

Recommendations on Screening for asymptomatic bacteriuria in pregnancy (2018)

Guideline Presentation Speaker Deck

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ASB Working Group

The ASB Working Group included members from the Canadian Task Force on Preventive Health Care (CTFPHC) and the Public Health Agency of Canada (PHAC). Systematic reviews were conducted by the University of Alberta Evidence Review and Synthesis Centre.

CTFPHC members of the working group include:

- Ainsley Moore (Chair)
- Roland Grad
- Brett Thombs
- Stéphane Groulx
- Kevin Pottie
- Cello Tonelli

Public Health Agency of Canada (PHAC) members of the working group (non-voting members) include:

- Marion Doull
- Susan Courage
- Alejandra Jaramillo Garcia

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OVERVIEW OF WEBINAR

- We will review the following:
 - Background on screening for asymptomatic bacteriuria in pregnancy
 - Methods of the CTFPHC
 - Key Findings
 - Recommendation
 - Implementation Considerations
 - Conclusions

[Slide 5] BACKGROUND TITLE SLIDE

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BACKGROUND Definition:

Asymptomatic bacteriuria is defined as a quantitative count of $> 100 \times 10^6$ colony forming units of bacteria per litre (CFU/L) of urine without specific symptoms of a urinary tract infection (1).

Prevalence of asymptomatic bacteriuria has been estimated to be 2-10% in premenopausal ambulatory women (1), although the task force did not identify published rates of asymptomatic bacteriuria during pregnancy in Canada.

Uncertainty:

There is considerable variation and hence uncertainty in the reported risk of pyelonephritis associated with untreated asymptomatic bacteriuria in pregnancy, depending on the setting and date of the report (2-5).

Pyelonephritis has been associated with maternal septicemia, renal dysfunction, and anemia (6), as well as adverse fetal outcomes, such as low birth weight and preterm birth (1, 7).

On the other hand, a recent study found asymptomatic bacteriuria was not associated with preterm birth (2). Hence, the relationship between asymptomatic bacteriuria and pregnancy complications is uncertain.

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GUIDELINE SCOPE

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 weeks) 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.

This recommendation focuses on women who are not at increased risk for asymptomatic bacteriuria.

[Slide 8] METHODS – TITLE SLIDE

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Methods of the CTFPHC

The CTFPHC is an independent panel of clinicians and methodologists with expertise in prevention, primary care, literature synthesis, and critical appraisal. The mandate of the CTFPHC is to apply the latest evidence in preventive health care research to primary care practice and policy across Canada.

The Asymptomatic Bacteriuria Working Group is composed of 6 CTFPHC members who are supported by PHAC science officers and clinical experts to establish key research questions, an analytical framework, and clinical and patient outcomes.

The Evidence Review and Synthesis Centre (ERSC) undertakes a systematic review of the literature based on the analytical framework and according to The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods.

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CTFPHC Review Process

The CTFPHC conducts both an (i) internal review and (ii) external review of all its guidelines. The internal review process involves the guideline working group, the full CTFPHC, and PHAC science officers.

The external review process involves the review of the protocol, systematic review, and guideline by key stakeholders including: generalist and disease specific organizations; academic peer reviewers; and Federal, Provincial and Territorial stakeholder groups.

The Canadian Medical Association Journal (CMAJ), where most of the CTFPHC guidelines are published, undertakes its own independent peer review journal process.

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What Evidence Does The CTFPHC Consider?

The CTFPHC considered four types of evidence for the ASB guideline: direct evidence, linked evidence, and patient focus groups.

Direct evidence was examined through a screening review conducted by the University of Alberta Evidence Review and Synthesis Centre. This review examined the benefits and harms of screening and women's values in preferences in relation to screening.

Linked evidence on screening was examined through a systematic review on the benefits and harms of treatment for ASB. Women's preferences and values related to key outcomes were collected through

online surveys and telephone focus groups conducted by the St. Michael's Hospital (SMH) Knowledge Translation (KT) Program.

Feasibility, acceptability, cost, health equity are considered in the evidence to decision process.

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In total, six key questions were addressed by the screening and treatment systematic reviews.

Research Questions:

1. What are the benefits and harms of screening compared with no screening for asymptomatic bacteriuria in pregnancy? Are there subgroup differences for patient characteristics (e.g., socioeconomic status [SES])?
2. What are the comparative benefits and harms of screening programs with different screening methods or algorithms for asymptomatic bacteriuria in pregnancy?
3. How do women weigh the benefits and harms of screening and treatment of asymptomatic bacteriuria in pregnancy?
4. How do women's valuation of benefits and harms of screening and treatment inform their decisions to undergo screening?
5. What are the benefits and harms of antibiotic treatment compared with placebo or no treatment for asymptomatic bacteriuria in pregnancy?
6. What is the accuracy of point-of-care screening tests compared with urine culture for asymptomatic bacteriuria in pregnancy?

One final research question on Cost-effectiveness was included in the systematic review but was not addressed because studies on the cost-effectiveness of screening were not identified: *What is the cost-effectiveness of screening for asymptomatic bacteriuria in pregnancy? [Staged, not completed]*

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The population of interest for the ASB systematic review was asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria.

Studies that focused *exclusively* on women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent UTI, diabetes, and sickle cell disease), or with symptoms of UTI were excluded from the review.

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How Does the CTFPHC Grade Evidence?

The CTFPHC utilizes the GRADE system for providing clinical practice guideline recommendations based on a systematic review of the available evidence. The GRADE acronym stands for: Grading of Recommendations, Assessment, Development and Evaluation.

The GRADE system is composed of two main components:

1. **The quality of the evidence:** The quality of the evidence measures the degree of confidence that the available evidence correctly reflects the theoretical true effect of the intervention or service. It is graded as high, moderate, low or very low based on how likely further research is to change our confidence in the estimate of effect.
2. **The strength of recommendation:** The strength of the recommendation (strong/weak) is based on the quality of supporting evidence, the degree of uncertainty about the balance between desirable and undesirable effects, the degree of uncertainty or variability in values and preferences, and the degree of uncertainty about whether an intervention represents a wide use of resources.

The strength of the recommendations (strong or weak) is based on four factors:

1. The quality of the supporting evidence
2. The certainty about the balance between desirable and undesirable effects
3. The certainty or variability in the values and preferences of individuals
4. Resource use: the higher the costs of an intervention, the less likely a strong recommendation is warranted.

[Slide 15] KEY FINDINGS – TITLE SLIDE

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Key Findings: Screening

Overall, very low quality evidence was available on the effect of screening pregnant women. No randomized trials that compared screening to no screening. The review summarized results from four observational studies (n=7611) that looked at outcomes before and after initiation of screening.

Very low quality evidence suggested that screening modestly reduces the incidence of pyelonephritis by 13 fewer women per 1,000 screened (confidence interval ranged from 8-16 fewer). This is based on 3 cohort studies, with a sample size of 5659 women. The number needed to screen to prevent one case of pyelonephritis was 77.

Data for other screening outcomes: perinatal mortality, preterm deliveries, harms associated with

antibiotics (e.g. fetal anomalies), spontaneous abortions, were also of very low quality. There were no statistically or clinically significant differences..

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Key Findings: Treatment

Overall, low quality evidence was available on the effect of treating pregnant women who screened positive

The review included 15 studies, 11 were randomized controlled trials (RCTs), 4 were non-randomized controlled clinical trials (CCTs).

Meta-analysis of 12 studies (9 RCTs, 3 CCTs) based on a total sample size of 2017 found low quality evidence suggesting that treatment modestly reduces the incidence of pyelonephritis by 176 fewer cases per 1,000 women (confidence interval ranged from 137 to 202 fewer). The number needed to treat to prevent one case of pyelonephritis was 6.

Meta-analysis of 7 studies based on a total sample size of 1522 women, found low quality evidence suggesting that treatment modestly reduces the number of low birth weight infants (44 fewer infant per 1,000 women with asymptomatic bacteriuria who were treated). The number needed to treat to prevent one low birth weight infant was 4.

Overall there was very low quality evidence found for harms of antibiotic treatment. No statistically or clinically important differences for perinatal mortality, spontaneous abortion, neonatal sepsis, preterm delivery or fetal anomalies.

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Patient Values and Preferences

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 (8 cross-sectional studies) on women's opinions related to use of antibiotics in pregnancy (12).

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.

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 weighed potential screening benefits as more important than possible harms of screening for asymptomatic bacteriuria, in part because the screening test was not in itself seen as harmful.

Uncertainty regarding antibiotic use was a concern for some women. Women in the focus groups indicated a preference for screening, but some indicated they would re-assess 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.

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Resource Use

Current cost-effectiveness studies were not available to inform resource considerations.

The task force considered the cost of screening for asymptomatic bacteriuria to be relatively low compared to overall costs of prenatal care in Canada.

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Feasibility, Acceptability and Equity

Urine culture, the gold standard for screening for asymptomatic bacteriuria, is part of standard prenatal care in Canada, and was judged by the task force to be **feasible and acceptable** to clinicians and women.

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.

[Slide 21] RECOMMENDATION TITLE SLIDE

[Slide 22] RECOMMENDATION

Recommendations for Screening for asymptomatic bacteriuria in pregnancy

These guidelines provide recommendations for practitioners on preventive health screening in a primary care setting.

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 UTI and are not at increased risk for asymptomatic bacteriuria.

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Overall Quality of Evidence

Overall quality of evidence supporting this recommendation is considered **very low** (i.e., highly uncertain), given the small, observational nature (cohort design) of the four included screening studies as well as other limitations.

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Rationale for Recommendation

Overall, very low quality evidence was available on the effect of screening pregnant women.

Very low quality evidence suggested that screening modestly reduces the incidence of pyelonephritis. Low-quality evidence suggested that treatment modestly reduces the incidence of pyelonephritis and the number of low birth weight infants.

Very low quality of evidence for harms of antibiotic treatment resulting in high uncertainty about these harms.

Resources required to provide screening for asymptomatic bacteriuria are modest in the context of prenatal care costs (cost effectiveness studies not available). There was wide variation in women's valuation regarding antibiotic use in pregnancy.

Therefore, considering the balance of consequences, the Task Force provides a weak recommendation in favour of screening.

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Rationale for weak recommendation in favour of screening

This recommendation places a relatively higher value on:

- the **small but uncertain benefit of screening** for asymptomatic bacteriuria

This recommendation places a relatively lower value on:

- **the lack of evidence regarding serious harms** associated with antibiotic use for pregnant women and their babies
- This recommendation 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

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Comparison: CTFPHC guideline vs. other recommendations

This recommendation **aligns** with guidelines from other international organizations, however, the task force places lower certainty on the evidence than other groups.

For example, the United States Preventive Services Task Force (USPSTF) provides a Grade A level recommendation advising screening all pregnant women at 12 to 16 weeks (or first prenatal visit) based on “high certainty for a substantial net benefit” of treatment with antibiotics to significantly reduce the incidence of symptomatic maternal UTIs (8).

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Knowledge Gaps

- High quality asymptomatic bacteriuria screening and treatment trials conducted in the current era of modern obstetrics were not available to inform this recommendation.
- A pragmatic preference-based/tolerant screening trial design (e.g., those without a preference towards/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 USA) (10).
- Studies evaluating prevalence of asymptomatic bacteriuria among pregnant women in Canada are recommended to inform accurate baseline risk.

[Slide 28] Knowledge Gaps

- 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 to confirm best practice for diagnosis such as the number of repeat urine cultures is recommended.
- Valuation studies on how Canadian women weigh asymptomatic bacteriuria screening outcomes would be clinically useful to understand the proportion of women choosing to be screened and not choosing to be screened.

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Considerations for Re-Evaluating the CTFPHC Guideline on Screening for Asymptomatic Bacteriuria

- Emergence of new high quality evidence on screening and treating asymptomatic bacteriuria in pregnancy to provide contemporary evidence on the effectiveness of screening.

[Slide 30] IMPLEMENTATION – TITLE SLIDE

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Considerations for Implementation

CTFPHC advises that screening should occur once in the first trimester with a urine culture or at the first prenatal visit if this visit occurs later in pregnancy. No evidence exists 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 UTI.

Women with diabetes, recurrent UTI, 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.

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Considerations for Implementation

When urine cultures are not available, clinicians should be aware that alternative tests have sufficient specificity but poor sensitivity for asymptomatic bacteriuria (e.g., 99% vs. 55%, respectively for urine dipstick) (9) and thus fail to detect a substantial number of cases (8).

The quality of evidence considering screening with a single urine culture compared to 2 urine cultures (for confirmation) was too poor to provide guidance on the appropriate strategy. Clinicians should follow relevant treatment guidance for screen positive women.

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Knowledge Translation (KT) Tools

- CTFPHC has created a Q&A KT tool to support clinicians/patients with implementing the guideline into **clinical practice**
- After guideline release, this tool will be **freely available** in both **French** and **English** on the website: www.canadiantaskforce.ca

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Conclusions – TITLE SLIDE

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Screening with urine culture during pregnancy and treatment of asymptomatic bacteriuria, ($> 100 \times 10^6$ CFU/L of urine without specific symptoms of a UTI) 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.

There is considerable variation in how women weigh the harms and benefits of antibiotic use in pregnancy

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Conclusions: Key Points

The CTFPHC recommends screening asymptomatic women *not at increased risk* with a single urine culture once during pregnancy.

This **weak recommendation** indicates uncertainty regarding benefits outweighing harms.

Some women concerned about antibiotic use in pregnancy may not want to be screened. Clinicians should consider the potential value for shared decision making in such circumstances given uncertain benefit.

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More Information

For more information on the details of this guideline please see: Canadian Task Force on Preventive Health Care website: <http://canadiantaskforce.ca>

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Questions & Answers

Thank you

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