



Canadian Task Force
on Preventive Health Care

Screening for asymptomatic bacteriuria in pregnancy (2018)

Canadian Task Force on Preventive Health Care (CTFPHC)

Putting Prevention into Practice

Use of Slide Deck

- These slides are made **available publicly** following the guideline's release as an educational support to assist with the dissemination, uptake and implementation of the guidelines into primary care practice
- Some or all of the slides in this slide deck may be used in educational contexts



Asymptomatic Bacteriuria in Pregnancy Working Group

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Overview of Webinar

- **Presentation**

- Background on screening for asymptomatic bacteriuria in pregnancy
- Methods of the CTFPHC
- Key Findings
- Recommendation
- Implementation Considerations
- Conclusions

- **Questions and Answers**





Screening for asymptomatic bacteriuria in pregnancy

BACKGROUND

Background

Definition:

- $> 100 \times 10^6$ colony forming units of bacteria per litre (CFL/L) of urine without symptoms of a urinary tract infection

Prevalence:

- 2-10% in premenopausal ambulatory women (1);
- CTFPHC did not identify published rates of ASB during pregnancy in Canada.

Uncertainty:

- Considerable variation in reported association between untreated ASB and pyelonephritis, depending on setting and date of the report (2-5).
- Pyelonephritis has been associated with maternal septicemia, renal dysfunction, and anemia (6), as well as 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.



Guideline Scope

- Screening for asymptomatic bacteriuria is a part of routine prenatal care in Canada.
- In 1994 the previous *Canadian Task Force on the Periodic Health Exam* concluded that there was good evidence to support a recommendation in favour of screening for asymptomatic bacteriuria early in pregnancy (12-16 weeks).
- The current task force saw the need for an **up-to-date guideline** that considers evidence on the potential harms and benefits of screening and also considers women's values and preferences.
- This recommendation focuses on women who are not at increased risk for asymptomatic bacteriuria.





Screening for asymptomatic bacteriuria in pregnancy

METHODS

Methods of the CTFPHC

Independent panel of:

Clinicians and methodologists

Expertise in prevention, primary care, literature synthesis, and critical appraisal

Application of evidence to practice and policy

Working Group

- 6 CTFPHC members
- Establish research questions and analytical framework

Evidence Review and Synthesis Centre (ERSC)

- Undertakes a systematic review of the literature based on the analytical framework
- Prepares a systematic review of the evidence with GRADE tables



CTFPHC Review Process

- **Internal review process** involving:
 - Guideline working group, CTFPHC, and PHAC scientific officers
- **External review is undertaken at key stages:**
 - Protocol, systematic review, and guideline
- **External stakeholder and peer reviewer groups:**
 - Generalist and disease specific stakeholders
 - Federal and P/T stakeholders
 - Academic peer reviewers
- **CMAJ undertakes an independent peer review process** to review guidelines prior to publication



What Evidence Does The CTFPHC Consider?

- Screening review
 - Benefits and harms of screening
 - Patient values and preferences
- Indirect evidence
 - Benefits and harms of treatment
- **Patient focus groups:** patient preferences and values related to key outcomes
- **Feasibility, acceptability, cost, health equity**



Research Questions: Systematic review screening for ASB

- (2) key research questions on **benefits and harms** of screening and treatment with antibiotics
- (1) key question on **women's values and preferences** focused on how **women weigh benefits and harms of screening** and how these valuations **affect decisions to be screened**
- (1) key question on **cost-effectiveness**; not completed as there was not enough evidence for benefits
- (1) key question on **diagnostic accuracy**
- For more detailed information, please access the systematic review www.canadiantaskforce.ca



Eligible Study Types

- **Population:** Asymptomatic pregnant women at any stage of pregnancy who are not at high risk for bacteriuria.
- **Exclude:** studies *exclusively* including women with conditions that place them at substantially higher than average risk of bacteriuria (kidney infection, urogenital anomalies, polycystic kidneys, recurrent UTI, diabetes, and sickle cell disease), or with symptoms of UTI

	KQ1a/b: Screening	KQ4: Treatment
Study Type	RCTs, CCTs, controlled observational (i.e., prospective and retrospective cohorts, case-control, controlled before-after)	RCTs (or systematic review(s))
Outcomes	<i>Benefits:</i> maternal mortality; maternal sepsis; pyelonephritis; perinatal mortality (≥ 20 weeks' gestation [e.g., intrauterine demise, stillbirth, early neonatal death]); spontaneous abortion/pregnancy loss before 20 weeks' gestation; neonatal sepsis; preterm delivery (live fetus passed < 37 week's gestation); low birth weight (< 2500 g) <i>Harms:</i> serious and non-serious adverse events	



How Does the CTFPHC Grade Evidence?

The “**GRADE**” System:

- **G**radings of **R**ecommendations, **A**ssessment, **D**evelopment & **E**valuation

1. Quality of Evidence

- Confidence that the available evidence **correctly reflects the theoretical true effect**

High, Moderate, Low, Very Low

2. Strength of Recommendation

- Quality of **supporting evidence**
- **Desirable and undesirable effects**
- **Values and preferences**
- **Cost, feasibility, acceptability, equity**

Strong, Weak





Screening for asymptomatic bacteriuria in pregnancy

KEY FINDINGS

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
 - Four observational studies (n=7611) that looked at outcomes before and after initiation of screening
 - Very low quality evidence from 3 cohort studies (n=5659) suggested that screening modestly reduces the incidence of pyelonephritis by 13 fewer women per 1,000 screened (confidence interval ranged from 8-16 fewer)
 - The number needed to screen to prevent one case of pyelonephritis was 77
 - Data for other screening outcomes: perinatal mortality, preterm deliveries, fetal anomalies, spontaneous abortions, were also of very low quality. There were no statistically or clinically significant differences.



Key Findings: Treatment

- **Overall, low quality evidence was available on the effect of treating pregnant women who screened positive:**
 - 15 included studies, 11 were randomized controlled trials (RCTs), 4 were non-randomized controlled clinical trials (CCTs)
 - Meta-analysis of 12 studies (9 RCTs, 3 CCTs) (n=2017) found low quality evidence suggested 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 suggested that treatment modestly reduces the number of low birth weight infants (44 fewer infants per 1,000 women with asymptomatic bacteriuria who were treated; number needed to treat was 4)
 - Very low quality of evidence for harms of antibiotic treatment.
 - No statistically or clinically important differences for perinatal mortality, spontaneous abortion, neonatal sepsis, preterm delivery, fetal anomalies.



Patient Values and Preferences

Systematic Review (8 cross-sectional studies):

Indirect evidence on women's opinions about antibiotic use in pregnancy

Women's preferences were **variable**

Important decision-making concerns:

- **Risk to baby with antibiotic use**

CTFPHC-Commissioned Survey and Focus groups (34 women):

More value placed on **benefits** than **harms** of screening

Screening test not seen as harmful; treatment decision viewed separately

Uncertainty about **antibiotic use** in pregnancy.



Resource Use

- Current cost-effectiveness studies were not available to inform resource considerations.
- Task force considered the cost of screening for asymptomatic bacteriuria to be relatively low compared to overall costs of prenatal care in Canada.



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.





Screening for asymptomatic bacteriuria in pregnancy

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.*



Overall Quality of Evidence

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



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 and high uncertainty for harms of antibiotic treatment
 - Resources required to provide screening for asymptomatic bacteriuria are modest in the context of prenatal care costs (cost effectiveness studies not available)
 - 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



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.



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).



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.



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.



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





Screening for asymptomatic bacteriuria in pregnancy

IMPLEMENTATION CONSIDERATIONS

Considerations for Implementation

- 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.
- This recommendation pertains to women who are **not at increased risk** for asymptomatic bacteriuria and who are not experiencing symptoms of a UTI.



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.



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

Clinician FAQ  Canadian Task Force on Preventive Health Care

SCREENING FOR ASYMPTOMATIC BACTERIURIA IN PREGNANCY



Recommendation

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

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

- 1. Who is at increased risk for asymptomatic bacteriuria?**
 - Women with diabetes, recurrent urinary tract infections, polycystic kidneys, other kidney defects from birth, and sickle cell disease are at higher risk for asymptomatic bacteriuria and associated complications for mothers and babies.
- 2. What are some considerations for implementing this recommendation?**
 - Patient preferences
 - Screening decisions are influenced by how women weigh possible benefits of preventing infection against potential harms of taking antibiotics during pregnancy.
 - Timing
 - For ease of implementation, we recommend one-time screening in the first trimester.
 - However we recognize that not all patients will present for prenatal care during their first trimester and that screening may occur after the first trimester.
- 3. What are the benefits and harms of screening for asymptomatic bacteriuria in pregnancy?**
 - Screening 1,000 pregnant women will potentially result in 1 to 5 fewer babies born with low birth weight (<2500 g).
 - Screening 1,000 pregnant women will potentially result in 4 to 16 fewer women developing a kidney infection.
 - Only limited and very low quality evidence is available to infer harms associated with screening and treatment of asymptomatic bacteriuria for women and their babies.
- 4. Why is it a weak recommendation?**
 - The recommendation is weak because of uncertainty regarding the benefits of screening as well as the various preferences of women regarding antibiotic treatment in pregnancy.
 - A weak recommendation for screening 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 mothers and their babies.
- 5. What does a weak recommendation mean?**
 - A weak recommendation in favour of screening highlights the need for shared decision-making with patients because many will want to be screened, but some will not.
- 6. What do you do with a positive test result?**
 - Treatment of a positive urine test should be guided by results of the urine culture and sensitivity.

*For information on how evidence is evaluated, how strength of recommendations are made, and to access our guidelines, tools, and resources, visit our website at www.canadiantaskforce.ca

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Screening for asymptomatic bacteriuria in pregnancy

CONCLUSIONS

Conclusions: Key Points

- 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



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.



More Information

For more information on the details of this guideline please see:

- Canadian Task Force on Preventive Health Care website: <http://canadiantaskforce.ca>



Questions & Answers

Thank you





Screening for asymptomatic bacteriuria in pregnancy

Reference Materials

CTFPHC Review Process

- Internal review process involving guideline working group, CTFPHC, PHAC scientific officers, and ERSC staff
- External review process involving key stakeholders
 - Generalist and disease-specific stakeholders
 - Federal and Provincial/Territorial stakeholders
- CMAJ undertakes an independent peer review process to review guidelines



Research Questions

Review question(s)

KQ1: 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])?

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

KQ2a: How do women weigh the benefits and harms of screening and treatment of asymptomatic bacteriuria in pregnancy?

KQ2b: How do women's valuation of benefits and harms of screening and treatment inform their decisions to undergo screening?

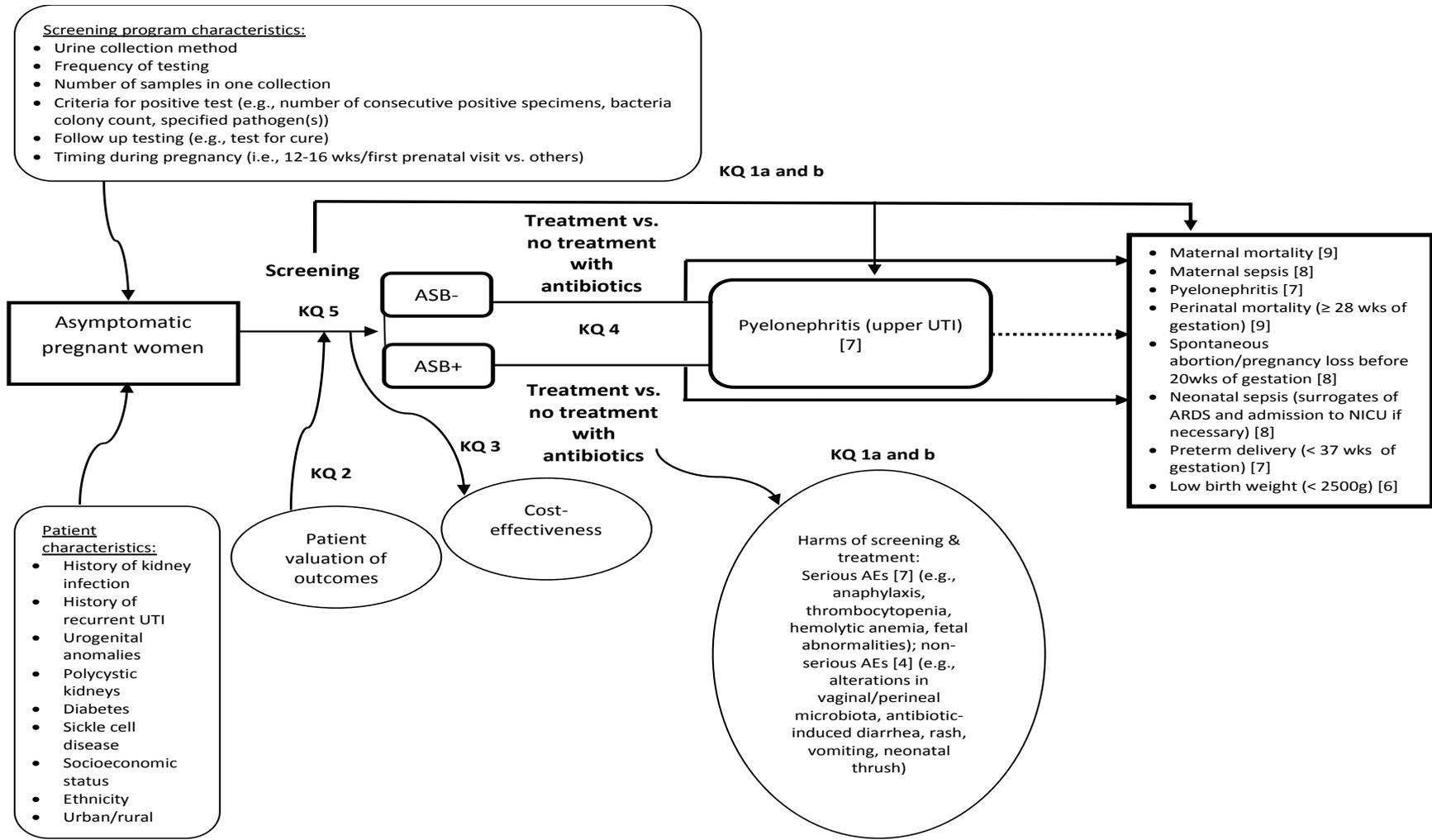
KQ3: What is the cost-effectiveness of screening for asymptomatic bacteriuria in pregnancy? [Staged, not completed]

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

KQ5: What is the accuracy of point-of-care screening tests compared with urine culture for asymptomatic bacteriuria in pregnancy?



Analytical Framework



Interpretation of Recommendations

Implications	Strong Recommendation	Weak Recommendations
For patients	<ul style="list-style-type: none"> • Most individuals would want the recommended course of action; • only a small proportion would not. 	<ul style="list-style-type: none"> • The majority of individuals in this situation would want the suggested course of action but many would not.
For clinicians	<ul style="list-style-type: none"> • Most individuals should receive the intervention. 	<ul style="list-style-type: none"> • Recognize that different choices will be appropriate for individual patients; • Clinicians must help patients make management decisions consistent with values and preferences.
For policy makers	<ul style="list-style-type: none"> • The recommendation can be adapted as policy in most situations. 	<ul style="list-style-type: none"> • Policy making will require substantial debate and involvement of various stakeholders.



Comparison: CTFPHC guideline vs. other recommendations

Organization	Recommendation
Canadian Task Force on Preventive Health Care (current)	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.
United States Preventive Services Task Force (2008)	USPSTF 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 USPSTF recommends the service. There is high certainty that the net benefit is substantial.
NICE, UK (2016)	Women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture early in pregnancy. Identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis.
SIGN, Scotland (2016)	Standard quantitative urine culture should be performed routinely at first antenatal visit (Grade A).



Values and Preferences

- In total, 34 individuals 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.
- The initial focus groups, prior to evidence synthesis, found that 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.
- 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.
- Screening was again not seen as harmful but **uncertainty regarding antibiotic use** was a concern for some women.
- The systematic review **did not find any studies** that provided direct evidence on how women weigh the benefits versus harms of screening but did find indirect evidence (8 cross-sectional studies) on women's opinions related to use of antibiotics in pregnancy.
- Similar 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.



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