection; wks: weeks

Foley, 1987	
Objective	Test of treatment vs. non-treatment of ASB for the prevention of symptomatic UTI in pregnancy
Methods	Design: RCT Recruitment: Pregnant women attending an antenatal clinic for the first time Inclusion criteria: Pregnant women with bacteriuria at the first prenatal visit Exclusion criteria: NR
Participants	Setting: National Maternity Hospital, Dublin, Ireland; urban Study period: 1985 Sample: n=220; treated (n=100); not treated (n=120) Mean age (SD), years: NR Risk factors: Previous history of UTI: 42% of bacteriuric patients (distribution among groups NR) Length of follow-up: Until delivery (patients interviewed post-delivery) Loss to follow-up: Reported follow-up rate of 81%, unclear if these were from treatment or control groups (total n used in analysis).
Interventions	Screening characteristics: Timing: First antenatal visit

	Urine collection: Midstream urine sample Urine testing method: NR Criteria for a positive test: One urine sample with >10^5 CFU/mL Treatment characteristics: Type of antibiotic and length of treatment: 300mg sulphamethizole or 150mg nitrofurantoin daily for 3 days, on the basis of sensitivity testing; further treatment, including maintenance treatment, provided if needed to render urine sterile Control group: Received no treatment Follow-up testing: Retested 'at follow-up'; not further defined
Outcomes	Benefits: Pyelonephritis: ND; 'admitted with pyelonephritis' Harms: NR
Notes	Reported as a letter to the editor, not a full publication.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; mg: milligram(s); ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; UTI: urinary tract infection

Furness, 1975	
Objective	To examine the effectiveness of urinary antiseptics in preventing pyelonephritis and adverse among pregnant women with ASB
Methods	Design: RCT Recruitment: Pregnant women attending their initial prenatal visit Inclusion criteria: Pregnant women with 'significant' bacteriuria at the second prenatal visit Exclusion criteria: NR
Participants	Setting: Queen Victoria Hospital, Adelaide, Australia; urban Study period: NR Sample: n=206; treated (n=139); not treated (n=67) Mean age (SD), years: NR Risk factors: NR Length of follow-up: Until 6 wks postpartum Loss to follow-up: None reported
Interventions	Screening characteristics: Timing: At the second antenatal visit Urine collection: Midstream urine sample Urine testing method: Dipslide Criteria for a positive test: One specimen with >10^5 CFU/mL or two specimens each with 10^4 to 10^5 CFU/mL Treatment characteristics

	Type of antibiotic and length of treatment: 1g methenamine mandelate 4 times daily or 1g methenamine hippurate twice daily until delivery; if pyelonephritis developed the patient was treated with the appropriate antibiotic and no further antiseptics were given Control group: Received no treatment Follow-up testing: A postnatal urine specimen was obtained at the 6-week postnatal visit from women who did not develop clinical pyelonephritis during pregnancy or the puerperium
Outcomes	Benefits: Pyelonephritis: Frequency and burning on micturition accompanied by pyrexia or loin tenderness, with presence of a significant number of bacteria in urine Spontaneous abortion: ND; 'abortions' Preterm delivery: <38 wks GA Harms: Serious adverse events: Major fetal abnormality (anencephaly)
Notes	The treatment group received one of two antiseptics, the two groups were combined for reporting of outcomes. Outcome of pyelonephritis includes both during pregnancy and the puerperium. Three intrauterine deaths reported but it is unclear which group the patients belonged to. GA at delivery reported for 118 treated and 52 placebo untreated patients with no explanation given, total n used as denominator in analysis.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; wks: weeks

Gold, 1966	
Objective	To determine whether chemotherapy for ASB, continued throughout the rest of the prenatal period, reduces the incidence of prematurity
Methods	Design: Quasi-RCT; placebo-controlled Recruitment: Pregnant women registering at a prenatal clinic Inclusion criteria: Pregnant women with two consecutive positive tests for bacteriuria at any prenatal visit Exclusion criteria: Failed to return to the clinic, aborted, delivered at other hospitals, found to not be pregnant, ectopic pregnancy, transferred to other care, delivered by a private physician
Participants	Setting: Prenatal clinic at a hospital in New York, NY, US; urban Study period: February 2, 1962-December 21, 1964 Sample: n=65; treated (n=35); placebo (n=30) Mean age (SD), years: NR Risk factors: Ethnicity: 85% non-white, 6% Puerto-Rican, 9% other white (distribution among groups NR) Length of follow-up: Until the 'postpartum period' (exact time NR) Loss to follow-up: None reported

Interventions	Screening characteristics: Timing: First prenatal visit and each visit thereafter Urine collection: Clean-voided midstream urine sample Urine testing method: Urine culture Criteria for a positive test: Two consecutive laboratory reports with $>10^5$ CFU/mL of the same species Treatment characteristics: Type of antibiotic and length of treatment: 0.5g sulfadimethoxine once per day until 36 wks GA, 1g sulfadiazine 3 times daily thereafter until delivery Control group: Received placebo tablets taken in the same manner Follow-up testing: Each patient had repeat tests at each antenatal visit until delivery (either for diagnosis or persistent bacteriuria); data presented for persistent bacteriuria at delivery.
Outcomes	Benefits: Pyelonephritis: ND Harms: NR
Notes	Also reported delivery data for non-bacteriuric patients. Only antepartum pyelonephritis included in the analysis (postpartum excluded). 'Preterm delivery' reported for 2/35 treated and 0/30 placebo patients, but this is not further defined.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; n: number; ND: not defined; NR: not reported; NY: New York; RCT: randomized controlled trial; SD: standard deviation; US: United States; wks: weeks

Kass, 1960	
Objective	To assess the effect of early detection and eradication of bacteriuria on excessive morbidity in pregnant women
Methods	Design: Quasi-RCT; placebo controlled Recruitment: Pregnant women ≤32 wks GA registering for a prenatal clinic Inclusion criteria: Pregnant women with bacteriuria at the first prenatal visit and confirmed on two repeat cultures Exclusion criteria: >32 wks GA, chronic renal insufficiency, given treatment in error, did not have further prenatal care, records were inadequate or unobtainable, urine samples were contaminated, unable to void, found to not be pregnant
Participants	Setting: Boston City Hospital, Boston, US; urban Study period: October 1956-April 1960 Sample: n=214 (n=11 recruited via renal clinic); treatment (n=93); placebo (n=98) Mean age (SD), years: NR; similar distribution between treated and placebo groups Risk factors: Ethnicity (black): Treated (~50%); placebo (slightly <50%) History of UTI: ~15% (distribution by group NR) Diabetes: n=2 (distribution by group NR)

	Uterine abnormalities: reported for n=2 bacteriuric women with cesarean section; prevalence in rest of population NR Length of follow-up: Until the post-delivery period and up to 12 months postpartum; records reviewed 3-4 years later Loss to follow-up: n=23 (11%) lost; 13 (12%) in the treatment group (7 not seen in last 4 wks before delivery, 5 delivered out of state, 1 incorrectly assigned), 10 (9%) in the placebo group (8 cleared spontaneously or false positive, 2 lost)
Interventions	Screening characteristics: Timing: At the time of registration for the clinic Urine collection: Clean-voided urine sample Urine testing method: Urine culture Criteria for a positive test: 10^3-10^5 CFU/mL at registration, then two additional cultures with >10^5 CFU/mL of the same species Treatment characteristics: Type of antibiotic and length of treatment: 0.5g sulfamethoxypyridazine daily until delivery; if infection did not clear in one week, the patient was given 100mg nitrofurantoin 3 times daily until delivery Control group: Received a placebo tablet supplied by the same manufacturer Follow-up testing: Treated patients were retested within the 4 wks preceding delivery. Data for 3-12 months postpartum bacteriuria presented for a subset of women (n=91) (Kass, 1960).
Outcomes	Benefits: Pyelonephritis: dysuria, frequency, and flank pain or other localizing evidence of inflammation, with either documented temperature of 100◦F or above or a history of chills and fever. When patients were seen outside the clinic (e.g., accident floor or emergency department), it was not always clear that patients were indeed febrile. Perinatal mortality: ND; 'perinatal death' and fetal loss >20 wks GA Low birth weight (defined as prematurity): <2500g Harms: NR
Notes	Kass, 1960 is a preliminary report, updated and more complete data retrieved from Savage, 1967 are presented. The study also includes a group of non-bacteriuric women. Some patients participated for >1 pregnancy, and were reassigned to the same treatment they received in the first pregnancy. Outcome of pyelonephritis reported only for the antenatal period, postpartum excluded. Outcome of low birth weight given for the total number of deliveries (3 twin deliveries in the placebo group and none in the treated group).

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; F: Fahrenheit; g: gram(s); GA: gestational age; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; US: United States; UTI urinary tract infection; wks: weeks

Kazemier, 2015	
Objective	To investigate the consequences of treated and untreated ASB in pregnancy
Methods	Design: Prospective cohort (screening vs. no screening) with embedded RCT Recruitment: Pregnant women attending antenatal clinics offering screening (not routinely available)

	Inclusion criteria: Pregnant women aged ≥18 years with a singleton pregnancy who were between 16 and 22 wks GA, tested positive for ASB, and did not have symptoms of UTI Exclusion criteria: History of preterm delivery <34 wks, warning signs of imminent preterm delivery, fetal congenital malformations, antibiotic use within 2 wks of screening, known glucose-6-phosphate dehydrogenase deficiency, hypersensitivity to nitrofurantoin, risk factors for complicated UTI (e.g., pre-gestational DM, use of immunosuppressive medication or functional or structural abnormalities of the urinary tract)
Participants	Setting: 8 hospitals and 5 ultrasound centres, the Netherlands Study period: October 11, 2011-August 22, 2014 Sample: n=248; treated (n=40); placebo (n=45), untreated (n=163) Mean age (SE), years: treated=29 (0.74), placebo or untreated=31 (0.33) Risk factors: Ethnicity (non-white): treated n=3 (8%), placebo or untreated n=36 (17%) Low education (≤pre-vocational level): treated n=6 (15%), placebo or untreated n=21 (10%) Length of follow-up: Until 6 wks postpartum Loss to follow-up: n=12 (5%) lost, all from the untreated or placebo group; 5 women could not be contacted for outcomes because of errors in their contact information. Missing data were imputed (see notes).
Interventions	Screening characteristics: Timing, median (IQR) wks + days GA: treated=20+2 (19+6 to 20+5), placebo or untreated=20+0 (19+3 to 20+3) Urine collection: Midstream urine sample Urine testing method: Dipslide Criteria for a positive test: $\geq 10^5$ CFU/mL of a single microorganism or when two different colony types were present but one had a concentration of $\geq 10^5$ CFU/mL Treatment characteristics: Type of antibiotic and length of treatment: 100mg nitrofurantoin twice daily for 5 days, based on sensitivity testing; if bacteriuria did not clear the treatment was repeated for a maximum of two rounds Control group: Received identical placebo capsules on the same dose and schedule as treated patients, or no treatment Follow-up testing: All participants provided a follow-up dipslide 1 week after the end of treatment; those who remained positive were retested after each new round of treatment, for a maximum of two rounds
Outcomes	Benefits: Pyelonephritis: Hospital admission with ≥2 of the following: fever (body temperature ≥38◦C), symptoms of pyelonephritis (nausea, vomiting, chills, and costovertebral tenderness), and a positive urine culture indicating the presence of bacteria in the urine. Perinatal mortality: neonatal death before discharge from the neonatal ward Preterm delivery: spontaneous birth between 32 and 37 wks GA Low birth weight: <10^{th} or 5^{th} percentile Neonatal sepsis: Confirmed with culture, includes group B streptococcal sepsis Harms:

	Serious adverse events: Congenital abnormalities (ND)
Notes	Cohort study addressed screening, results reported here for treatment RCT only. Study included both placebo and untreated groups who were combined in the analysis. When data were missing, these were imputed taking into account patient characteristics and outcomes. Differences in outcomes between groups were controlled for potential confounders (smoking, low education, conception through in-vitro fertilization or intracytoplasmic sperm injection, pre-existing hypertension). 5 women originally assigned to treatment group were later found to not have ASB, but remained in their assigned group (intention-to-treat analysis).

ASB: asymptomatic bacteriuria; C: Celsius; CFU/mL: colony forming units per millilitre; DM: diabetes mellitus; g: gram(s); GA: gestational age; IQR: interquartile range; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SE: standard error; UTI: urinary tract infection; wks: weeks

Kincaid-Smith, 1965	
Objective	To assess the effectiveness of antibacterial drugs for pregnant women with bacteriuria in preventing pyelonephritis, perinatal mortality, and low birth weight
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending their first antenatal visit before 26 wks GA Inclusion criteria: Pregnant women <26 wks GA with ASB at the first antenatal visit and confirmed by a subsequent positive test Exclusion criteria: NR
Participants	Setting: Queen Victoria Hospital, Melbourne, Australia; urban Study period: 1964-1965 Sample: n=145; treated (n=61), placebo (n=56) (see notes) Mean age (SD), years: NR Risk factors: (see notes) Socioeconomic status: All from lowest income category in community, but the community has a high standard of living Urogenital anomalies: At post-delivery testing, 51.4% of patients had an abnormal intravenous pyelogram and 5 patients had poorly functioning or non-functioning kidneys on one side due to ureteric obstruction. Length of follow-up: Until 6 months postpartum Loss to follow-up: Of initial 240 women with completed pregnancies, no outcomes reported for 95 women for various reasons (6 aborted before treatment, 20 developed symptoms before treatment, 22 attended infrequently, 33 failed to take tablets continuously, 14 had coagulase-negative staphylococcal bacteriuria); further information on non-compliant patients NR
Interventions	Screening characteristics: Timing: First antenatal visit Urine collection: Midstream urine sample; the second test was clean-voided (first was not) Urine testing method: Urine culture

	Criteria for a positive test: $>10^5$ CFU/mL on two occasions Treatment characteristics: Type of antibiotic and length of treatment: 0.5g sulphamexydiazine daily, changing to 1g sulphadimidine 3 times daily in the 13th week of gestation, continuing until delivery; if resistance to sulphonamides was indicated by sensitivity tests, 500mg ampicillin 3 times daily or 50mg nitrofurantoin 4 times daily was prescribed instead. Control group: Received identical placebo capsules and tablets Follow-up testing: Patients re-examined at monthly intervals, on any hospital admission, and at delivery. Retesting at 6 wks-3 months and 6 months postpartum ongoing at the time of publication. These subsequent samples involved cleansing of the periurethral area and insertion of a vaginal tampon to avoid contamination.
Outcomes	Benefits: Pyelonephritis: Loin pain and tenderness, with or without pyrexia, and rigors, with or without symptoms of dysuria and frequency Perinatal mortality: >28 wks GA Low birth weight (reported as preterm delivery): <2500g Harms: NR
Notes	Study also included a non-bacteriuric group. 29/145 (20%) patients were given treatment or placebo prior to confirmation of ASB (before the second culture was analyzed); outcomes for these patients were reported separately, leaving 116 in the current analysis. 11 fetal losses reported but group assignment NR.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; mg: milligram(s); NR: not reported; RCT: randomized controlled trial; SD: standard deviation; wks: weeks

Little, 1966	
Objective	To assess the effect of antibiotic treatment for pregnant women with ASB on incidence of pyelonephritis and adverse pregnancy outcomes
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending their first antenatal visit Inclusion criteria: Pregnant women with bacteriuria at the first antenatal visit and confirmed with a subsequent culture Exclusion criteria: NR
Participants	Setting: Charing Cross Hospital and Fulham Maternity Hospital, London, England; urban Study period: 1962-1965 Sample: n=265; treated (n=124), placebo (n=141) Mean age (SD), years: NR; 6.89% 10-20, 4.99% 21-30, 4.62% 31-40, 4.25% ≥40 Risk factors: Past history of urinary tract disease: 62 (23.4%) recalled a past episode (both groups combined) Length of follow-up: Until 6 wks postpartum

	Loss to follow-up: None reported.
Interventions	Screening characteristics: Timing: First antenatal visit, usually ~12th week of gestation Urine collection: Clean-voided midstream urine sample Urine testing method: Urine culture Criteria for a positive test: Two consecutive urine cultures with >10^5 CFU/mL Treatment characteristics: Type of antibiotic and length of treatment: At start of trial, patients were given 0.5g sulphamethoxypyridazine daily for 30 days; if bacteriuria did not clear, 1.5g ampicillin daily was given for 1 week, then a maintenance dose of 1g daily until delivery. Because treatment with ampicillin was generally not successful, later in the trial, a single dose of 100mg nitrofurantoin became the first form of treatment. Control group: Received placebo tablets Follow-up testing: Retested monthly throughout pregnancy
Outcomes	Benefits: Pyelonephritis: Loin pain and tenderness, a fever >100◦F, >10^5 CFU/mL. Usually there was also frequency and dysuria, and sometimes rigors and hematuria Perinatal mortality: ND Low birth weight (reported as prematurity): <2500g Harms: Serious adverse events: fetal abnormalities, ND
Notes	No additional notes

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; F: Fahrenheit; g: gram(s); mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation

Mulla, 1960	
Objective	To evaluate the clinical results of treatment of bacteriuria in pregnant women with long-acting sulfonamide
Methods	Design: RCT Recruitment: Pregnant women attending the obstetrical clinic Inclusion criteria: Pregnant women with ASB at their 30-32 wks GA obstetric visit Exclusion criteria: NR
Participants	Setting: St. Elizabeth Hospital, Ohio, US; urban Study period: NR Sample: n=100; treated (n=50), not treated (n=50) Mean age (SD), years: NR Risk factors: NR

	Length of follow-up: Until delivery and immediately after Loss to follow-up: None reported.
Interventions	Screening characteristics: Timing: Obstetric visit at 30-32 wks GA Urine collection: Catheter urinalysis (antimicrobial jelly used on the catheter) Urine testing method: Urine culture Criteria for a positive test: NR Treatment characteristics: Type of antibiotic and length of treatment: 250mg sulfadimethoxine twice daily for 1 week; the regimen was repeated if bacteriuria persisted Control group: Received no medication until symptoms appeared Follow-up testing: Followed at weekly intervals until delivery; were re-tested at least once, after the first course of treatment.
Outcomes	Benefits: Pyelonephritis: Clinical evidence of active infection, including acute symptoms of cystopyelitis; urine was tested at the time of the episode Harms: NR
Notes	Pyelonephritis after delivery was reported, but this was excluded from the present analysis.

ASB: asymptomatic bacteriuria; GA: gestational age; mg: milligram(s); n: number; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; US: United States; wks: weeks

Pathak, 1969	
Objective	To determine the effect of short-term antibacterial therapy on eradication of bacteriuria during pregnancy, and its effects on pregnancy outcomes
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending antenatal clinics Inclusion criteria: Pregnant women ≤24 wks GA with confirmed bacteriuria on two consecutive tests Exclusion criteria: Confirmation of bacteriuria at >24 wks GA, blood pressure >130/90mmHg at the initial antenatal visit, did not re-attend after first examination (wrong dates or could not be traced), early abortions, clinical pyelonephritis, 'mentally defective'
Participants	Setting: University College Hospital and Kingston Public Hospital, Jamaica; urban Study period: NR Sample: n=178; treated (n=76); placebo (n=76) Mean age (SD), years: NR Risk factors: Sickle-cell trait: 18/24 (21.4%) in bacteriuric patients, incidence by group NR Urogenital anomalies: 9/50 (18%) of bacteriurics had abnormalities on postpartum intravenous pyelogram (1 bilateral hydroureter with hydronephrosis, 1 localized calyceal

	clubbing, 1 bifid pelvis, 2 had changes consistent with papillary necrosis, 4 showed evidence of chronic pyelonephritis). Length of follow-up: Until delivery (all) and 3-9 months postpartum for a subset Loss to follow-up: n=26 (15%) lost; 12 (14%) treated (9 antibiotic received for positive serology, 3 defaulted from the clinic and could not be traced), 14 (16%) placebo (12 antibiotic received, 3 defaulted from the clinic)
Interventions	Screening characteristics: Timing: NR; ≤24 wks GA Urine collection: clean-voided urine sample Urine testing method: NR Criteria for a positive test: $>10^5$ CFU/mL on two consecutive specimens Treatment characteristics: Type of antibiotic and length of treatment: 100mg nitrofurantoin twice daily for 3 wks; patients who did not respond received 400mg nitrofurantoin daily for a further 4 days Control group: Received placebo identical in appearance Follow-up testing: Retested at weekly intervals during treatment (or placebo), then every 2 wks until delivery, and a subset (n=69, 24 treated and 45 placebo) at 3-9 months postpartum
Outcomes	Benefits: Pyelonephritis: ND Harms: NR
Notes	Reported preterm birth/fetal loss only by bacteriuric status, not by treatment group.

ASB: asymptomatic bacteriuria; CFU: colony forming units per millilitre; GA: gestational age; mg: milligram; mmHg: millimetre of mercury; n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; wks: weeks

Thomsen, 1987	
Objective	To assess the effect of treatment for group-B streptococcal bacteriuria in pregnant women on the incidence of preterm labour
Methods	Design: RCT; placebo-controlled Recruitment: Pregnant women attending Statens Seruminstitut Inclusion criteria: Pregnant women 27-31 wks GA who were positive for group-B streptococcal bacteriuria Exclusion criteria: NR; <27 or >31 wks GA
Participants	Setting: University Hospital, Denmark; urban Study period: October 1, 1984-October 1, 1986 Sample: n=69; treated (n=37), placebo (n=32) Mean age, years: 28.1, similar for both groups Risk factors:

	Ethnicity: All patients were white Socioeconomic status: Similar for both groups Length of follow-up: Until delivery (see notes) Loss to follow-up: None reported.
Interventions	Screening characteristics: Timing: NR; 27-31 wks GA Urine collection: Midstream urine sample Urine testing method: Urine culture Criteria for a positive test: 10^2-10^6 CFU/mL of group-B streptococci bacteria Treatment characteristics: Type of antibiotic and length of treatment: 10^6 IU penicillin 3 times daily for 6 days; treatment was repeated if bacteriuria persisted Control group: Received placebo tablets Follow-up testing: Retested weekly until delivery for persistent bacteriuria or recurrence
Outcomes	Benefits: Preterm delivery: <37 wks GA (mean wks GA for treated: 39.6, placebo: 36.2) Neonatal sepsis: ND Harms: NR
Notes	Patients positive for streptococci at delivery were treated with 2g ampicillin intravenously followed by 1g intravenously every 4 hours from the start of labour. Infants were given ampicillin (50mg/kg) intramuscularly every 12 hours to avoid sepsis. Umbilical cord blood was tested from group-B streptococci and babies with positive cultures were treated for 6 days. One infant tested positive for sepsis at 6 wks post-delivery.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram; GA: gestational age; IU: international unit; kg: kilogram; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; wks: weeks

Williams, 1969	
Objective	To investigate the effect of treatment of ASB in pregnancy on urine concentrating ability and the development of symptomatic UTI
Methods	Design: RCT Recruitment: Pregnant women attending their first antenatal visit Inclusion criteria: Pregnant women <30 wks GA with significant ASB at the first antenatal visit, confirmed by a second positive test within 10 days Exclusion criteria: NR
Participants	Setting: Maternity Hospital and St. David's Hospital, Cardiff, Wales, England; urban Study period: 1967 Sample: n=163; treated (n=85), untreated (n=78) Mean age (SE), years: 24.82 (0.49) for all bacteriurics, differences between groups NR

	Risk factors: NR Length of follow-up: Until 10 days postpartum Loss to follow-up: None reported
Interventions	Screening characteristics: Timing: First antenatal visit; mean (SE) 20.78 (0.45) wks GA Urine collection: Clean-voided midstream urine sample Urine testing method: Urine culture Criteria for a positive test: $>10^5$ gram-negative CFU/mL in at least two consecutive urine specimens; if the first specimen was positive, patients were recalled for a second specimen within 10 days Treatment characteristics: Type of antibiotic: 1g sulphadimidine 3 times daily for 7 days; if bacteriuria persisted, patients received 100mg nitrofurantoin twice daily for 7 days; if bacteriuria still persisted, patients received 250mg ampicillin 3 times daily for 7 days (ampicillin repeated as necessary) Control group: received no treatment until symptoms presented Follow-up testing: Retested 2-3 wks after the first course of treatment, and each subsequent course of treatment
Outcomes	Benefits: Pyelonephritis: loin pain and tenderness with or without fever (no record of fever in antenatal patients) Harms: NR
Notes	The study also included a non-bacteriuric and a non-pregnant group. Data for pyelonephritis includes postpartum infections (n=6) because group assignment NR.

ASB: asymptomatic bacteriuria; CFU/mL: colony forming units per millilitre; g: gram(s); GA: gestational age; mg: milligram(s); n: number; NR: not reported; RCT: randomized controlled trial; SE: standard error; UTI: urinary tract infection; wks: weeks

Wren, 1969	
Objective	To evaluate the effect of treatment of pregnant women with ASB on the incidence of premature deliveries and other adverse pregnancy outcomes
Methods	Design: Quasi-RCT Recruitment: Pregnant women booking at an antenatal clinic Inclusion criteria: Pregnant women with ASB at their first antenatal visit Exclusion criteria: NR
Participants	Setting: Royal Hospital for Women, New South Wales, Australia; urban Study period: November 1968-December 1968 Sample: n=183; treated (n=83), untreated (n=90) Mean age (SD): NR

	Risk factors: NR Length of follow-up: Until 6 wks postpartum Loss to follow-up: Of original n=183, 10 (5%) women lost; 2 sets of twins, 4 moved away and could not be traced, 3 received antibiotics before the trial started, 1 refused to take the treatment
Interventions	Screening characteristics: Timing: First antenatal visit Urine collection: Midstream urine sample Urine testing method: NR Criteria for a positive test: NR Treatment characteristics: Type of antibiotic and length of treatment: Rotational therapy with 100mg nitrofurantoin twice daily for 2 wks, 250mg ampicillin 4 times daily for 1 week, 500mg sulphurazole 4 times daily for 4 wks, and nalidixic acid 4 times daily for 2 wks. Each new patient started with one of the four drugs, then rotated through the remaining drugs in order. Every 9 wks, patients began a new course of rotational therapy until 1-6 wks after delivery. Control group: Untreated until clinical evidence of UTI developed Follow-up testing: Patients were retested one per month when possible, until the last month of pregnancy
Outcomes	Benefits: Spontaneous abortion: ND; 'abortion' Perinatal mortality: Stillbirth and neonatal death Preterm delivery: <37 wks GA Low birth weight (reported as prematurity): <2501g Harms: NR
Notes	The study also included a control group of non-bacteriuric women.

ASB: asymptomatic bacteriuria; g: gram(s); GA: gestational age; mg: milligram(s); n: number; ND: not defined; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; UTI: urinary tract infection; wks: weeks

Supplement 5. Risk of bias (ROB) assessments for included studies

Summary of ROB for studies of screening effectiveness

First Author, Year	Selection					Comparability		Outcome				Total Score[a] (max 9)	Selective Outcome Reporting[b]
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at start of study (pyelonephritis/ other outcomes)	Total	Comparability of cohorts	Total	Assessment of outcome	Adequacy of length of follow-up	Adequacy of follow-up of cohorts	Total		
Gérard, 1983	1	1	0	0/1	3	0	0	1	1	1	3	6	Suspected[c]
Gratacós, 1994	1	1	0	0/1	3	0	0	1	1	1	3	6	Suspected[d]
Rhode, 2007	1	1	1	0/1	4	1	1	1	1	1	3	8	Suspected[e]
Uncu, 2002	1	1	1	0/1	4	0	0	1	1	0	2	6	Not suspected[f]

[a]Assessed using the Newcastle-Ottawa Quality Assessment Scale[31]

[b]Assessed due to concern regarding reporting bias in the studies, but assessment not included in the total score

[c]Did not report on fetal abnormalities

[d]Did not report on spontaneous abortion, perinatal mortality, preterm delivery or fetal abnormalities

[e]Did not report on spontaneous abortion, perinatal mortality, or fetal abnormalities

[f]Reported on all outcomes, including fetal death >20 weeks of gestation (eligible for perinatal mortality)

ROB for studies of screening effectiveness

Domain	Author's judgement	Support for judgement
Gérard, 1983 (cohort)		
Representativeness of the exposed cohort	1	Included all pregnant women who visited the clinic at <25 wks GA.
Selection of the non-exposed cohort	1	Formed retrospectively, pregnant women attending the clinic in the 10 previous months (before implementation of screening).
Ascertainment of exposure	0	Not reported.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	0	No evidence of comparability.
Assessment of outcome	1	Appear to have used a chart review.
Adequacy of length of follow-up	1	Follow-up until delivery and for 3-6 months post-partum for those with ≥2 instances of asymptomatic bacteriuria.
Adequacy of follow-up of cohorts	1	No loss to follow-up.
Selective outcome reporting[b]	suspected	Did not report on fetal abnormalities.
Total score (maximum 10)	6	
Gratacós, 1944 (cohort)		
Representativeness of the exposed cohort	1	All pregnant women presenting to the clinic at <25 wks GA between January 1991 and December 1992.
Selection of the non-exposed cohort	1	Women who visited the same clinic in years (January 1987 to December 1990) before implementation of the screening program.
Ascertainment of exposure	0	Not reported.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	0	No evidence of comparability.
Assessment of outcome	1	Used a chart review – 'was recorded for 6 years'.
Adequacy of length of follow-up	1	Followed-up until delivery.
Adequacy of follow-up of cohorts	1	10 (6.9%) lost to follow-up.
Selective outcome reporting[b]	suspected	Did not report on spontaneous abortion, perinatal mortality, preterm delivery or fetal abnormalities.
Total score (maximum 10)	6	
Rhode, 2007 (cohort)		
Representativeness of the exposed cohort	1	All pregnant women who enrolled for care and delivered after August 15, 2002.
Selection of the non-exposed cohort	1	All pregnant women who enrolled for care at the same practice and delivered before August 15, 2002.

Domain	Author's judgement	Support for judgement
Ascertainment of exposure	1	Used delivery records.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	1	Compared 10 demographic factors, showing that groups were similar.
Assessment of outcome	1	Used a chart review.
Adequacy of length of follow-up	1	Followed-up until delivery of the patient left the practice.
Adequacy of follow-up of cohorts	1	112 (4.6%) lost to follow-up.
Selective outcome reporting[b]	suspected	Did not report on spontaneous abortion, perinatal mortality or fetal abnormalities.
Total score (maximum 10)	8	
Uncu, 2002 (cohort)		
Representativeness of the exposed cohort	1	All pregnant women <32 wks GA seen at an antenatal outpatient clinic.
Selection of the non-exposed cohort	1	Women who visited the clinic prior to the start of the screening study.
Ascertainment of exposure	1	Used delivery records.
Outcome not present at start of study (pyelonephritis/other outcomes)	0/1	Not ascertained for pyelonephritis, other outcomes could not have been present at the start of the study.
Comparability of the cohorts	0	No evidence of comparability.
Assessment of outcome	1	Used delivery records.
Adequacy of length of follow-up	1	Follow-up until post-delivery.
Adequacy of follow-up of cohorts	0	Not reported.
Selective outcome reporting[b]	not suspected	Reported on all outcomes, including fetal death >20 wks GA (eligible for perinatal mortality).
Total score (maximum 10)	6	

GA: gestational age; wks: weeks

[a]Assessed using the Newcastle-Ottawa Quality Assessment Scale

[b]Assessed due to concern regarding reporting bias in the studies, but assessment not included in the total score

Summary of ROB for studies of women's outcome valuation

First Author, Year	Did the study address a clearly focused question / issue?	Is the research method (study design) appropriate for answering the research question?	Is the method of selection of the subjects clearly described?	Could the way the sample was obtained introduce bias?	Was the sample of subjects representative of the population to which the findings will be referred?	Was the sample size based on pre-study considerations of statistical power?	Was a satisfactory response rate achieved?	Are the measurements (questionnaires) likely to be valid and reliable?	Was the statistical significance assessed?	Are confidence intervals given for the main results?	Could there be confounding factors that haven't been accounted for?	Can the results be applied to your organization?
Butters, 1990	1	1	1	2	1	2	1	2	1	3	1	1
Kazemier, 2015	2	2	1	3	1	2	2	2	3	3	2	3
Lupattelli, 2014	1	1	1	1	1	2	2	2	1	1	3	1
Mashayekhi, 2009	1	1	1	1	1	2	2	2	1	3	1	1
Nordeng, 2010	1	1	1	1	1	2	2	2	1	3	2	1
Sanz, 2000	1	1	3	2	1	2	2	2	1	3	1	1
Sharma, 2006	1	1	3	2	1	2	2	1	1	3	1	1
Twigg, 2016	1	1	1	1	1	2	2	1	1	3	1	1

[a]Assessed using a tool developed by the Center for Evidence-based Management[32] for cross-sectional studies (surveys)

1=Yes, 2=Can't Tell, 3=No

ROB for studies of women's outcome valuation

Domain	Author's judgement*	Support for judgement
Butters, 1990 (cross-sectional survey)		
Clearly focused question/issue	1	Awareness of the effects of commonly used drugs, cigarettes and alcohol on the fetus
Appropriate research method (study design)	1	Cross-sectional survey of women in postnatal wards
Selection of subjects clearly described	1	Provides inclusion and exclusion criteria, outlines selection methods
Sampling method introduces bias	2	Sampling was not random, may be consecutive
Sample of subjects representative of the population	1	Included women who were recently post-partum
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	1	Response rate was 87%
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Chi-square analysis
Confidence intervals for main results	3	No confidence intervals reported
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Identifies areas for further education in this population
Kazemier, 2015 (Prospective multi-centre screening cohort with embedded treatment RCT; valuation of outcomes obtained/reported in cross-sectional manner)		
Clearly focused question/issue	2	To assess maternal and neonatal consequences of treating and not treating asymptomatic bacteriuria in pregnancy; however, no direct examination of outcome valuation set out in protocol or study methods
Appropriate research method (study design)	2	Appears to be cross-sectional for information regarding why eligible women did not consent to participate in treatment trial
Selection of subjects clearly described	1	Clear inclusion and exclusion criteria for screening cohort and treatment RCT, with study flow documented
Sampling method introduces bias	3	Various clinics, hospitals and ultrasound centres in the Netherlands
Sample of subjects representative of the population	1	Women 18 years or older with singleton pregnancy without symptoms of urinary tract infection.
Sample size based on pre-study considerations of statistical power	2	Sample size estimates reported in statistical analysis, but none specified for cross-section of women for outcome valuation
Satisfactory response rate	2	Authors did not report response rate specifically for cross-section of women who declined treatment. Of 255 ASB-positive women, 163 received no treatment (of whom 155 did not want treatment for specified reason), but authors do not report if those who participated in treatment trial were asked/provided reason(s)

Questionnaires are likely to be valid and reliable	2	Validation of reason(s) for dissenting not reported
Statistical significance assessed	3	Fisher's exact test for outcomes from screening cohort and treatment trial; no significance for outcome valuation data
Confidence intervals for main results	3	CI's reported for outcomes from screening cohort and treatment trial; no CI's for outcome valuation data
Confounding factors not accounted for	2	Assessed confounders for outcomes from screening cohort and treatment trial, but not for outcome valuation data
Applicability of the results	3	Medication avoidance for asymptomatic conditions in pregnancy among Dutch women acknowledged by study authors to align with Dutch guidelines (not routinely screening and treating women with ASB); may be more applicable for the Netherlands but not for Canada where routine screening and treatment is standing practice
Lupattelli, 2014 (cross-sectional survey)		
Clearly focused question/issue	1	Association of health literacy and risk perception
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women
Selection of subjects clearly described	1	Self-selection, voluntary internet survey
Sampling method introduces bias	1	Informal sampling method – self-selection was not random or consecutive
Sample of subjects representative of the population	1	Pregnant women with internet access
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Mann-Whitney U test, Spearman's rank correlation coefficient, logistic regression
Confidence intervals for main results	1	Reported in Table 3
Confounding factors not accounted for	3	Adjusted for confounders in statistical analysis
Applicability of the results	1	Health literacy is significantly associated with adherence to pharmacotherapy in pregnant women
Mashayekhi, 2009 (cross-sectional survey)		
Clearly focused question/issue	1	Awareness of pregnant women on the effects of drugs during pregnancy
Appropriate research method (study design)	1	Cross-sectional survey of pre and postnatal women
Selection of subjects clearly described	1	Reports selection methods
Sampling method introduces bias	1	Sampling was not random or consecutive
Sample of subjects representative of the population	1	Included pre and postnatal women in hospital wards

Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Chi-square, Student's t-test, Pearson correlations, ANOVA
Confidence intervals for main results	3	Not reported
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Identifies roles for pharmacists in education of this population
Nordeng, 2010 (cross-sectional survey)		
Clearly focused question/issue	1	Women's perception of risk during pregnancy
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women and mothers
Selection of subjects clearly described	1	Self-selection, voluntary internet survey
Sampling method introduces bias	1	Informal sampling method – self-selection was not random or consecutive
Sample of subjects representative of the population	1	Pregnant women and young mothers (child less than 5 years) with internet access
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of survey questions was not reported
Statistical significance assessed	1	Linear regression, ANOVA, Student's t-test
Confidence intervals for main results	3	Confidence intervals were available in graph format only
Confounding factors not accounted for	2	Addressed in limitations
Applicability of the results	1	Indicates women overestimate risks and more education in this area is needed.
Sanz, 2000 (cross-sectional)		
Clearly focused question/issue	1	Drug utilization in pregnant women
Appropriate research method (study design)	1	Cross sectional, visual analogue scale
Selection of subjects clearly described	3	Selection methods are not reported for all populations
Sampling method introduces bias	2	Not reported for all populations
Sample of subjects representative of the population	1	Pregnant women attending out-patient clinic at a hospital
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Small n, no response rate reported
Questionnaires are likely to be valid and reliable	2	Validation of VAS questions was not reported
Statistical significance assessed	1	Mann-Whitney U, Kruskal Wallis, Chi-squared

Confidence intervals for main results	3	Only in graph format
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Pregnant women have high perceptions of teratogenic risk
Sharma, 2006 (cross-sectional survey)		
Clearly focused question/issue	1	Drug utilization in pregnant women
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women
Selection of subjects clearly described	3	Selected from an antenatal clinic but no sampling methods
Sampling method introduces bias	2	Not reported
Sample of subjects representative of the population	1	Pregnant women
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	1	Women's statements were confirmed through medical records when available
Statistical significance assessed	1	Chi-squared test
Confidence intervals for main results provided	3	Not reported
Confounding factors not accounted for	1	Confounders were not addressed with study design or analysis
Applicability of the results	1	Education of women of child-bearing age regarding benefits and harms of drug use during pregnancy is needed
Twigg, 2016 (cross-sectional survey)		
Clearly focused question/issue	1	Risk perception of medications in pregnant women and relationship with use
Appropriate research method (study design)	1	Cross-sectional survey of pregnant women and new mothers
Selection of subjects clearly described	1	Self-selection, voluntary internet survey
Sampling method introduces bias	1	Informal sampling method – self-selection was not random or consecutive
Sample of subjects representative of the population	1	Pregnant women or women <1 year post-natal with internet access
Sample size based on pre-study considerations of statistical power	2	Not reported
Satisfactory response rate	2	Large n, no response rate reported
Questionnaires are likely to be valid and reliable	1	Used validated BMQ-General questionnaire
Statistical significance assessed	1	Chi-square, Fisher's exact test, Mann-Whitney U, Independent t-test
Confidence intervals for main results	3	No confidence intervals for the main results, descriptive statistics only
Confounding factors not accounted for	1	Adjustment for confounding not reported in design or analysis

Applicability of the results	1	Medication use by pregnant women is impacted by beliefs about risk

[a]Assessed using a tool developed by the Center for Evidence-based Management for cross-sectional studies
* 1=Yes, 2=Can't Tell, 3=No
ANOVA: analysis of variance; ASB: asymptomatic bacteriuria; BMQ: beliefs about medicine questionnaire; n: sample size; RCT:randomized clinical trial; VAS: visual analogue scale

Summary of ROB for studies of treatment effectiveness

Study	Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel[1]	Blinding of Outcome Assessors[1]	Incomplete Reporting[2]	Selective Reporting[3]	Other Bias[4]	Overall Risk of Bias*
Brumfitt 1975								
Elder 1966								
Elder 1971								
Foley 1987								
Furness 1975								
Gold 1966								
Kass 1960								
Kazemier 2015								
Kincaid-Smith 1965								
Little 1966								
Mulla 1960								
Pathak 1969								
Thomsen 1987								
Williams 1969								
Wren 1969								

[a] Assessed using the Cochrane Risk of Bias[34] tool

[1] For the blinding domains, objective outcomes were considered to be at lower ROB than subjective outcomes

[2] For the incomplete reporting domain, 10-30% loss to follow-up were considered as Unclear ROB if no apparent between groups or reasons were provided

[3] For the selective reporting domain, a default of Low ROB was used for selective reporting when this was undetected or not highly suspected

[4] Assessed as: Low risk of bias if no other sources of bias are identified, High risk of bias if other sources of bias detected such as: participant characteristics (baseline imbalances), study design characteristics (crossover, cluster-randomized, or blocked randomization in trials without blinding); Unclear risk of bias assessment not applicable for this domain.

* Assessed as: Low if all domains are assessed as low, Unclear if at least one domain is assessed as unclear and no domains are assessed as high, or High if at least one domain is assessed as high.

Legend:

- Low risk
- Unclear risk
- High risk

ROB for individual studies of treatment effectiveness

Domain	Author's judgement	Support for judgement
Brumfitt, 1975 (RCT)		
Random sequence generation	Unclear	No description of the sequence generation process, how women were assigned to treatment or placebo, unequal numbers in treatment and placebo groups.
Allocation concealment	Unclear	No information provided to judge.
Blinding of participants and personnel	Low	"…were given placebo under double-blind conditions". Method not described in sufficient detail. Objective outcomes.
Blinding of outcome assessment	Low	"…were given placebo under double-blind conditions". Method not described in sufficient detail. Objective outcomes.
Incomplete outcome data	High	Inconsistencies in total number of women not explained (number of <2500g babies provided for 413/326 bacteriuric women); results not provided for pyelonephritis for all women in treated group (only subset).
Selective reporting	High	Results not provided for pyelonephritis for all women allocated to treatment.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Elder, 1966 (RCT)		
Random sequence generation	Unclear	"…a random sequence". Insufficient information to judge.
Allocation concealment	Unclear	No information provided to judge.
Blinding of participants and personnel	Low	"…double-blind trial"; no information provided to judge. Objective outcomes.
Blinding of outcome assessment	Low	"…double-blind trial"; no information provided to judge. Objective outcomes.
Incomplete outcome data	Low	Information provided on women lost to follow-up, reasonably balanced between groups.
Selective reporting	High	Result not provided for pyelonephritis for all participants; no pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Elder, 1971 (CCT)		
Random sequence generation	High	"…alternate bacteriuric…were assigned."
Allocation concealment	High	Participants were allocated by alternation.
Blinding of participants and personnel	Unclear	"identical-appearing placebo"; insufficient information to judge.
Blinding of outcome assessment	Unclear	"identical-appearing placebo"; insufficient information to judge.
Incomplete outcome data	Unclear	Insufficient information to judge.
Selective reporting	Unclear	Unable to judge; twin deliveries were excluded.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Foley, 1987		

Domain	Author's judgement	Support for judgement
Random sequence generation	Low	Allocated to treatment or no treatment by "toss of a coin".
Allocation concealment	Unclear	No information to judge.
Blinding of participants and personnel	Unclear	No description of any attempt at blinding; not placebo-controlled. Objective outcomes.
Blinding of outcome assessment	Unclear	No description of any attempt at blinding; not placebo-controlled. Objective outcomes.
Incomplete outcome data	Unclear	Loss to follow-up: 19%; no reasons provided for missing outcome data.
Selective reporting	High	No pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Furness, 1975 (RCT)		
Random sequence generation	Unclear	"by random allocation"; no additional information to judge.
Allocation concealment	Unclear	No information to judge.
Blinding of participants and personnel	Unclear	Not placebo-controlled. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge.
Incomplete outcome data	High	20/226 women withdrawn from trial, no details provided. All women included in outcome of pyelonephritis, 17% loss to follow-up or low birthweight and GA at delivery.
Selective reporting	Unclear	Unable to separate incidence of pyelonephritis during pregnancy and puerperium; results combined.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Gold, 1966 (CCT)		
Random sequence generation	High	Women allocated to treatment based on study number: odd number treatment, even number control.
Allocation concealment	High	Allocated to treatment based on study number.
Blinding of participants and personnel	Unclear	Placebo-controlled; no further details provided. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge. Objective outcomes.
Incomplete outcome data	Low	Does not appear to be any loss to follow-up.
Selective reporting	Unclear	No definition provided for prematurity.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Kass, 1960 (CCT)		
Random sequence generation	High	"alternate women received a placebo".
Allocation concealment	High	Allocation based on alternation: "alternate women received a placebo".

Domain	Author's judgement	Support for judgement
Blinding of participants and personnel	Low	Placebo was used and "the nature of the treatment was not known to the patient or to the attending obstetrical staff".
Blinding of outcome assessment	Unclear	Although a placebo was used, no further details are provided on blinding of outcome assessment. Objective outcomes.
Incomplete outcome data	Unclear	40 (21%) women were not enrolled either because they were >32 weeks GA before treatment could be started (n=30), or already received treatment for symptomatic infection (n=10). Loss to follow-up: 23 (11%) for pyelonephritis and low birthweight, no details provided; 69 (34%) for long-term persistent bacteriuria.
Selective reporting	Unclear	3 women had subsequent pregnancy and were reassigned to their original treatment group included in the analysis. In 5 placebo patients, symptomatic disease was assumed but no symptoms were documented. Not all women in symptomatic group were confirmed to have fever. Women treated for infections other than that in the urinary tract were included in the symptomatic group if they had cleared their bacteriuria.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Kazemier, 2015 (RCT)		
Random sequence generation	Low	Random assignment in 1:1 ratio; computer-generated list with random block sizes of 2/4/6 participants.
Allocation concealment	Low	Women, treating physicians and researchers remained unaware of bacteriuria status and treatment allocation. Central allocation - unmasking of treatment allocation was possible by 24h telephone service.
Blinding of participants and personnel	Low	Double-blinded. Women, treating physicians and researchers remained unaware of bacteriuria status and treatment allocation. Objective outcomes.
Blinding of outcome assessment	Low	Outcomes recorded by participants on questionnaires, and from data provided by hospitals and midwives up to 6 weeks post-delivery.
Incomplete outcome data	Low	ITT and dropout rate <10% (12/255 ASB-positive)
Selective reporting	Low	Cost-effectiveness was outlined in protocol but not reported in final study methods or results.
Other bias	Low	No other sources of bias identified.
Overall risk of bias	Low	
Kincaid-Smith, 1965 (RCT)		
Random sequence generation	Unclear	No description of sequence generation process.
Allocation concealment	Low	"a code of instructions to the pharmacist ensured that the trial remained double-blind despite…alterations in therapeutic regimen".
Blinding of participants and personnel	Low	"a code of instructions to the pharmacist ensured that the trial remained double-blind despite…alterations in therapeutic regimen".
Blinding of outcome assessment	Low	"a code of instructions to the pharmacist ensured that the trial remained double-blind despite…alterations in therapeutic regimen".
Incomplete outcome data	Unclear	240 women initially identified as bacteriuric; no information available on 55 (23%) women randomized to treatment but not included in the analysis because of poor compliance (attended infrequently or failed to take tablets continuously).
Selective reporting	Unclear	Insufficient information to judge.

Domain	Author's judgement	Support for judgement
Other bias	Low	Insufficient information to judge.
Overall risk of bias	Unclear	
Little, 1966 (RCT)		
Random sequence generation	Unclear	No information to judge.
Allocation concealment	Unclear	Allocation to treatment or control was drawn for "a pool of sealed envelopes containing a slip of paper", but there was no information provided to ensure appropriate safeguards to prevent investigators being aware of the treatment group.
Blinding of participants and personnel	Unclear	Participants in the control group "were given placebo"; no further details provided. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge. Objective outcomes.
Incomplete outcome data	Low	No missing outcome data.
Selective reporting	Unclear	Insufficient information to judge.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	Unclear	
Mulla, 1960 (RCT)		
Random sequence generation	Unclear	No description of sequence generation process.
Allocation concealment	Unclear	Women were "randomly divided into two groups"; no other details provided
Blinding of participants and personnel	Unclear	Not placebo-controlled. Objective outcomes.
Blinding of outcome assessment	Unclear	No information to judge. Objective outcomes.
Incomplete outcome data	Low	No missing outcome data.
Selective reporting	High	No definition for outcome of cystopyelitis; no pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Pathak, 1969 (RCT)		
Random sequence generation	Unclear	"on a random basis". Insufficient information provided to permit further judgement.
Allocation concealment	Unclear	Method of concealment not described.
Blinding of participants and personnel	Unclear	No information to judge.
Blinding of outcome assessment	Unclear	No information to judge.
Incomplete outcome data	Low	Missing outcome data balanced; reasons similar and unlikely to have introduced bias.
Selective reporting	High	No pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Thomsen, 1987 (RCT)		

Domain	Author's judgement	Support for judgement
Random sequence generation	Unclear	Described as "randomly allocated" but no description of the sequence generation process.
Allocation concealment	Unclear	Method of concealment of allocation not described.
Blinding of participants and personnel	Unclear	Placebo-controlled, described as "double-blinded" but no additional data. Objective outcomes.
Blinding of outcome assessment	Unclear	Described as "double-blinded" but no specific information provided to ensure outcome assessment was blinded. Objective outcomes.
Incomplete outcome data	Low	No missing outcome data.
Selective reporting	Unclear	Insufficient information to judge.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	Unclear	
Williams, 1969 (RCT)		
Random sequence generation	Unclear	"allocation at random"; no additional information to judge.
Allocation concealment	Unclear	No information to judge.
Blinding of participants and personnel	Unclear	No blinding, outcome may have been influenced by lack of blinding. No treatment group was given antibiotics to take if symptoms of infection developed. Objective outcomes.
Blinding of outcome assessment	Unclear	No blinding; assessment of outcome (pyelonephritis) may have been influenced by knowledge of treatment allocation. Objective outcomes.
Incomplete outcome data	Unclear	No explanation for unequal group sizes; no information provided on any missing data. An unknown number of women in the control group were given antibiotic treatment if they developed symptoms of UTI.
Selective reporting	High	No pregnancy outcomes (GA, birthweight).
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	
Wren, 1969 (CCT)		
Random sequence generation	High	Women "were divided into two groups, alternate patients being treated".
Allocation concealment	High	Women "were divided into two groups, alternate patients being treated".
Blinding of participants and personnel	Unclear	No blinding; knowledge of treatment group may have influenced outcome; women in untreated group who developed clinical UTI (33/90) were given antibiotics at the choice of the obstetrician, continued to delivery in 50% of cases. Objective outcomes.
Blinding of outcome assessment	Unclear	No blinding; however, outcome of birthweight unlikely to be influenced by lack of blinding.
Incomplete outcome data	Low	10 (6%) women not included in outcomes: 2 sets of twins excluded, 6 moved and 2 could not be traced, 3 delivered before antibiotics could be started, 1 refused treatment.
Selective reporting	Unclear	Insufficient information to judge; outcome of pyelonephritis not reported.
Other bias	Low	Insufficient information to judge.
Overall risk of bias	High	

[a]Assessed using the Cochrane Risk of Bias tool

ASB: asymptomatic bacteriuria; g: gram(s); GA: gestational age; UTI: urinary tract infection

Supplement 6. GRADE Summary of Findings & Evidence Profiles tables & forest plots

Evidence Set 1. Table 1.1 GRADE Summary of Findings – Benefits and harms of screening compared to no screening

Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Patient or population: asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: screening

Comparison: no screening

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no screening	**Risk with screening**				
Maternal mortality	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal mortality.
Maternal sepsis	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal sepsis.
Pyelonephritis	**Median**		**RR 0.28** (0.15 to 0.54)	5659 (3 observational studies)	⨁◯◯◯ VERY LOW [1,a]	We are very uncertain about the effects of screening on pyelonephritis.
	18 per 1,000	**13 fewer per 1,000** (from 8 fewer to 16 fewer)				
Perinatal mortality	**Median**		**RR 1.21** (0.01 to 102.93)	724 (2 observational studies)	⨁◯◯◯ VERY LOW [1,b]	We are very uncertain about the effects of screening on perinatal mortality.
	19 per 1,000	**4 more per 1,000** (from 19 fewer to 1,000 more)				
Spontaneous abortion	55 per 1,000	**2 fewer per 1,000** (from 32 fewer to 70 more)	**RR 0.96** (0.41 to 2.27)	370 (1 observational study)	⨁◯◯◯ VERY LOW [1,c]	We are very uncertain about the effects of screening on spontaneous abortion.

Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Patient or population: asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: screening

Comparison: no screening

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no screening	**Risk with screening**				
Neonatal sepsis	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on neonatal sepsis.
Preterm delivery	**Median** 13 per 1,000	**102 more per 1,000** (from 9 fewer to 1,000 more)	**RR 8.70** (0.32 to 240.07)	722 (2 observational studies)	⨁◯◯◯ VERY LOW [1, d]	We are very uncertain about the effects of screening on preterm delivery.
Low birthweight	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on low birthweight.
Maternal serious harm(s)	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal serious harms.
Neonatal serious harm: fetal abnormalities	11 per 1,000	**5 more per 1,000** (from 8 fewer to 85 more)	**RR 1.50** (0.25 to 8.87)	372 (1 observational study)	⨁◯◯◯ VERY LOW [1, e]	We are very uncertain about the effects of screening on fetal abnormalities.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Patient or population: asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: screening

Comparison: no screening

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no screening	**Risk with screening**				

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

Pyelonephritis [a] → Very Low Quality Evidence: Three non-concurrent cohort studies (Gérard 1983, Gratacós 1994, Uncu 2001) reported this outcome (n=5,659). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics. The optimal information size is met (sample size >5600), therefore downgrading for **imprecision** is not warranted. There were no serious concerns to warrant downgrading for **inconsistency**, **indirectness**, or **other considerations**.

Perinatal mortality [b] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=724; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on perinatal mortality. Further downgrading is warranted for **imprecision** due to optimal information size not being met with a small sample size. There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

Spontaneous abortion [c] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Gérard 1983). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk

factors or other patient characteristics, and suspected reporting bias as two studies did not report on spontaneous abortion. Only one study provided data on spontaneous abortion, so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to low event rates (total of 20) without optimal information size. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Preterm delivery [d] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=722; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on preterm delivery. Further downgrading is warranted for **imprecision** for inadequate sample size and optimal information size not being met (total of 38 events). There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

Neonatal serious harm: fetal abnormalities (harm) [e] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Uncu 2001). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as three studies did not report on fetal abnormalities. Only one study provided data on this outcome so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to the optimal information size not being met for rare events. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Evidence Set 1. Table 1.2 GRADE Evidence Profile – Benefits and harms of screening compared to no screening

Question: Screening compared to no screening for asymptomatic bacteriuria in pregnant women

Setting: Any primary or clinical care setting providing care to pregnant women

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**screening**	**no screening**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal mortality												
0									not estimable		-	CRITICAL
Maternal sepsis												
0									not estimable		-	CRITICAL
Pyelonephritis												
3	observational studies	serious	not serious	not serious	serious	none	10/2008 (0.5%)	1.8%	**RR 0.28** (0.15 to 0.54)	**13 fewer per 1,000** (from 8 fewer to 16 fewer)	⊕◯◯◯ VERY LOW [1, a]	CRITICAL
Perinatal mortality												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision [1]	Other considerations	screening	no screening	Relative (95% CI)	Absolute (95% CI)		
2	observational studies	serious	not serious	not serious	serious	none	6/349 (1.7%)	1.9%	**RR 1.21** (0.01 to 102.93)	**4 more per 1,000** (from 19 fewer to 1,000 more)	⨁◯◯◯ VERY LOW [1, b]	CRITICAL
Spontaneous abortion												
1	observational studies	serious	serious	not serious	serious	none	9/170 (5.3%)	11/200 (5.5%)	**RR 0.96** (0.41 to 2.27)	**2 fewer per 1,000** (from 32 fewer to 70 more)	⨁◯◯◯ VERY LOW [1, c]	CRITICAL
Neonatal sepsis												
0									not estimable		-	CRITICAL
Preterm delivery												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**screening**	**no screening**	**Relative (95% CI)**	**Absolute (95% CI)**		
2	observational studies	serious	not serious	not serious	serious	none	33/347 (9.5%)	1.3%	**RR 8.70** (0.32 to 240.07)	**102 more per 1,000** (from 9 fewer to 1,000 more)	⨁◯◯◯ VERY LOW [1, d]	CRITICAL
Low birthweight												
0									not estimable		-	IMPORTANT
Maternal serious harm(s)												
0									not estimable		-	CRITICAL
Neonatal serious harm: fetal abnormalities												
1	observational studies	serious	serious	not serious	serious	none	3/186 (1.6%)	2/186 (1.1%)	**RR 1.50** (0.25 to 8.87)	**5 more per 1,000** (from 8 fewer to 85 more)	⨁◯◯◯ VERY LOW [1, e]	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

Pyelonephritis [a] → Very Low Quality Evidence: Three non-concurrent cohort studies (Gérard 1983, Gratacós 1994, Uncu 2001) reported this outcome (n=5,659). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics. The optimal information size is met (sample size >5600), therefore downgrading for **imprecision** is not warranted. There were no serious concerns to warrant downgrading for **inconsistency**, **indirectness**, or **other considerations**.

Perinatal mortality [b] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=724; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on perinatal mortality. Further downgrading is warranted for **imprecision** due to optimal information size not being met with a small sample size. There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

Spontaneous abortion [c] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Gérard 1983). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on spontaneous abortion. Only one study provided data on spontaneous abortion, so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to low event rates (total of 20) without optimal information size. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Preterm delivery [d] → Very Low Quality Evidence: Two non-concurrent cohort studies (n=722; Gérard 1983, Uncu 2001) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as two studies did not report on preterm delivery. Further downgrading is warranted for **imprecision** for inadequate sample size and optimal information size not being met (total of 38 events). There were no serious concerns to warrant downgrading for **inconsistency, indirectness** or **other considerations**.

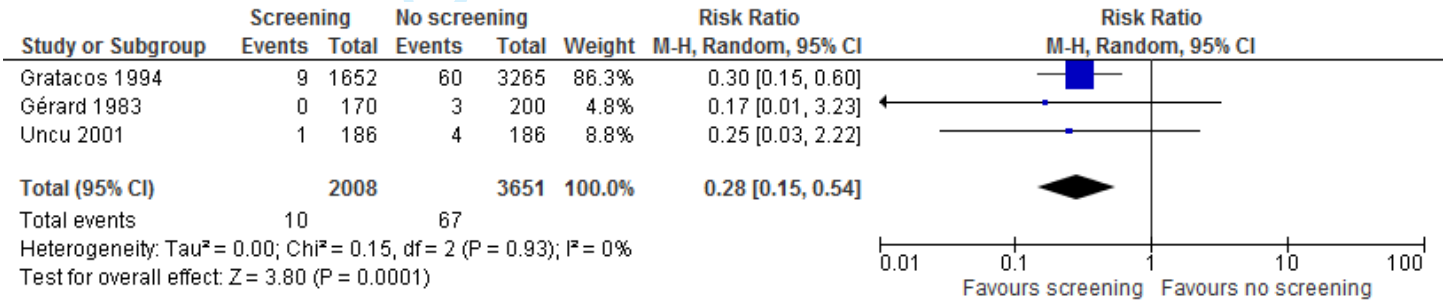
Neonatal serious harm: fetal abnormalities [e] → Very Low Quality Evidence: One non-concurrent cohort study reported this outcome (n=370; Uncu 2001). Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** across studies associated with: 1) no demonstration of comparability between screening and no screening groups, and 2) no adjustment to analyses for risk factors or other patient characteristics, and suspected reporting bias as three studies did not report on fetal abnormalities. Only one study provided data on this outcome so this warrants downgrading for **inconsistency**. Further downgrading for **imprecision** is warranted due to the optimal information size not being met for rare events. There were no serious concerns to warrant downgrading for **indirectness** or **other considerations**.

Evidence Set 1. Forest Plots 1.1-1.5 – Benefits and harms of screening compared to no screening

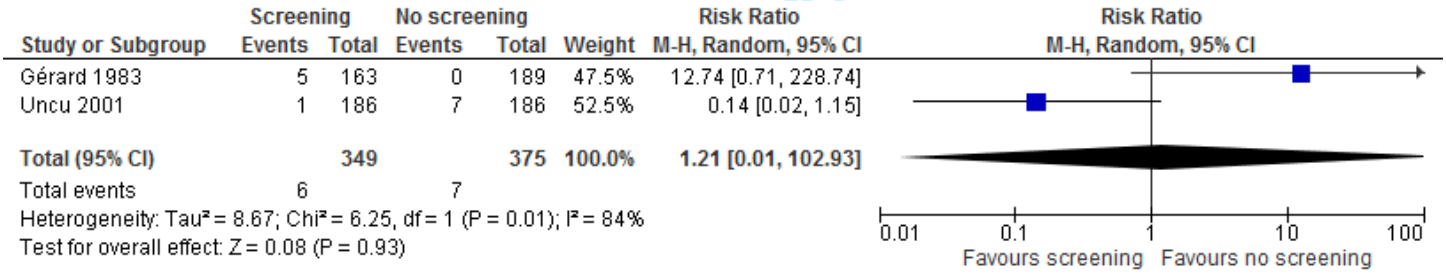
Outcome	No. of studies	No. of participants	Effect size (Risk Ratio; M-H, Random, 95%CI)
1.1 Pyelonephritis	3	5659	0.28 [0.15, 0.54]
1.2 Perinatal mortality >=20 wks GA note: Gérard >=31 wks; Uncu >20 wks	2	724	1.21 [0.01, 102.93]
1.3 Spontaneous abortion <20 wks GA note: 1 study <=28 wks (all occurred 7-21 wks)	1	370	0.96 [0.41, 2.27]
1.4 Preterm delivery <37 wks GA	2	722	8.70 [0.32, 240.07]
1.5 Neonatal serious harm: fetal abnormalities	1	372	1.50 [0.25, 8.87]

CI: confidence interval; GA: gestational age; M-H: Mantel-Haenszel; No.: number; wks: weeks

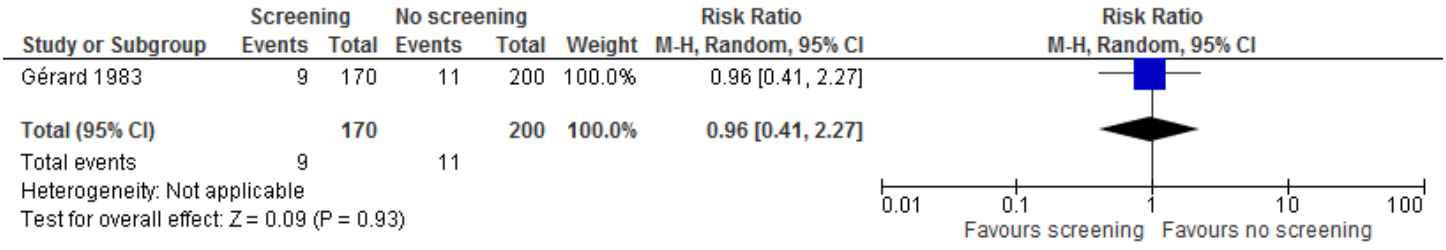
1.1 Pyelonephritis



1.2 Perinatal mortality (>=20 wks GA)



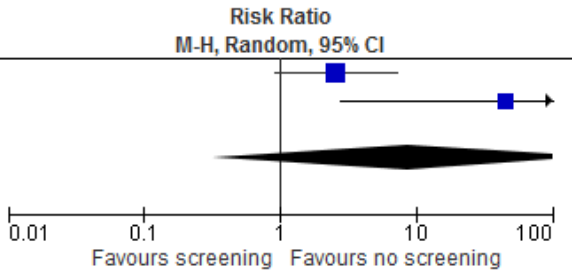
1.3 Spontaneous abortion (<20 wks GA)



1.4 Preterm delivery (<37 wks GA)

Study or Subgroup	Screening Events	Screening Total	No screening Events	No screening Total	Weight	Risk Ratio M-H, Random, 95% CI
Gérard 1983	11	161	5	189	57.5%	2.58 [0.92, 7.28]
Uncu 2001	22	186	0	186	42.5%	45.00 [2.75, 736.39]
Total (95% CI)		**347**		**375**	**100.0%**	**8.70 [0.32, 240.07]**
Total events	33		5			

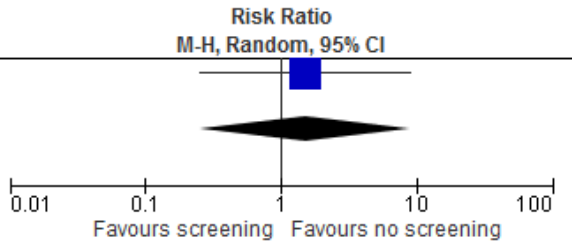
Heterogeneity: Tau² = 4.70; Chi² = 5.07, df = 1 (P = 0.02); I² = 80%
Test for overall effect: Z = 1.28 (P = 0.20)



1.5 Neonatal serious harm: fetal abnormalities

Study or Subgroup	Screening Events	Screening Total	No screening Events	No screening Total	Weight	Risk Ratio M-H, Random, 95% CI
Uncu 2001	3	186	2	186	100.0%	1.50 [0.25, 8.87]
Total (95% CI)		**186**		**186**	**100.0%**	**1.50 [0.25, 8.87]**
Total events	3		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.45 (P = 0.65)



Evidence Set 2. Table 2.1 GRADE Summary of Findings - Benefits and harms of frequent screening compared to one-time screening

Frequent screening compared to one-time screening for asymptomatic bacteriuria						
Patient or population: asymptomatic bacteriuria **Setting**: Any primary clinical care setting providing care to pregnant women **Intervention**: frequent screening **Comparison**: one-time screening						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with one-time screening	**Risk difference with frequent screening**				
Pyelonephritis	4 per 1,000	**0 fewer per 1,000** (from 3 fewer to 13 more)	**RR 1.09** (0.27 to 4.35)	1952 (1 observational study)	⨁◯◯◯ VERY LOW [1, a]	We are very uncertain about the effects of frequent screening compared to one-time screening on pyelonephritis.
Preterm delivery	49 per 1,000	**28 more per 1,000** (from 5 more to 60 more)	**RR 1.57** (1.11 to 2.23)	1952 (1 observational study)	⨁◯◯◯ VERY LOW [1, b]	We are very uncertain about the effects of frequent screening compared to one-time screening on preterm delivery.
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio						
GRADE Working Group grades of evidence **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect						

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when

optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

CI: Confidence interval; **RR:** Risk ratio

Pyelonephritis [a] → Very Low Quality Evidence: One non-concurrent cohort study (n=1952; Rhode 2007) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to serious **risk of bias** associated with: 1) no demonstration that pyelonephritis was not present at start of study, 2) no demonstration of comparability between frequent and one-time screening groups, and 3) no adjustment to analyses to account for risk factors or other patient characteristics. Only one study provided data for this outcome so downgrading is warranted for **inconsistency**. Further downgrading is warranted for **indirectness** as the women are predominantly medically underserved, Hispanic and receiving care from a midwifery clinic, with a high rate of gestational diabetes (9%). The optimal information size is not met (8 events) with sample size (n=1952), therefore this warrants downgrading for **imprecision**. There were no serious concerns to warrant downgrading for **other considerations**.

Preterm delivery [b] → Very Low Quality Evidence: One non-concurrent cohort study (n=1952; Rhode 2007) reported this outcome. Quality of evidence is downgraded from high to low due to observational level data. Further downgrading from low to very low is warranted due to very serious **risk of bias** associated with: 1) no demonstration of comparability between frequent and one-time screening groups, 2) no adjustment to analyses to account for risk factors or other patient characteristics, and 3) suspected reporting bias among outcomes reported by studies (did not report on spontaneous abortion, perinatal mortality or fetal abnormalities). Only one study provided data for this outcome so downgrading is warranted for **inconsistency**. Further downgrading is warranted for **indirectness** as the women are predominantly medically underserved, Hispanic and receiving care from a midwifery clinic, with a high rate of gestational diabetes (9%). The event rate is low (122 events) without meeting optimal information size, so this is downgraded for **imprecision**. There were no serious concerns to warrant downgrading for **other considerations**.

Evidence Set 3. Table 3.1 GRADE Summary of Findings – Benefits and harms of treatment compared to no treatment

Treatment compared to no treatment for asymptomatic bacteriuria

Patient or population: asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: treatment

Comparison: no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with treatment**				
Maternal mortality	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal mortality.
Maternal sepsis	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal sepsis.
Pyelonephritis	**Median**		**RR 0.24** (0.13 to 0.41)	2017 (12 RCTs)	⊕⊕◯◯ LOW [1, a]	There may be a reduction in pyelonephritis from treatment.
	232 per 1,000	**176 fewer per 1,000** (from 137 fewer to 202 fewer)				
Perinatal mortality	**Median**		**RR 0.96** (0.27 to 3.39)	1104 (6 RCTs)	⊕◯◯◯ VERY LOW [1, b]	We are very uncertain about the effects of treatment on perinatal mortality.
	40 per 1,000	**2 fewer per 1,000** (from 29 fewer to 97 more)				
Spontaneous abortion	**Median**		**RR 0.60** (0.11 to 3.10)	379 (2 RCTs)	⊕◯◯◯ VERY LOW [1, c]	We are very uncertain about the effects of treatment on spontaneous abortion.
	33 per 1,000	**13 fewer per 1,000** (from 30 fewer to 70 more)				

Treatment compared to no treatment for asymptomatic bacteriuria

Patient or population: asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: treatment

Comparison: no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with treatment**				
Neonatal sepsis	**Median**		**RR 0.22** (0.01 to 4.54)	154 (2 RCTs)	⨁◯◯◯ VERY LOW [1, d]	We are very uncertain about the effects of treatment on neonatal sepsis.
	22 per 1,000	**17 fewer per 1,000** (from 22 fewer to 79 more)				
Preterm delivery	**Median**		**RR 0.57** (0.21 to 1.56)	533 (4 RCTs)	⨁◯◯◯ VERY LOW [1, e]	We are very uncertain about the effects of treatment on preterm delivery.
	158 per 1,000	**68 fewer per 1,000** (from 125 fewer to 88 more)				
Low birth weight	**Median**		**RR 0.63** (0.45 to 0.90)	1522 (7 RCTs)	⨁◯◯◯ LOW [1, f]	There may be a reduction in low birth weight from treatment.
	118 per 1,000	**44 fewer per 1,000** (from 12 fewer to 65 fewer)				
Maternal serious harm(s)	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-	No study reported on maternal serious harms.
	Median					

Treatment compared to no treatment for asymptomatic bacteriuria

Patient or population: asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Intervention: treatment

Comparison: no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with treatment**				
Neonatal serious harm: fetal abnormalities	19 per 1,000	**9 fewer per 1,000** (from 15 fewer to 8 more)	**RR 0.49** (0.17 to 1.43)	821 (4 RCTs)	⨁◯◯◯ VERY LOW [1, g]	We are very uncertain about the effects of treatment on harms (fetal abnormalities).
Neonatal serious harm: hemolytic anemia	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	265 (1 RCT)	⨁◯◯◯ VERY LOW [1, h]	We are very uncertain about the effects of treatment on harms (hemolytic anemia).

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

CI: Confidence interval; **RR:** Risk ratio

Pyelonephritis, overall [a] → Low Quality Evidence: Twelve trials (Brumfitt 1975, Elder 1971, Foley 1987, Furness 1975, Gold 1966, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Mulla 1960, Pathak 1969, Williams 1969) reported this outcome (n=2,017). Quality of evidence is downgraded from high to moderate due to serious **risk of bias**

associated with use of alternation for sequence generation (Elder 1971, Gold 1966, Kass 1960), inadequate allocation concealment (Elder 1971, Gold 1966, Kass 1960), and incomplete reporting (Brumfitt 1975, Furness 1975). This body of evidence on treatment effectiveness is downgraded from moderate to low for **indirectness** due to studies that did not explicitly include asymptomatic women (only 3 studies included exclusively asymptomatic women; Kazemier 2015, Mulla 1960, and Williams 1969), and studies that included high-risk women (Elder 1971, Kincaid-Smith 1965, Little 1966, and Pathak 1969). The optimal information size criterion is met (control group event rate=20%; total number of events=253) with an adequate sample size (n=2,017), and the confidence interval (0.13 to 0.41) indicates there may be important benefit; therefore, downgrading is not warranted for **imprecision**. There were no concerns with **inconsistency** or **other considerations** to warrant further downgrading.

Perinatal mortality [b] → Very Low Quality Evidence: Six trials (n=1,104; Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Kass 1960, Wren 1969), and inadequate allocation concealment (Elder 1971, Kass 1960). This body of evidence on treatment effectiveness is downgraded for **indirectness** due to studies that did not explicitly include asymptomatic women as well as studies that included high-risk women. Further downgrading is warranted for **imprecision** due to the samples size not being met for optimal information size criterion (37 events). There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Spontaneous abortion [c]→ Very Low Quality Evidence: Two trials (n=379; Furness 1975, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969) and incomplete reporting (Furness 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size is inadequate with optimal information size not met (10 events) to warrant downgrading twice from low to very low for **imprecision**. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal sepsis [d] → Very Low Quality Evidence: Two trials (n=154; Kazemier 2015, Thomsen 1987) reported this outcome. Quality of evidence is downgraded for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size (<2000) is not met with only 2 events to warrant downgrading twice for **imprecision**. There were no concerns to warrant downgrading for **risk of bias, inconsistency** or **other considerations**.

Preterm delivery [e] → Very Low Quality Evidence: Four trials (n=533; Furness 1975, Kazemier 2015, Thomsen 1987, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969), and incomplete reporting (Furness 1975). There is substantial heterogeneity (I^2=70%) with point estimates on both sides of the line of no effect to warrant downgrading for **inconsistency**. Downgrading from moderate to low for **indirectness** is warranted due to studies that did not explicitly include exclusively asymptomatic women. There were no concerns to warrant downgrading for **imprecision or other considerations**.

Low birth weight [f] → Low Quality Evidence: Seven trials (n=1,522; Brumfitt 1975, Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Kass 1960, Wren 1969), inadequate allocation concealment (Elder 1971, Kass 1960, Wren 1969), and incomplete reporting (Brumfitt 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. The optimal information size was not quite met (<2000 patients and <200 events), but we did not think the concerns were serious enough to downgrade for this outcome for **imprecision.** There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: fetal abnormalities [g] → Very Low Quality Evidence: Four trials (n=821; Elder 1971, Furness 1975, Kazemier 2015, Little 1966) reported this outcome. Quality of evidence is downgraded from high to moderate for

serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971), inadequate allocation concealment (Elder 1971), and incomplete reporting (Furness 1975). Downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. Further downgrading from low to very low for **imprecision** is warranted due to optimal information size (sample size of 821) not being met for rare events. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: hemolytic anemia [h] → Very Low Quality Evidence: One trial (n=265; Elder 1971) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation and inadequate allocation concealment. Only one study provided data for this outcome so downgrading from moderate to low for **inconsistency** is warranted. Further downgrading from low to very low is warranted for **indirectness** due the study not explicitly including exclusively asymptomatic women as well as studies that included high-risk women. Due to optimal information size (sample size of 265) not being met for rare events, downgrading twice is warranted for **imprecision**. There were no concerns to warrant downgrading for **other considerations**.

Evidence Set 3. Table 3.1 GRADE Evidence Profile – Benefits and harms of treatment compared to no treatment

Question: Treatment compared to no treatment for asymptomatic bacteriuria

Setting: Any primary or clinical care setting providing care to pregnant women

Bibliography:

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**treatment**	**no treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal mortality												
0									not estimable		-	CRITICAL
Maternal sepsis												
0									not estimable		-	CRITICAL
Pyelonephritis												
12	randomised trials	serious	not serious	serious	not serious	none	55/1023 (5.4%)	23.2%	**RR 0.24** (0.13 to 0.41)	**176 fewer per 1,000** (from 137 fewer to 202 fewer)	⊕⊕◯◯ LOW [1, a]	CRITICAL
Perinatal mortality												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision [1]	Other considerations	treatment	no treatment	Relative (95% CI)	Absolute (95% CI)		
6	randomised trials	serious	not serious	serious	serious	none	16/529 (3.0%)	4.0%	**RR 0.96** (0.27 to 3.39)	**2 fewer per 1,000** (from 29 fewer to 97 more)	⊕◯◯◯ VERY LOW [1, b]	CRITICAL
Spontaneous abortion												
2	randomised trials	serious	not serious	serious	very serious	none	4/222 (1.8%)	3.3%	**RR 0.60** (0.11 to 3.10)	**13 fewer per 1,000** (from 30 fewer to 70 more)	⊕◯◯◯ VERY LOW [1, c]	CRITICAL
Neonatal sepsis												
2	randomised trials	not serious	not serious	serious	very serious	none	0/77 (0.0%)	2.2%	**RR 0.22** (0.01 to 4.54)	**17 fewer per 1,000** (from 22 fewer to 79 more)	⊕◯◯◯ VERY LOW [1, d]	CRITICAL
Preterm delivery												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision** [1]	**Other considerations**	**treatment**	**no treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
4	randomised trials	serious	serious	not serious	very serious	none	34/299 (11.4%)	15.8%	**RR 0.57** (0.21 to 1.56)	**68 fewer per 1,000** (from 125 fewer to 88 more)	⊕◯◯◯ VERY LOW [1, e]	CRITICAL
Low birth weight												
7	randomised trials	serious	not serious	serious	not serious	none	64/769 (8.3%)	11.8%	**RR 0.63** (0.45 to 0.90)	**44 fewer per 1,000** (from 12 fewer to 65 fewer)	⊕⊕◯◯ LOW [1, f]	IMPORTANT
Maternal serious harm(s)												
0									not estimable		-	CRITICAL
Neonatal serious harm: fetal abnormalities												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision [1]	Other considerations	treatment	no treatment	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	serious	not serious	serious	very serious	none	4/425 (0.9%)	1.9%	**RR 0.49** (0.17 to 1.43)	**9 fewer per 1,000** (from 15 fewer to 8 more)	⨁◯◯◯ VERY LOW [1, g]	CRITICAL
Neonatal serious harm: hemolytic anemia												
1	randomised trials	serious	serious	serious	very serious	none	0/122 (0.0%)	0/143 (0.0%)	not estimable		⨁◯◯◯ VERY LOW [1, h]	CRITICAL

[1] The imprecision domain is assessed using GRADE guidance[42] relevant for systematic reviews as follows: when optimal information size (OIS) criterion is met, and the 95% confidence interval overlaps no effect, consideration of important benefit or important harm will be assessed using a relative risk of 1.0 (0.75 to 1.25).

CI: Confidence interval; **RR:** Risk ratio

Pyelonephritis, overall [a] → Low Quality Evidence: Twelve trials (Brumfitt 1975, Elder 1971, Foley 1987, Furness 1975, Gold 1966, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Mulla 1960, Pathak 1969, Williams 1969) reported this outcome (n=2,017). Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Gold 1966, Kass 1960), inadequate allocation concealment (Elder 1971, Gold 1966, Kass 1960), and incomplete reporting (Brumfitt 1975, Furness 1975). This body of evidence on treatment effectiveness is downgraded from moderate to low for **indirectness** due to studies that did not explicitly include asymptomatic women (only 3 studies included exclusively asymptomatic women; Kazemier 2015, Mulla 1960, and Williams 1969), and studies that included high-risk women (Elder 1971, Kincaid-Smith 1965, Little 1966, and Pathak 1969). The optimal information size criterion is met (control group event rate=20%; total number of events=253) with an adequate sample size (n=2,017), and the confidence interval (0.13 to 0.41) indicates there may be important benefit; therefore, downgrading is not warranted for **imprecision**. There were no concerns with **inconsistency** or **other considerations** to warrant further downgrading.

Perinatal mortality [b] → Very Low Quality Evidence: Six trials (n=1,104; Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence

generation (Elder 1971, Kass 1960, Wren 1969), and inadequate allocation concealment (Elder 1971, Kass 1960). This body of evidence on treatment effectiveness is downgraded for **indirectness** due to studies that did not explicitly include asymptomatic women as well as studies that included high-risk women. Further downgrading is warranted for **imprecision** due to the samples size not being met for optimal information size criterion (37 events). There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Spontaneous abortion [c]→ Very Low Quality Evidence: Two trials (n=379; Furness 1975, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate due to serious **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969) and incomplete reporting (Furness 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size is inadequate with optimal information size not met (10 events) to warrant downgrading twice from low to very low for **imprecision**. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal sepsis [d] → Very Low Quality Evidence: Two trials (n=154; Kazemier 2015, Thomsen 1987) reported this outcome. Quality of evidence is downgraded for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women. The sample size (<2000) is not met with only 2 events to warrant downgrading twice for **imprecision**. There were no concerns to warrant downgrading for **risk of bias, inconsistency** or **other considerations**.

Preterm delivery [e] → Very Low Quality Evidence: Four trials (n=533; Furness 1975, Kazemier 2015, Thomsen 1987, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation (Wren 1969), inadequate allocation concealment (Wren 1969), and incomplete reporting (Furness 1975). There is substantial heterogeneity (I^2=70%) with point estimates on both sides of the line of no effect to warrant downgrading for **inconsistency**. Downgrading from moderate to low for **indirectness** is warranted due to studies that did not explicitly include exclusively asymptomatic women. There were no concerns to warrant downgrading for **imprecision or other considerations**.

Low birth weight [f] → Low Quality Evidence: Seven trials (n=1,522; Brumfitt 1975, Elder 1971, Kass 1960, Kazemier 2015, Kincaid-Smith 1965, Little 1966, Wren 1969) reported this outcome. Quality of evidence is downgraded from high to moderate for serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971, Kass 1960, Wren 1969), inadequate allocation concealment (Elder 1971, Kass 1960, Wren 1969), and incomplete reporting (Brumfitt 1975). Further downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. The optimal information size was not quite met (<2000 patients and <200 events), but we did not think the concerns were serious enough to downgrade for this outcome for **imprecision.** There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: fetal abnormalities [g] → Very Low Quality Evidence: Four trials (n=821; Elder 1971, Furness 1975, Kazemier 2015, Little 1966) reported this outcome. Quality of evidence is downgraded from high to moderate for serious **risk of bias** associated with use of alternation for sequence generation (Elder 1971), inadequate allocation concealment (Elder 1971), and incomplete reporting (Furness 1975). Downgrading from moderate to low is warranted for **indirectness** due to studies that did not explicitly include exclusively asymptomatic women as well as studies that included high-risk women. Further downgrading from low to very low for **imprecision** is warranted due to optimal information size (sample size of 821) not being met for rare events. There were no concerns to warrant downgrading for **inconsistency** or **other considerations**.

Neonatal serious harm: hemolytic anemia [h] → Very Low Quality Evidence: One trial (n=265; Elder 1971) reported this outcome. Quality of evidence is downgraded from high to moderate for **risk of bias** associated with use of alternation for sequence generation and inadequate allocation concealment. Only one study provided data for this outcome so downgrading from moderate to low for **inconsistency** is warranted. Further downgrading from low to very low is warranted for **indirectness** due the study not explicitly including exclusively asymptomatic women as well as studies that included high-risk women. Due to

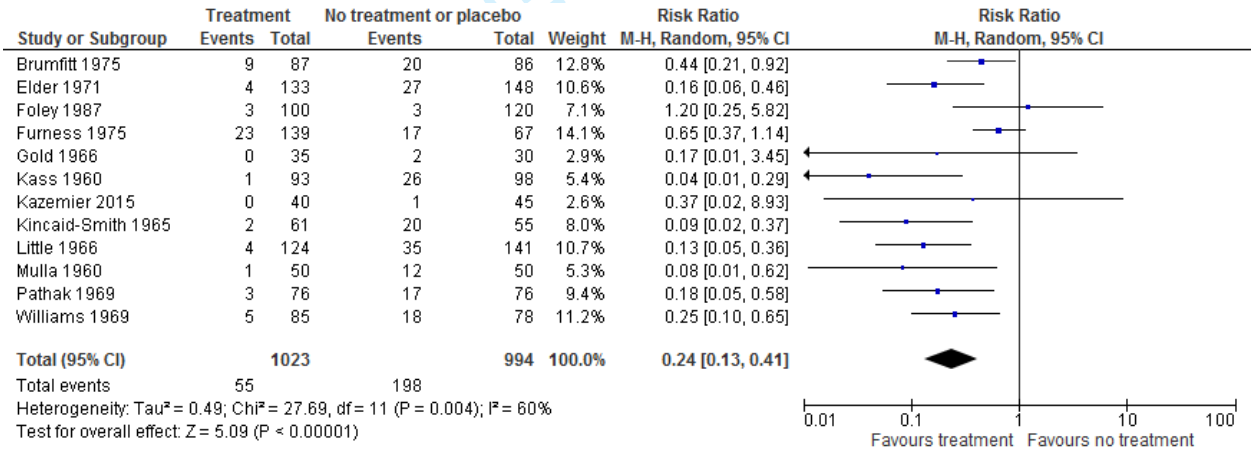
optimal information size (sample size of 265) not being met for rare events, downgrading twice is warranted for **imprecision**. There were no concerns to warrant downgrading for **other considerations**.

Evidence Set 3: Forest Plots 3.1-3.8 - KQ4: Benefits and harms of treatment compared to no treatment

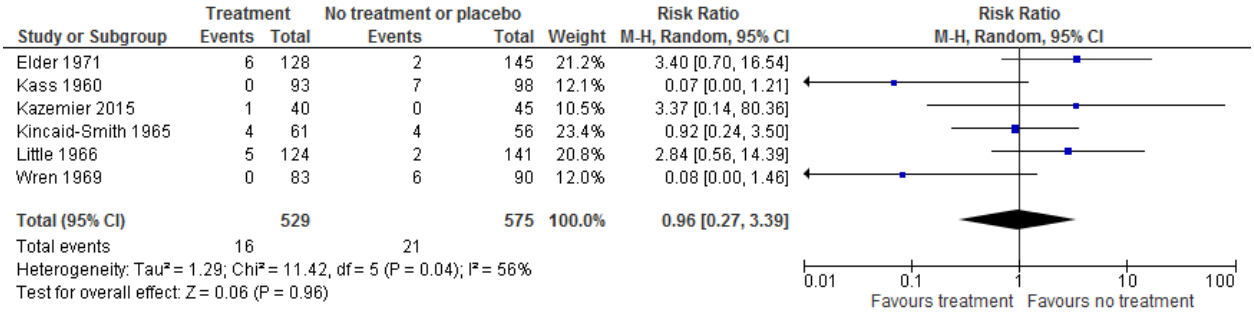
Outcome	No. of studies	No. of participants	Effect size (Risk Ratio; M-H, Random, 95%CI)
3.1 Pyelonephritis	12	2017	0.24 [0.13, 0.41]
3.2 Perinatal mortality (≥20 wks, including intrauterine demise, stillbirth, early neonatal death)	6	1104	0.96 [0.27, 3.39]
3.3 Spontaneous abortion (<20 wks)	2	379	0.60 [0.11, 3.10]
3.4 Neonatal sepsis	2	154	0.22 [0.01, 4.54]
3.5 Preterm delivery (<38 wks)	4	533	0.57 [0.21, 1.56]
3.6 Low birth weight (≤2500g; SGA <10th percentile & <5th percentile)	7	1522	0.63 [0.45, 0.90]
3.7 Neonatal serious harm: fetal abnormalities	4	821	0.49 [0.17, 1.43]
3.8 Neonatal serious harm: hemolytic anemia	1	265	Not estimable

CI: confidence interval; g: grams; M-H: Mantel-Haenszel; No.: number; SGA: small for gestational age; wks: weeks

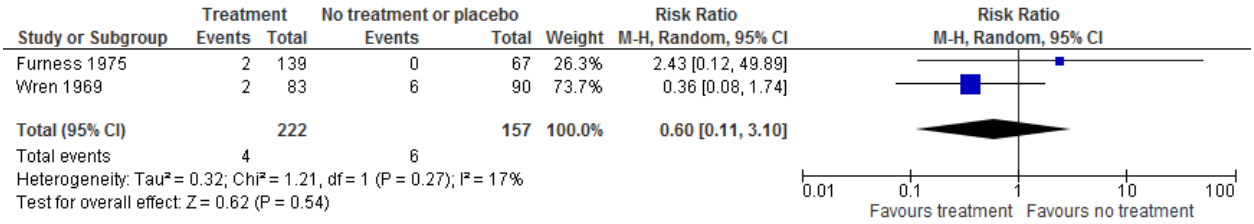
3.1 Pyelonephritis



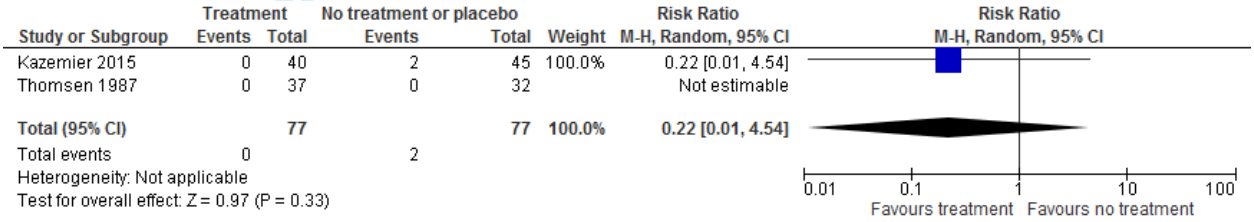
3.2 Perinatal mortality



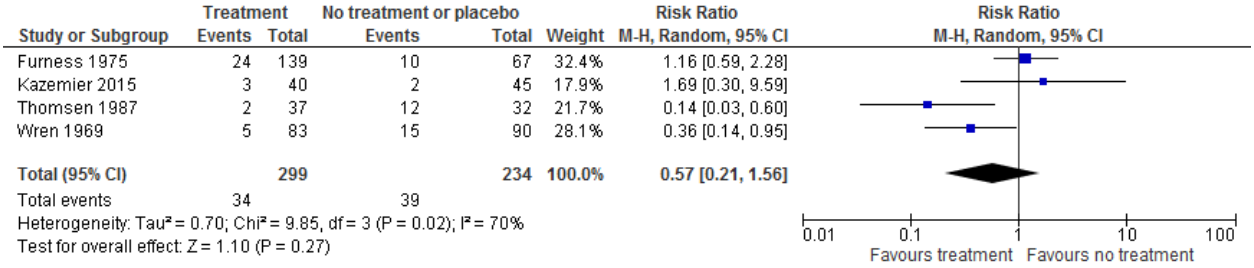
3.3 Spontaneous abortion



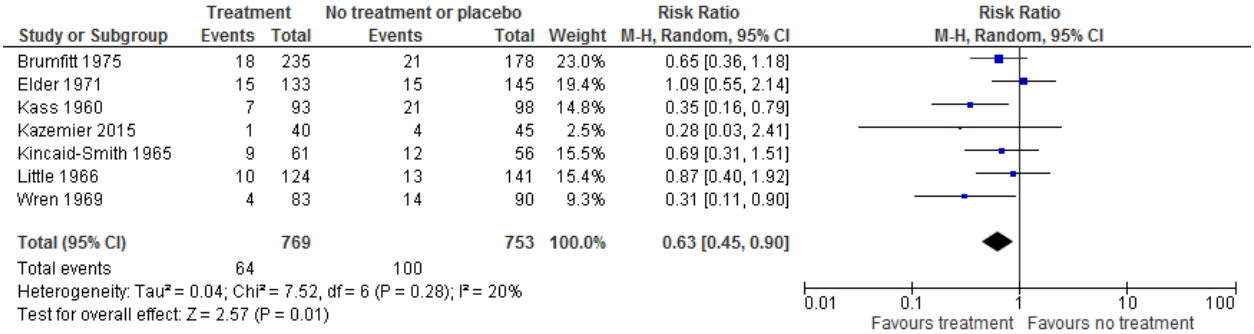
3.4 Neonatal sepsis



3.5 Preterm delivery



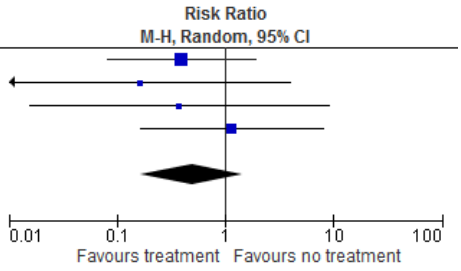
3.6 Low birthweight



3.7 Neonatal serious harm: fetal abnormalities

Study or Subgroup	Treatment Events	Total	No treatment or placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Elder 1971	2	122	6	143	46.4%	0.39 [0.08, 1.90]
Furness 1975	0	139	1	67	11.4%	0.16 [0.01, 3.92]
Kazemier 2015	0	40	1	45	11.5%	0.37 [0.02, 8.93]
Little 1966	2	124	2	141	30.7%	1.14 [0.16, 7.95]
Total (95% CI)		**425**		**396**	**100.0%**	**0.49 [0.17, 1.43]**
Total events	4		10			

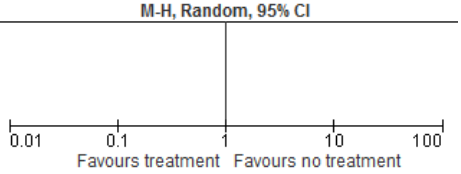
Heterogeneity: Tau² = 0.00; Chi² = 1.29, df = 3 (P = 0.73); I² = 0%
Test for overall effect: Z = 1.31 (P = 0.19)



3.8 Neonatal serious harm: hemolytic anemia

Study or Subgroup	Treatment Events	Total	No treatment or placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Elder 1971	0	122	0	143		Not estimable
Total (95% CI)		**122**		**143**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

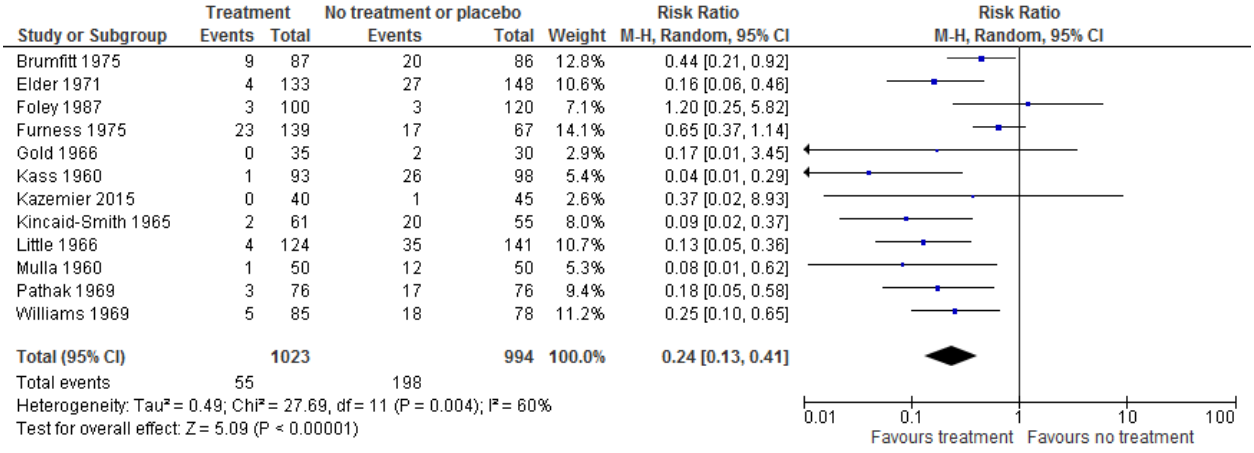


Evidence Set 3. Forest Plots for Subgroup Analyses 3.1.1-3.1.4 – KQ4: Benefits and harms of treatment compared to no treatment

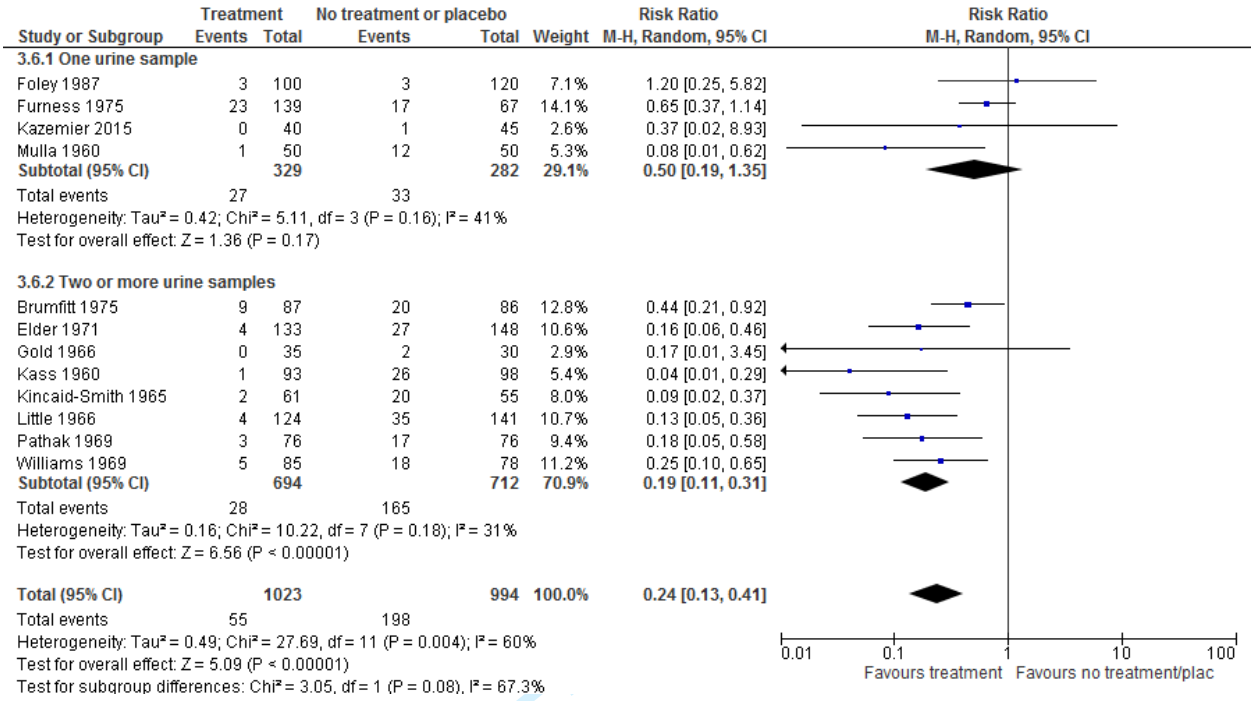
Outcome	No. of studies	No. of participants	Effect size (Risk Ratio; M-H, Random, 95%CI)
3.1 Pyelonephritis (overall)	**12**	**2017**	**0.24 [0.13, 0.41]**
3.1.1 Subgroup analysis: no. of urine samples before confirming bacteriuria and giving treatment			
One urine sample	4	611	0.50 [0.19, 1.35]
Two or more urine samples	8	1406	0.19 [0.11, 0.31]
3.1.2 Subgroup analysis: testing for persistent bacteriuria			
Tested for persistent bacteriuria during pregnancy	8	1352	0.26 [0.15, 0.45]
Testing for persistent bacteriuria post-delivery only	1	206	0.65 [0.37, 1.14]
Testing for persistent bacteriuria during pregnancy and post-delivery	3	459	0.11 [0.05, 0.25]
3.1.3 Subgroup analysis: follow-up			
Follow-up until delivery or puerperium (≤6 wks post-delivery)	9	1558	0.31 [0.18, 0.54]
Follow-up until >6 wks post-delivery	3	459	0.11 [0.05, 0.25]

CI: confidence interval; M-H: Mantel-Haenszel; No.: number; wks: weeks

3.1 Pyelonephritis (overall)

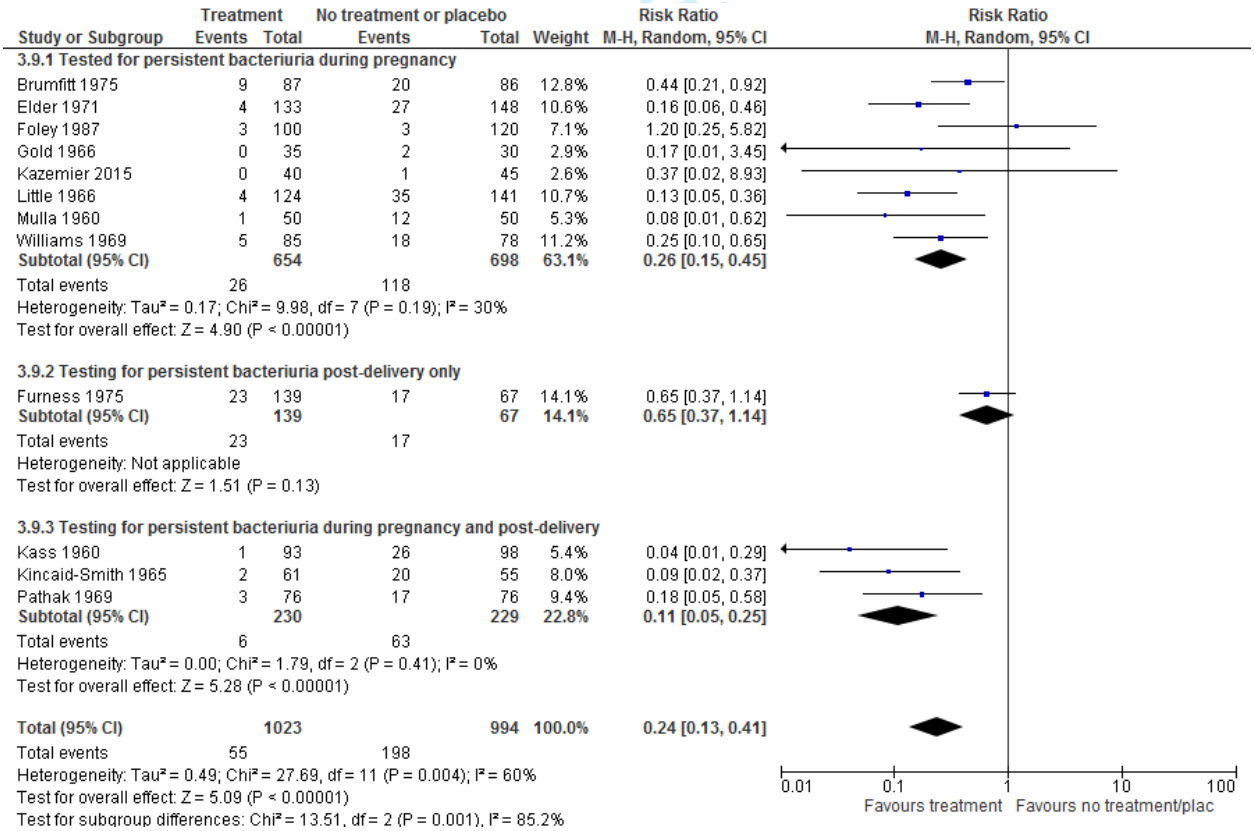


3.1.1 Pyelonephritis subgroup: number of urine samples at each screening visit*

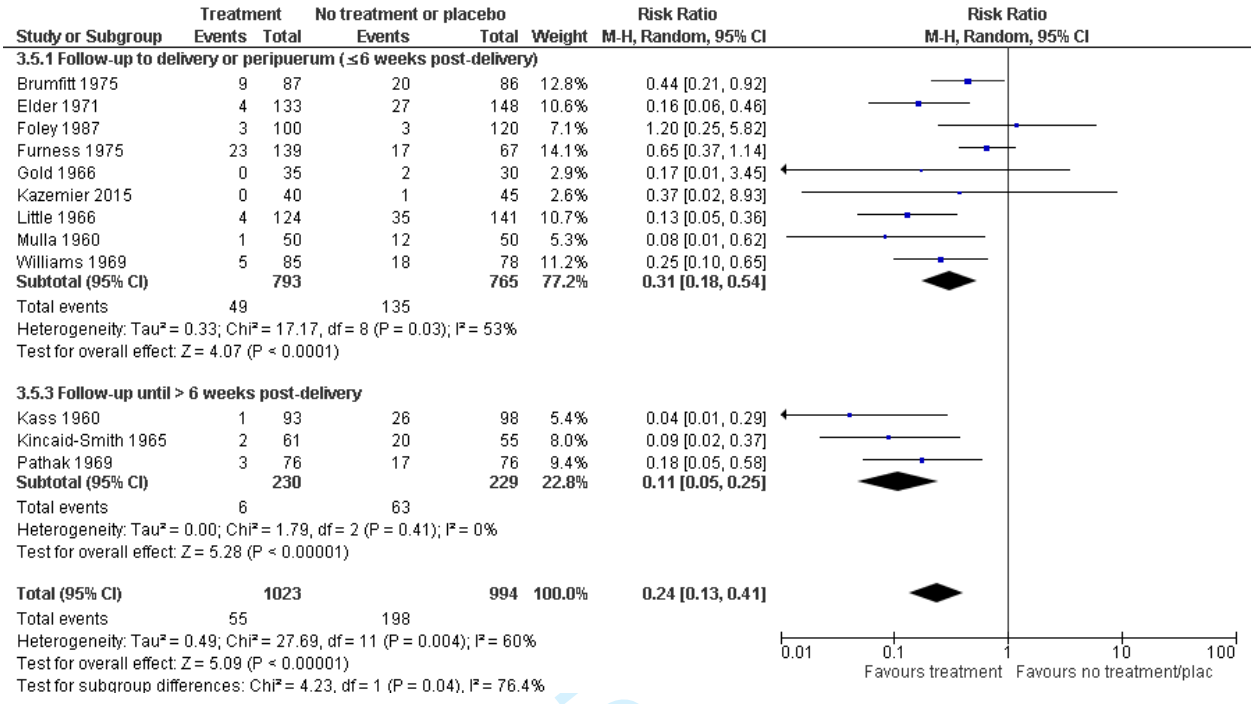


*The additional culture(s) was used to confirm levels of bacteriuria.

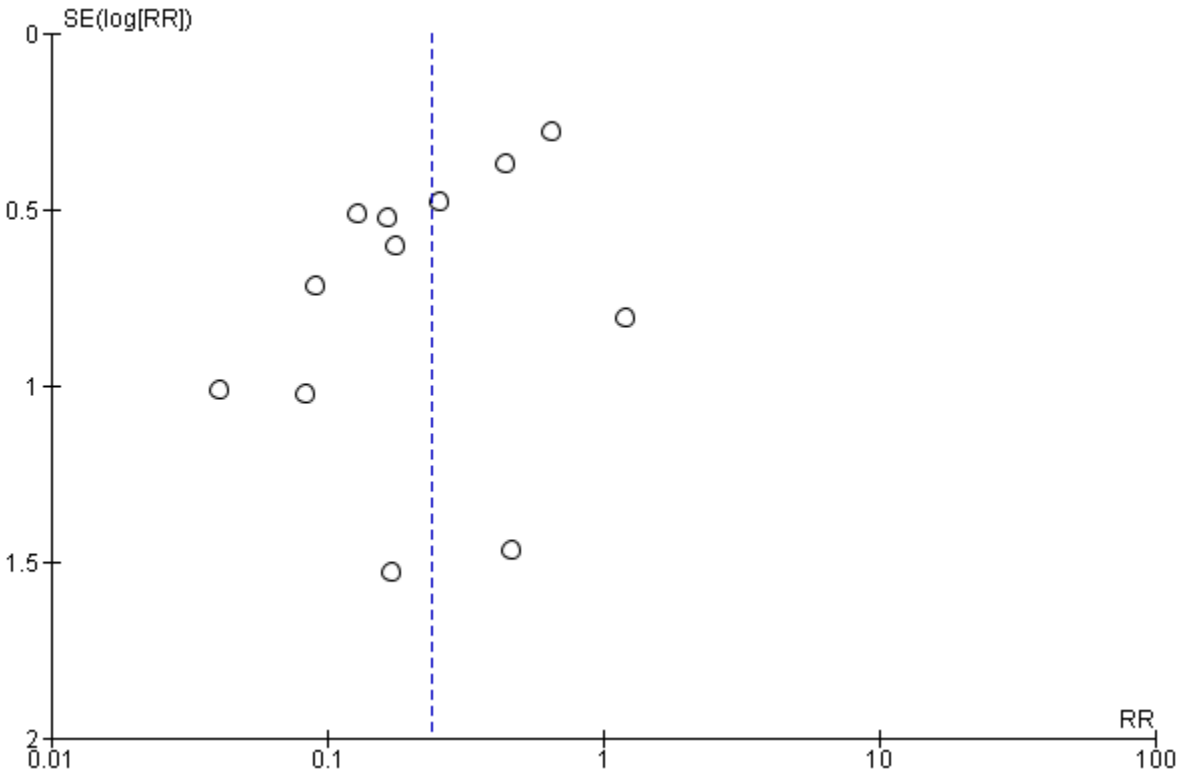
3.1.2 Pyelonephritis subgroup: timing of testing for persistent bacteriuria



3.1.3 Pyelonephritis subgroup: duration of follow-up



Supplement 7. Funnel Plot Asymmetry Test for outcome of pyelonephritis for treatment effectiveness



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	p. 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	p. 3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	p. 3-4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Abstract; p.4; Supplement 1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	p. 4; Supplement 3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	p. 4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	p. 4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	p. 5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	p. 4-5 Supplement 3
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	p. 5

PRISMA 2009 Checklist

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	p. 5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency ($e.g., I^2$) for each meta-analysis.	p. 5

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	p. 4-5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	p. 5-6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	p. 6; Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	p. 6; Table 1; Supplement 4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	p. 7-11; Supplement 5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	p. 7-11; Table 2; Supplement 4 & 6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	p. 9-12; Table 2; Supplement 6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	p.7-11; Supplement 5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	p. 9-10 Supplement 6 & 7

PRISMA 2009 Checklist

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	p. 13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	p. 13;
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	p. 13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	p.15-16

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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