This guideline from the Canadian Task Force on Preventive Health Care focuses on screening for asymptomatic bacteriuria in pregnancy and re-examines the evidence supporting this routine practice in prenatal care.

Asymptomatic bacteriuria is defined as a quantitative count of > 100 × 10^6 colony-forming units of bacteria per litre (CFU/L) of urine without specific symptoms of a urinary tract infection.1 Women with diabetes, recurrent urinary tract infections, polycystic kidneys, other congenital renal anomalies and sickle cell disease are at higher risk for asymptomatic bacteriuria and associated complications in pregnancy.1–3 Prevalence of asymptomatic bacteriuria has been estimated to be 2%–10% in premenopausal ambulatory women,3 although the task force did not identify published rates of asymptomatic bacteriuria during pregnancy in Canada.

Depending on the setting and date of the report, there is considerable variation in the reported risk of pyelonephritis associated with untreated asymptomatic bacteriuria in pregnancy.4–7 Pyelonephritis has been associated with maternal septicemia, renal dysfunction and anemia,8 as well as adverse fetal outcomes, such as low birth weight and preterm birth.3,9 Conversely, a recent study found asymptomatic bacteriuria was not associated with preterm birth.4 Hence, the relationship between asymptomatic bacteriuria and pregnancy complications is uncertain.

Screening for asymptomatic bacteriuria is done with the intention to treat with antibiotics when bacteriuria is identified. A screening guideline for asymptomatic bacteriuria must consider both potential benefits and possible harms of antibiotic treatment in pregnancy. Randomized controlled trials (RCTs) of antibiotic treatment for asymptomatic bacteriuria in pregnancy, however, have been criticized for poorly reporting harms of antibiotics and for other sources of bias.1

Current Canadian practice is to screen for asymptomatic bacteriuria in the first trimester of pregnancy, with antibiotic treatment for positive screens. In women with a history of recurrent urinary tract infections, the Society of Obstetricians and Gynaecologists of Canada recommends screening for asymptomatic bacteriuria in each trimester.10

Screening for asymptomatic bacteriuria is a part of routine prenatal care in Canada. In 1994, the Canadian Task Force on the Periodic Health Examination concluded that there was good evidence to support a recommendation in favour of screening for asymptomatic bacteriuria early in pregnancy (12–16 wk) using urine culture.11 The current task force saw the need for an updated guideline that considers evidence on the potential harms and benefits of screening for asymptomatic bacteriuria in pregnancy and that also considers women’s values and preferences regarding screening and resulting outcomes.

KEY POINTS

- Systematic reviews on screening and treating asymptomatic bacteriuria in pregnancy found very low-quality evidence for a modest reduction in pyelonephritis among pregnant women and the number of low-birth-weight infants.
- Only scant and very low-quality evidence was available to infer harms associated with screening and treatment of asymptomatic bacteriuria in pregnancy.
- Patient values and preferences regarding screening for asymptomatic bacteriuria are variable and influenced by individual perspectives regarding the small potential benefit of antibiotic use, as well as potential harms associated with antibiotic use in pregnancy.
- A weak recommendation in favour of screening is warranted given the small but uncertain benefit of screening for asymptomatic bacteriuria, variation in women’s values and preferences, and the judgment that harms associated with this long-standing practice in Canada are likely minimal.
- Some women who are not at increased risk of urinary tract infections in pregnancy and are more concerned with potential harms of antibiotics may choose not to be screened for asymptomatic bacteriuria; women at increased risk of urinary tract infections in pregnancy should follow guidance for higher-risk populations.

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CMAJ Podcasts: author interview at https://soundcloud.com/cmajpodcasts/171325-guide
The task force is an independent panel of clinicians and methodologists that makes recommendations on primary and secondary prevention in primary care (www.canadiantaskforce.ca). This document was developed by a working group of five task force members with scientific support from the Public Health Agency of Canada. The recommendations were informed by a systematic review with three key questions and patient engagement activities with women that addressed specific aspects of the guideline’s development (analytical framework, Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.171325/-/DC2).

The Evidence Review and Synthesis Centre conducted the systematic reviews at the University of Alberta between June and October 2016, and prepublication search updates in September and October 2017. The systematic review was carried out according to a registered protocol (PROSPERO: CRD42016045263). For review questions on screening effectiveness, values and preferences, and treatment effectiveness, the review centre conducted peer-reviewed database searches (from inception to September 2017) in MEDLINE, Embase, CINAHL, PubMed, the Cochrane Library and PsycINFO. PsycINFO was included only in the systematic review of values and preferences. Screening and treatment reviews excluded studies that focused on women at higher than average risk for bacteriuria, or who had recurrent urinary tract infections, or had symptoms of a urinary tract infection, polycystic kidneys, other congenital renal anomalies or sickle cell disease should follow guidance for higher-risk groups.

**Methods**

**Scope**

This guideline provides patients, clinicians and policy-makers with guidance on screening for asymptomatic bacteriuria in pregnancy. It focuses on women who are not at increased risk for asymptomatic bacteriuria. Women with diabetes, recurrent urinary tract infection, polycystic kidneys, other congenital renal anomalies or sickle cell disease should follow guidance for higher-risk groups.

**Recommendation**

We recommend screening pregnant women once during the first trimester with urine culture for asymptomatic bacteriuria (weak recommendation; very low-quality evidence).

This recommendation applies to pregnant women who are not experiencing symptoms of a urinary tract infection and are not at increased risk for asymptomatic bacteriuria.
Screening

The systematic review on outcomes of screening for asymptomatic bacteriuria did not identify any RCTs that compared the effects of screening with those of no screening. It did identify four observational studies, with a total of 7611 women, that compared screening to no screening.16–19 All four studies used nonconcurrent cohort designs to evaluate outcomes before and after screening practices began. Three studies examined outcomes of implementing universal screening versus no screening in Spain,14 Turkey17 and France.18 The fourth study, conducted in the United States, examined the effectiveness of screening at every prenatal visit versus at the first prenatal visit only.19

Meta-analysis16 of the three cohort studies (n = 5659) that compared screening to no screening16–18 found very low-quality evidence of an absolute risk reduction (ARR) for pyelonephritis of 13 fewer women per 1000 screened (ARR 1.3%, 95% confidence interval [CI] 8 to 16 fewer). The number needed to screen to prevent one case of pyelonephritis was 77 (95% CI 65 to 121) (Table 1).

Data for other screening outcomes, including harms, were also of very low quality. There were few events, and effect estimates were highly imprecise (Table 1). In two studies (n = 724), women screened for asymptomatic bacteriuria had four more cases of perinatal mortality per 1000 women screened (absolute risk increase [ARI] 0.4%, 95% CI 19 fewer to 1000 more).17,18 In the same two studies (n = 722), there were 102 more preterm deliveries per 1000 women screened (ARI 10.2%, 95% CI 9 fewer to 1000 more).17,18 Based on data from one study (n = 372), there were five more babies with fetal anomalies per 1000 women screened (ARI 0.5%, 95% CI 8 fewer to 85 more) and two fewer spontaneous abortions per 1000 women screened (n = 370, ARR 0.2%, 95% CI 32 fewer to 70 more).17

One study (n = 1952) compared the incidence of pyelonephritis among women who were screened using urine dipstick testing at every prenatal visit compared with women who were screened at the first prenatal visit only.17 This study found zero fewer cases of pyelonephritis per 1000 women who were screened at all visits compared with women screened at the first visit only (95% CI 3 fewer to 13 more).19 Risk of preterm delivery was higher in the group screened at all visits versus those screened only at the first visit (ARI 28 more women per 1000 [2.8%], 95% CI 5 more to 60 more).18 Evidence was rated as very low quality for both outcomes.

Treatment

Linked evidence on screening effectiveness was provided from an update of a 2015 Cochrane review,1 which compared antibiotic treatment with no treatment or placebo among pregnant women with asymptomatic bacteriuria. In total, there were 15 eligible studies, including one new study identified during the search update.4 Eleven studies were RCTs, and four were non-randomized controlled clinical trials. All but one, in Jamaica,20 were conducted in high-income countries, including the US,21–24 United Kingdom,25–27 Ireland,28 Australia,29–31 Denmark32 and the Netherlands.4 Studies varied in terms of testing protocols (e.g., timing during pregnancy, number of confirmatory urine
samples), treatment (e.g., dose, type of antibiotic) and follow-up periods.

Meta-analysis of 12 studies (n = 2017), including nine RCTs and three nonrandomized controlled clinical trials, found low-quality evidence for a statistically and clinically significant reduction in the rate of pyelonephritis among pregnant women with asymptomatic bacteriuria who were treated, compared with those not treated. The ARR was 176 fewer cases of pyelonephritis per 1000 women with asymptomatic bacteriuria who were treated, compared with those not treated (ARR 17.6%, 95% CI 137 fewer to 202 fewer, number needed to treat 6). Across seven studies (n = 1522), there was also low-quality evidence for a statistically significant reduction of 44 fewer low-birth-weight infants born per 1000 women with asymptomatic bacteriuria who were treated (ARR 4.4%, 95% CI 12 fewer to 65 fewer).

Very low-quality evidence was found for other treatment outcomes of interest, including harms of antibiotic treatment. No statistically significant or clinically important differences were found for perinatal mortality, spontaneous abortion, neonatal sepsis, preterm delivery or fetal anomalies (Table 2).

### Patient values and preferences

In total, 34 women from across Canada (ages 21–41), of whom 14 were pregnant, participated in online surveys and telephone focus groups across the two phases of engagement work. Women rated all the outcomes examined in the systematic reviews on screening effectiveness as critical, except for pyelonephritis, which they rated as important. The initial focus groups, before evidence synthesis, found that women weighed potential screening benefits as more important than possible harms of screening.

### Table 1: Outcome summary of screening versus no screening for asymptomatic bacteriuria among pregnant women

| Outcome               | No. of studies | Women screened (n/N) | Women not screened (n/N) | RR (95% CI) | Absolute difference per 1000 (95% CI) | ARR, % | ARI, % | Quality of evidence |
|-----------------------|----------------|----------------------|-------------------------|-------------|---------------------------------------|--------|--------|---------------------|
| Pyelonephritis        | 3, 16–18       | 10/2008              | 67/3651                 | 0.28        | (0.15 to 0.54)                        | 13 fewer (8 fewer to 16 fewer) | 1.3     | –                   | Very low            |
| Perinatal mortality   | 2, 17, 18      | 6/349                | 7/375                   | 1.21        | (0.01 to 2.27)                        | 4 more (19 fewer to 1000 more) | –       | 0.4                 | Very low            |
| Spontaneous abortion  | 1, 17          | 9/170                | 11/200                  | 0.96        | (0.32 to 2.27)                        | 2 fewer (19 fewer to 1000 more) | –       | 0.2                 | Very low            |
| Preterm delivery      | 2, 17, 18      | 33/347               | 5/375                   | 8.70        | (0.82 to 24.07)                       | 102 more (9 fewer to 1000 more) | –       | 10.2                | Very low            |
| Fetal anomalies       | 1, 17          | 3/186                | 2/186                   | 1.50        | (0.25 to 8.87)                        | 5 more (8 fewer to 85 more)    | –       | 0.5                 | Very low            |

Note: ARR = absolute risk reduction, ARI = absolute risk increase, CI = confidence interval, RR = risk ratio.

### Table 2: Outcome summary treatment v. no treatment for asymptomatic bacteriuria among pregnant women

| Outcome               | No. of studies | Women treated (n/N) | Women not treated (n/N) | RR (95% CI) | Absolute difference per 1000 (95% CI) | ARR, % | Quality of evidence |
|-----------------------|----------------|---------------------|-------------------------|-------------|---------------------------------------|--------|--------------------|
| Pyelonephritis        | 12, 4, 6, 20, 22–29, 31 | 55/1023             | 198/994                 | 0.24        | (0.13 to 0.41)                        | 176 fewer (137 fewer to 202 fewer) | 17.6    | Low                |
| Low birth weight      | 7, 6, 22, 25, 27, 29, 31 | 64/769              | 100/753                 | 0.63        | (0.45 to 0.90)                        | 44 fewer (12 fewer to 65 fewer)   | 4.4     | Low                |
| Perinatal mortality   | 6, 6, 22, 25, 29, 31     | 16/529              | 21/575                  | 0.96        | (0.27 to 3.39)                        | 2 fewer (29 fewer to 97 more)     | 0.2     | Very low           |
| Spontaneous abortion  | 2, 20, 31          | 4/222               | 6/157                   | 0.60        | (0.11 to 3.10)                        | 13 fewer (30 fewer to 70 more)    | 1.3     | Very low           |
| Neonatal sepsis       | 2, 3, 2           | 0/77                | 2/77                    | 0.22        | (0.01 to 4.54)                        | 17 fewer (22 fewer to 79 more)    | 1.7     | Very low           |
| Preterm delivery      | 4, 30–32           | 34/299              | 39/234                  | 0.57        | (0.21 to 1.56)                        | 68 fewer (125 fewer to 88 more)   | 6.8     | Very low           |
| Fetal anomalies       | 4, 22, 25, 30      | 4/425               | 10/396                  | 0.49        | (0.17 to 1.43)                        | 9 fewer (15 fewer to 8 more)      | 0.9     | Very low           |

Note: ARR = absolute risk reduction, CI = confidence interval, RR = risk ratio.
for asymptomatic bacteriuria, in part because the screening test was not in itself seen as harmful.

In the second phase of engagement, women were presented with synthesized evidence of screening and treatment effectiveness and were asked to consider whether they would undergo screening in light of this evidence. Women again did not see screening as harmful, but uncertainty regarding antibiotic use was a concern for some women. Women in the focus groups indicated a preference for screening, but some said they would reassess treatment decisions once they knew test results. Consequently, important variation in values and preferences was identified when women considered the evidence on overall benefits and harms of screening and subsequent treatment. Past experience with antibiotic use and pregnancy complications, as well as unknown harms to babies and women themselves, influenced their preferences both in favour and against treatment of asymptomatic bacteriuria in pregnancy.14

The systematic review did not find any studies that provided direct evidence on how women weigh the benefits versus harms of screening for asymptomatic bacteriuria, but did find indirect evidence (eight cross-sectional studies) on women’s opinions related to use of antibiotics in pregnancy.12 Similarly to the findings from the focus groups, these studies reached conflicting conclusions regarding antibiotic use during pregnancy, although there appears to be greater concern among pregnant women about risks of teratogenesis compared with risks to themselves.

Resource use
Current cost-effectiveness studies were not available to inform resource considerations. Lack of data on prevalence of asymptomatic bacteriuria and uncertain estimates of risk reduction limit capacity for accurately estimating cost-effectiveness.

Feasibility, acceptability, cost and equity
Urine culture, the gold standard for screening for asymptomatic bacteriuria, is part of standard prenatal care in Canada, and the task force judged it to be feasible and acceptable to clinicians and women. Task force members considered the cost of screening for asymptomatic bacteriuria to be relatively low compared with the overall costs of prenatal care in Canada. All systematic reviews informing this guideline were designed to conduct subgroup analyses to identify vulnerable groups. However, no data were available to inform specific recommendations or considerations for vulnerable groups.

Rationale
Overall, very low-quality evidence was found for the benefits and harms of screening for asymptomatic bacteriuria in pregnancy. Linked evidence on screening that considers the effectiveness of treating asymptomatic bacteriuria identified by screening was found. Low-quality evidence suggested that treatment modestly reduces the incidence of pyelonephritis and the number of low-birth-weight infants. It is a long-standing practice in Canada to provide routine screening and treatment of asymptomatic bacteriuria in pregnancy, and this may contribute to the apparently low prevalence of pyelonephritis among pregnant women in Canada. In addition, the resources required to provide such screening are modest. Therefore, in the judgment of the task force, the potential benefits of screening outweigh possible harms, and a weak recommendation in favour of screening is warranted. This recommendation places a relatively higher priority on the small but uncertain benefit of screening for asymptomatic bacteriuria and a relatively lower priority on the lack of evidence regarding serious harms associated with antibiotic use for pregnant women and their babies.

The recommendation is weak because of uncertainty regarding the benefits of screening, as well as the various preferences of women with respect to antibiotic treatment in pregnancy. Women who are interested in small, uncertain, potential reductions in risk of pyelonephritis and low birth weight will be more likely to choose screening for asymptomatic bacteriuria. However, women who are more concerned with potential harms of antibiotics may be more likely to choose not to be screened; in such circumstances, there is potential value for discussion between clinicians and patients in order to reach evidence-informed decisions that are congruent with patient values and preferences.

Considerations for implementation
The task force advises that screening should be conducted once in the first trimester with a urine culture, or at the first prenatal visit, if this visit occurs later in pregnancy. There is no evidence for an optimal screening time in pregnancy. For ease of implementation, this recommendation advises first-trimester screening, recognizing that not all women will present for prenatal care during the first trimester, and that screening may occur after the first trimester.

This recommendation pertains to women who are not at increased risk for asymptomatic bacteriuria and who are not experiencing symptoms of a urinary tract infection. Women with diabetes, recurrent urinary tract infections, polycystic kidneys, other congenital renal anomalies or sickle cell disease are not included in the recommendation, and their care should follow guidance for higher-risk groups. A history of recurrent urinary tract infection is defined as two uncomplicated infections in the past six months, or three positive cultures in the past 12 months.10

When urine cultures are not available, clinicians should be aware that alternatives have sufficient specificity but poor sensitivity for asymptomatic bacteriuria (e.g., 99% v. 55%, respectively, for urine dipstick)33 and thus fail to detect a substantial number of cases.24 The quality of evidence considering screening with a single urine culture compared with two urine cultures (for confirmation) was too poor to provide guidance on the appropriate strategy. All the evidence supporting a reduction in pyelonephritis from treatment studies included a test for cure. Clinicians should follow relevant treatment guidance for women with a positive screen for asymptomatic bacteriuria.10

Monitoring and evaluation
This is a weak recommendation, which recognizes that some women will choose to undergo screening, whereas others may
not. Therefore, clinician awareness of this recommendation is a performance measure for this guideline.

**Other guidelines**

Although this recommendation aligns with guidelines from other international organizations, the task force places lower certainty on the evidence than other groups (Table 3). This uncertainty contributes to a weak recommendation in favour of screening.

For example, the United States Preventive Services Task Force provides a grade A–level recommendation that advises screening all pregnant women at 12 to 16 weeks (or at first prenatal visit), based on “high certainty for a substantial net benefit” of treatment with antibiotics to reduce substantially the incidence of symptomatic maternal urinary tract infection and are not at increased risk for asymptomatic bacteriuria.

**Gaps in knowledge**

High-quality trials for screening and treatment of asymptomatic bacteriuria conducted in the current era of modern obstetrics were not available to inform this recommendation. It is possible that risks associated with asymptomatic bacteriuria may have decreased since the publication of studies informing this guideline. This, coupled with advances in prenatal care, may reduce the absolute benefits of screening. Studies evaluating rates of asymptomatic bacteriuria among pregnant women in Canada are required to inform accurate baseline risk. More information is also needed on independent factors that place some groups of women at clinically important risk for asymptomatic bacteriuria.

The studies included in the evidence review used various algorithms to confirm a positive asymptomatic bacteriuria diagnosis; further research is required to confirm best practice for diagnosis, such as the number of repeat urine cultures. Preference-based studies on how Canadian women weigh asymptomatic bacteriuria screening outcomes would be clinically useful to understand the proportion of women who choose and do not choose screening. A pragmatic trial design comparing treatment-based versus tolerant screening (e.g., those without a preference toward or against screening are randomized, while others self-select an intervention arm) that includes data on all critical outcomes is needed to determine more contemporary estimates of effectiveness. We are aware that one such trial has been deemed feasible and is underway for risk-based versus routine breast cancer screening in the US.

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**Table 3: National and international recommendations on screening for asymptomatic bacteriuria in pregnancy**

| Guideline group | Recommendation |
|-----------------|----------------|
| Canadian Task Force on Preventive Health Care (current guideline, 2018) | We recommend screening pregnant women once during the first trimester with urine culture for asymptomatic bacteriuria (weak recommendation; very low-quality evidence). This recommendation applies to pregnant women who are not experiencing symptoms of a urinary tract infection and are not at increased risk for asymptomatic bacteriuria. |
| Canadian Task Force on the Periodic Health Examination11 | Good evidence to include screening once by culture method for asymptomatic bacteriuria at 12–16 weeks of pregnancy. |
| United States Preventive Services Task Force34 | The United States Preventive Services Task Force recommends screening for asymptomatic bacteriuria with urine culture for pregnant women at 12 to 16 weeks’ gestation or at their first prenatal visit, if later. (Grade A: The United States Preventive Services Task Force recommends the service. There is high certainty that the net benefit is substantial.) |
| Scottish Intercollegiate Guidelines Network, Scotland35 | Standard quantitative urine culture should be performed routinely at first antenatal visit (Grade A). Confirm the presence of bacteriuria in the urine with a second urine culture (Grade A). Do not use dipstick testing to screen for bacterial urinary tract infection at the first or subsequent visits (Grade A). Treat asymptomatic bacteriuria detected during pregnancy with an antibiotic (Grade A). Women with bacteriuria that is confirmed by a second urine culture should be treated and have repeat urine culture at each antenatal visit until delivery (Grade C). |
| The National Institute for Health and Care Excellence, UK36 | Women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture early in pregnancy. Identification and treatment of asymptomatic bacteriuria reduce the risk of pyelonephritis. |
| The American Academy of Family Physicians37 | Pregnant women should be screened for asymptomatic bacteriuria in the first trimester of pregnancy (Grade A: consistent, good-quality patient-oriented evidence). Pregnant women who have asymptomatic bacteriuria should be treated with antimicrobial therapy for 3 to 7 days (Grade B: inconsistent or limited-quality patient-oriented evidence). |
| The Infectious Disease Society of America38 | The diagnosis of asymptomatic bacteriuria should be based on results of culture of a urine specimen collected in a manner that minimizes contamination (Grade A-II). Pregnant women should be screened for bacteriuria by urine culture at least once in early pregnancy, and they should be treated if the results are positive (Grade A-I). Periodic screening for recurrent bacteriuria should be undertaken after therapy (Grade A-III). No recommendation can be made for or against repeated screening of women who are culture negative in later pregnancy. |
Conclusion

Screening with urine culture during pregnancy and treatment of asymptomatic bacteriuria, defined as > 100 × 10^6 CFU/L of urine without specific symptoms of a urinary tract infection, is a long-standing practice in Canada that may provide a modest reduction in pyelonephritis for women and may reduce the number of low-birth-weight infants. Serious harms from antibiotics, although possible, were not reported in our systematic reviews.

This weak recommendation in favour of screening for asymptomatic bacteriuria in pregnancy recognizes that some women who are not at increased risk of asymptomatic bacteriuria in pregnancy and are more concerned with potential harms of antibiotics may choose not to be screened or treated for asymptomatic bacteriuria. In such circumstances, there is potential value for discussion between clinicians and patients in order to reach evidence-informed and values-based decisions. This guideline does not apply to women at increased risk of asymptomatic bacteriuria in pregnancy, who should follow guidance for higher-risk populations.

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