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 $\geq 10^4$ 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: 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