

Screening for Asymptomatic Bacteriuria in Adults: Evidence for the U.S. Preventive Services Task Force Reaffirmation Recommendation Statement

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Background: Asymptomatic bacteriuria is common, and screening for this condition in pregnant women is a well-established, evidence-based standard of current medical practice. Screening other groups of adults has not been shown to improve outcomes.

Purpose: To review new and substantial evidence on screening for asymptomatic bacteriuria, to support the work of the U.S. Preventive Services Task Force.

Data Sources: English-language studies of adults (age >18 years) indexed in PubMed and the Cochrane Library and published from 1 January 2002 through 30 April 2007.

Study Selection: For benefits of screening or treatment for screened populations, systematic reviews; meta-analyses; and randomized, controlled trials were included. For harms of screening, systematic reviews; meta-analyses; randomized, controlled trials; cohort studies; case-control studies; and case series of large multisite databases were included. Two reviewers independently reviewed titles, abstracts, and full articles for inclusion.

Data Extraction: Two reviewers extracted data from studies on benefits of screening and treatment (including decreases in the

incidence of adverse maternal and fetal outcomes, symptomatic urinary tract infections, hypertension, and renal function decline).

Data Synthesis: An updated Cochrane systematic review of 14 randomized, controlled trials of treatment supports screening for asymptomatic bacteriuria in pregnant women. A randomized, controlled trial and a prospective cohort study show that screening nonpregnant women with diabetes for asymptomatic bacteriuria is unlikely to produce benefits. No new evidence on screening men for asymptomatic bacteriuria or on harms of screening was found.

Limitation: The focused search strategy may have missed some smaller studies on the benefits and harms of screening for asymptomatic bacteriuria.

Conclusion: The available evidence continues to support screening for asymptomatic bacteriuria in pregnant women, but not in other groups of adults.

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The presence of bacteria in the urine of an individual without signs or symptoms of a urinary tract infection is called *asymptomatic bacteriuria*. This condition is normally present in 3% to 5% of women younger than age 60 years and is more common in patients with diabetes and elderly persons. In pregnant women, asymptomatic bacteriuria has been associated with an increased incidence of pyelonephritis and low-birthweight offspring (1).

In 2004, the U.S. Preventive Services Task Force (USPSTF) recommended “screening for asymptomatic bacteriuria with urine culture for pregnant women at 12 to 16 weeks’ gestation” (a grade A recommendation) on the basis of good evidence that treatment for asymptomatic bacteriuria reduces the incidence of symptomatic urinary tract infections, low-birthweight children, and preterm delivery (2). Citing a lack of evidence that screening for

asymptomatic bacteriuria improves clinical outcomes in men and nonpregnant women, the USPSTF recommended against screening these groups (a grade D recommendation) (2).

In 2008, the USPSTF reexamined the evidence to reaffirm its recommendations on screening for asymptomatic bacteriuria in adults. The USPSTF decided to perform a reaffirmation update because there is a strong evidence base for the 2004 recommendations on screening for asymptomatic bacteriuria, and therefore only contradictory information from large, high-quality studies could change these recommendations. The USPSTF performs reaffirmation updates for recommendation statements that remain USPSTF priorities and are within the scope of the USPSTF and for which there is compelling reason for the USPSTF to have a current recommendation statement. The goal of this reaffirmation update was to find new, substantial, high-quality evidence regarding the benefits and harms of screening for asymptomatic bacteriuria in adults.

See also:

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Related article. 43
Summary for Patients. 1-37

Web-Only

Conversion of graphics into slides
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METHODS

The USPSTF requested that this update address 2 primary key questions:

1. What are the benefits of screening and treatment for asymptomatic bacteriuria in pregnant women, nonpregnant women, and men?

2. What are the harms of screening for asymptomatic bacteriuria in pregnant women, nonpregnant women, and men?

The Task Force determined that this update need not review new evidence for the harms of antibiotic treatment for asymptomatic bacteriuria because the adverse effects of commonly used antibiotic medications are well established.

Data Sources and Searches

We performed literature searches for the benefits of screening for asymptomatic bacteriuria and the harms of screening, limited 1 January 2002 through 30 April 2007, using the search terms *asymptomatic bacteriuria*, *screening*, and *urine culture*. Initial searches were limited to English-language articles indexed in the Cochrane Database of Systematic Reviews and PubMed core clinical journals. Core journals are a subset of 120 English-language journals defined by the National Library of Medicine, previously known as the Abridged Index Medicus. When initial searches revealed few articles, we expanded searches to include noncore journals. We supplemented these searches by reviewing reference lists of recent systematic and narrative reviews and clinical guidelines.

Study Selection

We searched for studies on the benefits and harms of screening and the benefits of treatment for asymptomatic bacteriuria. We included studies of adults 18 years of age or older from the United States and from other countries with patient populations generalizable to the United States. We excluded studies of very high-risk or special patient populations, including patients with a history of recurrent urinary tract infections, immunocompromised patients, and patients with sickle cell disease.

For benefits of screening or treatment of screened populations, we included randomized, controlled trials (RCTs); meta-analyses; and systematic reviews. For harms of screening, we included systematic reviews, meta-analyses, RCTs, cohort studies, case-control studies, and case series of large multisite databases. We excluded editorials, case reports, narrative reviews, and guideline reports.

We evaluated all articles for predetermined exclusion criteria at each stage of review (title, abstract, and full article). Articles selected by at least 1 team member advanced to the next stage of review. At the full article stage, we resolved differences of opinion by consensus.

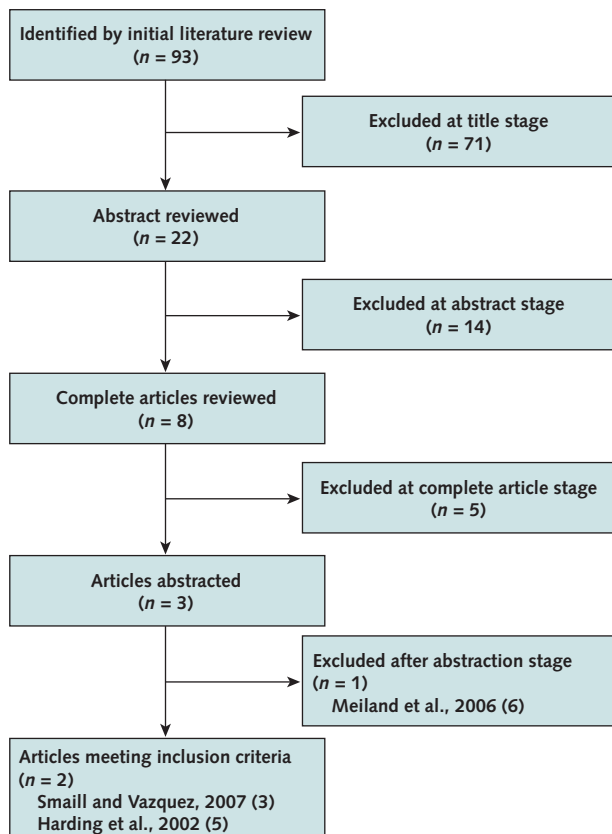
Data Extraction

We abstracted information on sample size, entry criteria, demographic characteristics, comorbid conditions, study design, treatment group allocation, and clinical outcomes of interest.

Data Synthesis and Analysis

Data from included studies were synthesized qualitatively in a narrative format.

Figure. Study flow diagram.



Reasons for exclusion (number of studies excluded):

- Not a study (n = 9): Narrative review, editorial, comment, or case report
- No outcomes (n = 32): Study reported only microbiologic or ecologic outcomes
- Study design (n = 4): Benefits: not an RCT, meta-analysis, or systematic review
Harms: did not meet study design inclusion criteria
- Not condition of interest (n = 33): Not asymptomatic bacteriuria (e.g., symptomatic UTI)
- High-risk population (n = 12): Not generalizable to general adult populations (e.g., recurrent UTIs, sickle cell disease, immunocompromised patients)
- Not adults (n = 1): Study exclusively involving persons younger than age 18 years

RCT = randomized, controlled trial; UTI = urinary tract infection.

Role of the Funding Source

The work of the USPSTF is supported by the Agency for Healthcare Research and Quality. This review did not receive separate funding.

RESULTS

We identified 93 potentially eligible articles and entered them into a reference database. After sequential application of exclusion criteria (Figure), 1 systematic review

of treatment for asymptomatic bacteriuria in pregnant women and 1 RCT of treatment for asymptomatic bacteriuria in nonpregnant women with diabetes met inclusion criteria for this update. An additional prospective cohort study of outcomes of asymptomatic bacteriuria in diabetic women that did not meet the inclusion criteria is also reviewed in detail. These 3 new studies are discussed in the next sections (Table).

1. What Are the Benefits of Screening and Treatment for Asymptomatic Bacteriuria in Pregnant Women, Nonpregnant Women, and Men?

Pregnant Women

We identified no new RCTs of screening for asymptomatic bacteriuria in pregnant women. A 2007 Cochrane systematic review and meta-analysis of randomized trials comparing antibiotic treatment with placebo or no treatment included 14 studies involving 2302 pregnant women.

The review found statistically significant reductions in the incidence of pyelonephritis (relative risk [RR], 0.23 [95% CI, 0.13 to 0.41]) and low-birthweight babies (RR, 0.66 [CI, 0.49 to 0.89]) (3).

Although all of the studies included in the Cochrane review were published in 1987 or earlier, we considered the meta-analysis to represent new evidence because it came to a different conclusion than a previous Cochrane review (4) about the effect of antibiotic treatment on the incidence of preterm delivery. The previous review relied on the standard definition of *preterm delivery* from the 1960s, birthweight less than 2500 g, rather than the currently accepted definition of birth before a certain gestational age. When the Cochrane review investigators included only the 3 studies that used a gestational age–based definition of preterm delivery, antibiotic treatment for asymptomatic bacteriuria had no effect on rates of preterm delivery (RR, 0.37 [CI, 0.10 to 1.36]) (3).

Table. New Studies on the Benefits of Screening and Treatment for Asymptomatic Bacteriuria

Author, Year (Reference)	Study Design	Sample Characteristics	Intervention and/or Comparison	Main Results	Additional Information	Summary
Small and Vazquez, 2007 (3)	Systematic review of randomized, controlled trials	14 trials of antibiotic treatment involving 2302 pregnant women, published between 1960 and 1987 Most trials rated poor quality because of unclear or inadequate allocation concealment	Treatment for asymptomatic bacteriuria identified during pregnancy (multiple different antibiotics and durations) vs. no treatment	Intervention groups had a reduced incidence of pyelonephritis (RR, 0.23 [95% CI, 0.13–0.41]) and low-birthweight babies (RR, 0.66 [CI, 0.49–0.89]) Results from 3 trials that measured the outcome of preterm delivery showed no statistically significant effect of the intervention (RR, 0.37 [CI, 0.10–1.36])	A prior Cochrane review (4) had found a reduction in the incidence of preterm delivery when birthweight of <2500 g was assumed to be preterm birth	Treating asymptomatic bacteriuria in pregnancy reduced the incidence of pyelonephritis and low-birthweight babies
Harding et al., 2002 (5)	Randomized, double-blind, placebo-controlled trial	105 nonpregnant women age >16 y with diabetes, normal renal function, and asymptomatic bacteriuria confirmed in 2 consecutive urine cultures	Trimethoprim–sulfamethoxazole (or ciprofloxacin if resistant organism or patient was allergic to sulfa drugs) twice daily for 14 d vs. no treatment	After a mean follow-up of 27 mo, no statistically significant differences were seen between intervention and placebo groups in symptomatic UTIs, pyelonephritis, or hospitalization for a UTI	Patients in the placebo group averaged 34 d of antibiotic use per 1000 d of follow-up, compared with 158 d of antibiotic use in the treatment group	Treating asymptomatic bacteriuria in nonpregnant women with diabetes increased antibiotic use but did not improve outcomes
Meiland et al., 2006 (6)	Prospective cohort	644 nonpregnant women age ≥18 y with diabetes	17% of the study sample had asymptomatic bacteriuria based on a screening urine culture; outcomes for these participants were compared with those in participants without asymptomatic bacteriuria	After a mean follow-up of 6.1 y, there was no association (after multivariate adjustment) between the presence of asymptomatic bacteriuria and creatinine clearance or the development of hypertension	The multivariate analysis adjusted for patient age, length of follow-up, duration of diabetes, and presence of microalbuminuria at study entry	Asymptomatic bacteriuria was not associated with renal function decline or the development of hypertension in nonpregnant women with diabetes

RR = relative risk; UTI = urinary tract infection.

Nonpregnant Women

We found 1 good-quality RCT of treatment that compared antibiotics with placebo in diabetic women with asymptomatic bacteriuria (5). Endocrinology offices in 2 tertiary care hospitals and community practices in Canada recruited 105 participants. Eligible patients were nonpregnant women older than 16 years of age with diabetes, normal renal function, no symptoms consistent with a urinary tract infection, and 2 consecutive positive urine cultures ($\geq 10^5$ colony-forming units of an organism per mL of urine). After randomization, patients received either trimethoprim-sulfamethoxazole (or ciprofloxacin if they could not use sulfa drugs) or placebo. Four weeks after treatment, and every 3 months for up to 36 months, investigators rescreened patients for bacteriuria with urine cultures. Patients in the experimental group with positive results received additional antibiotics for progressively longer periods. Patients in either group who developed symptomatic urinary infections were also treated with the study drugs.

After the initial round of therapy, significantly ($P < 0.001$) more women in the placebo group continued to have bacteriuria. However, during follow-up, the time to symptoms consistent with a urinary tract infection was similar in both groups. The placebo group was no more likely than the treatment group to have a symptomatic urinary tract infection (RR, 1.19 [CI, 0.28 to 1.81]), pyelonephritis (RR, 2.13 [CI, 0.81 to 5.62]), or hospitalization for a urinary tract infection (RR, 1.93 [CI, 0.47 to 7.89]). Patients in the placebo group averaged 34 days of antibiotic use per 1000 days of follow-up, compared with 158 days of antibiotic use per 1000 days of follow-up in the treatment group.

Two additional clinically important outcomes thought to be related to asymptomatic bacteriuria are renal function decline and development of hypertension. We identified a multicenter prospective cohort study of interest that did not meet inclusion criteria for this review because it was not a randomized trial (6). We present it here as a good-quality study that contributed to the USPSTF's understanding of screening for asymptomatic bacteriuria in women with diabetes.

A total of 644 women with type 1 and type 2 diabetes, who were from hospital outpatient diabetic clinics in the Netherlands, were evaluated for asymptomatic bacteriuria and monitored for a mean of 6.1 years for changes in creatinine clearance and blood pressure. A multivariate analysis, adjusted for patient age, length of follow-up, duration of diabetes, and presence of microalbuminuria at study entry, found no association between the presence of asymptomatic bacteriuria and subsequent changes in creatinine clearance. Similarly, investigators observed no relationship between asymptomatic bacteriuria and the development of hypertension. These findings suggest that screening and treatment for asymptomatic bacteriuria in women with diabetes would have no effect on either outcome.

Men

We identified no studies of screening or treatment for asymptomatic bacteriuria in men.

2. What Are the Harms of Screening for Asymptomatic Bacteriuria in Pregnant Women, Nonpregnant Women, and Men?

We identified no new studies of the harms of screening for asymptomatic bacteriuria in pregnant women, nonpregnant women, or men.

DISCUSSION

Although urine culture remains the gold standard for screening for and diagnosis of asymptomatic bacteriuria in pregnant women, it is time- and labor-intensive and patients may have difficulty providing uncontaminated samples for testing. It would be useful to identify a rapid test with a high negative predictive value for asymptomatic bacteriuria that could replace urine culture as a screening test. Urine cultures would then be performed only on patients with positive screening results.

The 2004 USPSTF evidence update on screening for asymptomatic bacteriuria (7) highlighted the Uriscreen (Savyon Diagnostics, Ashdod, Israel) enzymatic screening test as having good potential because of its reported 100% sensitivity and negative predictive value in 1 study of 313 consecutive pregnant patients in Israel. However, in a 2005 study of 150 asymptomatic pregnant women in Venezuela, the test detected only 17 of 28 patients whose catheterized urine samples showed bacteriuria, yielding a sensitivity of 60.7% and negative predictive value of 90.8% compared with urine culture (8).

Whether pregnant women benefit from additional screening for asymptomatic bacteriuria after the first trimester is unknown. A 2005 Canadian study conducted in outpatient clinics at an urban teaching hospital compared the diagnostic yield of a single urine culture, 2 urine cultures, and 3 urine cultures at fewer than 20 weeks', 28 weeks', and 36 weeks' gestation (9). Additional cultures were performed at routine prenatal visits if a leukocyte esterase-nitrite test result was positive; the gold standard for asymptomatic bacteriuria was any single positive urine culture.

Forty-nine of the 1050 patients in the Canadian study had asymptomatic bacteriuria. A single urine culture before 20 weeks' gestation (consistent with the USPSTF recommendation) detected only 40.8% of cases, whereas the 3-urine-culture strategy detected 87.8% of cases. However, the study did not assess the effect of increased detection on clinical outcomes.

In summary, we found some new evidence that continues to support screening for asymptomatic bacteriuria in pregnant women, as well as evidence that suggests no benefit from screening other groups of adults. No currently available screening tests have a high enough sensitivity and negative predictive value for asymptomatic bacteriuria in

pregnant women to replace the urine culture. Future research is needed to clarify the optimal timing and periodicity of screening in pregnant women.

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