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CADTH HEALTH TECHNOLOGY ASSESSMENT

Screening for *Chlamydia Trachomatis* and *Neisseria Gonorrhoeae* During Pregnancy: A Health Technology Assessment

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Acknowledgements / Contributors

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Conflicts of Interest

The authors declared no conflicts of interest relevant to this report.

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Abbreviations

ACOG	American College of Obstetricians and Gynecologists
CCI	Canadian Classification of Health Interventions
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CNIB	Canadian National Institute for the Blind
COS	Canadian Ophthalmological Society
CPS	Canadian Paediatric Society
CT	*Chlamydia trachomatis*
EPDS	Edinburgh Postnatal Depression Scale
GC	*Neisseria gonorrhoeae*
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HTA	health technology assessment
HUI3	Health Utilities Index 3
ICD10CA	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada
ICER	incremental cost-effectiveness ratio
ICUR	incremental cost-utility ratio
M/L	moderate-to-late
NAAT	nucleic acid amplification test
NR	not reported
OCCI	Ontario Case Costing Initiative
ON	ophthalmia neonatorum
OR	odds ratio
PCR	polymerase chain reaction
PHAC	Public Health Agency of Canada
PRISMA	Preferred Reporting Items for Systematic Reviews
QALY	quality-adjusted life-year
RoBANS	Risk of Bias Assessment Tool for Non-randomized studies
SD	standard deviation
SDA	strand displacement amplification
SR	systematic review
SROC	Summary receiver operating characteristic
STI	sexually transmitted infection
TMA	transcription-mediated amplification
TOC	test-of-cure
USPSTF	United States Preventive Services Task Force

Glossary

The economic analysis in this report uses a four-letter acronym convention to label the screening strategies. Each letter corresponds to a type of screening scheduled at each of the trimesters and during labour and delivery in a chronological order; whereby, the first letter corresponds to the first trimester, the second letter corresponds to the second trimester, the third letter corresponds to the third trimester, and the fourth letter corresponds to labour and delivery. Each letter is coded in the following manner:

N no screening

M mixed screening of age-based subgroups of the pregnant population (i.e., those who are younger than 25 years and those who are 25 years or older) based on other criteria (e.g., prior screening history).

T age-targeted screening; whereby, only the pregnant population that included those who are younger than 25 years are screened.

U universal screening

For example, screening strategy TNUM would indicate age-targeted screening in the first trimester, no screening in the second trimester, universal screening in the third trimester, and mixed screening during labour and delivery.

Protocol Amendments

Section	Amendment	Page
Clinical Review	The protocol indicated that studies using more than one test type would be excluded if results using nucleic acid amplification tests (NAATs) and culture are not reported independently. As only eight citations met the inclusion/exclusion criteria, two additional studies were also included — one that reported findings separately for NAATs and culture and one that did not report the screening test.	p. 9
Clinical Review	Data abstraction was not piloted on a random sample of three publications. Due to the small number of eligible studies, piloting was deemed unnecessary. The data abstraction was completed by one reviewer and verified by a second reviewer.	p. 13
Clinical Review	GRADE evidence profile tables were not created using the GRADEpro software package. Tables were created using Microsoft Word.	p. 15
Economic Analysis	The research question was revised to better align the economic analysis to the narrower scope of the health technology assessment.	p.7, p.16 and p. 20
Economic Analysis	The time horizon was shifted to capture the period from the time of first trimester screening (12 weeks gestation) to 19 weeks postpartum.[1]	p. 16

Executive Summary

Issue

Chlamydia trachomatis (CT) and *Neisseria gonorrhoeae* (GC) are the most commonly reported sexually transmitted infections (STIs) in Canada. Untreated infections are associated with substantial morbidity which in pregnant persons can have serious implications. The potential to cause downstream sequelae to the birthing parents and their fetus or neonate (i.e., newborn) are of particular concern. There is a pan-Canadian need for guidance on the optimal approach (i.e., universal or targeted), test (e.g., type of nucleic acid amplification tests [NAATs], culture), specimen (e.g., urine, vaginal, cervical), frequency (i.e., once or multiple times), and timing (e.g., first trimester, test-of-cure, third trimester, at delivery) for CT and GC screening during pregnancy. A comprehensive and multidisciplinary review of the literature is required to guide policy-makers on important considerations for formulating new guidelines for a national screening strategy.

Objectives

The purpose of this health technology assessment (HTA) is to conduct a systematic assessment of the clinical effectiveness, safety, cost-effectiveness, and perspectives and experiences of pregnant persons, partners, and health care providers regarding the screening of pregnant persons for CT and GC during pregnancy.

Clinical Evidence

Methods

A systematic review of primary comparative clinical studies was conducted using MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and PubMed. The Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS) was used to guide the quality assessment of the included non-randomized studies. The overall quality of the body evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to provide an assessment of the overall confidence in the estimated effect for each outcome of interest.

Studies were selected if they included pregnant adults and adolescents (≥ 12 years of age, up to and including delivery), involving the use of a universal or targeted approach to screening, a NAAT for CT, and a NAAT or culture for GC; urine, vaginal, or cervical samples for NAATs and urethral or endocervical samples for cultures; any timing, or any frequency; and with any or no subsequent management of pregnant persons with confirmed infection. Comparisons of interest included an alternative screening strategy conducted with an alternative test, specimen, approach, at an alternative point, with a different frequency, or with any or no subsequent management strategy for pregnant persons with confirmed infection, or no screening strategy. Study designs of interest were any primary clinical studies that included eligible active intervention and eligible comparison group (including randomized controlled trials and non-randomized controlled studies of any design).

A descriptive summary of study and participant characteristics was prepared and a narrative synthesis was conducted.

Results

In total, 10 primary studies were found to be eligible and were included in the clinical review. Of the 10 included studies nine reported on detection yield outcomes and six reported on clinical utility outcomes. The literature search did not identify any studies reporting on the harms of screening during pregnancy. One of the studies was conducted in Canada.

Overall, the clinical review findings suggest that screening at both entry into prenatal care and at another time point in pregnancy may result in better yields than screening at a single time point. The evidence that new infections and reinfections occur throughout pregnancy suggests that regardless of the outcome of testing at entry to prenatal care, repeat testing may be warranted. When screening is targeted (i.e., age-based or other risk factor-based), infections may be missed in pregnant persons who do not meet the screening criteria.

There was conflicting evidence to determine whether early detection and treatment had an impact on neonatal outcomes. In a study involving 3,354 females in an urban county in the US, infant mortality was higher while mean gestational age was lower by 0.2 weeks in pregnant persons that were tested at or before 20 weeks of gestation compared with those that were tested after 20 weeks of gestation. In contrast, in a study of 752 pregnant persons in the US who were at high risk for infection, detection, and treatment at entry into prenatal care had no statistically significant impact on gestational age compared with detection and treatment at 34 weeks of gestation. Caution must be taken in selecting one form of specimen sampling over others. While a small group of 207 pregnant persons preferred screening by urine over vaginal and cervical samples, three studies provided conflicting evidence on relative detection yield across the various samples.

Results from a large study of almost 1.3 million pregnant persons across the US suggest that just over 60% of pregnant persons are not being screened in accordance with guidelines. Therefore, significant effort must be made to ensure that any new or updated guidelines are implemented accordingly.

Economics

Methods

A decision-analytic model was constructed to facilitate the comparisons between the clinical outcomes (quality-adjusted life-years [QALYs]) and costs associated with screening of CT and GC infection in pregnancy to both the pregnant person and the infant, from the first trimester of pregnancy up to the postpartum period (i.e., 19 weeks after birth or stillbirth). The target population was pregnant adults and adolescents of age 12 years and older in Canada and their offspring. The clinical pathway and decision tree model were developed by reviewing existing clinical and economic literature, and the conceptualization of the model and its structure was subsequently validated by clinical experts from different medical specialties (e.g., obstetrics, laboratory medicine, infectious pediatrics). Given uncertainties regarding a number of model parameters and assumptions, including the natural history of CT and GC infection and the variability in current screening practice and clinical management, sensitivity analyses were conducted. Exploratory analyses were also conducted to explore the impact of considering the potential long-term clinical impacts of infection such as blindness to the offspring and pelvic inflammatory disease to the birthing parent, and the potential association between infection in the pregnant person and adverse obstetric outcomes such as extremely preterm birth, preterm birth, and stillbirths during the second and third trimesters. For the economic evaluation, preterm births refer to live births that occurred between 28 and 36 weeks of gestation, extremely preterm births refer to live

births that occurred between 20 and 27 weeks, and births that occurred between 37 and 41 weeks were labelled as term.[2]

Results

More intensive screening programs (i.e., increasing the proportion screened and/or increasing the frequency of screening) were associated with increased health benefits and costs, and led to higher true-negative and false-positive results. Screening earlier in pregnancy was more costly, the incremental health benefits were small, resulting in large incremental cost-utility ratios (ICURs) for strategies in which screening was conducted in the first trimester. Although the base-case analysis found that not offering a prenatal visit screening program for CT and GC infections in pregnant persons was the least costly and the least effective option, and would only be cost-effective if the willingness-to-pay threshold was less than $2.3 million per QALY. The model results were sensitive to higher-risk populations, lower screening costs, or higher pediatric treatment-related costs as these parameters had the largest impact of shifting the benefit to harm or benefit to costs profile associated with screening. In such circumstances, the model found that it may be cost-effective to provide programmatic CT and GC screening during pregnancy.

The exploratory analyses also demonstrated that the model was sensitive if CT and GC were assumed to also impact obstetric outcomes. If future research supports this causal relationship, universal screening in the first trimester would be cost-effective if one's willingness-to-pay threshold was between $76,111 and $1.6 million per QALY gained. Furthermore, adopting a lifetime time horizon to capture the benefits of screening that extends beyond the postpartum period found that the universal screening in both first and third trimesters would be considered cost-effective if the willingness-to-pay threshold was greater than $11,468 per QALY.

Patients' Preferences and Experiences Review

Methods

A systematic review and qualitative meta-synthesis of empirical studies describing pregnant persons' experiences and perceptions of screening for STIs during pregnancy was conducted. Studies that include the perspectives of pregnant persons' partners and health care providers on screening for STIs were also included. Following an iterative approach consistent with the inductive principles of qualitative research, the *a priori* planned methods were actively refined and amended at various stages. Of note, given the scarcity of qualitative evidence on screening specifically for GC and CT during pregnancy, in order to ensure a sufficient evidence base to inform the policy question the research question specific to perspectives was refined and the scope of this section of the review was expanded to include screening for other STIs (such as HIV) during pregnancy.

Assessments of the major strengths and limitations of studies, in terms of their credibility, transferability, dependability, and confirmability, were guided by the Critical Appraisal Skills Programme quality appraisal checklist for qualitative research.[3] Included qualitative studies were analyzed using techniques of integrative qualitative meta-synthesis,[4-7] and also defined as qualitative research integration. The analysis followed a staged coding process similar to grounded theory and passed through three stages: open or line-by-line coding, descriptive coding, and development of analytic themes

Results

Of the included studies, 36 were part of the thematic synthesis. The review outlines a number of factors related to STI screening that may impact pregnant persons' experiences and participation. We identified a multilayered thematic framework that situates incentives and disincentives to STIs screening within two connected levels of factors that inform pregnant persons' decisions to engage with STI screening: one upstream and another downstream. Upstream factors are broader social and systemic conditions that offer opportunities for or barriers to STI screening for pregnant persons, which in turn have a cascade effect on downstream factors. Upstream factors included logistic and pragmatic barriers to antenatal care, knowledge and beliefs, psychosocial barriers, relationships with health care providers, and communication. Downstream factors encompass individual behavioural incentives or disincentives to screening, which included: personal assessment of health and risk, screening administration modalities, screening as a risk-seeking and risk-reducing behaviour, and screening options.

Conclusions

A limited number of studies were available from which to draw conclusions on screening for CT and GC. However, the findings that emerged from the clinical review, economic analysis, and the review of patients' perspectives and experiences (PPE) offer complementary sets of conclusions that may inform policy decisions.

In summary, this HTA finds that universal screening at entry into prenatal care and at another time point during pregnancy results in the highest detection yield and provides the most health benefits. However, a trade off that exists between the expected costs and clinical benefits among different screening strategies was most sensitive to the potential harms associated with the outcomes of developing an infection. Although universal screening in first and third trimesters (strategy UNUM) was found to be the costliest strategy, it generated the greatest amount of health. The incremental gain in health associated with UNUM compared with other screening strategies was dependent on the potential magnitude of harm from undiagnosed CT and GC infections (e.g., high-risk populations, impact on obstetric adverse event, lifetime analysis) and the costs associated with managing such infections (e.g., cost of managing pediatric infection). Although the base-case analysis capturing up to the postpartum period would suggest that the magnitude of clinical benefit is marginal (i.e., an ICUR of more than $65 million per QALY gained), exploratory analysis found that UNUM may be the most likely cost-effective screening strategy at a willingness-to-pay threshold of $11,468 per QALY or greater when factoring a lifetime time horizon. The universal strategy also aligns with the perspectives and experiences of pregnant persons, their partners, and health providers, as it has the potential to minimize stigma and discrimination, important psychosocial factors that influence screening behaviours. The evidence on the relative difference in detection yield between urine samples and endocervical and vaginal samples is inconclusive. Given the large proportion of pregnant persons who are not undergoing current screening guidelines, significant effort must be made to ensure that any new or updated guidelines are implemented accordingly.

Context Rationale and Policy Issues

Background / Setting in Canada

In Canada, chlamydia and gonorrhea are the most commonly reported sexually transmitted infections (STIs).[8] The bacterium *Chlamydia trachomatis* (CT) causes chlamydia infections, while the bacterium *Neisseria gonorrhoeae* (GC) causes gonorrhea infections.[8] These infections are a significant public health concern as their rates continue to increase despite numerous prevention and treatment strategies.[8] In 2016, 121,244 cases of CT and 23,708 cases of GC were reported in Canada, corresponding to rates of 344.9 and 67.4 per 100,000 individuals, respectively.[9,10] The overall rate of CT infections are disproportionately higher in females than in males (414.5 versus 271.9 per 100,000).[9,10] The overall GC rates are higher in males than in females (87.6 versus. 47.8 per 100,000).[9,10] High-risk groups for contracting CT and GC infections include sexually active youth under 25 years of age, sex workers, homeless persons, persons with a previous history of STIs, persons afflicted with substance abuse disorder, and men who have sex with other men (including bisexual men).[11,12]

CT and GC infections are commonly found at genitourinary, rectal, and pharyngeal sites.[13] Though often asymptomatic in females, early detection and treatment of CT and GC infections are necessary to prevent potential complications, sexual transmission, and transmission to neonates (i.e., newborns) in the perinatal period.[14] When signs and symptoms do develop, in females they are often nonspecific and include vaginal discharge, vaginal bleeding, and abdominal or pelvic pain.[15] In males, CT infections are more commonly asymptomatic than GC infections.[15] Symptomatic infections in males may present as dysuria; urethral discharge or pruritus; or testicular, epididymal, or scrotal pain.[15]

The potential for downstream sequelae in pregnant persons is of particular concern. Untreated CT or GC infections can lead to pelvic inflammatory disease and its deleterious sequelae, including infertility, ectopic pregnancy, and chronic pain.[15] During pregnancy, these infections and their complications can result in spontaneous abortion, stillbirth, preterm delivery,[16] low birth weight, and perinatal mortality.[17] CT and GC during pregnancy can be transmitted to the neonate resulting in substantial morbidity.[17,18] GC infection can be transmitted to the fetus in utero if there is prolonged rupture of the membranes.[18] Neonatal conjunctivitis or ophthalmia neonatorum develops in 15% to 44% of neonates born to a birthing parent infected with CT,[17] and 30% to 42% of neonates born to a birthing parent infected with GC.[18] Of all the cases of ophthalmia neonatorum (ON) in Canada and the US, CT and GC are responsible for up to 40% and 1%, respectively.[13] Of the neonates born to a birthing parent infected with CT during pregnancy, 50% are at risk for the infection, and 10% to 20% are at risk of developing pneumonia.[19]

Early detection of CT or GC can prevent significant adverse gynecological and non-gynecological health outcomes, neonatal morbidity, and perinatal mortality. Historically to prevent ON, the clinical management has focused on universal neonatal ocular prophylaxis.[20] The Canadian Paediatric Society (CPS) no longer recommends neonatal ocular prophylaxis for the prevention of ON.[19] The CPS' decision to shift the focus away from universal neonatal ocular prophylaxis to prenatal screening was based on the low prevalence rates of ON in Canada, the availability of prenatal screening and treatment, and the questionable effectiveness of erythromycin as prophylaxis for ON.[19]

Several guidelines exist at the provincial or national level for the screening of CT and GC during pregnancy. The CPS recommends universal screening for CT and GC at the first

prenatal visit.[19] Furthermore, the CPS recommends repeat screening in the third trimester, or failing that, at delivery, after treatment and test-of-cure visit for persons who test positive, and for persons who initially test negative and are at high risk of acquiring the infections later in their pregnancy (e.g., persons who are not in a monogamous relationship).[19] The CPS' recommendations were not formulated based on a systematic review (SR) of the evidence, and therefore the quality of evidence upon which the recommendations are based or the strength of the recommendations remain unclear. In the *Canadian Guidelines on Sexually Transmitted Infections*, the Public Health Agency of Canada (PHAC) recommends that all pregnant women be screened for CT and GC during their first prenatal visit.[21] Women with risk factors should be rescreened during the second and third trimesters.[21] If either CT or GC is detected, treatment is recommended for both the pregnant woman and sexual partner(s).[21]

The 2015 Society of Obstetricians and Gynaecologists of Canada's *Adolescent Pregnancy Guidelines* recommends screening for CT and GC when an adolescent (i.e., a pregnant person younger than 20 years of age) first presents for prenatal care, in the third trimester, at any other time during the pregnancy if risks arise, and postpartum.[22]

The Province of Quebec's evidence-based screening guidelines for STIs and blood-borne infections recommends universal screening for CT and GC as part of basic prenatal care, and repeat screening if the pregnant person is exposed to infection, or if the pregnant person and/or partner exhibit risky behaviour or have certain risk factors. The guidelines do not explicitly describe risky behaviour, but they describe risk factors for contracting STIs.[23] These risk factors include, but are not limited to, having a new sexual partner, having multiple concurrent sexual partners, having sexual encounters with anonymous partners, being 25 years or younger, coming from areas where STIs are endemic, living in Cree-James Bay Terrestrial Region or Nunavik (Quebec), having a history of incarceration, and drug and alcohol use.[23] If repeat screening is necessary, the guidelines recommend screening is performed around the 28th week of pregnancy and at the time of delivery. Furthermore, screening is also recommended for persons presenting for termination of pregnancy.[23]

In section 5 of the *Canadian Guidelines on Sexually Transmitted Infections*, the PHAC recommends that all pregnant persons are screened for CT during their first prenatal visit and those who are positive or who are at high risk for reinfection, be rescreened in their third trimester.[21] These updated guidelines were based on the Canadian Task Force on Preventive Health Care's 1996 Guidelines for Screening for CT[24] along with five accompanying primary studies, and the Centers for Disease Control and Prevention's 2006 Sexually Transmitted Diseases Treatment Guidelines. The guidelines on management and treatment of GC do not discuss screening of pregnant persons.[21]

In addition to the variation in screening guidelines, the use of diagnostic tests and specimens vary across Canada. A number of nucleic acid amplification tests (NAATs) (e.g., polymerase chain reaction [PCR], transcription-mediated amplification) are used to detect CT and GC on urine, vaginal, or cervical samples.[25] According to section 3 of the Canadian *Guidelines on Sexually Transmitted Infections*, NAATs are considered the most sensitive and specific tests for CT infection and the most sensitive tests for GC infection.[25] False-positive results may arise due to possible cross-reaction with other *Neisseria* bacterial species.[25] Based on an SR, the Agency for Healthcare Research and Quality reports that, across all specimens, the sensitivity of NAATs cleared by the FDA ranges from 86% to 100% for CT, and the specificity is greater than 97%.[14] Across all specimens and tests, the

sensitivity for GC ranges from 90% to 100%, and the specificity is greater than 97%.[14] GC can also be detected using cultures from endocervical or urethral specimens.

All confirmed cases of CT and GC require treatment with antibiotics.[12,26] A test-of-cure visit for CT using a NAAT is recommended for pregnant women three to four weeks post-treatment.[26] The test-of-cure visit for GC has been recommended three to seven days post-treatment if using culture and two to three weeks after treatment if using NAATs.[12]

Given the potential for the variation in approach (i.e., universal or targeted), tests (e.g., type of NAATs, culture), specimen (e.g., urine, vaginal, cervical), frequency (i.e., once or multiple times) and timing (e.g., first trimester, test-of-cure visit, third trimester, at delivery) for CT and GC screening during pregnancy, there is a pan-Canadian need for updated guidance. A comprehensive and multidisciplinary review of the literature is required to guide policy-makers on important considerations for formulating new guidelines for a national screening strategy.

In this report, gender-neutral language has been used where possible in order to be inclusive of all gender identities. When reporting results from published manuscripts, gender-neutral language was not used in order to be consistent with the terms used in the source material.

Policy Question

How should Canadian health care providers screen pregnant persons for *Chlamydia trachomatis (CT)* and/or *Neisseria gonorrhoeae (GC)* — at what time(s) during pregnancy, using what specimen, with what frequency, and using a universal or a targeted approach?

Objective(s)

The purpose of this HTA is to conduct a systematic assessment of the clinical effectiveness, safety, cost-effectiveness, and perspectives and experiences of pregnant persons, partners, and health care providers regarding the screening of pregnant persons for CT and GC.

Research Questions

This HTA addresses the following research questions:

Clinical Review

1. What are the comparative detection yield, clinical utility, and harms of differing screening strategies for the detection of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* during pregnancy?

Economic Analysis

2. What is the most cost-effective screening strategy during pregnancy for *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* in pregnant persons and their infants up to the postpartum period?

Patients' Perspectives and Experiences Review

3. What are the experiences and perspectives of pregnant persons and their partners with respect to undergoing screening for sexually transmitted infections (STIs)? And, what are their health care providers' perspectives on screening for STIs during pregnancy?

Analytical Framework

The analytic framework informing this HTA is presented in Appendix 1.

Clinical Review

The clinical review addresses the following research question:

Research question 1: What are the comparative detection yield, clinical utility, and harms of differing screening strategies for the detection of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* during pregnancy?

Systematic Review

A de novo SR of primary comparative clinical studies was conducted to address question 1. This clinical review was prepared in consideration of relevant reporting guidelines for SRs (i.e., Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA][27] and PRISMA harms).[28] A protocol was developed a priori and registered on the PROSPERO database (CRD42018087016).[29] All deviations have been identified in the Protocol Amendments table.

Methods

Literature Search Methods

The literature search was performed by an information specialist, using a peer-reviewed search strategy.

Information was identified by searching the following bibliographic databases: MEDLINE (1946–) with In-Process records and daily updates, Embase (1974–), and the Cochrane Central Register of Controlled Trials through Ovid; Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1981–) through EBSCO; and PubMed. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were chlamydia, gonorrhea, pregnancy, and screening.

Retrieval was limited to English- or French-language documents added to the databases since January 1, 2003. Where possible, retrieval was limited to the human population. No methodological filters were applied to limit retrieval by study type. Conference abstracts were excluded from the search results.

The search was completed January 25, 2018. Regular alerts were established to update the searches until the publication of the final report. Regular search updates were performed on databases that do not provide alert services. Studies identified in the alerts and meeting the selection criteria of the review haven been incorporated into the analysis if they were identified before the completion of the stakeholder feedback period of the final report. Any studies that were identified after the stakeholder feedback period are described in the discussion, with a focus on comparing the results of these new studies to the results of the analysis conducted for this report.

Grey literature (literature that is not commercially published) was identified by searching the Grey Matters checklist (https://www.cadth.ca/grey-matters), which includes the websites of HTA agencies, clinical guideline repositories, SRs repositories, economics-related resources, public perspective groups, and professional associations. Google and other Internet search engines were used to search for additional Web-based materials. These

searches were supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry. The complete search strategy is presented in Appendix 2.

Inclusion criteria

Full-text publications were included if they were published between January 1, 2003 and the present in English and met the eligibility criteria outlined in Table 1. The 2003 date was chosen because prior to this date, now obsolete tests such as antigen detection, direct fluorescent antibody tests, and nucleic acid hybridization tests were routinely used to detect CT and GC.[25] The current laboratory diagnosis recommendations published by the PHAC do not include these tests, and accordingly studies using these tests were excluded.[25] Studies were eligible for inclusion if NAATs were used to diagnose CT and/or GC or culture was used for the diagnosis of infection with GC. The population of interest included all pregnant adults and pregnant adolescents, 12 years and older. If the population was mixed (e.g., included both pregnant and non-pregnant persons), the study was included if the results for pregnant persons were reported separately. Studies reporting on a mixed population were also included if more than 80% of the total population comprised of the population of interest, even if results were not reported separately.

Primary clinical studies with a comparison group conducted in countries with a health care context comparable to Canada's were eligible for inclusion. Therefore, inclusion was restricted to studies conducted in Australia, Canada, New Zealand, the US, the UK, or members of the European Economic Area. Countries were considered to have comparable health care contexts based on the clinical opinion of the expert co-authors consulted on this review. (T.H: expert opinion, Dec 19, 2017; S.B: expert opinion, Dec 19, 2017).

Exclusion criteria

Publications describing case reports, case series, literature reviews letters, editorials, conference abstracts, and presentations were not eligible for inclusion. Duplicate publications and multiple publications of the same study were also excluded unless they provided unique findings of interest.

Eligibility criteria for clinical studies are outlined in Table 1.

Table 1: Eligibility Criteria for the Clinical Review

Population(s)	Pregnant adult and adolescent females (≥ 12 years of age, up to and including delivery)
Intervention(s)	A screening strategy involving: • NAAT for CT and NAAT or culture for GC • urine, vaginal, or cervical samples for NAATs; urethral or endocervical samples for cultures • using a universal or targeted approach • any timing (i.e., the point during pregnancy at which the screening test is performed) • any frequency (i.e., number of times the screening test is conducted during pregnancy) • any subsequent management of pregnant persons with confirmed infection, including no active management.
Comparator(s)	• An alternative screening strategy conducted with an alternative test, specimen, approach, timing, with a different frequency, or with any subsequent management strategy for pregnant persons with confirmed infection (including no management) • No screening strategy

Outcome(s)	**1. Primary outcomes:**
	Detection yield[a]:
	Any measure of detection yield including but not limited to:
	• number/per cent of positive tests for CT and/or GC
	• number/per cent of false-positive tests for CT and/or GC
	• number/per cent of false-negative tests for CT and/or GC.
	
	2. Secondary outcomes:
	Clinical Utility:
	Any measure of clinical utility including but not limited to:
	• number/per cent of pregnant persons eligible for screening who obtain screening in accordance with recommendations
	• number/per cent of pregnant persons eligible for screening who decline screening
	• number/per cent of pregnant persons referred for treatment
	• number/per cent of pregnant persons referred for treatment who obtain treatment
	• number/per cent of pregnant persons obtaining resolution or cure of infection
	• optimal timing of the test-of-cure visit
	• number/per cent of repeat infections identified, number/per cent of repeat infections missed
	• patient satisfaction with screening strategy (as assessed by a standardized questionnaire)
	• any measure of adverse gynecological and obstetric and non-gynecological health outcomes associated with CT and/or GC infection including but not limited to:
	  ○ infertility
	  ○ ectopic pregnancy
	  ○ spontaneous abortion
	  ○ preterm labour
	  ○ pelvic inflammatory disease
	  ○ chronic abdominal pain.
	• Any measure of adverse neonatal health outcomes associated with CT and/or GC infection including but not limited to:
	  ○ neonatal pneumonia
	  ○ neonatal ocular infection
	  ○ ocular infection sequelae (e.g., blindness, corneal infection)
	  ○ stillbirth
	  ○ prematurity
	  ○ low birth weight
	  ○ infection with CT and/or GC
	  ○ perinatal mortality.

Outcome(s)	Harms:
	• Any measure of harm from undergoing screening by any method or strategy including but not limited to:
	  ○ anxiety (as measured by a standardized scale)
	  ○ fear of stigmatization (as measured by a standardized scale)
	  ○ number and type of adverse pregnancy outcomes (e.g., miscarriage)
	  ○ negative impacts of false-positive and false-negative results.

Time Frame	2003 to present
Study Design(s)	Primary clinical studies that include eligible active intervention and eligible comparison group (including randomized controlled trials and non-randomized controlled studies of any design)[b]
Countries	Australia, Canada, European Economic Area, New Zealand, the UK, and the US.

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; NAATs = nucleic acid amplification tests.

[a] Calculations of prevalence and the per cent of screened pregnant persons who tested positive were included when reporting on detection yield.

[b] Case reports, case series, reviews, letters, editorials, conference abstracts, and presentations were excluded.

Selection Method

Two reviewers independently screened titles and abstracts of all citations retrieved from the literature search using the pre-determined eligibility criteria outlined in Table 1. The citations were screened in DistillerSR using standardized screening forms.[30] Titles and abstracts deemed to be potentially eligible by either reviewer were retrieved for full-text review. The same two reviewers independently reviewed the full-text reports using the eligibility criteria and compared the list of included and excluded citations. Any disagreements were resolved through discussion until a consensus was reached.

Data Extraction

Data extraction for the included studies was conducted using standardized data extraction forms, which were designed to extract relevant information from the studies, including but not limited to:

- first author's name, publication year, country, funding sources, and reported conflicts of interest
- study design
- patient characteristics including, number of pregnant persons, age, comorbidities, and risk factors for infection (where reported)
- description of intervention, including screening test, specimen, timing of screening, frequency of screening, setting of screening, and subsequent management of people (pregnant persons and neonates) identified as positive
- description of comparator(s), including screening test, specimen, timing of screening, frequency of screening, setting of screening, and subsequent management of people (pregnant persons and neonates) identified as positive
- description of outcomes reported, follow-up duration, and study loss to follow-up
- description of subgroups of interest and outcomes reported by subgroups, where available
- results for each outcome (i.e., detection yield, clinical utility, and harms).

Outcomes

Detection yield was the primary outcome of interest for this review. Detection yield was defined as the number and per cent of positive tests for CT and/or GC identified by differing screening strategies or the number and per cent of false-positive and false-negative tests for CT and/or GC. Secondary outcomes included clinical utility and harms. Further details on the outcomes are presented in Table 1.

Quality Assessment of Individual Studies

The Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS) was used to guide the quality assessment of the included non-randomized studies.[31] The RoBANS tool contains six domains, and a judgment of "high," "low," or "unclear" that can be assigned to each domain in alignment with the Cochrane Risk of Bias Tool and GRADE.[31]

The two reviewers piloted the RoBANS tool independently and in duplicate on a random sample of three publications and discussed discrepancies until they reached consistency in their assessments. After piloting, both reviewers independently conducted the quality assessment on the remaining included studies and compared findings. Discrepancies between the two reviewers were discussed until consensus was reached. The findings of the methodological assessments for each included study are reported, including an assessment of the strengths, and limitations across studies using a table and a narrative description.

Additional criteria to assess external validity, sources of funding, and competing interests were also included in the quality assessment of the included primary studies. The results from the quality assessment were not used to further include or exclude studies, but rather to assess the certainty of the evidence. Details are provided in Appendix 6.

Quality Assessment of the Body of Evidence

The overall quality of the body evidence was assessed using the GRADE framework to provide an assessment of the overall confidence in the estimated effect for each outcome of interest.[32] To determine the outcomes of interest for inclusion in the GRADE assessment, the list of primary and secondary outcomes from Table 1 were sent to decision-makers and stakeholders. They were asked to rate the relative importance of each outcome on a scale of 1 to 9. A rating from 1 to 3 represents an outcome of limited importance for decision-making, 4 to 6 represents an important outcome for decision-making, and 7 to 9 represents an outcome of critical importance for decision-making.[32] Any outcome rated important or critical by any of the decision-makers and stakeholders was considered an outcome of interest and included in the GRADE assessment.

The GRADE approach categorizes the quality of evidence, by outcome, from high to very low.[32] According to GRADE, randomized controlled trials begin with a high-quality rating but can be rated down for numerous reasons, including risk of bias, inconsistency of results, indirectness of evidence, imprecision, and publication bias.[32]

Non-randomized studies start with a low-quality rating but can be rated up if there is a very large magnitude of effect, dose-response gradient, or presence of plausible biases that would decrease an apparent effect. The assessments were performed independently by two reviewers.[32] Any discrepancies between the reviewers was discussed until consensus was reached. The final GRADE quality was classified as high, moderate, low, or very low. All assessments were presented in GRADE evidence profile tables.

Data Analysis Methods

A descriptive summary of study and patient characteristics was prepared that included the study design, year and country of publication, sample size, population, intervention, comparator, and outcomes of each study, where applicable.

Results were not meta-analyzed due to the presence of substantial clinical and methodological heterogeneity. Rather, a narrative synthesis of the results of the included primary studies was conducted. The findings, where possible, were grouped by infection outcome. Direct comparisons and indirect comparisons between interventions were reported as presented in the studies. No formal testing was conducted to indirectly compare interventions not directly compared against each other in the studies. Tables were organized to emphasize screening strategy characteristics, including screening test, test specimen, timing, frequency, and infection management strategy, and accompany the narrative summaries to ensure the consistency of the presented information across all studies and to facilitate study comparisons.

Subgroup analyses by age were reported in five of the included studies and are presented, as reported, in each included study along with the results from the full study population.

Assessment of publication bias graphically or objectively using Egger's regression test and Begg's rank correlation test[33] was not feasible as at least 10 citations of a given study design and a particular outcome were not identified.

Results

Quantity of Research Available

The literature search identified a total of 1,696 citations. After review of titles and abstracts, 69 citations were deemed potentially relevant and retrieved for full-text review. Two potentially relevant reports were retrieved from other sources (i.e., grey literature, hand searching, and search alerts). Of these 71 potentially relevant reports, 10[34-43] reports were found to be eligible and were included in this review.

The study selection process is outlined in Appendix 3 using a PRISMA flow diagram. Lists of included and excluded citations are provided in Appendix 4 and Appendix 5, respectively.

Study Characteristics

The characteristics of the 10[34-43] included primary studies, with respect to the country, study design, funding, analytical methods, patient characteristics, clinical setting, interventions, comparators, outcomes, and subgroup analyses conducted are summarized in Appendix 7.

Nine[35-43] of the 10 included studies were applicable to detection yield outcomes and six[34-36,41-43] were applicable to clinical utility outcomes. The literature search did not identify any studies reporting the harms of screening during pregnancy. Two of the studies reported on the same population of pregnant persons.[42 43]

Study Dates, Locations, Funding, and Design

The 10 included primary studies were published between 2003 and 2014.[34-43] One study was published in 2014,[34] one in 2012,[35] two in 2011,[36,37] two in 2010,[38,39] one in 2009,[40] two in 2005,[41,42] and one in 2003.[43]

Seven studies were conducted in the US,[34-37,39,42,43] one was conducted in Canada,[38] one in Germany,[40] and one in the UK.[41]

Three studies reported their sources of funding,[36,39,42] three reported there were no conflicts of interest,[37,38,40] and one reported sources of funding and declared competing interests.[35] Three primary studies did not report their sources of funding or competing interests.[34,41,43]

Five studies were retrospective chart reviews.[35,38,39,42,43] Two of these studies were retrospective cohort studies,[34,40] two were cross-sectional studies,[37,41] and one was a secondary analysis of a prospective cohort study.[36]

Population

Pregnant adults and adolescents (less than 20 years of age) were the population of interest in eight studies[34,35,37,39-43] and pregnant adolescents were the population of interest in two studies.[36,38] The study group sizes ranged from 95[36] to 760,864.[35]

Three studies reported the age ranges for included pregnant persons:[35,36,38] the youngest was 12 years of age,[36] and eldest was 40 years of age.[35] The mean ages were reported in three studies as 16.1 years,[38] 26.9 years,[37] and 29.3 years.[41] Two studies reported median ages of 17 years[36] and 28 years,[40] and one reported an age range of 16 to 40 years.[35] While some studies reported age using more than one measure (mean, median, range or standard deviation), four studies did not report on ages of included pregnant persons.[34,39,42,43]

Screening Strategies, Comparisons, Outcomes, and Subgroups

Four major groups of screening strategies were compared:

- Initial screening for CT and/or GC in comparison with screening at another point during pregnancy (including test-of-cure visits) for CT and/or GC.[35,36,38,42,43]
- Routine screening for CT compared with targeted screening using the United States Preventive Services Task Force (USPSTF) criteria.[39] The USPSTF criteria recommends that pregnant persons should be tested for CT if they are 24 years of age or younger, are single, and are black or Hispanic).[44] Data describing detection yield were provided.
- Specimen type, including urine, vaginal or endocervical specimens.[37,40,41] Detection yield and preference data were available.
- Timing of detection and treatment, specifically early versus late detection and treatment of CT.[34,42,43] Clinical utility data were available.

Detection yield outcomes (i.e., number and per cent of CT and/or GC infections) were reported in nine studies.[35-43] Clinical utility outcomes that were addressed included the number and/or per cent of pregnant persons screened in accordance with guidelines,[35] the number of pregnant persons treated for CT and/or GC infections,[36,42,43] the number of pregnant persons declining screening,[41] preference for screening strategies,[41] number and/or per cent of pregnant persons with obstetric and gynecological outcomes,[34] and number and/or per cent of adverse neonatal outcomes.[34,42,43] With regard to detection yield, two studies described how true-test outcomes were determined.[38 41] Logan et al. (2005) stated that a specimen recorded as negative for CT on single testing (with NAAT) was reported as negative.[41] All positive CT results were retested (presumably using the same NAAT) and a confirmed positive result was considered to be a true positive.[41] In another study, GC testing was conducted using a cervical culture with confirmation by immunofluorescence.[38] The remaining tests did not discuss test verification or confirmation. Two studies on the same population reported that the direct DNA assay (Gen-Probe, San Diego, CA) had a sensitivity of 96% and a specificity of 98% for CT using cervical swabs[42]

and had sensitivity ranging from 93% to 99% and a specificity of 99% for GC using cervical swabs.[43]

Outcomes based on age groups were reported in five studies.[34,35,40,42,43] In Blatt et al. (2012),[35] the number and per cent of CT and/or GC infections were evaluated based on age in accordance with the USPSTF and Centers for Disease Control and Prevention (CDC) guidelines. The CDC guidelines suggest that all pregnant women should be screened for CT during their first prenatal visit.[45] High-risk women (i.e., those ≤ 25 years and/or have a new or multiple sexual partners) should be rescreened during the third trimester.[45] Miller et al. (2003)[43] and Miller et al. (2005)[42] reported the number and/or per cent of CT or GC infections and neonatal outcomes by age group. Folger (2014)[34] stratified the effect of early detection and treatment of CT infections by age group on moderate-to-late preterm and spontaneous moderate-to-late preterm birth. Lastly, Böhm et al. (2009)[40] compared the prevalence of CT infections in the cohort of females sampled with cervical swabs versus urine samples, by age group.

Quality Assessment of Individual Studies

The RoBANS tool[31] was used to guide the quality assessment conducted on the ten included studies[34-43] as summarized in Appendix 6. The RoBANS rating was low risk for the blinding of outcome assessment and selective outcome reporting criteria in all of the included studies.[34-43] The quality assessment rating was mixed for the remaining four criteria — selection of participants, confounding variable, intervention measurement, and incomplete outcome data. For selection of participants, nine[34-39,41-43] of the 10 studies had retrospective study designs, including one[36] that involved a secondary analysis of a prospective cohort study. The studies were rated as having a high risk of bias because they relied on medical records that were not configured to provide data on the primary and secondary outcomes of interest. Some studies also failed to provide sufficient information on inclusion/exclusion criteria, and demographic and clinical characteristics; leaving uncertainty regarding selection of patients. The lack of demographic and clinical information makes it challenging to assess whether the results can be generalized. There was a risk that the researchers were biased toward selecting pregnant persons and/or their partners and health care providers because they had specific characteristics. For example, one study enrolled pregnant persons who sought medical care at family planning and obstetric complication clinics,[37] while another performed retrospective analysis on data from a private laboratory.[35] The populations in three studies[36,42,43] were from areas with high prevalence of STIs, and one study was conducted in a miscarriage population;[37] meaning these results may not be generalized to a broader population of pregnant persons. These reasons suggest that the nine studies were at a high risk of bias regarding participant selection.

In addition, data inaccuracy, incompleteness, and errors in abstraction are potential concerns. External validity, funding sources and competing interests were also taken into consideration. Three studies[36,39,42] declared their sources of funding, three studies[37,38,40] declared no competing interests, and three studies[34,41,43] failed to declare sources of funding. One study[34] was rated as having a high risk of bias with respect to confounding, eight were rated as having a low risk of bias,[35-40,42,43] and one was rated as having an unclear risk of bias.[41] For intervention measurement, six studies were rated as having a low risk of bias,[34,35,37,41-43] and four studies were rated as unclear.[36,38-40] For the incomplete outcome data criterion, nine studies were rated as having a low risk of bias,[35-43] and one study was rated as having a high risk of bias.[34]

Data Analysis and Synthesis

Findings are presented by outcomes of detection yield and clinical utility, first summarizing study findings in which pregnant persons were screened for both CT and GC infections, and then CT or GC infections only.

Detection Yield

Nine[35-43] of the 10 included primary studies contributed detection yield outcome data. Details are provided in Table 2.

Impact of Repeat Screening

CT and GC Infections

To determine the impact of repeat screening (i.e., screening in the same population at a second time point) following screening at entry into prenatal care, an assessment of the increase in the number of infections detected was conducted. Five articles[35,36,38,42,43] (from four studies) provided data to calculate the detection yield of screening for CT and GC at entry into prenatal care and the detection yield of screening at another point in pregnancy. One of the studies conducted population-level screening in pregnant persons 16 to 40 years old across the US,[35] one selected adolescents in Washington,[36] one selected adolescents in Toronto,[38] and the fourth study (two articles) enrolled pregnant persons of undisclosed ages in New Orleans.[42,43]

In the Blatt et al.(2012)[35] study, 2.7% (20,489 out of 761,315) and 4.4% (5,027 out of 113,275) pregnant persons tested positive for CT at initial and repeat screening, respectively. A total of 2,187 new CT infections and 2,885 reinfections were identified when repeat screening was conducted. This means 19.7% (5,027) of the total 25,561 infections would have been missed had a second screening not been done at another time point in pregnancy. In addition, 0.47% (3,435 out of 730,796) and 1.04% (1,093 out of 104,828) of pregnant persons tested positive for GC at initial and repeat screening, respectively. While 3,435 GC infections were identified at entry into prenatal care, 24.1% (817 new GC infections and 276 reinfections) of the total 4,528 infections would have been missed had a second screening not been done at another time point in pregnancy.

In the Berggren and Patchen (2011)[36] study, the prevalence of CT at initial and repeat screening was 19.2% (24 out of 125) and 13.7% (13 out of 95), respectively. Four new CT infections and nine reinfections would have been missed had additional screening not been done in the third trimester. The prevalence of GC at initial and repeat screening was 10.4% (13 out of 125) and 7.4% (7 out of 95), respectively. Four new GC infections and three reinfections would have been missed.

In the study by Aggarwal et al. (2010),[38] the prevalence of CT at initial and repeat screening was 14.2% (30 out of 211) and 3.5% (6 out of 173), respectively. The prevalence of GC at initial and repeat screening was 0.94% (2 out of 211) and 2.9% (5 out of 173), respectively. Five new infections and one reinfection with CT and five new cases with GC would have been left undiagnosed had repeat screening not been conducted in the third trimester.[38] Of the five new GC infections, one was a new coinfection in an adolescent previously diagnosed with CT.[38]

In Miller et al. (2005),[42] the prevalence of CT at initial and repeat screening was 14.0% (105 out of 752) and 5.7% (43 out of 752), respectively. A total of 29 new CT infections and 14 repeat CT infections would have been missed had repeat screening not been conducted at 34 weeks of gestation. Likewise in Miller et al. (2005),[43] The prevalence of GC at initial and

repeat screening was 5.1% (38 out of 751) and 2.7% (20 out of 751), respectively. 19 new GC infections and one GC reinfection would have been missed.

The Blatt et al.(2012)[35] study was conducted on a large nationally representative sample of pregnant females aged 16 to 40 years of age in the US, that may be generalizable to the Canadian population (albeit with uncertainty in risk factors). The prevalence of CT and GC infections in the Blatt et al.(2012)[35] study was lower than the Aggarwal et al.(2010),[38] the Berggren and Patchen (2011),[36] and the Miller et al. (2005)[42,43] studies likely due to differences in the populations studied. The Berggren and Patchen (2011)[36] study and the study by Miller et al. (2005)[42 43] were conducted in areas with high prevalence of STIs. The Berggren and Patchen (2011),[36] Aggarwal et al.(2010),[38] and the Miller et al. (2005)[42 43] studies were limited to high-risk populations making it unlikely for their findings to be generalizable to populations with a lower risk and/or low prevalence of STIs.

A subgroup analysis performed by maternal age demonstrated that females aged 19 years and younger had a significantly higher prevalence of CT infections at both initial and repeat testing (at 34 weeks of gestation) compared with females aged 20 years and older.[42] The prevalence rates were 19.4% (62 out of 319) and 9.9% (43 out of 433), respectively at entry into prenatal care. The prevalence rates were 8.2% (21 out of 257) and 2.1% (8 out of 390) at 34 weeks of gestation following a negative test at entry into the prenatal program. Limiting the repeat testing to females 19 years of age and younger would have missed eight CT infections in 390 females outside this age range. Whereas, limiting the repeat testing to persons 20 years of age and older would have missed 21 CT infections in 257 females.

A subgroup analysis performed by maternal age demonstrated that females 19 years and younger had a higher prevalence of GC infections at both initial and repeat testing (at 34 weeks of gestation) than females aged 20 years and older.[43] The prevalence rates were 7.2% (23 out of 318) and 3.5% (15 out of 433), respectively at entry into prenatal care. The prevalence rates were 3.5% (11 out of 318) and 1.8% (8 out of 433) at 34 weeks of gestation following a negative test at entry into the prenatal program. Limiting the repeat testing to pregnant persons 19 years of age and younger would have missed eight GC infections in 433 females. Limiting the repeat testing to pregnant persons 20 years of age and older would have missed 11 GC infections in 318 females. However, no analyses were reported to determine statistical significance of the difference in prevalence.

The prevalence of CT and GC infections, the number of new and repeat infections, and the proportion of total infections detected at repeat screening can be found in Table 2.

Table 2: Detection Yield: Initial Versus Repeat Screening

Author, Publication Year, Country, Study Design,	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT and GC Infections			
Blatt et al., 2012[35] US Retrospective chart review	761,315 and 730,796 pregnant females aged 16 to 40 years of age tested for CT and GC infections, respectively Median age: NR (range 16 to 40 years)	Intervention: Initial screening at entry into prenatal care n = 761,315 for CT and 730,796 for GC Comparator:[a] Repeat screening at another point during pregnancy (including TOC for CT within 6 weeks of initial screen) n = 113,275 for CT and 104, 828 for GC Specimen: NR Diagnostic tests: • 70% — SDS • 20% — DNA hybridization • 10% — target capture, TMA dual-kinetic assay	**CT (screening at entry into prenatal care vs. repeat screening at another time point)** Prevalence: 2.7% (20,489/761,315) vs. 4.4% (5,027/113,275) Proportion of total infections: 80.2% (20,489/25,561) vs. 19.7% (5,027/25,561) At repeat screening, 2,187 were new and 2,885 were repeat infections **GC (screening at entry into prenatal care vs. repeat screening at another time point)** Prevalence: 0.47% (3,435/730,796) vs. 1.04% (1,093/104,828) Proportion of total infections identified: 75.6% (3,435/4,528) vs. 24.1% (1093/4,528) At repeat screening, 817 were new and 276 were repeat infections
Berggren et al.2011[36] US Prospective cohort study	125 pregnant adolescents; 12 to 18 years old Median age at delivery: 17 years	Intervention: Screening at entry to prenatal care n = 125 Comparator:[a] Screening during the third trimester (~36 weeks of gestation)[b] n = 95[c] Specimen: Endocervical culture or urine samples **Diagnostic test: urine NAAT**	**CT (screening at entry into prenatal care vs. repeat screening during the third trimester)** Prevalence: 19.2% (24/125) vs. 13.7% (13/95) Proportion of total infections identified: 64.9% (24/37) vs. 35.1% (13/37) At repeat screening, 4 were new and 9 were repeat infections **GC (screening at entry into prenatal care vs. repeat screening during the third trimester)**

Author, Publication Year, Country, Study Design,	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
			Prevalence: 10.4% (13/125) vs. 7.4% (7/95) Proportion of total infections identified: 65% (13/20) vs. 35% (7/20) At initial screening, 5 persons were co-infected with CT. At repeat screening, 4 were new and 3 were repeat infections
Aggarwal et al.2010[38] Canada Retrospective chart review	211 pregnant adolescents (including 10 repeat pregnancies) Mean age: 16.1 years (range, 13 to 18 years)	Intervention: Screening at first prenatal (i.e., baseline) visit for CT and GC n = 211 (14 pregnant adolescents had their baseline screening during the third trimester) Comparator:[a] Screening during the third trimester n = 173 (excludes 14 who had their baseline screen during the third trimester)[c] Specimen: Cervical swab Diagnostic tests: CT: NAAT (SDA assay) GC: Cervical culture with confirmation by immunofluorescence	**CT (screening at entry into prenatal care vs. repeat screening during the third trimester)** Prevalence: 14.2% (30/211) vs. 3.5% (6/173) Proportion of total infections identified: 83.3% (30/36) vs. 16.7% (6/36) At repeat screening, 5 were new and 1 was a repeat infection **GC (screening at entry into prenatal care vs. repeat screening during the third trimester)** Prevalence: 0.94% (2/211) vs. 2.9% (5/173) Proportion of total infections identified: 28.6% (2/7) vs. 71.4% (5/7) At repeat screening, 5 were new and 1 was co-infected with CT
Miller, Maupin, and Nsuami, 2005[42] US Retrospective chart review	752 pregnant females Mean age: NR	Intervention: Screening for CT at entry into a prenatal program n = 752 Comparator: Repeat screening at 34 weeks n = 752 Specimen: NR Diagnostic test: Direct DNA assay (Gen-Probe, San Diego, CA)	**CT (screening at entry into prenatal care vs. repeat screening at 34 weeks of gestation)** Prevalence: 14.0% (105/752) vs. 5.7% (43/752) Proportion of total infections identified: 70.9% (105/148) vs. 29.1% (43/148) At repeat screening, 29 were new and 14 were repeat infections **Subgroup Analysis:**[e] Screened at entry into prenatal program (maternal age ≤ 19 years vs. ≥ 20 years) Prevalence: 19.4% (62/319) vs. 9.9% (43/433) were diagnosed with CT, $P < 0.001$; OR = 2.29 (95% CI, 1.44 to 3.23)

Author, Publication Year, Country, Study Design,	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
			Repeat screening at 34 weeks of gestation following a negative test at entry into prenatal program (maternal age ≤ 19 years vs. ≥ 20 years) Prevalence: 8.2% (21/257) vs. 2.1% (8/390) were diagnosed with CT, *P* < 0.001; OR = 4.24 (95% CI, 1.85 to 9.74)
Miller et al., 2003,[43] US Retrospective chart review	751 pregnant females Mean age : NR	Intervention: Screening for GC at entry into a prenatal program n= 751 Comparator: Repeat screening at 34 weeks n = 751 Specimen: NR Diagnostic test: Direct DNA assay (Gen-Probe, San Diego, CA)	**GC (screening at entry into prenatal care vs. repeat screening at 34 weeks of gestation)** Prevalence: 5.1% (38/751) vs. 2.7% (20/751) Proportion of total infections identified: 65.5% (38/58) vs. 34.5% (20/58) At initial screening, 19 of the 38 were co-infected with CT. At repeat screening, 19 were new and 1 was a repeat infection; 8 of the 19 newly infected were co-infected with CT **Subgroup Analyses:**[e] Screened at entry into prenatal program (maternal age ≤ 19 years vs. ≥ 20 years) Prevalence: 7.2% (23/318) vs. 3.5% (15/433) were diagnosed with GC, *P* = NR Repeat screening at 34 weeks of gestation following a negative test at entry into prenatal program (maternal age ≤ 19 years vs. ≥ 20 years) Prevalence: 3.5% (11/318) vs. 1.8% (8/433) were diagnosed with GC, *P* = NR

CI = confidence interval; CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; NAAT = nucleic acid amplification test; NR = not reported; OR = odds ratio; SDA = Strand Displacement Amplification; STI = sexually transmitted infection; TMA = transcription-mediated amplification; TOC = test-of-cure.

[a] The comparator group is comprised of a subset of the population in the intervention group.

[b] A test-of-cure was also performed 4 weeks after positive initial test and treatment but the study reported no data for this outcome.

[c] The number of pregnant persons differed in the intervention and comparator group due to loss to follow-up.

[e] Subgroup analyses were also conducted on variables including sociodemographic characteristics, other STIs, and gynecological/obstetric factors but are not included in this report.

Universal Versus Targeted Risk, Factor-Based Screening

CT Infections

One study[39] reported outcome data on the prevalence of CT infections diagnosed during routine, universal screening in comparison to targeted risk, factor-based screening using the USPSTF recommendations.[39] The USPSTF recommends screening pregnant persons ≤ 24 years old, single and black or Hispanic.[39] The medical records of 2,127 pregnant females with singleton live births and full antenatal records were analyzed.[39] A total of 2,104 were screened for CT during pregnancy. The majority (72.6%) were screened at or before 20 weeks of gestation.[39] The remaining females were screened after 20 weeks of gestation. Of the 2,104 females screened, 98 cases of CT were identified, suggesting a prevalence of 4.7%.[39] Based on medical records, applying the USPSTF criteria would have resulted in a prevalence rate of 1.33% or diagnosis of 28 cases of CT.[39] Risk factor-based targeted screening would have potentially missed 70 (3.32%) CT infections.[39] Of note, in the population of 2,104 that was screened, 750 met the USPSTF criteria for screening.

The primary limitation of this study is that the criteria used to define which individuals were routinely screened was not reported, limiting reproducibility and generalizability. Furthermore, the study did not report the occurrence of repeat screening. The findings are summarized in Table 3.

Specimen Detection Yield

CT Infections Only

Three studies[37,40,41] reported outcome data on the detection yield of CT infections in females by specimen type. They present data from Germany,[40] the UK,[41] and the US.[37] Two of the studies compared detection yield between cervical swabs and urine samples,[37,40] while one study (Logan et al.)[41] additionally compared vaginal samples. The tests they used were the Aptima Combo 2 Assay,[37] a semi-automated real-time polymerase chain reaction (PCR),[40] and the BD Probe Tec ET system.[41] Roberts et al. (2011)[37] found no significant difference in the prevalence rates of CT infection detected by NAATs between endocervical (4.3%) and urine (4.1%) samples from 2018 pregnant adults and adolescents between May and September 2009. Böhm et al. (2009)[40] found a significant difference in the detection yield of CT when comparing cervical swabs to pooled urine samples in 21 to 25 year olds, 26 to 30 year olds, and 31 to 35 year olds. In these subgroups, the detection yield was significantly higher with cervical swabs than with pooled urine samples, as cervical swabs were reported to identify 1.12%, 1.07% and 0.82% more infections than urine samples in each age group, respecitvely.[40] For females between ages 36 and 40 years, the detection yield was higher with cervical swabs than with pooled urine samples, but the difference was not statistically signficant.[40] For females ≤ 20 years old, the prevalence was lower with cervical swabs than with pooled urine samples, but the difference was not statistically significant.[40] Testing was conducted with semi-automated PCR between April and December 2008. Urine samples that were designated for screening were automatically pooled by five.[40] Urine samples from pools with a positive result were retested individually.[40] All samples in a negative pool were considered negative. Samples with a negative result and a concomitant drop out of the internal control were retested.[40]

Although the pooled urine approach is expected to be less accurate than individual testing, only four out of 216 negative pooled samples contained positive samples when retested.[40] The authors calculated a negative predictive value of 98.1% for the pooling system.[40] Logan et al. (2005)[41] reported the detection yield of CT was 2.2%, 3.9%, and 1.5% from cervical, vaginal, and urine samples, respectively.[41] Though no statistical analyses were performed, the study authors report that urine samples may have decreased test performance in comparison to cervical and vaginal samples.[41] Testing was conducted between September and December 2001.

The results from these three studies on the detection rate of endocervical, vaginal, and urine samples are summarized in Table 4.

Clinical Utility

Adherence to Guideline-based Screening

CT and GC Infections

One study[35] reported on the number of females across the US who were screened according to the Centers for Disease Control and Prevention (CDC), The American College of Obstetricians and Gynecologists (ACOG), and USPSTF recommendations. The CDC guidelines suggest that all pregnant women should be screened for CT during their first prenatal visit.[45] High-risk women (i.e., those ≤ 25 years and/or have a new or multiple sexual partners) should be rescreened during the third trimester.[45] Those who test positive during the first trimester should be retested within three to six months. A test-of-cure visit should be conducted within three weeks.[45] In addition, those who are at risk or live in an areas with high prevalence should be tested for GC during their first prenatal vist.[45] The USPSTF recommends screening pregnant persons who are 16 to 24 years old, single, and black or Hispanic during their first prenatal visit.[39] Blatt et al. (2012)[35] reviewed data of 1,293,423 pregnant females from a private clinical laboratory data warehouse in the US. Of these 37% were screened at their first prenatal visit for CT in accordance with the 2010 CDC[45] and 2007 ACOG[47] guidelines, and 39% were screened in accordance with the 2007 USPSTF[44] guidelines. For GC infections, 37% were screened in accordance with the 2010 CDC[45] and 2007 USPSTF[44] guidelines.[35]

Adherence with repeat testing recommendations was also evaluated.[35] Females with a positive result at initial screening were not included so as to isolate the influence of age on retesting.[35] Of the high-risk females who had a negative initial test, 19.1% and 22.1% were retested for CT and GC, respectively in accordance with the 2010 CDC guidelines.[35] Of the females considered at high risk who were rescreened, 3.4% and 1.1% had at least one subsequent positive test for CT and GC, respectively. Of those that were rescreened more than once, 1.9% and 0.6% were positive for CT and GC, respectively, at their last test.[35]

The study demonstrated that at least 60% of females were not screened in accordance with any guidelines, potentially resulting in a number of undiagnosed CT and GC infections. The findings are summarized in Table 5.

Table 3: Detection Yield: Universal Versus Targeted Risk, Factor-Based Screening

Author, Publication Year, Country, Study Design, Quality	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT Infections Only			
Silveira et al. 2010[39] US Retrospective chart review	2,127 pregnant adults and adolescents with antenatal records who gave birth to a singleton at ≥ 20 weeks of gestation and were routinely screened for CT (and GC). Mean age: NR (64.3% > 24 years old)	Intervention: Universal (routine) screening for CT at any time point during pregnancy; inclusive population n = 2,104 Comparator:[a] Screening for CT at any time point in pregnancy using USPSTF criteria (≤ 24 years old, single, and black of Hispanic) n = 2,104 Specimen: NR Diagnostic test: NAAT	Women routinely screened for CT[b] during pregnancy (criteria for screening NR) • The prevalence of CT infections was 4.7% (95% CI, 3.8% to 5.6%; n = 98/2104) Applying the USPSTF criteria (≤ 24 years old, single, and black or Hispanic) to the screening for CT: • The prevalence of CT infections would have been 1.33% (28/2014).[a] • 29.0% (28/98) (95% CI, 21.0% to 38.0%) of the CT cases that were detected through routine screening would have been identified. • Infections that would have been missed: 3.32% (70/2104).

CI = confidence interval; CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; NAAT = nucleic acid amplification test; NR = not reported; USPSTF = United States Preventive Services Task Force

[a] Of the total population, 750 were 24 years old or younger.

[b] GC infections were also documented; 24 pregnant persons had GC infections; 13 were co-infected with GC and CT; however the study did not report on GC outcomes.

Table 4: Detection Yield: Specimen Detection Yield

Author, Publication Year, Country, Study Design,	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT Infections Only			
Roberts et al. 2011[37] US Cross-sectional study	2018 pregnant adults and adolescents Mean age (± SD): 26.9 (± 6.1) years	Intervention: Screening of urine samples for CT at 35 to 37 weeks of gestation n = 2018 Comparator[a]: Screening of endocervical[b] samples for CT at 35 to 37 weeks of gestation n = 2018 Specimen: Urine samples and endocervical[a] samples Diagnostic test: NAAT (Aptima Combo 2 Assay, Tigris DTS system)	• 83 samples were positive for CT by endocervical swab and urine sample; 3 samples were positive by endocervical swab but negative by urine • CT prevalence was 4.3% (95% CI, 3.4% to 5.2%) for endocervical samples (86/2,018) and 4.1% (95% CI, 3.3% to 5.1%) for urine samples (83/2,018) • There was no statistically significant difference in detection rate between the two samples by McNemar's test: 0.15% (95% CI, –0.02% to 0.32%), *P* = 0.083 • Agreement between endocervical and urine samples: κ statistic 0.982 (95% CI, 0.961 to 1.00)
Böhm et al.2009[40] Germany Retrospective cohort study	50,025 females Median age: 28 years (range, 13 to 50 years)	Intervention: Screening for CT using cervical swabs n = 31,856 Comparator:[a] Screening for CT using pooled urine samples n = 18,169 Specimen: Cervical swabs and urine samples Diagnostic test: Semi-automated real-time PCR [*artus* C.Trachomatis Plus RG PCR Kit (Qiagen, Hilden, Germany)]	Prevalence of CT in cervical swabs 3.26% (1,039/31,856) vs. pooled urine samples was 2.93% (533/18,169) **Subgroup Analysis:**[c] • CT prevalence stratified by age (cervical swab vs. urine samples): ○ ≤ 20 years: 10.18% (95% CI, 9.34% to 11.11%) vs. 10.91% (95% CI, 9.77% to 12.20%), q = NR. ○ 21 to 25 years: 5.66% (95% CI, 5.22% to 6.14%) vs. 4.54% (95% CI, 4.05% to 5.11%), q < 0.05. ○ 26 to 30 years: 2.63% (95% CI, 2.13% to 2.61%) vs. 1.56% (95% CI, 1.32% to 1.85%), q < 0.01. ○ 31 to 35 years: 1.76% (95% CI, 1.53% to 2.03%) vs. 0.94% (95% CI, 0.72% to 1.22%), q < 0.01. ○ 36 to 40 years: 1.27% (95% CI, 1.00% to 1.64%) vs. 0.73% (95% CI, 0.51% to 1.20%), q = NR. ○ > 40 years: 0.40% (95% CI, 0.17% to 1.26%) vs 0.83% (95% CI, 0.34% to 2.59%), q = NR.

Author, Publication Year, Country, Study Design,	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT Infections Only			
Logan et al. 2005[41] UK Cross-sectional study	207 adults and adolescents who were admitted into an early pregnancy assessment unit and had a positive pregnancy test, history of vaginal bleeding and were < 24 weeks pregnant Mean age (± SD) (n = 207): 29.3 (± 5.9) years	Intervention: Screening followed by semi-structured questionnaire Comparator: Screening by an alternate specimen Specimen: Endocervical (n = 139)[b], self-collected vaginal (n= 205), or first-void urine (n = 205) samples Diagnostic test: BD ProbeTec ET System	A total of 207 females provided ≥ 1 sample. 2 samples that could not be assayed were excluded from the analysis. • The per cent and number of positive CT tests by specimen type: Endocervical vs. vaginal vs. urine samples: 2.2% (3/139) vs. 3.9% (8/205) vs. 1.5% (3/205); all positive cases were from patients < 30 years old

CI = confidence interval; CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; NAAT = nucleic acid amplification test; NR = not reported; PCR = polymerase chain reaction; SD = standard deviation

[a] The comparator group is comprised of the same population of females as in the intervention group.

[b] The endocervix is the inner part of the cervix.[46]

[c] *"Multiple application of Fisher's exact test was allowed for in the line-wise comparison of the observed infection prevalence in cervical swabs and urine samples by controlling the false discovery rate q, using a SIMES procedure."* (p.S29).[40]

Table 5: Clinical Utility: Adherence to Guidelines-Based Screening

Author, Publication Year, Country, Study Design	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT and GC Infections			
Blatt et al., 2012[35] US Retrospective chart review	761,315 and 730,796 pregnant females tested for CT and GC infections Median age: NR (range 16 to 40 years)	Intervention: Initial screening for CT and GC at entry into prenatal care n = 761,315 for CT and 730,796 for GC Comparator[a]: Repeat screening for CT and GC at another point during pregnancy (including TOC for CT within 6 weeks of initial screen) n = 113, 275 for CT and 104, 828 for GC Specimen: NR Diagnostic tests: • 70% — SDA • 20% — DNA with chemiluminescent detection • 10% — Target capture, TMA, dual-kinetic assay	**CT** Number and per cent of females screened at their first prenatal visit in accordance with current guidelines: • 37% (483,845/1,293,243) were screened for CT in accordance with 2010 CDC[45] and 2007 ACOG[47] guidelines • 39% (143,019/368,550) aged 16 to 24 years were screened for CT in accordance with the 2007 USPSTF[44] guidelines. Repeat testing of females 16 to 25 years of age, considered to be at highest risk for CT infection in accordance with the 2010 CDC[45] guidelines: • 19.1% (50,959/266,472) of females testing negative were retested[b] • 3.4% (1746/50,959) retested had ≥ 1 positive subsequent test result • 1.9% (978/50,959) retested were still positive on their last test. **GC** Number and per cent of females screened at their first prenatal visit in accordance with current guidelines: • 37% (137,612/368,550) aged 16 to 24 years were screened for GC in accordance with the 2010 CDC[45] and 2007 USPSTF[44] guidelines. Repeat testing of females 16 to 24 years of age, considered to be at highest risk for GC infection according to 2010 CDC[45] guidelines: • 22.1% (51,077/231,014) of females testing negative were retested[b] • 1.1% (564/51,077) retested had ≥ 1 positive subsequent test result • 0.6% (288/51,077) retested were still positive on their last test.

ACOG = American College of Obstetricians and Gynecologists; CDC = Centers for Disease Control and Prevention; CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; SDA = Strand Displacement Amplification; STI = sexually transmitted infection; TMA = transcription-mediated amplification; TOC = test-of-cure; USPSTF = United States Preventive Services Task Force.

[a] The comparator group is comprised of a subset of the population in the intervention group.

[b] Positive results were excluded to remove the impact of age on retesting.

Gynecological and Obstetric Outcomes

CT Infections Only

One study[34] reported on the effect of early detection (i.e., at or before 20 weeks of gestation) and treatment for CT in comparison to late detection (i.e., after 20 weeks of gestation) and treatment of CT on birth outcomes (preterm birth, spontaneous preterm birth, moderate-to-late preterm birth, spontaneous moderate-to-late preterm birth, very preterm birth, and spontaneous very preterm birth). In this study, moderate-to-late preterm refers to live births that occurred between 32 and 36 weeks of gestation, inclusive; while very preterm refers to live births that occurred prior to 32 weeks of gestation.[34] Spontaneous (preterm) birth refers to premature rupture of membranes and/or spontaneous onset of labour.[34] The population of interest comprised 3,354 pregnant adults and adolescents (i.e., 19 years of age and younger) in an urban county in the US who were retrospectively found to have had live births and CT infections.[34] The early detection and treatment group had significantly lower moderate-to-late and spontaneous moderate-to-late preterm births than the late detection and treatment group.[34] The early detection group reported 12.2% moderate-to-late preterm births as compared with 14.4% in the late detection group (P = 0.05), and 8.2% spontaneous moderate-to-late preterm births as compared with 10.8% in the late detection group (P = 0.01). The differences in the other birth outcomes were not statistically significant.[34]

A subgroup analysis stratified by maternal age (i.e.,< 20 years, 20 to 29 years, and > 29 years).[34] The findings demonstrated that early detection of CT reduced the risk of moderate-to-late preterm (adjusted relative risk [aRR] 0.64; 95% CI, 0.47 to 0.86) and moderate-to-late (aRR; 0.54; 95% CI, 0.37 to 0.80) spontaneous preterm birth in females less than 20 years of age but not in females 20 to 29 years of age and those 29 years of age and older.[34] Females in the less than 20 years of age group were more frequently diagnosed with chorioamnionitis, suggesting that they had a greater incidence of more invasive and severe upper genital tract infections.[34] As a result, the early diagnosis and treatment of infection reduced the risk of moderate-to-late and spontaneous moderate-to-late preterm birth.[34]

The findings are summarized in Table 6.

Table 6: Clinical Utility: Obstetric and Gynecological Outcomes

Author, Publication Year, Country, Study Design	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT Infections Only			
Folger 2014[34] US Retrospective cohort study	3,354 pregnant adults and adolescents with live births and documented CT infections (identified retrospectively) Mean age: NR	Intervention: Early detection i.e., screening and treatment for CT at or before 20 weeks of gestation without subsequent detection n = 2,009 Comparator[a]: Late detection i.e., screening and treatment for CT at or after 20 weeks of gestation or recurrent/persistent infection[b] n = 1,345 Specimen: NR Diagnostic test: NR[c]	Prevalence of preterm births in early detection vs. recurrent/persistent or late detection groups: • Preterm: 15.5% (312/2009) vs. 16.6% (223/1345), *P* = 0.42 • Spontaneous preterm: 10.5% (211/2009) vs. 12.0% (162/1345), *P* = 0.16 • M/L preterm: 12.2% (244/2009) vs. 14.4% (194/1345), *P* = 0.05 • Spontaneous M/L preterm: 8.2% (165/2009) vs. 10.8% (145/1345), *P* = 0.01 • Very preterm [d]: 3.4% (68/2009) vs. 3.2% (29/1345), *P* = 0.74 • Spontaneous very preterm: 2.3% (46/2009) vs.1.9% (17/1345), *P* = 0.44. Risk of preterm births in the early detection group[e] (aRR): [no late detection values to compare] • Preterm: 0.96 (95% CI, 0.81 to 1.13) • Spontaneous preterm: 0.92 (95% CI, 0.75 to 1.13) • M/L preterm: 0.85 (95% CI, 0.71 to 1.02) • Spontaneous M/L preterm: 0.80 (95% CI, 0.63 to 1.00) • Very preterm: 1.06 (95% CI, 0.62 to 1.80) • Spontaneous very preterm: 1.17 (95% CI, 0.61 to 2.23). **Subgroup Analyses:** Age-specific risk of preterm birth in the early detection group[f] (aRR): • M/L preterm: ○ < 20 years : 0.64[a] (95% CI, 0.47 to 0.86) ○ 20 to 29 years:1.02 (95% CI, 0.80 to 1.30) ○ > 29 years: 0.94 (95% CI, 0.44 to 2.02). • Spontaneous M/L preterm: ○ < 20 years: 0.54* (95% CI, 0.37 to 0.80) ○ 20 to 29 years: 0.98 (95% CI, 0.73 to 1.32) ○ > 29 years: 1.15 (95% CI, 0.42 to 3.10).

aRR = adjusted relative risk; CI = confidence interval; CT = Chlamydia trachomatis; M/L = moderate to late; NR = not reported.
[a] Statistically significant.
[a] The intervention group and comparator group are two distinct populations.
[b] Recurrent/persistent infection was defined as infections detected at or before 20 weeks of gestation and after 20 weeks of gestation, but at least seven days apart.
[c] It is assumed that the diagnostic test used is a NAAT.
[d] Reference group restricted to 920 mothers with CT infections detected at 21 to 31 weeks of gestation.
[e] Adjusted for combination of variables including age, race, preconception infection (CT/GC), coinfection (CT/GC), plurality, maternal education, marital status, previous preterm birth, smoking, payer source, pre-pregnancy/gestational diabetes, pre-pregnancy/gestational hypertension, pre-pregnancy weight, and primiparousity.
[f] Adjusted for variables including race, preconception infection, plurality, maternal education, previous preterm birth, smoking, and Medicaid payer source.

Neonatal Outcomes

CT Infections Only

Two studies reported on the effect of detecting and treating CT infections on various neonatal outcomes. The first study by Folger (2014)[34] evaluated the effect of early detection and treatment of CT (i.e., at or before 20 weeks of gestation) in comparison to late detection and treatment for CT (i.e., after 20 weeks of gestation) on neonatal birth outcomes (rate of low birth weight, infant mortality, mean gestational age, and mean birth weight) in 3,354 females in an urban county in the US. Infant mortality was significantly higher (2.2% versus 0.9%, $P = 0.003$) and mean gestational age was significantly lower (37.9 weeks versus 38.1 weeks, $P = 0.048$) in the early detection group compared with the late detection group. There were no statistically significant differences in the proportion of neonates born with low birth weight and in their mean birth weight. In the second study, Miller et al. (2005)[42] evaluated the gestational age and birth weight of babies born to mothers in a cohort of 752 pregnant females from a population with a high prevalence of CT (i.e., 19.7%, 148/752). There were no statistically significant differences in gestational age and birth weight of neonates born to females with infections identified at initial screening versus repeat screening.[42]

The findings from the two studies on the effect of detecting and treating CT infections on neonatal outcomes was mixed. Miller et al.(2005)[42] reported no difference in outcomes in neonates born to females who had their infections identified at initial screening versus repeated screening. Folger et al.(2014)[34] found significant differences between groups with respect to infant mortality and mean gestational age. The authors speculate that the increase in infant mortality may be due to increased severity of the infection in the early detection group, but did not report infection severity data.[34] The difference in mean gestational age between the early antenatal detection group and the recurrent or late detection group was 0.2 weeks.[34] Though this finding is statistically significant, the difference may not be clinically significant.

GC Infections Only

One study reported on birth weight and gestational age of neonates born to females who underwent initial testing for GC at entry into a prenatal program and again at 34 weeks of gestation.[43] The population of interest was comprised of 751 pregnant females from a population with high prevalence of GC (i.e., 7.8%).[43] No significant differences were found in birth weight and gestational age between females with infections identified at initial screening versus repeat screening.[43]

The findings are summarized in Table 7.

Table 7: Clinical Utility: Neonatal Outcomes

Author, Publication Year, Country, Study Design	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT and GC Infections			
Folger 2014[34] US Retrospective cohort study	3,354 pregnant females with documented CT infections Mean age: NR	Intervention: Early detection i.e., screening and treatment for CT at or before 20 weeks of gestation without subsequent detection n = 2,009 Comparator[a]: Late detection i.e., screening and treatment for CT at or after 20 weeks of gestation or recurrent/persistent infection[b] n = 1,345 Specimen: NR Diagnostic test: NR	Neonatal outcomes in early detection vs. recurrent/persistent or late detection groups: • Proportion with low birth weight: 13.8% (277/2009) vs. 14.6% (196/1345), *P* = 0.52. • Infant mortality[c]: 2.2% (45/2009) vs. 0.9% (12/1345), *P* = 0.003. • Mean gestational age at birth: 37.9 weeks vs. 38.1 weeks, *P* = 0.048. • Mean birth weight: 3,060.2 grams vs. 3,039.7 grams, *P* = 0.40.
Miller, Maupin, and Nsuami, 2005[42] US Retrospective chart review	752 pregnant females Mean age: NR	Intervention: Screening for CT at entry into a prenatal program n = 752 Comparator:[d] Screening at entry and repeat screening at 34 weeks of gestation n = 752 Specimen: NR Diagnostic test: Direct DNA assay (Gen-Probe, San Diego, CA)	**CT** Neonatal outcomes (Negative initial and repeat screen vs. initial test positive vs. repeat test positive): • Mean gestational age (SD) at delivery: 276.9 (10.9) days vs. 275.9 (± 13.4) days vs. 276.0 (± 13.4) days, *P* = NS. • Mean birth weight (SD): 3237 (479) grams vs. 3257 (489) grams vs. 3,153 (547) grams, *P* = NS.
Miller et al., 2003[43] US Retrospective chart review	751 pregnant females Mean age: NR	Intervention: Screening for GC at entry into a prenatal program n = 751 Comparator[d]: Screening at entry and repeat screening at 34 weeks of gestation n = 751 Specimen: NR Diagnostic test: Direct DNA assay (Gen-Probe, San Diego, CA)	**GC** Neonatal outcomes (Negative initial and repeat screen vs. initial test positive vs. repeat test positive): • Mean gestational age (SD) at delivery [days]: 276.7 (11.4) vs. 276.5 (11.7) vs. 279.7 (8.0), *P* = NS. • Mean birth weight (SD) [grams]: 3242 (490) vs. 3172 (424) vs. 3,160 (312), *P* = NS.

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; NR = not reported; NS = not significant; SD = standard deviation.

[a] The intervention group and comparator group are two distinct populations.

[b] Recurrent/persistent infection was defined as infections detected at or before 20 weeks of gestation and after 20 weeks of gestation, but at least seven days apart.

[c] Data are available for years 2007 to 2011.

[d] The comparator group is comprised of the same population of females as in the intervention group.

Preference for Specimen Sampling

CT Infections Only

Logan et al. (2005)[41] reported on patient preferences with respect to the type of specimen sampled in a cohort of females with suspected miscarriages.[41] Two hundred and seven females who agreed to participate in the study were asked to provide three samples — urine, endocervical, and self-collected vaginal samples. Of the study patients, 32.8% (68/207) agreed to provide urine and vaginal samples and declined to provide the more invasive endocervical samples. An acceptability questionnaire completed after screening, revealed that urine sampling was significantly preferred over vaginal and endocervical sampling ($P < 0.001$);[41] whereas, vaginal sampling was significantly preferred over endocervical sampling ($P < 0.001$).[41]

A smaller number of females (n = 139) agreed to provide the more invasive endocervical samples in comparison to the self-collected vaginal (n = 207) and urine sampling (n = 207).[41] The study demonstrated that non-invasive sampling by urine is preferred over vaginal and endocervical sampling. The findings are summarized in Table 8.

Number of Females Declining Screening

CT Infections Only

Logan et al. (2005)[41] also reported on the number of females who declined screening. Of the 310 females with suspected miscarriages invited to participate in the screening, 21 were excluded due to antibiotic use in the past four weeks. Of the 289 females who were eligible to be screened, 26.6% or 77 of the females declined the invitation to participate. Reasons for declining included, *"I have enough to deal with already"* (p.104),[41] "*I do not think I have C.trachomatis"* (p.104)[41] and *"I have been tested before*" (p.104). The distress of undergoing a miscarriage may have contributed to a number of females declining screening.[41] The findings are summarized in Table 9.

Number of Females Treated for CT and/or GC Infections

CT and GC Infections

Of the studies reviewed, one study[36] provided outcome data on the number of CT and GC infections identified through screening and subsequently treated. In the study by Berggren and Patchen (2011),[36] all (100%) positive CT and GC infections were treated with 1 g oral azithromycin and 125 mg intramuscular ceftriaxone, respectively. At entry into prenatal care, 24 (100%) women were treated for CT, eight (100%) were treated for GC, and five (100%) were treated for coinfection with CT and GC.[36] At repeat screening, 13 (100%) were treated for CT infections and seven (100%) were treated for GC.[36]

Without repeat screening the diagnosis and treatment of 13 CT infections and seven GC infections would have potentially been missed.

CT Infections Only

Of the studies reviewed, one study[42] reported on the number of CT infections identified through screening and how they were subsequently treated. In the study by Miller et al. (2005)[42] all (100%) infections were treated with 1 g oral azithromycin. At entry into the prenatal program, 105 infections with CT were diagnosed and treated.[42] Repeat screening at 34 weeks of gestation resulted in the detection and treatment of 43 (100%) infections of CT.[42]

Without repeat screening at 34 weeks of gestation the diagnosis and treatment of 43 cases of CT would have potentially been missed.[42] Of these 43 cases, 29 were new infections and 14 were repeat infections. However, additional details regarding whether the infection was from the same sexual partner or new partner were not provided.

GC Infections Only

One study[43] reported on the number of GC infections identified through screening and subsequently treated. In the study by Miller et al. (2003)[43] all (100%) positive infections were treated with a 400 mg dose of oral cefixime. At entry into the prenatal program, 38 (100%) infections with GC were diagnosed and treated.[43] Of these 38 females, 19 were also treated for coinfection with CT.[43] Repeat screening at 34 weeks of gestation resulted in the detection and treatment of 20 (100%) infections of GC.[43] Eight of these females were also treated for coinfection with CT.[43]

The lack of repeat screening at 34 weeks of gestation would have potentially missed the diagnosis and treatment of 20 cases of GC and eight coinfections with CT.[43] Of these 20 cases, 19 (95%) were new infections and one (5%) was a repeat infection.[43]

The findings are summarized in Table 10.

Table 8: Clinical Utility: Preference for Specimen Sampling

Author, Publication Year, Country, Study Design	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT Infections Only			
Logan et al. 2005[41] UK Cross-sectional study	207[a] adults and adolescents who were admitted into an early pregnancy assessment unit and had a positive pregnancy test, history of vaginal bleeding and were < 24 weeks pregnant Median age: 28 years	Intervention: Screening for CT with endocervical[b], self-collected vaginal, or urine sample followed by semi-structured questionnaire Comparator: Screening for CT by an alternate specimen Specimen: Endocervical (n = 139)[c], self-collected vaginal (n = 205), or first-void urine (n = 205) samples Diagnostic test: BD ProbeTec ET System	32.8% (68/207) agreed to non-invasive sampling with urine samples or self-collected vaginal samples and declined providing endocervical samples Preferred method of sampling[c]: • Urine sampling was significantly preferred compared with vaginal sampling (P < 0.0001) and endocervical sampling (P < 0.0001). • Vaginal sampling significantly preferred when compared with endocervical sampling (P < 0.0001). .

CT = *Chlamydia trachomatis*; NR = not reported.

[a] Two samples were excluded as they leaked, leaving 205 samples for analysis.

[b] The endocervix is part of the cervix.[46]

[c] The number of females who provided samples differed from the number who stated their preference for method of sampling.

Table 9: Clinical Utility: Number of Females Declining Screening

Author, Publication Year, Country, Study Design	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT Infections Only			
Logan et al. 2005[41] UK Cross-sectional study	207[a] adults and adolescents who were admitted into an early pregnancy assessment unit and had a positive pregnancy test, history of vaginal bleeding and were < 24 weeks pregnant Median age: 28 years	Intervention: Screening followed by semi-structured questionnaire Comparator: Screening by an alternate specimen Specimen: Endocervical (n = 139)[b], self-collected vaginal (n = 205), or first-void urine (n = 205) samples Diagnostic test: BD ProbeTec ET System	Females declining invitation to participate in screening: Of the 289 of the females eligible to participate: • 77 (26.6%) of 289 declined to participate; 212 were eligible for inclusion in the study; 5 samples were then excluded[b] leaving 207 females.

CT = *Chlamydia trachomatis;* NR = not reported.

[a] Two samples were excluded as they leaked, leaving 205 samples for analysis.

[b] Three endocervical samples were not taken by staff and two samples leaked and were excluded from the study.

Table 10: Clinical Utility: Number of Females Treated for CT and GC Infections

Author, Publication Year, Country, Study Design	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT and GC Infections			
Berggren and Patchen, 2011[36] US Prospective cohort study	125 pregnant adolescents Median age at delivery: 17 years (range, 12 to 18 years)	Intervention: Screening for CT and GC at entry to prenatal care n = 125 Comparator[a]: Repeat screening for CT and GC during the third trimester[b] n = 95 Specimen: Endocervical culture or urine samples Diagnostic test: NAAT[c]	All females testing positive for CT were treated with 1 g oral azithromycin and 125 mg intramuscular ceftriaxone for GC Screened at entry into prenatal care: • The prevalence of CT was 19.2% (24/125) • The prevalence of GC was 10.4% (13/125); 5 were co-infected with CT as well 24 (100%) were treated for CT infections; 8 (100%) were treated for GC; and 5 (100%) were treated for coinfection Repeat screening during third trimester or at 4 weeks TOC for CT: • The prevalence[d] of CT was 13.7% (13/95); 9.5% (9/95) were diagnosed with CT reinfections and 4.2% (4/95) with new CT infections • The prevalence[d] of GC was 7.4% (7/95); 3.2% (3/95) were diagnosed with GC reinfections and 4.2% (4/95) with new GC infections 13 (100%) were treated for CT infections and 7 (100%) were treated for GC infections
Miller, Maupin, and Nsuami, 2005[42] US Retrospective chart review	752 pregnant females Mean age: NR	Intervention: Initial screening for CT at entry into a prenatal program n = 752 Comparator[c]: Repeat screening at 34 weeks of gestation n = 752 Specimen: NR Diagnostic test: Direct DNA assay (Gen-Probe, San Diego, CA)	**CT** All females testing positive for CT were treated with 1g oral azithromycin Screened at entry into prenatal program (n = 752): • The prevalence of CT was 14.0% (105/752) 105 (100%) were treated for CT infections Repeat screening at 34 weeks of gestation (n = 752): • The prevalenced of CT was 5.7% (43/752); of these, 3.85% (29/752) were new cases and 1.86% (14/752) were diagnosed with CT at entry had a positive repeat test indicating reinfection or treatment failure 43 (100%) were treated for CT infections

Author, Publication Year, Country, Study Design	Patient Characteristics	Intervention, Comparator(s), Specimen, Screening Test	Results
CT and GC Infections			
Miller et al., 2003,[43] US Retrospective chart review	751 pregnant females Mean age : NR	Intervention: Initial screening for GC at entry into a prenatal program n = 751 Comparator:[e] Initial screening at entry and repeat screening at 34 weeks of gestation n =751 Specimen: NR Diagnostic test: Direct DNA assay (Gen-Probe, San Diego, CA)	GC All females testing positive for GC were treated with 400 mg dose of oral cefixime Screened at entry into prenatal program (n = 751): • The prevalence of GC was 5.1% (38/751); 19 were co-infected with CT 38 (100%) were treated for GC infections; 19 were also treated for CT infections Repeat screening at 34 weeks of gestation (n = 751): • The prevalence of GC was 2.7% (20/751); 2.5% (19/751) were new cases; 0.13% (1/151) were diagnosed with GC at entry had a positive repeat test indicating reinfection or treatment failure • 1.1% (8/751) were co-infected with CT 20 (100%) were treated for GC infections; 8 were also treated for CT infection

CT = *Chlamydia trachomatis;* GC = *Neisseria gonorrhoeae;* NAAT = nucleic acid amplification test; NR = not reported; TOC = test-of-cure.

[a] The comparator group is comprised of the same population of females as in the intervention group; however, the difference in sample size between the intervention and comparator groups is due to loss to follow-up.

[b] A test-of-cure visit was administered 4 weeks after the initial positive test and treatment, but the study does not include the results.

[c] This study did not independently report the results of culture and NAATs for CT and GC infection. It was assumed that the majority of samples were tested by NAAT.

[d] The number and per cent of CT and GC infections was calculated from data presented in the study.

[e] The comparator group is comprised of the same population of females as in the intervention group.

Assessment of the Overall Body of Evidence

The outcomes for detection yield, clinical utility, and harms were rated as important or critical by the decision-makers and stakeholders who were consulted for this review, and therefore, they were all included in the evidence profile tables. The GRADE evidence profile tables can be found in Appendix 8, Table 47 to Table 57.

The initial level of confidence of the evidence included in the report for detection yield and clinical utility started out as low based on study design, as all 10 included citations were non-randomized studies.

Based on the quality assessment of the included citations, there was a high risk of bias related to patient selection in nine of the 10 included studies. Patient selection was considered to be a serious limitation and the level of confidence for all outcomes was further downgraded by one, from low to very low.

Serious inconsistency was identified for three outcomes — detection yield: endocervical versus urine versus vaginal samples; clinical utility: mean gestational age; and clinical utility: mean birth weight. For the detection yield outcome (Table 49), the level of confidence was downgraded as the wide range of values reported could not be explained by a specific source of heterogeneity. For the clinical utility outcomes (Table 53), inconsistency was considered serious due to the heterogeneity in the intervention and comparators across studies.

Indirectness was a serious concern for assessing the impact of repeat screening on detection yield (Table 47). All the included studies reported outcomes for screening once at entry into prenatal care and for screening in the same population (full or subset) once at another time point. There was no direct comparison between screening once versus screening multiple times. The information on the number of infections that would have been missed without repeat screening had to be extracted from the studies. The authors did not explicitly discuss the impact of repeat screening. Data were extracted from the studies to determine the cumulative effect of repeat screening. Furthermore, prevalence data were extracted from some studies that were not conducting population-level screening exercises. For example, Berggren et al. (2011),[36] Aggarwal et al. (2010),[38] and Miller et al. (2005)[42] enrolled 125, 211, and 752 patients, respectively.

Imprecision could not be assessed as most results were not reported as point estimates with 95% confidence intervals.

A formal assessment of publication bias was not feasible as at least 10 citations of a given study design and a particular outcome were not identified.

The final GRADE evidence quality level for all detection yield and clinical utility outcomes was very low. There was no evidence identified with respect to the harms of differing screening strategies during pregnancy.

Summary of Clinical Results

The evidence from the literature enabled a comparative assessment of detection yield based on varying specimen (i.e., urine versus endocervical samples or vaginal samples); approach (universal versus targeted), timing (at entry to prenatal care only versus during the third trimester only); and frequency (i.e., once versus twice during pregnancy). The literature also enabled a comparative assessment of clinical utility based on varying specimen (i.e., urine versus endocervical or vaginal samples); approach (universal versus targeted); timing (i.e., early screening versus screening after 20 weeks); timing and frequency.

Information on the impact of alternative tests and management strategies was not collected. All included studies used NAAT and all positive cases were treated and a test-of-cure was administered.

Detection Yield

Specimen: There is conflicting evidence on the relative detection rates of CT infections among cervical, vaginal, or urine samples. One study found no statistically significant difference in the prevalence of CT infections using endocervical and urine samples. Findings from two other studies suggest that urine samples may have decreased test performance as compared with endocervical and vaginal samples. There was insufficient information to perform subgroup analysis across multiple studies.

Approach: Given that adolescents (< 20 years of age) are more likely to have a positive test for CT and/or GC at any time point,[42,43] targeting this population for screening may potentially result in higher detection yield than universal screening. However, the results from one study suggest that targeted screening using the USPSTF criteria (24 years old or younger, being single, and being black or Hispanic) could potentially miss a substantial number of CT and GC infections in pregnant persons who did not fit the screening criteria.[39] This form of targeted screening would leave excluded pregnant persons at risk for infection. Similarly, while early detection of CT infection (at or before 20 weeks of gestation) was associated with a lower risk of moderate to late (M/L) preterm and M/L spontaneous preterm births in adolescents, the effect was not significant in pregnant persons 20 years of age and older.[34] In one study, universal screening at least once during pregnancy resulted in CT prevalence of 4.7% (out of 2,104) compared with 1.33% using a targeted risk factor-based screening.[39]

Timing and frequency: Repeat screening at another time point in pregnancy resulted in the detection and treatment of a substantial number of new infections and reinfections with CT and GC, which would have been potentially left undiagnosed if screening had been limited to entry at prenatal care only.[35,36,38] Irrespective of having been tested at entry into prenatal care, as many as 13.7% and 7.4% of pregnant persons had an infection for CT and GC, respectively, that was detected in their third trimester. These results favour an increase in the frequency of screening from once at entry to prenatal care to include screening at a second time point during pregnancy. It is not clear from the studies whether repeat screening was conducted in the third trimester for pregnant persons who had made a test-of-cure visit. In practice, repeat testing may be performed in the third trimester, independently of a test-of-cure visit.

Clinical Utility

Specimen: Approximately one-third of 207 pregnant persons in one study agreed to non-invasive sampling by self-collected vaginal swabs or urine samples.[41] Although the same number of women provided urine and vaginal samples, urine samples were preferred over vaginal and cervical samples.[41] A quarter of the pregnant persons invited to screen declined to participate in the study.[41] Given that there is conflicting evidence on relative detection yield across the various samples,[37,40,41] caution must be taken in selecting the patients' preferred form of screening over others.

Approach: Findings from a large study of almost 1.3 million persons across the US suggest that just over 60% of females were not being screened in accordance with guidelines, potentially resulting in a number of undiagnosed CT and GC infections. The early detection and treatment of CT infections in females less than 20 years of age reduced the risk of

moderate-to-late preterm birth and moderate-to-late spontaneous preterm birth by 64% and 54%, respectively.

Timing and frequency: The evidence was mixed with regard to the effect of detection and treatment of CT infections at entry into prenatal care versus another time point in pregnancy on neonatal outcomes. One study reported that the detection and treatment of CT infections earlier in the pregnancy was associated with lower mean gestational age and higher infant mortality, but had no statistically significant impact on birth weight.[34] The authors speculate that the increase in infant mortality may be due to increased severity of the infection in the early detection group.[34] The difference in mean gestational age between the early antenatal detection group and the recurrent or late detection group, though statistically significant, may not be clinically significant.[34] Another study confirmed that there was no impact on birth weight; however, there was also no association with mean gestational weight.[42] The findings from another study reported that GC infections early in pregnancy in comparison to late in pregnancy had no effect on mean gestational age and birth weight.[43]

Assumptions: The type of specimen utilized was not reported in five of the 10 included studies.[34,35,39,42,43] This report assumes that only cervical, urine, and/or vaginal samples were used when screening pregnant persons.

Harms

No evidence was found regarding the harms of differing screening strategies during pregnancy.

The implications of the results are outlined in the Discussion section, in consideration of results from the other analyses conducted as part of this HTA.

Economic Analysis

The economic analysis addresses the following research question:

Research Question 2: What is the most cost-effective screening strategy during pregnancy for *Chlamydia trachomatis* and/*or Neisseria gonorrhoeae* in pregnant persons and their infants up to the postpartum period?

Review of Economic Studies

A review of the published literature was conducted to identify relevant economic evaluations that assessed the cost-effectiveness of strategies for screening of CT and GC infections during pregnancy. Three unique economic evaluations were identified that evaluated the cost-effectiveness of at least one CT screening strategy in comparison to another CT screening strategy in adult and adolescent pregnant persons.[48-50] These economic evaluations, none of which were conducted in a Canadian setting, generally considered the time from gestation to the postpartum period at minimum, and included outcomes for the mother (e.g., pelvic inflammatory disease), pregnancy (e.g., preterm birth), and the infant (e.g., conjunctivitis and pneumonia). Appendix 9 provides further details on each economic evaluation. An economic evaluation that addressed the economic impact of GC screening in pregnant persons was not identified in the published literature.

All three economic evaluations on CT screening were decision tree models, of which two were based on a one-year time horizon and focused specifically on a high-risk population of adolescent and young pregnant women under a third-party payer perspective.[48,49] The third study assessed the effectiveness of screening strategies in a general pregnant population under a societal perspective and adopted an undefined time horizon that appeared to be longer than one-year as it accounted for subsequent pregnancies and long-term consequences such as infertility and chronic pelvic pain.[50] All three studies were also unclear regarding the strategy for CT infection screening as it did not describe the timing or type of screening interventions assessed.[48]

In the cost-utility analysis by Ong et al., with a one-year time horizon, antenatal screening of pregnant women 16 to 25 years old was found to be cost-effective at the willingness-to-pay threshold of $50,000 (in 2014 Australian dollars) per quality-adjusted life year (QALY) compared with no antenatal screening or to selective screening of 16 to 19 year olds or those who have had multiple sexual partners within a year.[48] Antenatal screening was also found to be dominant (i.e., less costly and more effective) compared with no antenatal screening if the prevalence of CT was higher than 11%.[48] In another cost-utility analysis by Rours et al., that adopted a longer time horizon, universal antenatal screening was found to be dominant compared with no antenatal screening.[50] In the cost-benefit analysis by Ditkowsky et al., prenatal screening for CT in 15 to 24-year-old high-risk pregnant women was found to be more costly but also resulted in reduced morbidity to mother and infant pairs compared with no prenatal screening.[49] The analysis also found that such prenatal screening could be cost-saving if CT prevalence was higher than 16.9%.[49]

Given that none of the studies fully addressed our stated decision problem, a de novo economic model was deemed necessary.

Methods

The objective of the economic analysis was to evaluate the associated costs, health outcomes, and cost-effectiveness of different screening strategies for CT and GC infection in

pregnant persons for the duration of the pregnancy and its subsequent impact on both the birthing parent and the infant up to 19 weeks of age.

A protocol developed a priori for the economic analysis was adhered to.[29] As noted in the Protocol Amendments table, the only deviations to the protocol were the changes in the research question and the associated time horizon for the analysis. Greater clarity was provided in the revised research question to highlight the fact that the economic analysis aligned with the more focused scope defined by this HTA by addressing immediate impacts of screening during pregnancy and did not consider any potential further long-term impacts of CT and GC infection beyond the postpartum period. The start of the time horizon was shifted from the beginning of the pregnancy to the time at first trimester screening (i.e., gestational age of 12 weeks) to limit the model to only account for the periods that would be affected by the screening decisions. The end of the time horizon was changed from three months postpartum to 19 weeks postpartum to account for the full incubation period for CT pneumonia in infants.[1]

Type of Analysis

To facilitate comparisons of the wide-ranging health benefits associated with screening of CT and GC infection in pregnancy to both the pregnant person and the infant, QALYs were estimated in the base case, reflecting a cost-utility analysis. In addition, cost-effectiveness analyses in which clinical outcomes were defined as the number of prevented adverse pediatric and obstetric outcomes were also evaluated.

Target Population and Settings

The target population of this economic analysis was pregnant adults and adolescents 12 years and older in Canada and their offspring from the pregnancy. The age distribution in the model represented the Canadian pregnant population, based on the number of live births and fetal loss, between 15 and 44 years of age (excluding induced abortions) as reported by Statistics Canada for the years 2001 to 2005.[51] This distribution was deemed appropriate as pregnancies in individuals younger than 15 years and older than 44 years of age are relatively rare.[51]

Individuals at high risk of CT and GC infection were defined in this model based on age as those younger than the age of 25 years. This definition of high risk reflects one of the risk criteria within the Public Health Agency of Canada's (PHAC) *Canadian Guidelines on Sexually Transmitted Infections*.[21] Although other high-risk factors exist, such as sexual history and injection drug use[21] that may also be of interest, this study limited the exploration of additional subgroups to age specifically due to the availability of data. To explore screening strategies that target screening or repeat screening in high-risk individuals, age subgroups were defined (i.e., < 25 years of age and ≥ 25 years or older) and modelled separately with model parameters specific to these age groups incorporated where possible.

Table 11: Modelled Age Distribution

Age Group	Value (Probabilistic)	Reference
< 25 Years	21.37% (Range: 20.35% to 22.45%)	Statistics Canada, 2010[51]
≥ 25 Years	78.63% (Range: 77.55% to 79.65%)	

The obstetric outcome and infection status of the birthing parents were also linked to the infants. The level of prematurity was assumed to affect the infant's health utility. Infants born

to individuals with CT or GC infections were at risk of vertical transmission and, among those neonates infected, they are associated with a higher risk of the infection manifesting as conjunctivitis or pneumonia.

The setting for the analysis reflected the Canadian health care system. The care of the mother-infant pair can span multiple clinical settings including prenatal visits, labour and delivery ward, neonatal intensive care unit, and pediatric outpatient clinic. The initial contact with the health care system and all subsequent prenatal care was assumed to occur as an outpatient visit. All modelled obstetrical events (i.e., term birth occurring between 37 and 41 weeks, preterm birth occurring between 28 to 36 weeks, extremely preterm birth occurring between 20 to 27 weeks, and second and third trimester stillbirths) were assumed to be cared for in an in-patient setting. Prophylactic care of the neonate with suspected exposure to CT or GC during delivery was assumed to occur during the postpartum care period. Symptomatic pediatric CT and GC infections were assumed to be managed in a follow-up outpatient setting except for GC conjunctivitis which was assumed to be treated in an in-patient setting due to higher risk of blindness (Table 14). Conjunctiva in extremely premature infants were also assumed to be treated in an in-patient setting as their length of stay in in-patient postpartum care tends to be longer and encompass the expected onset of symptoms for these infections.

Time Horizon

As per the economic research question, the analysis reflected the period between a prenatal visit in the first trimester of pregnancy (i.e., start of the time horizon) and anchored to 19 weeks after birth or stillbirth (i.e., end of the time horizon) to capture the immediate impacts of screening. The timing of the first trimester screen (i.e., gestational age of 12 weeks) was informed by a clinician feedback. The period of up to 19 weeks after birth was selected as one of the manifestation of CT infection, pneumonia, can arise between two to 19 weeks after birth.[1]

Therefore, while all liveborn infants have an identical time horizon of 19 weeks, the time horizon for the pregnant persons can differ given that the 19-week postpartum period was anchored to births and stillbirths, both of which can occur at different time points within one's pregnancy. For example, those who delivered preterm had a shorter time horizon than those who delivered at term. To determine the expected gestational age for each obstetrical event, 2012 to 2016 Statistics Canada data on live births by weeks of gestational age[2] was consulted.

Defining the time of occurrence of events in the model was necessary to calculate the risk of new infections or reinfections over the duration of the pregnancy and, thus, the potential cost and clinical impacts of screening. The expected gestational ages of each obstetrical event within the model and the timing of prenatal visits in which CT and GC test would be performed within each trimester of pregnancy are further described in Table 12.

By setting a time horizon that was approximately one-year in duration, maternal consequences of CT and GC infection that would require longer time to develop (e.g., pelvic inflammatory disease, ectopic pregnancy, and infertility) were not captured as part of this analysis. Consequences of pediatric infection that occur over longer term such as blindness were also not captured as part of the analysis. It is important to note that these consequences have a lifelong impact and may alter the cost-effectiveness of CT and GC screening strategies if the decision problem was considered over a longer time horizon.

Given that the time horizon was approximately one-year, discounting was not applied.

Table 12: Timing of Key Events in the Economic Model

Event	Gestational Age	Source
First Trimester Prenatal Visit	12 Weeks	(Dr. Isabelle Boucoiran, University of Montreal, Montreal, QC: personal communication, 2018 Jun 27).
Second Trimester Prenatal Visit	20 Weeks	Statistics Canada's obstetric outcome timing data.[2] The prenatal visit was assumed to occur before any of the second trimester obstetric outcomes that the screening at the visit could have influenced.
Extremely Preterm Birth	24.1 Weeks	Weighted average of gestational ages at extremely preterm birth reported by Statistics Canada.[2]
Second Trimester Stillbirth	24.1 Weeks	Assumption
Third Trimester Prenatal Visit	28 Weeks	Statistics Canada's obstetric outcome timing data.[2] The prenatal visit was assumed to occur before any of the third trimester obstetric outcomes that the screening at the visit could have influenced.
Preterm Birth	34.2 Weeks	Weighted average of gestational ages at preterm birth reported by Statistics Canada.[2]
Third Trimester Stillbirth	38.7 Weeks	Assumption
Term Birth	39 Weeks	Weighted average of gestational ages at term birth reported by Statistics Canada.[2]

Screening Strategies

As per clinical experts consulted as part of this review, the prevalent CT and GC screening technology in Canada is a combination NAAT that screens for both CT and GC at the same time, and this screening technology was assumed for this analysis.

Screening strategies varied according to the population, timing and frequency of screening. The current recommended screening strategy involves universal CT and GC screening for all mothers during the first trimester prenatal visit, with consideration for rescreening in every trimester for mothers deemed to be at high risk,(e.g., age < 25 years) and follow-up screening in the third trimester for those who were tested positive for CT or GC in an earlier trimester in their pregnancy.[21] PHAC recommends that in all pregnant persons identified by screening to be positive for CT and GC infection, a test-of-cure visit is provided following treatment.[21] In those with no history of screening over the course of their pregnancy, variations exist in whether pregnant persons are screened at labour and delivery. Eleven other screening strategies were further incorporated into the model in consultation with clinical experts and are described in Table 13. Screening strategies were compared against the strategy of no prenatal visit screening (NNNM) to examine the added health benefits and costs of introducing programmatic screening before labour and delivery.

Detailed clinical management associated with screening for CT and GC infections in pregnant persons and infants are described in the Decision-Analytic Model section below.

Table 13: Modelled Screening Strategies in Pregnant Persons

Strategy Name[a]	First Trimester	Second Trimester	Third Trimester	At Labour and Delivery
UTTM (Current Practice)	Universal	Targeted	Targeted	Screen, if no prior history of CT or GC screening[b]
TTUM	Targeted	Targeted	Universal	Screen, if no prior history of CT or GC screening[b]
TTTM	Targeted	Targeted	Targeted	Screen, if no prior history of CT or GC screening[b]
UNUM	Universal	None	Universal	Screen, if no prior history of CT or GC screening[b]
UNTM	Universal	None	Targeted	Screen, if no prior history of CT or GC screening[b]
TNUM	Targeted	None	Universal	Screen, if no prior history of CT or GC screening[b]
TNTM	Targeted	None	Targeted	Screen, if no prior history of CT or GC screening[b]
UNNM	Universal	None	None	Screen, if no prior history of CT or GC screening[b]
NNUM	None	None	Universal	Screen, if no prior history of CT or GC screening[b]
TNNM	Targeted	None	None	Screen, if no prior history of CT or GC screening[b]
NNTM	None	None	Targeted	Screen, if no prior history of CT or GC screening[b]
NNNM	None	None	None	Screen, if no prior history of CT or GC screening[b]

[a] Strategies are named after the type of screening scheduled at the prenatal visit in each trimester. Each type of screening schedule is coded as: N = No screening at trimester; T = Targeted screening (age < 25 years) at trimester; U = Universal screening at trimester; M = mixed. Strategy NTUM for example, indicates no screening at first trimester, targeted screening at second trimester, universal screening at third trimester, and screening at labour and delivery if individual who presents for term birth has no prior history of screening.

[b] Assumed in the model to occur only in individuals presenting for term births. Due to the uncertainty regarding the actual rate of screening at labour and delivery, it was assumed that only 50% of individuals with no history of screening would be screened at labour and delivery. CT and GC screening at labour and delivery was assumed to not occur in extremely preterm births and preterm births.

Perspective

The perspective of a publicly funded Canadian health care payer was adopted, consistent with CADTH guidelines for the conduct of economic evaluations.[52] As such, direct medical costs were captured including the costs of diagnostic tests, physician services, management of CT and GC infections (including ocular prophylactic treatment for neonates) and hospital-related costs.

Decision-Analytic Model

A decision tree was developed to capture the impact of CT and GC screening on treatment, the risk of reinfection between prenatal visits, and the potential vertical transmission to infants during delivery in infected pregnant persons. In a decision tree, consequences of a decision are arranged in a logical order to highlight the relationships between competing courses of action (in terms of the possible sets of decisions that could be made) and the resulting set of chance events. To facilitate an efficient model that would explicitly address key outcomes related to CT and GC screening over the entire modelled time horizon, a series of subtrees were built reflecting the decision to screen the pregnant person at each trimester, the screening practice for the pregnant person during labour and delivery, and the screening practice for the infant after birth. The outcomes from a prior subtree were then linked to the next subtree in a chronological fashion. An overview of how the modelled pregnant population and their infant flows through the resulting decision tree is summarized in Figure 1. In summary, infection statuses of the modelled pregnant population were subject to change pending participation in screening at each trimester, additional screening at labour and delivery, and the risk of new infections or reinfection between the trimesters of pregnancy. Furthermore, at labour and delivery, infected parents are at risk of vertically transmitting the infection to the infant. Current clinical management of CT and GC infections

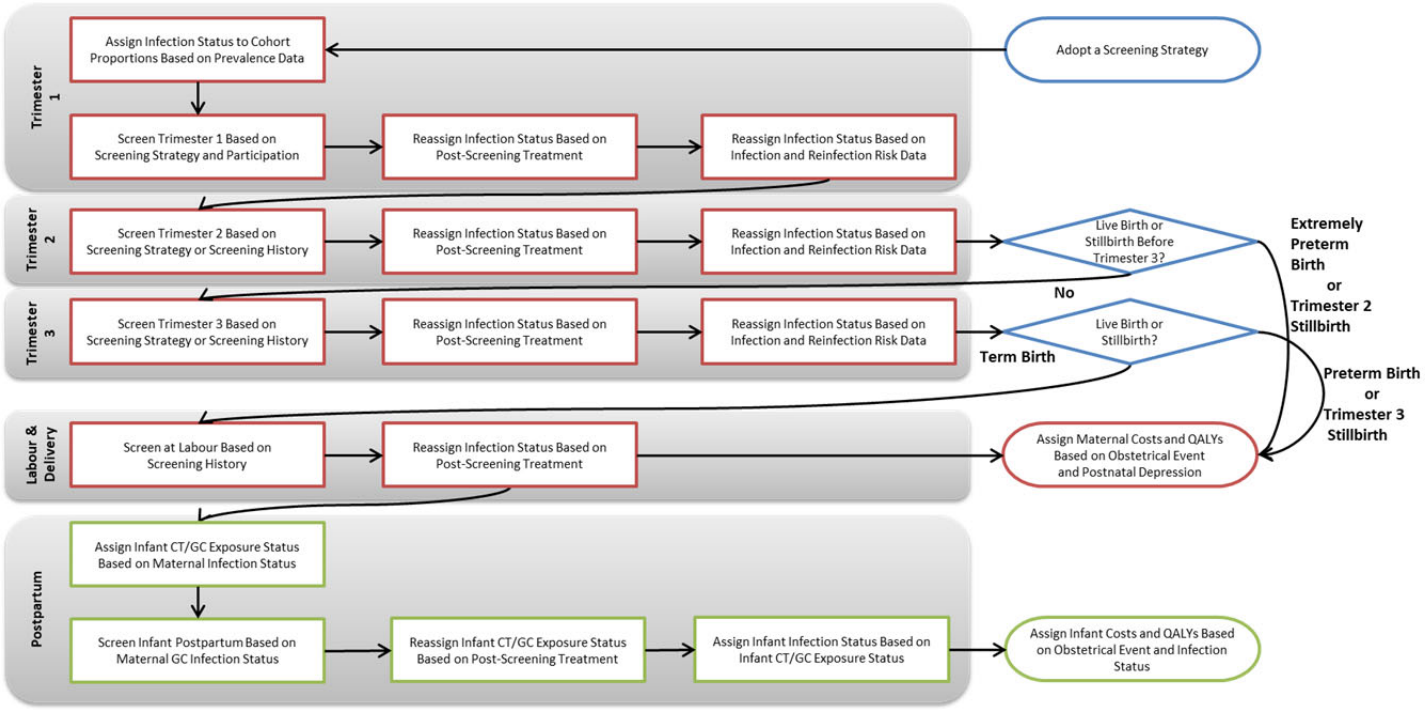
were assumed in the model (see the Modelled Screening Strategies section). Expected health benefit and costs were accrued within the model based on the mother's and infant's infection status, the obstetrical outcomes, and the pediatric outcomes.

As noted, the population represented the general Canadian pregnancy population containing a mixed cohort with varying infection statuses (i.e., uninfected, CT infected, GC infected, CT and GC co-infected). Although an infection may be detected and treated with each screening, the cohort is subjected to continued risk of infection (if previously uninfected) or reinfection (if previously infected) from continued sexual activity over the course of their pregnancy.

Relationships between CT and GC infections and a number of pediatric outcomes were captured within the modelled time horizon. Manifestations of infections included in the analysis captured the most common infections observed in clinical practice. CT conjunctivitis, CT pneumonia, and GC conjunctivitis were ultimately considered the most prevalent consequences of CT and GC neonatal infection (Dr. Joan Robinson, University of Alberta, Edmonton, AB: personal communication, 2018 Jun) and were included in the economic model. Infantile hypertrophic pyloric stenosis, an adverse event from CT infections requiring antibiotic treatment, was considered rare (Dr. Joan Robinson: personal communication, 2018 Jun) and thus excluded from the analysis.

As existing evidence suggests an unclear relationship between CT and GC infection and adverse obstetric outcomes (i.e., extremely preterm birth, preterm birth, term birth, second trimester stillbirth, and third trimester stillbirth),[53] the base-case model assumed CT and GC infections had no impact on these obstetrical outcomes. An exploratory analysis was conducted in which a potential association between obstetrical events and CT or GC infection were assessed.

Figure 1: Overview of Decision Tree



CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; QALY = quality-adjusted life-year.

Note: Red boxes denote processes relevant for the mother, and green boxes denote processes relevant for the infant.

Modelling Screening Strategies

The modelled screening practice reflected an understanding of the pregnant person's medical history in terms of their past screening results and obstetrical outcomes (Table 14) given that this has an impact on the individual and the infant's subsequent clinical management.

Table 14: Assumptions Applied to All CT and GC Screening Strategies

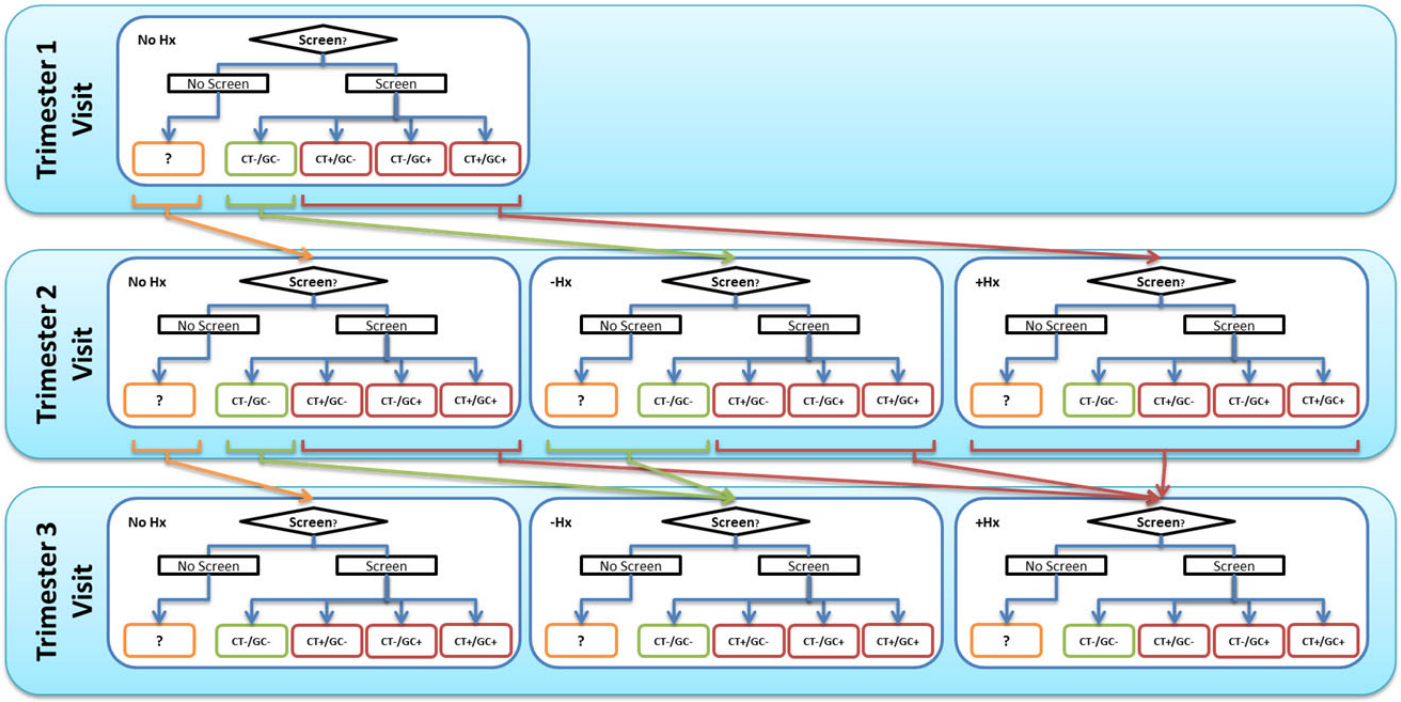
Screening Practice Assumptions
• 22.1% of mothers are not screened for CT or GC during a prenatal visit, independent of selected screening strategy, reflecting general screening participation rate.[54] • Individuals screened positive for CT and GC infection would receive treatment, which was assumed 100% successful. Treatment for CT and GC was assumed to be followed by a test-of-cure visit.[21] • If a screening strategy involved first or second trimester screening (i.e., all strategies except for strategy NNNM, NNTM, and NNUM), 35% of mothers with positive CT or GC test results during pregnancy who also received a test-of-cure visit will be rescreened at their third trimester prenatal visit. This reflects current adherence rate for rescreening based on recommended screening guideline in which mothers with a known history of infections during pregnancy are encouraged to be rescreened in their third trimester.[54] • Mothers who present for extremely preterm birth or preterm birth were not assumed to be screened at labour and delivery for CT and GC in the base-case model, regardless of the maternal infection status. As CT and GC screenings may be performed for spontaneous extremely preterm birth and spontaneous preterm births in some Canadian hospitals, (Dr. Isabelle Boucoiran, University of Montreal, Montreal, QC: personal communication, 2018 Jun 27) a sensitivity analysis was conducted to explore the impact of CT and GC screening in such circumstances. • Mothers presenting for term labour who do not have a history of CT and GC screening were assumed to be screened for both organisms. (Dr. Isabelle Boucoiran: personal communication, 2018 Jun). Due to the uncertainty regarding the rate of such screenings, the rate was assumed to be approximately 50%. Note that this means that, in the case of no scheduled prenatal visit screening (e.g., strategy NNNM) that nearly half of pregnant persons would be screened at the time of labour and delivery. Mothers presenting for term labour who have a history of CT or GC were assumed to be rescreened for both organisms. (Dr. Isabelle Boucoiran: personal communication, 2018 Jun). • It was assumed that mothers who tested positive for GC at presentation for labour received an antibiotic treatment. However, due to the uncertainty regarding whether timely treatment can be offered to effectively prevent GC exposure to the infants, these infants were assumed to be screened for potential vertical transmission and prophylactically treated with an antibiotic if found to be infected. (Dr. Joan Robinson: personal communication, 2018 Jun). Prophylaxis would treat GC infections and, in neonates with coinfections of CT and GC, the prophylactic antibiotic would also resolve CT infections. • Infants born to mothers who tested positive for CT at presentation for labour were assumed to not be screened for potential vertical transmission as would be recommended by PHAC.[21] The infants were instead assumed to be observed for any development of symptoms that would be consistent with CT infection in clinical practice. (Dr. Joan Robinson: personal communication, 2018 Jun). • All infants receive a routine visit by health care providers following birth. Any symptomatic infection was assumed to be detected either at such visits or brought to clinical attention by the parents to receive further screening and treatment as appropriate.

Three groups were tracked in the pregnant population according to their screening history until presentation at birth or stillbirth as in Figure 2:

- pregnant population without any screening history (No Hx)
- pregnant population with exclusively infection-negative history (-Hx)
- pregnant population with at least one infection-positive screening result during their pregnancy (+Hx)

These groupings were used to guide further maternal screening decisions at presentation for birth.

Figure 2: Diagram Representing the Mechanics Behind the Decision Tree to Track Screening History and its Impact on the Next Trimester of Pregnancy and Subsequent Screens



CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; Hx = screening history; ? = screening result not available; - = Infection-negative screening result; + = Infection-positive screening result.

At presentation for birth, if a pregnant person's CT and GC screening history indicated a prior infection during their pregnancy, the individual received further screening for CT and GC. If the screening history instead indicated at least one infection-negative test result and no infection-positive test result, the individual did not undergo additional screening. As such, if their prior screening results were false negatives, this would mean that their infants would be at risk from vertical transmission of CT and GC given that the pregnant person remained infected.

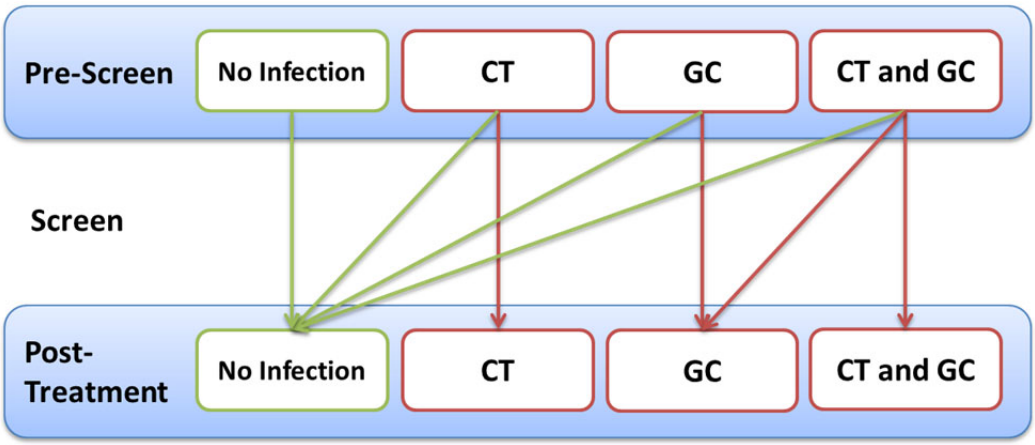
Modelling Infections

The points of screening in the model served to detect and manage CT and GC infections to reduce the prevalence of infections in mothers and the likelihood of vertical transmission and symptomatic infections in infants. In the model, infection status changed following screening, as illustrated in Figure 3 for pregnant person, and Figure 4 for infants born to individuals with known active GC infection.

Therefore, in the economic analysis, infection and exposure status changes were informed by the screening decision, the diagnostic performance of NAATs at the time of screening, and the subsequent treatment regimen administered based on the screening results. For instance, in individuals with both CT and GC coinfection, choosing to not screen at a particular point in the model time horizon or a false-negative screening result for both CT and GC infections when participating in programmatic screening would allow the existing infections to continue. Similarly, screening tests in an individual with both CT and GC

coinfection that produced a CT-positive and GC-negative screening result would lead to inadequate treatment as only the CT portion of the coinfection would be treated. Of note, those co-infected who screen positive for GC but negative for CT would be treated for both infections as the treatment regimen for GC for mothers includes azithromycin which is also used to resolve CT infections.[21]

Figure 3: Potential Change in Infection Statuses for Pregnant Persons at Screening



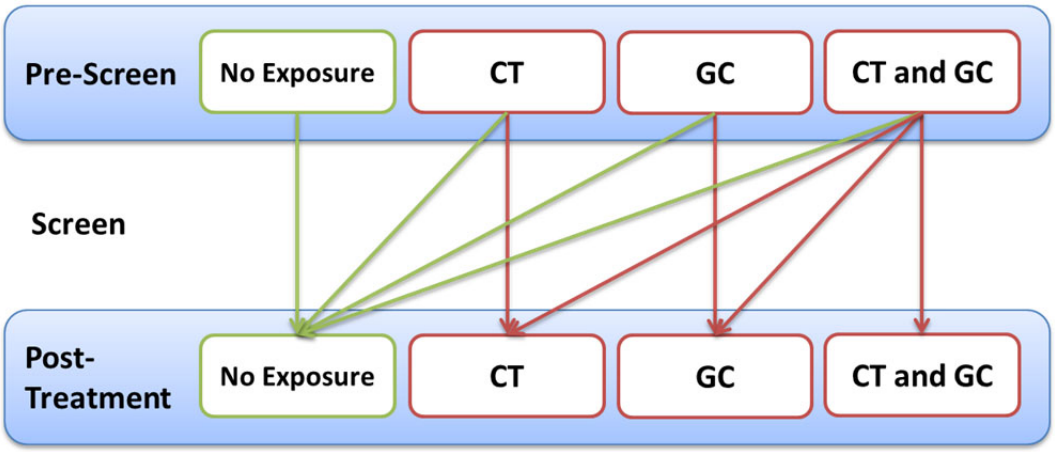
CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*.

Green arrow = curative treatment. The base-case analysis assumes treatment is 100% effective; Red arrow = inadequate treatment based on a false-negative or false-positive screening result.

The analysis modelled vertical transmissions based on the mother's infection status and screening history. For infants born to infected mothers who were not screened at presentation for labour and delivery, they were assumed to be exposed to the same microbes the mother was infected with. For those infants born to mothers who were screened and treated during labour and delivery, there is uncertainty regarding the timeliness of screening and administration of antibiotic treatments to effectively prevent vertical transmission to the infant. It was therefore assumed that the risk of vertical transmission in this situation was approximately 50%.

As described previously in Table 14, infants born to mothers with GC-positive screening results during labour and delivery were further screened for exposure to GC after birth, reflecting current clinical practice. Figure 4 illustrates how the various pre-screen exposure statuses of these infants could change pending treatment based on the infants' screening results.

Figure 4: Potential Change in CT and GC Exposure Statuses for Infants With Mothers Who Were GC-Positive at Presentation for Labour



CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*.

Green arrow = curative treatment that clears any previous exposure to CT and/or GC. The base-case analysis assumes treatment is 100% effective; Red arrow = inadequate treatment based on a false-negative or false-positive screening result.

For those infants who were exposed to CT or GC from vertical transmission, a range of infection manifestations were modelled. An exposure to CT or GC can either develop to a symptomatic manifestation, or resolve without infection. As noted, exposure to CT in infants can lead to the development of CT conjunctivitis or CT pneumonia as infections, while an infant exposed to GC could only potentially develop GC conjunctivitis as an infection.

Clinical Inputs

Natural History

Obstetric Outcomes

The probabilities for the obstetric outcomes in the model were informed by the number of fetal deaths and live births that have been reported across a range of gestational ages by Statistics Canada between 2012 and 2016.[2,55] Live births that occurred between 20 and 27 weeks of gestational age were labelled as extremely preterm births, those that occurred between 28 and 36 weeks were labelled as preterm births, and those that occurred between 37 and 41 weeks were labelled as term births. Post-term births, defined as those occurring after 41 weeks of gestational age, were not accounted for in the model as these were rare events that occurred in only 0.4% of births.[2] Stillbirths were labelled as occurring in the second trimester if the fetal death occurred between 20 and 27 weeks of gestation age and occurring in the third trimester if occurring at a later time point.

Odds of obstetric outcomes were calculated, based on the number of live births and fetal deaths reported by Statistics Canada.[2,55]These odds were in turn converted to probabilities at second and third trimester using the formula:

$$\text{Probability} = \frac{\text{Odds}}{1 + \text{Odds}}$$

The resulting conditional probabilities of obstetric outcomes by trimester are reported in Table 15.

Table 15: Calculated Mean Obstetric Outcome Probabilities by Trimester

Obstetric Outcome for a Pregnant Person at the Beginning of:	Mean Probability
Second Trimester	
Extremely Preterm Birth	0.5 %
Second Trimester Stillbirth	0.5 %
Continue Gestation to Third Trimester	99.0 %
Third Trimester	
Term Birth	92.4 %
Preterm Birth	7.4 %
Third Trimester Stillbirth	0.3 %

Infections

The underlying prevalence of CT and GC infections at the beginning of the model was informed by a retrospective study of at least 19-weeks pregnant women in a Quebec hospital (n = 2,221).[56] CT was found in 1.9% of the pregnant women, GC in 0.2%, and CT and GC coinfections in 0.1%.[56]

Among those without a history of CT and GC infection, the model incorporated a probability of acquiring a new infection at both the second and third trimester. This was based upon the annual incidence of CT and GC infections from PHAC's 2015 national surveillance data.[57,58] The annual incidence rates in the pregnant population were assumed to be equal to those in the general female population, and were converted to annual probabilities. Data for multiple age groups were incorporated into the modelled age group of those younger than 25 years old (15 to 19 years and 20 to 24 years) and those 25 years old and older (25 to 29 years, 30 to 39 years, and 40 to 59 years) by weighting infection rates to the proportion in each age cohort (Table 16).

CT and GC infections were assumed independent and the probability of new coinfections in the second and third trimesters was based on multiplying the probability of CT incidence and GC incidence. Although this assumption likely leads to an underestimation (i.e., as the association between CT and GC is unlikely to be independent due to shared risk factors), a joint correlation between CT and GC infection was not available in this patient population to calculate the probability of coinfection.

Antibiotic treatment was assumed to be 100% effective. Reinfection in pregnant persons who had been previously infected during the model time horizon was based on reinfection rates informed by a retrospective study of GC infection based on 1997 to 2003 Alberta surveillance data.[59] The annual probability of GC reinfection was calculated to be 2.31% (95% CI, 2.07% to 2.56%), with those under the age of 25 years showing a trend of increased risk of reinfections compared with those 25 years or older (mean relative risk 1.12; 95% CI, 0.95 to 1.43). The probability of CT reinfection was assumed to be equal to the calculated probability of GC reinfection given the paucity of literature on this topic. As noted in the Time Horizon section, the above annual probabilities of infection and reinfection were converted to appropriate time-dependent infection and reinfection probabilities for each trimester and for labour and delivery.

Table 16: Infection Probabilities Input Parameters

Parameter	Value (Probabilistic)	Reference
CT Prevalence	1.9%	Boulay et al., 2018[56]
GC Prevalence	0.2%	
CT and GC Coinfection Prevalence	0.1%	
Probability of CT Infection Age < 25 Years Age ≥ 25 Years	 2.15% (Range: 1.78% to 2.25%) 0.63% (Range: 0.06% to 1.06%)	Choudhri et al., 2018[57]
Probability of GC Infection Age < 25 Years Age ≥ 25 Years	0.16% (Range: 0.11% to 0.18%) 0.14% (Range: 0.03% to 0.21%)	Choudhri et al., 2018[58]
Annual GC Reinfection Rate (All ages)	0.0234 (95% CI, 0.0209 to 0.0259)	De et al., 2007[59]
GC Reinfection Relative Risk (Age < 25 years vs. ≥ 25 Years)	1.12 (95% CI, 0.95 to 1.43)	
Annual CT Reinfection Rate (All ages)	0.0234 (95% CI, 0.0209 to 0.0259)	Assumed same as GC
CT Reinfection Relative Risk (Age < 25 years vs. ≥ 25 Years)	1.12 (95% CI, 0.95 to 1.43)	
Probability of treatment success	100%	Assumption

CI = confidence interval; CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*.

Vertical Transmission and Pediatric Infections

The model parameters for CT pediatric infections were informed by a 2003 CT oral prophylaxis modelling study that had conducted a literature search for incidence of CT conjunctivitis and pneumonia in infants who were exposed to CT at birth and derived a pooled incidence for both manifestations of CT infection.[60] For GC, a range of GC ophthalmia rates cited by the Canadian Pediatric Society (CPS)[19] were used to inform incidence of GC conjunctivitis in infants exposed to GC at birth. The probabilities of pediatric infections in CT or GC exposed infants are listed in Table 17. Similarly, treatment effectiveness in infants was assumed to be 100%.

Table 17: Probability of Symptomatic CT and GC Infections in Exposed Infants

Probability	Value (Probabilistic)	Reference
GC Conjunctivitis	40% (Range: 30% to 50%)	Moore and Macdonald, 2015[19]
CT Conjunctivitis	15% (Beta distribution: α = 156; β = 899)	Rosenman et al., 2003[60]
CT Pneumonia	7% (Beta distribution: α = 42; β = 555)	

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*.

Diagnostic Test Performance

To inform the accuracy of NAAT in the model, a meta-analysis was conducted on the reported NAAT diagnostic test accuracy for the female population, extracted from the US Preventive Services Task Force (USPSTF) recommendation for CT and GC screening.[14] Methodology for the meta-analysis are further detailed in Appendix 10.

The calculated pooled sensitivity and specificity for CT NAAT were 0.93 (95% CI, 0.91 to 0.946) and 0.996 (95% CI, 0.994 to 0.998) respectively, while for GC NAAT were 0.917 (95% CI, 0.87 to 0.948) and 0.998 (95% CI, 0.996 to 0.999) respectively. Due to the limited

available information for NAAT performance in infants, the same diagnostic test accuracy as the pregnant person was assumed.

The parameters for the summary receiver operating characteristic (SROC) curve generated for the above meta-analysis were incorporated into the model to permit probabilistic analysis while preserving the correlation between diagnostic measures. Specifically, the bivariate model described by Harbord et al., 2007[61] was used to derive stochastically generated sets of sensitivity and 1-specificity parameters.

Health Utilities

Pregnant Persons

Baseline health utilities were informed by the Health Utilities Index 3 (HUI3) measurements taken from the 2013-2014 Canadian Community Health Survey.[62] Specifically, utilities values from a female population were weighted by the expected Canadian pregnancy age distribution to derive utilities for women younger than 25 years of age and for those who were 25 years and older. These utility values were applied to the duration of life-years accumulated by pregnant persons between the first trimester screening and 19 weeks after delivery. No disutility was applied to false test results (i.e., no harms assumed from the test itself).

Infants

Health utilities based on gestational maturity (Table 18) were applied to infants from birth to the end of the modelled time horizon. HUI3 utility values for various levels of gestational outcomes were informed by a 2017 meta-regression of pediatric health utilities.[63] Specifically, the baseline coefficient of the meta-regression was used to inform the utility weight associated with term birth. Utility decrements were calculated for preterm birth and, for extremely preterm births. Specifically, the study separated utilities for extremely preterm birth by the presence of major comorbidity. In the economic model, it was assumed that 67.6% of extremely preterm births were associated with a major comorbidity.[64]

As CT and GC conjunctiva tend to resolve quickly within a few days after treatment (Dr. Joan Robinson: personal communication, 2018 Jun), utility decrement associated with these infections were assumed to have a negligible impact to the model outcomes and thus were not incorporated into the analysis. For CT pneumonia, the associated utility decrement was proxied by the utility decrement of influenza and pneumonia in the aforementioned meta-regression, and was applied to a period of one week to reflect the average time to recovery after treatment (Dr. Joan Robinson: personal communication, 2018 Jun).

Table 18: Postpartum Infant Utility Values

Parameter	Value (Probabilistic)	Reference
Baseline Infant Utility (Term Birth)	0.876 (SE: 0.045)	Kwon et al., 2017[63]
Utility Decrement of Preterm Birth[a]	0.021 (SE: 0.014)	
Utility Decrement of Extremely Preterm Birth With Major Comorbidity Without Major Comorbidity	 0.268 (SE: 0.065) 0.081 (SE: 0.037)	
Proportion of Major Comorbidity in Extremely Preterm Birth	67.6%	Anderson et al., 2016[64]
Utility Decrement of CT Pneumonia[b]	0.256 (SE: 0.071)	Kwon et al., 2017[63]

CI = confidence interval; SE = standard error.

[a] Utility decrement of preterm birth was proxied by the utility decrement of very preterm birth.

[b] Utility decrement of CT pneumonia was proxied by the utility decrement of influenza and pneumonia.

Costs and Resources

All costs and resource use data informing the economic analysis were derived from Canadian data. If 2018 costs were not available, costs from another year were inflated to estimate March 2018 price based on the Canadian consumer price index (CPI).[65,66] Where costs may also be attributed to other payers (e.g., private, individual payers), such as outpatient care drug costs, they were assumed to be covered by a publicly funded insurance plan to capture the analytic perspective of the publicly funded Canadian health care payer to the fullest extent. Resources with equal rates of utilization across the compared screening strategies (e.g., routine visit by health care providers following birth) were omitted from the analysis.

Costs associated with obstetric outcomes

Although obstetric outcomes did not differ between pregnant persons with different infection statuses in the base-case model (i.e., no differences in rates of obstetric adverse events by different screening strategy), costs associated with these outcomes were estimated for the purposes of informing the exploratory analysis that assumed an association of CT and GC infection with adverse obstetric outcomes.

All births and stillbirths in the analysis were assumed to have involved a single fetus and to have occurred in an in-patient setting. Procedure costs were informed by 2016 Ontario Case Costing Initiative (OCCI)[67] that accounted for both direct medical costs such as nursing, laboratory, and pharmacy costs, and administration costs. Given the complexity of physician billing codes for extremely preterm and preterm births, more accurate estimates of obstetric outcome costs were not pursued. Given the high costs associated with extremely premature births, the impact of unaccounted physician billings is expected to be marginal.

Cases were defined by relevant International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada (ICD10CA) diagnostic codes and Canadian classification of health interventions (CCI) procedure codes (Appendix 11) were consulted when the appropriate case costs could not be identified by ICD10CA (Table 19).

Table 19: Obstetric Outcome Costs

Obstetric Outcome	Value (Probabilistic)	Reference
Pregnant Person		
Term Birth	$3,493 (SE: $3,271)	OCCI[67]
Preterm Birth	$4,620 (SE: $4,802)	
Extremely Preterm Birth[a]	$4,620 (SE: $4,802)	
Stillbirth	$5,817 (SE: $5,144)	
Infant		
Term Birth	$1,120 (SE: $710)	OCCI[67]
Preterm Birth	$7,830 (SE: $14,204)	
Extremely Preterm Birth	$70,385 (SE: $80,615)	

OCCI = Ontario case costing initiative; SE = standard error.

[a] Assumed same as preterm birth cost.

Costs reported in 2018 C$.

Screenings Costs

As each screening and test-of-cure visit was assumed to be conducted with the same CT and GC combination NAAT technology, the cost of these tests were informed by 2018 British Columbia Ministry of Health's Schedule of Fees for Laboratory Services. Urine

NAATs ($29.94) were assumed for maternal tests and swab-based NAATs ($28.85) were assumed for infants.[68] Of note, these costs do not include confirmatory testing for GC that are done in some Canadian jurisdictions and represent a conservative cost estimate. Physician fees associated with prenatal visits were not incorporated into the analysis as these would have been billed as part of regular prenatal visit costs.

Cost to Manage Infections in the Pregnant Person

Oral pharmacotherapy associated with CT and GC infections in pregnant persons were informed by PHAC's *Guidelines on Sexually Transmitted Infections*[21] and Ontario Drug Benefit list prices.[69] Description of the treatment for each infection and its cost, including the test-of-cure visit, is listed in Table 20.

Table 20: Maternal Infection Treatment Costs

Infection	Treatment Regimen	Cost
CT	Azithromycin 1 g p.o. single dose	$14.01
	Test-of-cure visit	$29.94
	Total	**$43.95**
GC	Cefixime 800 mg p.o. single dose	$5.43
	Azithromycin 1 g p.o. single dose	$14.01
	Test-of-cure visit	$29.94
	Total	**$49.38**
CT and GC	**Total**[a]	**$49.38**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; p.o.; orally.

[a] Includes the test-of-cure cost. Assumed same as GC as azithromycin is already present in GC therapy.

Costs reported in 2018 C$.

Pediatric Infections

As antibiotic treatment in infants are often prescribed by weight, Fenton growth charts for preterm infants[70] were consulted to inform expected infant weight at birth and at the time of symptomatic CT and GC infection. Expected incubation periods for the pediatric infections were informed by PHAC's *Canadian Guidelines on Sexually Transmitted Infections*,[21] and from consulting clinical experts involved in this review. Sex-specific infant weights from Fenton growth charts were weighted by average proportion of male (51.3%) and female (48.7%) Canadian live births reported by Statistics Canada for 2012 to 2016.[2]

CT conjunctivitis and pneumonia were assumed to be managed in the outpatient setting, while GC conjunctivitis was assumed to be managed as an in-patient care lasting two to four days (Dr. Joan Robinson: personal communication, 2018 Jun). A bottom-up costing approach was used to estimate cost for GC conjunctivitis care. Costs for hospitalization based on a per-diem charge for uninsured Canadian residents ($825 per day),[71] diagnostic test and test-of-cure visits, pediatrician ($167.00) and infectious disease specialist ($165.50) consultation from the Ontario schedule of benefits for physician services,[72] and a single intramuscular injection of ceftriaxone (average of 25 mg/kg to 50 mg/kg assumed [37.5 mg], maximum 125 mg;[21] cost variable by weight: $4.29 to $5.90[69]) based on Ontario Drug Benefit list price were included.

For those infants who were screened shortly after birth due to suspected GC vertical transmission and had a positive test outcome for GC, the costs of an infectious disease specialist consultation, intramuscular injection drug and service, and test-of-cure visits were included. Pediatrician cost and hospitalization costs were assumed to have been already included as part of neonate clinical care.

For CT conjunctivitis, 2016 OCCI ambulatory care case cost corresponding to neonatal CT conjunctivitis and dacryocystitis (ICD10CA code P39.1, 2018 mean cost of $558.47),[67] pediatrician and infectious disease specialist consultation costs, and the treatment cost consisting of 14 days of oral erythromycin therapy (erythromycin base 20 mg/kg/day to 40 mg/kg/day variable by age and weight;[21] total costs: $0.31 to $2.88[69]) were included.

As the 2016 OCCI ambulatory care case cost corresponding specifically to CT pneumonia in neonates was unavailable, this cost was proxied with 2015 OCCI ambulatory care case cost for congenital pneumonia of unspecified organism (ICD10CA code P23.9, mean 2018 cost $538.47).[67] Pediatrician and infectious disease specialist consultations costs, and cost for a day of oral azithromycin therapy (average of 12 mg/kg to 15 mg/kg assumed [13.5 mg/kg];[21] $0.46 to $1.06[69]) were also included in the event of managing CT pneumonia.

For the above CT costs, screening and test-of-cure visits costs were not included as these have been assumed to be included in the case cost. Mean calculated pediatric infection costs are listed in Table 21.

Table 21: Mean Calculated Pediatric Infection Treatment Costs

Treatment	Term Infant	Preterm Infant	Extremely Preterm Infant
GC Intramuscular Prophylaxis	$200.20	$199.56	$198.61
GC Conjunctivitis	$2,871.10	$2,870.48	$2,869.49
CT Conjunctivitis	$574.47	$573.66	$332.81
CT Pneumonia	$865.56	$865.37	$864.96

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*.

Statistical Analysis and Management of Uncertainty

The base-case analysis was conducted probabilistically to account for parameter uncertainty. Conventional parameter distributions were applied: beta distributions defined parameters bound between 0 and 1, such as probabilities; gamma distributions were used to vary those parameters bound to a single lower bound such as costs; and normal distribution was used to vary random variables that were normally defined such as the SROC curve parameters. Sensitivity analyses were performed to account for additional parameter and structural uncertainties.

Sensitivity Analyses

In terms of parameter uncertainty on the epidemiology of infections, the prevalence for CT and GC infections have been reported higher among some Canadian adolescent pregnant persons (i.e., 14.69% CT-only infection; 0.47% GC-only infection; 0.47% coinfections).[38] Therefore, a sensitivity analysis that would reflect a higher-risk pregnant population was performed that incorporated this higher prevalence rate and set the probability of infection and reinfection to be at the upper limit of the 95% confidence interval of the base-case values (CT infection: 2.25% annually age < 25 years, 1.06% age ≥ 25; GC infection: 0.18% annually age < 25 years, 0.21% age ≥ 25; CT and GC reinfections: 2.79% annually age < 25 years, 2.49% age ≥ 25 years).

Given the paucity of literature on CT reinfection rates, a sensitivity analysis was also conducted that equated the CT reinfection rate to the initial CT incidence rate (approximately 2.15% annually age < 25 years; 0.63% age ≥ 25 years) instead of the GC reinfection rate (approximately 2.53% annually age
< 25 years; 2.25% age ≥ 25 years) as was done for the base-case analysis.

A sensitivity analysis with a lower probability of symptomatic infection among infants was also conducted since the base-case literature sources for these rates[19,60] were synthesized from settings that may not reflect Canadian perinatal care (e.g., China,[73] Kenya,[74] and Cameroon[75]) or the drug presently used for ocular prophylaxis in Canada (i.e., erythromycin). Given the prevalence of legal enforcement of neonatal ocular prophylaxis using erythromycin in Canada despite calls to reconsider this practice,[19,76] and the finding that erythromycin ocular prophylaxis is more efficacious than other prophylactic drugs previously used for CT conjunctivitis,[77] it is possible that these infection rates could be an overestimate. Indeed, this has been a limitation criticized in other studies of CT modelling.[78] In this regard, this sensitivity analysis used lower pediatric infection probabilities that were observed in an American ocular prophylaxis study that included erythromycin as part of the study (Table 22).[79]

Conversely, it may also be possible that the observed probability of symptomatic neonatal infection may be higher than the base-case values if the practice of neonatal ocular prophylaxis were to decline in Canada. In this regard, another sensitivity analysis was conducted with higher pediatric infection probabilities, sourced from the maximum values reported in the studies that informed the base-case analysis.[19,60] This high pediatric infection analysis was also combined with the previously described high maternal CT and GC prevalence risk analysis for an additional sensitivity analysis to capture high infection risk in both pregnant persons and infants.

Table 22: Alternate Probabilities of Symptomatic CT and GC Infections in Exposed Infants

	Low Pediatric Infection		High Pediatric Infection	
Infection	**Probability**	**Source**	**Probability**	**Source**
GC Conjunctivitis	0.1%	Hammerschlag et al., 1989[79]	50%	Moore and Macdonald, 2015[19]
CT Conjunctivitis	14%		44%	Rosenman et al., 2003[60]
CT Pneumonia	0%		17%	

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*.

As the base-case analysis was modelled with the age distribution of the Canadian pregnant population from 2001 to 2005, another sensitivity analysis was conducted to use an age distribution that may be more reflective of the pregnant population today. Due to the unavailability of more recent data for pregnant persons, the age distribution of mothers at birth from 2016[80] was used to approximate this distribution.

Uncertainties regarding cost considerations were also further explored through sensitivity analyses. A lower cost of screening ($8.10, Quebec[81]) than the base-case value ($29.94, British Columbia[68]) was used in a low screening cost sensitivity analysis. The larger cost of pediatric infections was also explored in a sensitivity analysis that assumed that all cases of neonatal conjunctivitis and pneumonia would result in hospitalization. Specifically, ambulatory care costs of CT conjunctivitis and CT pneumonia that were treated in an outpatient setting in the base-case analysis, were replaced by OCCI's in-patient cost (Table 23).[67]

Table 23: Mean Calculated Pediatric CT Infection Treatment Costs for Hospitalized Patients

Treatment	OCCI In-patient Care Case Cost[a] (SD)	Term Infant	Preterm Infant	Extremely Preterm Infant
CT Conjunctivitis	$3,108.25 ($1,715.07)	$10,579.90	$10,580.32	$10,580.50
CT Pneumonia	$10,246.96 ($6,598.42)	$3,441.06	$3,442.81	$3,443.62

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; OCCI = Ontario case costing initiative; SD = standard deviation.

[a] Costs reported in 2018 Canadian Dollars.

A series of sensitivity analyses were also conducted to determine whether considering each of the following additional clinical services to treat CT and GC infections would impact the economic model's results:

- GC culture investigation to determine antimicrobial sensitivities[21] was added to each case of GC treatment, at an additional fee of $12.41.[82]
- Each CT or GC conjunctivitis treatment included a general consultation by a pediatric ophthalmologist to assess for corneal damage, at an additional cost of $82.30.[72]
- Each treatment for infant conjunctivitis or pneumonia included additional costs of treating the mother for a corresponding infection as well. Depending on the organism, a 2016 OCCI ambulatory care case cost corresponding to chlamydial infection of lower genitourinary tract (ICD10CA code A56.0, mean 2018 cost $169.00[67]) or gonococcal infection of lower genitourinary tract without periurethral or accessory gland abscess (ICD10CA code A54.0, mean 2018 cost $126.00[67]) was included, in addition to drug costs associated with either infection and a unit of STI management consultation ($62.75[72]). Overall, treating the mother of an infant infected with a CT infection cost an additional $208.19, and $245.76 for the mother of an infant infected with a GC infection.

Furthermore, given the lack of literature to inform input parameters associated with Canadian screening practice, sensitivity analyses were conducted to assess the robustness of the cost-effectiveness results. This included:

- 100% prenatal visit screening participation rate of pregnant persons.
- 25% third trimester rescreening rate of pregnant persons with positive CT or GC test results during pregnancy. This is a reduced rate derived from the same source as the base case (i.e., 35%),[54] and the assumption that pregnant persons do not always receive a test-of-cure visit following CT or GC treatment.
- 0% third trimester rescreening rate of pregnant persons with positive CT or GC test results during pregnancy.
- 100% third trimester rescreening rate of pregnant persons with positive CT or GC test results during pregnancy.
- 100% screening of extremely preterm or preterm births at presentation for labour.
- 100% screening rates at presentation for labour for pregnant persons without prior history of screening.
- 0% screening rates at presentation for labour for pregnant persons without prior history of screening.
- No screening of infants born to mothers with GC-positive test results.

- 100% rate of vertical transmission prevention in pregnant persons who have received antibiotic treatment during labour and delivery which would mean that treatment was not effective in preventing vertical transmission.
- 0% rate of vertical transmission prevention in pregnant persons who have received antibiotic treatment during labour and delivery which would mean that treatment was 100% effective in preventing vertical transmission.

Subgroup analyses of pregnant persons who were younger than 25 years and who were 25 years or older were also performed to examine whether the cost-effectiveness of screening would be different between the risk subgroups.

Lastly, exploratory analyses were conducted to test whether altering key structural assumptions of the base-case model would impact the results. Specifically, the following assumptions were conducted in the exploratory analyses:

- Inclusion of an additional screening strategy; whereby, universal screening is conducted in first and third trimesters and an age-targeted screening is conducted in the second trimester (strategy UTUM).
- CT or GC infection in the pregnant person is assumed to be associated with a greater risk of adverse pregnancy outcomes of extremely preterm birth, preterm birth, and stillbirths.
- Time horizon expanded to lifetime to account for potential long-term sequelae of infections such as blindness and infant mortality in the offspring, and pelvic inflammatory disease in the birthing parent.
- An expanded scope capturing the lifetime impact of treating partners of infected pregnant persons.

Details on how the model was programmed differently in these exploratory analyses are described below.

For the exploratory analysis that assumed an association between CT and GC infection and adverse obstetric outcomes, odds ratios for preterm birth and stillbirths associated with CT and GC infection compared with uninfected pregnant persons were extracted from a 2013 Australian study of singleton birth records.[38,53] These odds ratios were then applied to the existing odds of preterm birth and stillbirth reported for the general Canadian population[2,55] and then converted into CT and/or GC-specific probabilities that were incorporated into the exploratory analysis (Table 24).

Table 24: Calculated Probability of Adverse Obstetric Outcome, by Infection Status (For Exploratory Analysis)

Obstetric Outcome for a Pregnant Person	CT Infection	GC Infection	No Infection
Second Trimester Prenatal Visit			
Extremely Preterm Birth	0.5%	1.1%	0.5%
Second Trimester Stillbirth	0.4%	0.7%	0.3%
Continue Gestation to Third Trimester	99.1%	98.3%	99.2%
Third Trimester Prenatal Visit			
Term Birth	91.1%	92.4%	92.4%
Preterm Birth	8.5%	7.4%	7.3%
Third Trimester Stillbirth	0.4%	0.7%	0.3%

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*.

In this exploratory analysis, differences in the pregnant persons' utilities due to adverse obstetric outcome were also accounted for. As no literature was identified reporting the utility weights of pregnant persons following adverse obstetric outcomes, utilities were estimated based on the relationship between adverse obstetric outcomes and postnatal depression. Specifically, the Edinburgh Postnatal Depression Scale (EPDS) scores from an Austrian longitudinal study of pregnant women[83] were used to determine whether pregnant persons with specific obstetric outcomes in the model would experience postnatal depression. The EPDS score for term birth was proxied as the reported EPDS scores for "pregnancies without complications" while the EPDS scores for extremely preterm birth and stillbirth were conservatively assumed to be equal to that of the preterm birth. See EPDS scores in Table 25.

Table 25: EPDS Scores by Obstetric Outcome

Obstetric outcome	Value (Probabilistic)	Reference
Term Birth	5.085 (SE: 4.655)	Mautner et al., 2009[83]
Preterm Birth	8.220 (SE: 5.675)	
Extremely Preterm Birth[a]	8.220 (SE: 5.675)	
StillBirth[a]	8.220 (SE: 5.675)	

EPDS = Edinburgh Postnatal Depression Scale; SE = standard error.
[a] EPDS score of stillbirth and extremely preterm birth were assumed to be at least that of extremely preterm or preterm birth.

A pregnant person was considered to have postnatal depression if their EPDS score was at least equal to the threshold score of 14/30, a score clinically interpreted as a probable depression.[84] For pregnant persons with postnatal depression, a health utility decrement (0.17) associated with depression was applied to the postpartum period based on the difference of HUI3 utilities between non-depressed and depressed populations reported in a Canadian study (Table 26).[85] The utility values in the Canadian study were similar to those reported for postnatal depression in the UK.[86]

Table 26: Postnatal Depression Utility Decrement[a] Parameters

Parameter	Value (Probabilistic)	Reference
Utility in Individuals Without Depression	0.85 (95% CI, 0.84 to 0.86)	Patten et al., 2014[85]
Utility in Individuals With Depression	0.68 (95% CI, 0.64 to 0.71)	

CI = confidence interval.
[a] Utility decrement of postnatal depression was calculated from the difference of the two health utility values in the table (Mean 0.17).

To model a lifetime time horizon in the second exploratory analysis, a proportion of antibiotic treatments for conjunctivitis and pneumonia in infants were assumed to have failed, leading to the development of long-term consequences such as infant mortality related to respiratory failure from pneumonia and blindness from conjunctivitis. Treatment failure rates for CT conjunctivitis and CT pneumonia in infants were derived from clinical studies that reported failure rates for the erythromycin[60] and azithromycin,[87] respectively, and are summarized in Table 27. The treatment failure rates for GC conjunctivitis in infants were assumed to reflect that of the proportion of GC isolates reported by PHAC[88] to have demonstrated decreased susceptibility to ceftriaxone. No further treatments for conjunctivitis or pneumonia were assumed to be sought after treatment failure. Consequently, all failed conjunctivitis treatments were assumed to lead to blindness in the infants, and all failed pneumonia treatments were assumed to lead to infant mortality due to respiratory failure.

Health utilities and costs associated with each health state were applied over the life expectancy of the modelled population as estimated by Statistics Canada.[89] Infants were expected to live up to 82 years, and pregnant persons were expected to live between 43.1 to 67.5 years depending on their age during pregnancy.[89] The utilities and costs were discounted at 1.5% per annum. Details on the lifetime utilities and cost impacts to an offspring with GC and CT infection treatment are detailed in Table 27.

Table 27: Infant-Specific Model Parameters Incorporated Into the Exploratory Analyses for Long-Term Consequences Associated With GC/CT Infection

Parameter	Value (Probabilistic)	Reference
Probability of Treatment Failure		
CT Conjunctivitis (Initial Treatment: erythromycin)	15.0% (Range: 9.0% to 12.0%)	Rosenman et al., 2003[60]
CT Pneumonia (Initial Treatment: azithromycin)	3.2% (Range: 0.4% to 7.4%)	Geisler et al., 2015[87]
GC Conjunctivitis (Initial treatment: ceftriaxone)	3.46%	PHAC 2017[88]
Annual Utilities		
Blindness (pediatrics)	0.473 (SD: 0.077)	Kwon et al., 2017[63]
Blindness (adults, ≥ 16 years of age)	0.46531	Feeny et al., 2002[90]
Death (associated with respiratory failure from CT pneumonia)	0	
Annual Costs		
Blindness	$12,602.26	CNIB & COS, 2009[91]

CI = confidence interval; CNIB; Canadian National Institute for the Blind; COS = Canadian Ophthalmological Society; CT = *Chlamydia trachomatis;* GC = *Neisseria gonorrhoeae*; PHAC = Public Health Agency of Canada; SD = standard deviation.

For the birthing parent, a long-term consequence of remaining infected by GC and CT infection post-pregnancy is pelvic inflammatory disease. In the proportion of patients who remained infected at the end of the pregnancy (i.e., due to lack of screening, false-negative test results, or no CT/GC symptoms in their infected infants), the exploratory analyses assumed that these patients would never receive treatment. The probabilities of developing a pelvic inflammatory disease (PID), its symptoms, and potential chronic sequelae (Table 28) were sourced from a Canadian CT burden of illness study.[92] All birthing parents who developed PID were assigned a mean lifetime decrement of one QALY (Range: 0.4 to 1.8 QALY),[92] which reflected the lifetime discounted QALY decrement that considered potential sequelae of PID such as chronic pelvic pain, ectopic pregnancy, and infertility. The same study reported that the lifetime discounted cost of treating a symptomatic PID and PID with sequelae were $2,067.85 and $2,799.73 respectively.

Table 28: Birthing Parent-Specific Model Parameters Incorporated Into the Exploratory Analyses for Long-Term Consequences Associated With GC/CT Infection

Parameter	Value (Probabilistic)	Reference
Probabilities		Tuite et al., 2012[92]
Probability of developing PID from an untreated CT or GC infection	10% (Range: 1% to 30%)	
Probability that PID is symptomatic	40% (Range: 15% to 40%)	
Probability that PID leads to sequelae (ectopic pregnancy, chronic pelvic pain, and infertility)	32%	
Lifetime QALY decrement		
PID	1	
Lifetime costs		
Symptomatic PID	$2,067.85	
PID with Sequelae	$2,799.73	

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; PID = Pelvic inflammatory disease; QALY = quality-adjusted life-year.

The long-term exploratory analysis additionally incorporated the broader clinical services captured in the sensitivity analyses that accounted for GC culture investigation, consults by a pediatric ophthalmologist (for GC and CT conjunctivitis), and infection screening and treatment for the birthing parent of infants with conjunctivitis or pneumonia.

For the final exploratory analysis that expanded the above lifetime time horizon to include partner treatments, each pregnant person was assumed to be involved in a heterosexual relationship with a single male partner of the same age. Consequently, each male partner was expected to live between 39.6 to 63.5 years over the lifetime time horizon. Costs of adult infection treatment and test-of-cure visits in the model was doubled to account for additional testing and treatment of the partner during and after pregnancy, and the partner was assumed to have the same infection as the infected pregnant person. Those who were partnered to pregnant persons with untreated CT or GC infection at the end of their pregnancy were assumed to be at risk of epididymo-orchitis with a mean 2% probability (Range: 1% to 5%) that would cost $267.19.[92]

Validation

Face validity was achieved through numerous consultations with Canadian clinical experts who practice in obstetrics and gynecology, pediatrics, infectious diseases, medical microbiology, and communicable diseases. These consultations were used to ensure that the model was consistent with Canadian practice and that no significant evidence was omitted from consideration. Internal validity was ensured through tests of extreme parameter values and the model underwent an independent technical review.

Summary of Key Assumptions

The base-case analysis was conducted under the following key assumptions listed in Table 29.

Table 29: Summary of Key Assumptions and Sensitivity Analyses

Assumption	Sensitivity Analysis/Notes
A representative Canadian pregnancy population (range of ages between 15 and 44) was modelled and the overall prevalence of CT and GC infection was 1.9% and 0.2% respectively.	Sensitivity analysis: High-risk pregnant population.
Only the pregnant persons and their infants are modelled.	Exploratory analysis: A lifetime time horizon exploratory analysis and partner treatment captured partner screening and treatment costs, and a long-term consequence of an infection, epididymo-orchitis, for the partner as well.
Modelled time horizon was between first prenatal visit (12 weeks) and 19-weeks postpartum. Long-term implications of infection and screening was not captured given the defined time horizon within the model.	Exploratory analyses: • Lifetime time horizon for both the pregnant person and their offspring. • Lifetime time horizon for the pregnant person, their partner, and their offspring.
Each pregnancy produced a single birth.	
No impact of CT or GC infections on the development of adverse obstetric outcomes (i.e., extremely preterm birth, preterm birth, stillbirth).	Exploratory analysis – ORs of CT and GC-associated adverse obstetric outcomes from an Australian birth record study[53] were applied.
Pregnant persons were assumed to be at continued risk of CT and GC infections from sexual activities until live birth or stillbirth event.	
CT reinfection probability equalled GC reinfection probability.	Sensitivity analysis: CT reinfection probability equivalent to that of the initial CT incidence.
CT and GC infections were assumed to be independent for the pregnant person.	This may have overestimated the incidence of infections in the pregnant population as it did not account for the correlation in coinfections.
CT and GC pediatric infections were mutually exclusive — although infants could be exposed to both, they could only develop either a CT or GC symptomatic infection.	
All screenings for the mother involved urine sample NAAT that tested both for CT and GC. The diagnostic test accuracy of NAAT was assumed to be similar to the reported diagnostic test accuracy of NAATs in the general female population.	
All screenings for the infant involved swab-based NAAT that tests both for CT and GC. It was assumed that the tests would have the same diagnostic test accuracy as the maternal urine sample NAAT.	
Mothers or infants who test positive for CT or GC at any point received corresponding antibiotic treatment. All CT and GC treatments were assumed to be curative and treatment-related complications were not captured.	Exploratory analyses: lifetime time horizon incorporated probability of treatment failure for pediatric antibiotic treatment with long-term consequences (e.g., blindness, mortality).
Approximately 50% of treatments administered to mothers who test positive for CT or GC at presentation for labour and delivery did not prevent vertical transmission to infant.	Sensitivity analyses: 0% and 100% of treatments administered to mothers at presentation prevented vertical transmission.

Results

Base-Case Results

Cost-Utility Analysis

The sequential results of the base case are presented in tables below, ordered by lowest to highest total cost. Table 30 highlights those strategies that have not been dominated (i.e., more costly and less effective against another strategy) or extendedly dominated (i.e., more costly and less effective than a combination of screening strategies) when defining

effectiveness based on QALYs. The highlighted strategies represent the efficiency frontier, a series of strategies that produces the highest health benefits at different costs. The current Canadian screening strategy (UTTM) was dominated by strategy TNUM, indicating that offering targeted screening in the first trimester for individuals younger than 25 years and universal screening to all pregnant women in the third trimester would be less costly but would also generate more health benefits compared with current practice. Complete cost-utility and cost-effectiveness results are presented in Appendix 12.

Table 30: Expected Costs and QALYs Associated With Different Screening Strategies per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Probabilistic Base Case)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM[b]	113,489.73	561,663,682	Reference		
NNTM	113,489.83	561,899,189	0.10	235,506	2,328,518
NNUM	113,490.15	562,780,969	0.32	881,780	2,775,685
TNUM	113,490.15	563,302,330	0.01	521,361	63,774,285
UNUM	113,490.18	565,220,444	0.03	1,918,114	65,154,327
Current Strategy					
UTTM[c] (vs. TNUM)	113,490.12	563,823,557	-0.03	521,228	Dominated

ICUR = incremental cost-utility ratio.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

[b] This strategy represents no prenatal visit screen with 50% of patients offered screening at labour and delivery.

[c] Current strategy UTTM is not part of the efficiency frontier, included here for information.

Not offering a prenatal visit screening program for CT and GC in pregnant women (i.e., strategy NNNM) was the least costly but also the least effective option. If one's willingness-to-pay (λ) was under $2.3 million per QALY, this screening strategy was also most likely to be considered cost-effective.

Other screening strategies generated more QALYs from preventing more pediatric infections. In terms of the frequency of screening, offering screening once during the pregnancy was associated with lower costs but also fewer clinical benefits. This was due to the fact that less frequent screening resulted in fewer averted pediatric infections compared with strategies that screened at multiple time points during a pregnancy. Similarly, as the base-case analysis assumed no impact of CT and GC infections on obstetric outcomes, the analysis found that screening in the third trimester would be less costly and more effective than a corresponding strategy involving screening in an earlier trimester (e.g., NNTM versus TNNM). Therefore, between a λ of $2.3 million to $63.8 million per QALY, offering a prenatal visit screening during the third trimester would be considered cost-effective; otherwise, offering screening at both the first and third trimester of the pregnancy would be considered cost-effective at a higher λ threshold.

Within the general trends noted above, another emerged with respect to the screening approach. The analysis found that targeted screening compared with universal screening was associated with lower costs and QALYs as fewer individuals would undergo screening and, similarly, fewer benefit from averted pediatric infections. Targeted approaches were associated with more true positive detection; whereas, universal approaches were associated with more true-negative detection.

Of the screening strategies on the efficiency frontier, implementing those with increasingly larger coverage and frequency were found to decrease the prevalence of CT and GC infections in the pregnant population but correspondingly increased the rate of false-positive findings and reduced the rate of false-negative findings (Table 31). Adopting targeted screening in the third trimester (NNTM), for example, was found to increase the proportion of false-positive results from 4.01% to 4.04% compared with the no prenatal visit screening strategy (NNNM) and reduce the proportion of false-negative results from 0.18% to 0.16%. As a reminder, it was possible for the no prenatal visit screening strategy to generate false-positive and false-negative findings in this analysis as approximately 50% of individuals presenting at labour and delivery without a history of CT and GC screening during the pregnancy would have CT and GC screening performed. Per 100,000 pregnant persons screened, this would mean an additional increase in 30 false-positive cases and a reduction of five false-negative cases. Expanding the strategy to universal screening in the third trimester (NNUM) was found to produce 59 more false-positive cases and 14 fewer false-negative cases per 100,000 pregnant persons screened compared with a targeted screening in the third trimester (NNTM).

Table 31: Overall Diagnostic Outcomes Across Entire Pregnancy (Probabilistic Base Case)

Strategy[a]	True Positive (%)	False Positive (%)	True Negative (%)	False Negative (%)
NNNM	2.40	4.01	93.41	0.18
NNTM	2.33	4.04	93.45	0.18
NNUM	2.15	4.10	93.59	0.16
TNUM	1.84	4.11	93.91	0.14
UNUM	1.22	4.14	94.54	0.09
Current Strategy				
UTTM[b]	1.50	4.13	94.25	0.12

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

[b] Current strategy UTTM is not part of the efficiency frontier, included here for information.

The reported ICURs for introducing CT and GC screening during pregnancy in the third trimester before labour and delivery were in the millions due to the small incremental QALY gain (i.e., 0.10 QALYs per 100,000 pregnant persons). To aid interpretation of such results in more concrete epidemiological context, cost-effectiveness analysis results are provided below in which the clinical outcomes compared are in terms of pediatric infections averted.

Cost-Effectiveness Analysis

Table 32 shows that compared with the current screening strategy (UTTM), strategies with universal screening in third trimester visits (i.e., NNUM, TNUM, and UNUM) reduced more cases of pediatric infections. These results also align with the trends reported in the cost-utility analysis: increasing coverage and frequency of screening decreased pediatric infections in the population, albeit at an incremental cost. For example, adopting targeted third trimester screening (NNTM) compared with no prenatal visit screening (NNNM) would reduce approximately 74 pediatric infections per 100,000 pregnant persons and would cost $3,171 per prevented pediatric infection.

Table 32: Expected Pediatric Outcomes of Screening Strategies on the Efficiency Frontier per 100,000 Pregnant Persons — Sequential Cost-Effectiveness Ratio (Probabilistic Base Case)

Strategy[a]	Total (n)					Incremental (n)					ICER ($ Per Pediatric Infection Prevented[a])
	GC Conjunctivitis	CT Conjunctivitis	CT Pneumonia	Pediatric Infections[b]	Cost ($)	GC Conjunctivitis	CT Conjunctivitis	CT Pneumonia	Pediatric Infection Prevented[b]	Cost ($)	
NNNM	80.4	276.7	132.0	489.1	561,663,682	Reference Strategy					
NNTM	69.1	234.1	111.7	414.8	561,899,189	–11.4	–42.6	–20.3	74.3	235,506	3,171
NNUM	27.7	100.4	47.9	176.0	562,780,969	–41.3	–133.7	–63.8	238.9	881,780	3,692
TNUM	27.3	96.9	46.2	170.5	563,302,330	–0.4	–3.4	–1.6	5.5	521,361	94,679
UNUM	25.8	84.5	40.3	150.7	565,220,444	–1.5	–12.4	–5.9	19.8	1,918,114	96,807
Current Strategy											
UTTM[c] (vs. TNUM)	36.8	110.8	52.8	200.4	563,823,557	9.5	13.8	6.6	-29.9	521,228	Dominated

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

[b] Accounts for GC conjunctivitis, CT conjunctivitis, and CT pneumonia in aggregate.

[c] Current strategy UTTM is not part of the efficiency frontier, included here for information.

Sensitivity Analyses

All sensitivity analyses reflected the trends observed in the base-case analysis (Appendix 12) with the exception of six analyses that either altered population risk profiles, screening costs or treatment-related costs for pediatrics. The results of the analyses that led to different conclusions from the base-case analyses are detailed below:

Higher-risk pregnant population: Introducing screening in an earlier trimester (strategy UNNM) was found to be less costly and more effective than the corresponding strategy that screened at a later trimester (strategy NNUM). When the λ was between $66,565 and $481,855 per QALY screening in the first trimester was found to be the most likely cost-effective strategy (Table 33). Targeted screening strategies were also found not to be cost-effective at any λ threshold.

Table 33: Expected Costs and QALYs per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (High Risk Pregnant Population)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	113,486.17	563,876,964	Reference		
UNNM	113,489.00	564,065,420	2.83	188,456	66,565
NNUM	113,489.08	564,101,229	0.07	35,808	481,855
UNUM	113,489.36	566,206,134	0.28	2,104,905	7,446,073

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Incidence of pediatric infections: When the incidence of pediatric infection were lower (i.e., pediatric infection probabilities: 0.1% GC conjunctivitis, 14% CT Conjunctivitis, 0% CT pneumonia; Table 34), no prenatal visit screening strategy (strategy NNNM) was found to always be the most cost-effective strategy across all λ values and dominated all other strategies. Of note, this reflected a setting where CT pneumonia would not occur and, as this outcome was the only one that contributed to lowered utilities, there were no differences in expected utilities across all strategies.

Table 34: Expected Costs and QALYs per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Low Pediatric Infection)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	113,490.38	561,307,532	Reference		

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

In another setting with higher incidence of pediatric infections (i.e., pediatric infection probabilities: 50% GC conjunctivitis, 44% CT conjunctivitis, 17% CT pneumonia; Table 35), the ICUR values reduced for all screening strategies. While adopting targeted screening in the third trimester (strategy NNTM) would have costed an additional $2.3 million per QALY in the base-case analysis, the same strategy was associated with an ICUR of $631,368 per QALY.

Table 35: Expected Costs and QALYs per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (High Pediatric Infection)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	113,488.80	562,199,711	Reference		
NNTM	113,489.05	562,353,412	0.24	153,701	631,368
NNUM	113,489.81	562,974,312	0.76	620,900	811,956
TNUM	113,489.83	563,489,419	0.02	515,107	26,155,405
UNUM	113,489.90	565,385,013	0.07	1,895,594	26,724,631

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Combined high risks of pediatric infection to and maternal CT and GC prevalence: When the underlying risks of infection are higher, universal screening in the third trimester (strategy NNUM) became the least costly strategy (Table 36). The efficiency frontier also included UNUM which was associated with an incremental cost-effectiveness ratio (ICER) of 2.8 million per QALY. All other screening strategies, including screening strategies with targeted screens, were found to be dominated.

Table 36: Expected Costs and QALYs per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (High Risk Pregnant Population and High Pediatric Infection)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	113,487.24	565,098,963	Reference		
UNUM	113,487.92	566,994,344	0.68	1,895,382	2,782,785

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Lower screening costs ($8.10 per screening): Although the order of strategies on the efficiency frontier remained identical to the base-case results, the reported ICURs were drastically reduced (Table 37). The ICER for NNTM reduced to $132,109 per QALY compared with $2.3 million per QALY estimated in the base-case analysis.

Table 37: Expected Costs and QALYs per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Low Screening Cost)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	113,489.73	560,546,454	Reference		
NNTM	113,489.83	560,559,816	0.10	13,362	132,109
NNUM	113,490.15	560,630,598	0.32	70,783	222,811
TNUM	113,490.15	560,778,896	0.01	148,298	18,140,233
UNUM	113,490.18	561,324,659	0.03	545,763	18,538,415

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Pediatric infections managed in in-patient setting: When the cost of managing pediatric complications associated with GC and CT infection were higher, the efficiency frontier consisted of screening strategies NNUM, TNUM (targeted screening in first trimester and

universal screening in the third trimester), and UNUM . The strategy, NNUM, was found to be the least costly of the strategies and, if the payer's willingness-to-pay threshold was less than $60.6 million per QALY gained, NNUM was considered to be the most likely cost-effective intervention in the analysis (Table 38).

Table 38: Expected Costs and QALYs per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (High Pediatric Infection Hospitalization)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	113,490.18	561,324,659	Reference		
TNUM	113,490.15	564,026,795	0.01	495,678	60,632,673
UNUM	113,490.18	565,852,348	0.03	1,825,554	62,010,243

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Subgroup Analysis

Subgroup analyses of pregnant persons younger than 25 years, and 25 years and older were conducted to explore potential differences in cost-effectiveness between age subgroups due to patient heterogeneity. Of note, targeted screening strategies were not evaluated in this subgroup analysis as targeted screening for high-risk patients was defined by age. The findings in terms of frequency and timing reflected the trends observed in the base-case analysis (Table 39). No prenatal visit screening strategy (strategy NNNM) was found to be cost-effective if λ was below $2.3 million per QALY in the younger than 25 years of age subgroup, and $2.8 million per QALY in the subgroup 25 years and older. Screening in the third trimester was cost-effective at higher λ thresholds up to $64.0 million per QALY in the under 25 years of age subgroup, and $65.1 million per QALY in the subgroup aged 25 years and older. Screening in both first and third trimesters was cost-effective at λ thresholds beyond these levels and, for the younger than 25 years of age subgroup, screening at each trimester (strategy UUUM) was found to be cost-effective if λ threshold was beyond $214.7 million per QALY.

Of note, the ICURs of screening strategies were found to be lower in the younger than 25 years subgroup compared with the 25 years and older subgroup. This result highlights the potential value of offering targeted screening to younger patients who are considered at higher risk of infection and reinfection.

Table 39: Expected Costs and QALYs Associated With Different Screening Strategies per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Subgroup Analyses)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
Age < 25					
NNNM	122,922.90	614,662,833	Reference		
NNUM	122,923.42	615,868,858	0.52	1,206,025	2,327,685
UNUM	122,923.46	618,538,529	0.04	2,669,671	63,946,120
UUUM	122,923.48	621,108,593	0.01	2,570,064	214,670,689
Age ≥ 25					
NNNM	124,522.19	614,547,290	Reference		
NNUM	124,522.63	615,774,304	0.44	1,227,013	2,775,918
UNUM	124,522.67	618,443,467	0.04	2,669,163	65,105,665

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Exploratory Analyses

As noted above, exploratory analyses were conducted to incorporate additional comparators, address structural uncertainty or expand the analyzed time horizon beyond the research question to address the potential long-term cost-effectiveness of pregnancy screening.

Inclusion of UTUM screening strategy: In considering compared screening strategy whereby universal screening occurred in first and third trimesters and an age-targeted screening occurred in the second trimester (strategy UTUM), UTUM was found to produce the most QALYs but was also the most expensive. Under a sequential analysis, UTUM was found to produce an additional 0.002 QALYs, or 0.73 day of a perfect health, compared with UNUM. The ICER associated with the UTUM strategy was approximately $214.1 million per QALY (Table 40).

Table 40: Expected Costs and QALYs per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Exploratory Analysis: Strategy UTUM Included as a Comparator)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	113,489.73	561,663,682	Reference		
NNTM	113,489.83	561,899,189	0.10	235,506	2,328,518
NNUM	113,490.15	562,780,969	0.32	881,780	2,775,685
TNUM	113,490.15	563,302,330	0.01	521,361	63,774,285
UNUM	113,490.18	565,220,444	0.03	1,918,114	65,154,327
UTUM	113,490.19	565,722,366	0.00[b]	501,922	214,095,828

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

[b] Incremental QALY is larger than what can be displayed on this table (0.002 QALYs).

Impact of CT and GC infection on adverse pregnancy outcomes: An exploratory analysis was also conducted that incorporated the potential impact of CT or GC infections on adverse obstetric outcomes. The base-case analysis omitted this consideration due to clinical studies that have reported on an unclear association between these infections and adverse pregnancy outcomes. Under this exploratory analysis, the efficiency frontier differed from the base-case analysis (Table 41).

The exploratory analysis observed larger utility differences between strategies as adverse obstetric outcomes had a utility impact on both the neonate and birthing parent compared with the base-case results in which utility decrements were associated to the neonate from CT and GC infection. As such, the reported ICURs for introducing programmatic CT and GC screening before labour and delivery were correspondingly lower.

Table 41: Expected Costs and QALYs Associated With Different Screening Strategies per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Exploratory Analysis: CT and GC Infection Impact Adverse Obstetric Outcomes)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	113,486.92	561,859,113	Reference		
UNNM	113,495.35	562,500,445	8.43	641,331	76,111
UNTM	113,495.66	562,991,380	0.32	490,935	1,554,224
UNUM	113,496.30	564,850,954	0.64	1,859,574	2,905,194

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Lifetime analysis (considering offspring and birthing parent): By extending the time horizon to a lifetime, the exploratory analysis demonstrated significant changes from the base-case results. At a program-level, the expected benefits associated with each screening strategy increased due to both the longer time horizon considered and the averted long-term impact to screening when compared with the base-case strategy; whereas, the expected costs remained similar. This suggests that the costs of screening occur upfront; whereas, the clinical benefits to screening may extend over a longer time period. This exploratory analysis may be considered the least conservative as it assumed that, upon treatment failure to the first antibiotic, infants with conjunctivitis would develop blindness; whereas, infants with pneumonia would die. This therefore resulted in a larger difference in incremental QALYs between strategies.

When a lifetime time horizon was evaluated, programmatic screening would be considered cost-effective. The efficiency frontier consisted of screening strategies NNUM, TNUM, and UNUM that dominated all others (Table 42). Strategy NNUM was found to be the least costly strategy and adopting strategy TNUM was expected to cost an additional $10,764 per QALY compared with strategy NNUM. Adopting strategy UNUM compared with strategy TNUM was expected to cost an additional $11,468 per QALY.

Table 42: Expected Costs and QALYs Associated With Different Screening Strategies per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Exploratory Analysis: Lifetime Time Horizon)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	8,504,789.66	572,443,916	Reference		
TNUM	8,504,808.26	572,644,155	18.60	200,238	10,764
UNUM	8,504,874.79	573,407,114	66.53	762,959	11,468

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Lifetime analysis (considering offspring, birthing parent, and partner): Similar results to the lifetime analysis were found when the exploratory analysis was extended beyond the offspring and birthing parents to include the impact of screening on the partner (Table 43). However, the expected costs were increased when factoring the costs of treatment and the test-of-cure visit for the partner. While this shifted the ICURs, the overall interpretation of the lifetime model remained robust. Although NNUM was the least costly strategy, at a λ threshold was greater than $14,655 per QALY, UNUM was considered the most likely cost-effective intervention.

Table 43: Expected Costs and QALYs Associated With Different Screening Strategies per 100,000 Pregnant Persons — Sequential Incremental Cost-Utility Ratio (Exploratory Analysis: Lifetime Time Horizon and Partner Treatment)

Strategy[a]	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	12,063,343.03	572,938,618	Reference		
TNUM	12,063,361.63	573,196,669	18.60	258,051	13,871
UNUM	12,063,428.16	574,171,682	66.53	975,013	14,655

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-years.

[a] Other strategies that were either dominated or extendedly dominated are omitted from this table.

Summary of Results from the Economic Analysis

The tradeoff of marginal health benefits and costs between different screening strategies support the generalization that more intensive screening programs (i.e., increasing the proportion of the pregnant population screened and/or increasing the frequency of screening) were associated with increased health benefits and costs, and higher true-negative and false-positive detection rates. The economic evaluation allowed quantification of this tradeoff between screening strategies in the incremental health benefits and incremental costs through the calculation of ICUR (where health benefits were measured as QALYs) or ICER (where health benefits were measured as averted pediatric infection). Although screening earlier in pregnancy was found to be more costly, the incremental health benefits were small, resulting in high ICURs for strategies associated with screening in the first trimester unless the clinical impact associated with CT or GC infection was found to be more severe (e.g., higher risk of infection in the pregnant population [resulting in higher risk of vertical transmission to the infant], incorporating the potential impact of CT or GC infection on adverse obstetric outcomes, extending model's time horizon).

Overall, in the base-case analysis that considered only the impact of screening during the pregnancy and postpartum period, not offering a prenatal visit screening program for CT and GC infections in pregnant persons (i.e., strategy NNNM) was found to be the least costly and the least effective option that would be considered the most likely cost-effective option at willingness-to-pay thresholds less than $2.3 million per QALY, or $3,171 per averted pediatric infection. The results also indicate that the currently recommended screening strategy (UTTM)[21] may not be cost-effective as there are other strategies such as TNUM that generate more health benefit at a lower cost.

Extensive sensitivity analyses were conducted on model parameters to test alternative parameter values and potential variations in screening practice and clinical management. In the majority of the sensitivity analyses, the model remained robust although these analyses demonstrated that the model was most sensitive to the population risk profile, screening costs, and pediatric treatment-related costs as these had the largest impact of shifting the benefit to harm profile associated with screening. Specifically, in a sensitivity analysis setting the risk of infection and reinfection to the highest reported values, offering universal screening in the first trimester (strategy UNNM) was associated with an ICUR of $66,565 per QALY as the potential clinical consequences from no screening in terms of vertical transmission of the infection would be more severe. This analysis may approximate a “high risk” population. Screening costs were one of the key drivers in the model and, unsurprisingly, lowering the costs to screening was found to reduce the ICUR (e.g., base-case ICURs for NNTM in which screening costs are $29.94: $2,328,518 per QALY; lower screening cost ($8.10) ICUR for NNTM: $132,109 per QALY). Similarly, when the cost of managing pediatric infections were higher, this shifted the cost of harms to be higher such that universal screening in the third trimester (strategy NNUM) was found to be the less costly and more effective than the reference strategy in the base-case analysis (strategy NNNM). In this case, NNUM was found to be the most likely cost-effective screening intervention at a willingness-to-pay threshold under $60 million per QALY.

The economic evaluation was limited in a number of instances by the availability of clinical information, specifically with respect to whether a causal link exists between CT and GC infections on adverse obstetric outcomes. As per consultation with clinical experts in this field, the base-case analysis assumed that the impact of CT and GC infections in the pregnant person was the risk of vertically transmitting the infection to their offspring. In an exploratory analysis in which CT and GC were assumed to further impact obstetric outcomes, universal screening in the first trimester (strategy UNNM) was found to be potentially cost-effective if the willingness-to-pay threshold was between $76,111 and $1.6 million per QALY (Table 41) as there was a greater incremental QALY difference between no prenatal screening (strategy NNNM) and UNNM as more adverse obstetric outcomes would be averted by programmatic screening that would otherwise negatively impact the QALYs of the pregnant person and the child. Lastly, one limitation that could not be addressed in the current economic evaluation is whether the optimal screening strategy for CT and GC infections in pregnant women would vary in different high-risk subgroups. Although the definition of “high risk” includes multiple different patent-level factors, limited clinical data were found on these factors to support further stratification of the economic analysis.

Of note, the base-case analysis was restricted to consider only the impact of screening during pregnancy and the postpartum period (i.e., 19 weeks post birth or stillbirth) in the pregnant person and their offspring to align with the decision problem stemming from the policy question. However, as per the CADTH guidelines,[52] a lifetime time horizon may be considered appropriate given that the impact of screening at pregnancy may extend beyond the modelled time period to the pregnant person, their child and even to their partner. Indeed, in exploratory analyses to evaluate how the cost-effectiveness of programmatic screening may differ by adopting an extended lifetime time horizon to better capture all relevant differences in clinical outcomes associated with screening during pregnancy, the findings highlight the fact that the cost of screening occurs upfront during pregnancy; whereas, the benefits of screening may extend further beyond the time horizon considered in the base-case model. As such, universal screening in the third trimester (strategy NNUM) was the least costly strategy and the ICUR for UNUM ranged from $11,468 per QALY to $14,655 per QALY depending on whether or not the population considered extended to the partner.

Patients' Preferences and Experiences Review

The patients' perspectives and experiences review addresses the following research question:

Research Question 3: What are the experiences and perspectives of pregnant persons and their partners with respect to undergoing screening for sexually transmitted infections (STIs)? And, what are their health care providers' perspectives on screening for STIs during pregnancy?

To ensure the relevance of the analysis to the objectives of the broader HTA, a secondary set of research questions was explored during data extraction and analysis:

- What do pregnant persons and their partners value or expect with regards to screening for STIs?
- How do pregnant persons and their partners experience and perceive screening options (vaginal and cervical swabs, and urine specimen) for STIs?
- What are the ways in which screening for STIs and its frequency and timing affect pregnant person's lives and the lives of their partners?
- What are health care providers' experiences and perceptions on when and how to screen for STIs during pregnancy?
- What are health care providers' perspectives regarding targeted or universal screening?
- Are there differences in perceptions and experiences relating to screening for STIs between pregnant persons and their partners, or between pregnant persons and their partners and health care providers?

Systematic Review and Qualitative Meta-Synthesis

An SR and qualitative meta-synthesis of empirical studies describing pregnant persons' experiences and perceptions of screening for STIs during pregnancy was conducted. Studies that include the perspectives of their partners and health care providers on screening pregnant persons for STIs were also included. Following an iterative approach consistent with the inductive principles of qualitative research, the a priori planned methods[29] were actively refined and amended at a few stages. Of note, while a research question was established a priori, given the scarcity of qualitative evidence on screening specifically for GC and CT during pregnancy, and to ensure a sufficient evidence base to inform the policy question, this research question was refined and the scope of this review expanded to include screening for other STIs during pregnancy.

Methods

Literature Search Methods

The literature search was performed by an information specialist, using a peer-reviewed search strategy.

Information related to patient preferences was identified by searching the following bibliographic databases: MEDLINE (1946–) with In-Process records and daily updates through Ovid; Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1981–) though EBSCO; PubMed; and Scopus. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. In both iterations of this search, methodological filters were applied to limit retrieval to qualitative studies, including surveys or questionnaires.

The initial formal search was completed on January 15, 2018 and included the concepts of chlamydia, gonorrhea, pregnancy, and screening. Retrieval was limited to human, English or French-only publications from January 1, 2003 onward. The second search was performed on February 23, 2018 and was broadened to include the concept of all STIs, in addition to the previously specified chlamydia and gonorrhea. Retrieval was limited to English-only publications and did not have a date limit. This final search was set as a regular alert to update the searches until the publication of the final report. Regular search updates were performed on databases that do not provide alert services. Studies identified in the alerts and meeting the selection criteria of the review have been incorporated into the analysis if they were identified prior to the completion of the stakeholder feedback period of the final report. Any studies that were identified after the stakeholder feedback period are described in the discussion, with a focus on comparing the results of these new studies to the results of the analysis conducted for this report.

Grey literature (literature that is not commercially published) was identified by searching the Grey Matters checklist (https://www.cadth.ca/grey-matters), which includes the websites of HTA agencies, clinical guideline repositories, SR repositories, economics-related resources, public perspective groups, and professional associations. Google and other Internet search engines were used to search for additional Web-based materials. These searches were supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry. The complete search strategy is presented in Appendix 2.

Selection Criteria

English language reports describing studies using any descriptive or interpretive qualitative methodology that explored the experiences or perspectives of pregnant persons and their partners or health care providers with respect to screening for STIs during pregnancy were eligible. Eligibility criteria are presented in Table 44.

Papers that were not peer-reviewed (e.g., reports, theses), case reports commentaries or editorials, not in English, reported animal or in vitro data, reported non-empirical studies, used non-qualitative methods, or were off-topic (that is, not addressing the topic of experiences of screening for STIs) were excluded. The qualitative data from studies using a survey design were included, while quantitative data from the same studies were excluded. Due to the limited information available in abstracts, studies or results presented only in abstract form were excluded.

Table 44: Selection Criteria for Patients' Perspectives and Experiences Review

Topical parameters	Screening for STIs during pregnancy; context in which technology is used (e.g., setting (home, primary care settings, sexual health centres, or general community settings), resource allocation considerations, health and human resources issues); how technology fits in the process of patient care; screening method (i.e., testing options, including urine tests, self-administered swabs, pelvic exams and clinician-collected swabs, home-testing options, self-testing options, mobile health vans); screening strategy (e.g., targeted or universal), timing of the screening (at any point and frequency during pregnancy); pregnant persons' experiences, expectations and perceptions of screening for STIs; partners of pregnant persons' experiences and perceptions of screening for STIs during pregnancy; health care providers' perceptions of screening for STIs during pregnancy.
Population parameters	Pregnant persons, partners of pregnant persons, health care providers screening for STIs (family doctors, midwives, obstetrician-gynecologists, etc.)
Temporal parameters	No limits on time frame
Methodological parameters	Primary qualitative empirical research (using any descriptive or interpretive qualitative methodology) and the qualitative component of mixed-methods studies, in which authors use methods for both qualitative data collection and analysis that include the following: • in-depth or open-ended interviews or focus groups, lengthy participant or field observations, or document or artifact review • techniques for analysis and interpretation of data that move beyond the data generated • descriptive qualitative surveys to answer open-ended "why" questions • qualitative syntheses that provide novel interpretations of existing data.

Screening and Selecting Studies for Inclusion

Two reviewers screened all citations retrieved from the literature searches based on the eligibility criteria. Titles and abstracts were reviewed to identify papers addressing pregnant persons' experiences and perceptions of screening for STIs during pregnancy, as well as the perspectives of their partners or of their health care providers. The full-text of all potentially relevant reports was retrieved for detailed review and screened in duplicate according to the eligibility criteria. The screening and sorting of eligible papers was managed using Endnote X7 for Mac,[93] which is a reference management software package.

Data collection and extraction

Two types of data were extracted from each primary study: descriptive study characteristics and the study results relevant to the research topic. One reviewer extracted descriptive data into an a priori developed standardized electronic form, which was checked for accuracy by a second reviewer. Descriptive data included such items as first author, year of publication, article title, study objectives, study participants' characteristics, and study design.

Both reviewers used NVivo 11[94] (QSR International Pty Ltd. Version 11, 2017) to extract and manage the second type of qualitative data from included reports, that is, the qualitative result statements of each included study relevant to the research question. Result statements are typically presented within the "results" section of a report, and are characterized as data-driven and integrated findings based on participant experiences.[5] Before being coded, each result statement was assessed to ensure it was differentiated from raw data, methods, external data, and researchers' conclusions and implications. Only qualitative data were extracted; the quantitative component of mixed-methods studies was not included in our analysis. Given that discrepancies have been noted between results presented within abstracts and main reports, only results presented within the main report

were extracted.[95] Extraction was subsequently compared and verified between the two reviewers.

Quality assessment

Two reviewers with experience in qualitative research design and synthesis independently assessed the quality of included papers. Assessments on the major strengths and limitations of studies in terms of their credibility, transferability, dependability, and confirmability were guided by the Critical Appraisal Skills Programme (CASP) quality appraisal checklist for qualitative research,[3] the Critical Appraisal of a Survey tool,[96] and the CASP Systematic Review Checklist .[97] Papers were not excluded from the review on the basis of indicators of quality. This approach recognizes that procedural details are typically under-reported and that theoretically sophisticated findings are not necessary to contribute valuable information to a synthesis of multiple studies, or to inform health policy questions. Disagreements in assessments were resolved through discussion.

Data analysis

Included qualitative studies were analyzed using techniques of integrative qualitative meta-synthesis,[4-7] and also defined as qualitative research integration. Qualitative meta-synthesis summarizes and integrates findings across a set of qualitative studies with the aim of combining results across multiple articles. The objective of qualitative meta-synthesis is twofold: first, the aggregated sum of results reflects the range of findings across studies while retaining the original meaning; second, by comparing and contrasting findings across studies, a new integrative interpretation is produced.

The analysis followed a staged coding process similar to grounded theory and passed through three stages: open or line-by-line coding, descriptive coding, and development of analytic themes.[98] The constant comparison method was adapted to include comparing codes across reviewers, comparing codes across codes and across studies.[98]

In analyzing the data, secondary research questions were used as sensitizing concepts to assist the researchers in interpreting findings and concepts in the data. They provided general guidelines for approaching the data, to open up and refine inquiry, without imposing or prescribing a specific analytical lens.[98,99] Secondary questions provided a beginning point for constructing the analysis during the line-by-line and descriptive coding process. During this stage, reviewers sought empirical accounts of pregnant persons,' their partners,' and health care providers' perspectives on experiences of undergoing STIs screening during pregnancy, STIs screening options (vaginal and cervical swabs, and urine specimen), its frequency and timing. The perspectives of partners and health care providers were used here to corroborate context and to add depth to the issues of screening relative to the experience of pregnant persons. Sensitizing concepts derived from secondary questions further informed the analysis helping to refine the initial descriptive codes into abstract categories and themes.

Line-by-line and Descriptive Analysis

Two reviewers independently conducted line-by-line coding of an initial set of four papers. Line-by-line coding encourages "staying close to the data," a process that encourages the inductive development of codes that identify and describe the data's meaning and content. Upon completing this initial set, the reviewers met to discuss and reflect on the coding process, and identify patterns appearing in the codes used. At this time, it was determined that line-by-line coding was sufficient (i.e., patterns emerged in the codes used and there was stability in their application), and subsequently each reviewer independently

descriptively coded the first set of coded studies and four more papers. During this stage, larger passages of text were used to group and cluster codes in categories using descriptive concepts that still remained close to the data. Descriptive codes were compared and contrasted between each other and across the papers. Upon completion of the descriptive coding, the reviewers met and discussed the coding process and reflected on emergent concepts to refine the coding set, noting that through discussion and comparison of codes new interpretative insights emerged leading to a more abstract level of analysis. As the descriptive codes became hierarchical and the relationship between codes became the subject of the analysis, the coding of the individual reviewers was deemed to be sufficiently aligned and coding proceeded with both researchers descriptively coding the remainder of the studies and with a move from descriptive coding to analytic synthesis.

A note on the iterative nature of the coding process for the analysis of qualitative data. Sometimes coding moves in a linear fashion from descriptive codes close to the data to higher-level conceptual categories and ultimately to abstract themes; but sometimes the process of identifying categories and themes happens simultaneously, especially in the second and final stages of coding.[98] For example, descriptive coding provides accounts of what is happening in the data but does not integrate the ideas into a set of interrelated concepts from which the researcher develops explanations. However, during this stage, some focused and theoretical coding work is also accomplished as the initial codes are condensed and grouped into preliminary abstract conceptual categories.[98] At the same time, sometimes the analysis directs the reviewers to rethink a high-level category or theme, pushing them to go back to the data, the line-by-line coding or descriptive coding to identify or organize the data in a different way.[98]

Thematic Analysis

Analytic synthesis is the development of themes or abstracted constructs that are interpretations of the data. The two reviewers independently began to develop analytic themes using sensitizing concepts and memos to assemble and sort the previously established descriptive codes, going back to the data to further develop the relationship between themes and codes. Once a first stage of analytical coding was completed, the two reviewers met and discussed whether the preliminary categories and themes were theoretically relevant to the research and policy questions and theoretically rich enough to support further inquiry across the body of literature.[7] At times when there was disagreement on both points, the reviewers refined the categories, themes and their relationships, and then re-applied them to the data independently before meeting to re-assess sufficiency and alignment. Once the reviewers were confident with the analytic scheme, larger sets of data were coded before meeting to discuss. Throughout all stages of analysis, the reviewers met regularly to discuss emerging results, and preliminary analytic ideas. To facilitate these discussions, explicit notes were kept using the memo and annotation features in NVivo to record decisions made regarding coding and theme development, as a means of ensuring rigour in the analysis. In all stages of coding, the reviewers paid attention to the transferability of results across different contexts as a way to determine whether some results might only apply to certain subgroups. Analytical synthesis ended once themes and their relationships had been richly described and were stable, with no additional descriptive or interpretive insights arising from further analysis.

Reflexivity is an epistemological principle and methodological approach in qualitative research that recognizes the role of the researcher as instrument.[98] Reflexive practices and techniques are those that allow for and facilitate making researcher's observations and interpretations transparent and explicit versus implicit and unacknowledged. They aim to

provide cognitive and emotional space of the researcher from the act of analysis to reflect on this act of observation and interpretation itself. This review employed the reflexive practices of memoing and frequent dialogue among reviewers to probe and position reviewers in relation to the analysis. Within the context of the current study, the two reviewers considered the ways in which their perspectives were influenced by their own professional and personal background, experiences and prior assumptions. An important question they addressed in drawing conclusions from the data concerned whether or not their personal background could have influenced their approach to the analysis. As a result of this reflexive practice, both reviewers (FB and DD) acknowledged their similar perspective and approach to data analysis as both are qualitative researchers from non-clinical backgrounds, women, and without children.

Results

The bibliographic database searches yielded 4,068 papers (with duplicates removed). Two reviewers screened all titles and abstracts, and subsequently the full-texts, to confine the database to qualitative research articles eligible according to the criteria listed in Table 44. In total, 35 papers were deemed eligible and are included in the analysis. Appendix 13 presents the PRISMA flow diagram for the patients' perspectives and experiences review.

Descriptive analysis

Of the 35 included papers, four[41,100-102] addressed chlamydia and one study[103] addressed both chlamydia and gonorrhea. Twenty-seven reported experiences and perspectives pertaining to HIV screening.[76,104-129] An additional two papers reported perspectives about syphilis screening,[130,131] while one paper sought perspectives relevant to general STI screening.[132] Twenty-eight studies reported the experiences and perspectives of pregnant persons.[41,76,100,101,104-108,110,112-123,125-129] Five studies reported the perspectives of health care providers,[102,103,109,111,124] and three studies reported the experiences and perspectives of both pregnant persons and health care providers (e.g., physicians, nurses, midwives).[130-132] 14 of the 35 included studies also included perspectives of non-pregnant women, although studies reporting experiences of pregnant persons were in the majority.[76,101,104,106,112,113,117,119,121,123,125,126,131,133] None of the included studies reported only the experiences or perceptions of partners of pregnant persons.

Twenty-one included papers reported on primary qualitative research studies.[76,104,106-108,110,111,115-123,126,128-131,133] One paper reported on a SR of qualitative studies, of which none of the included studies were doubly included in this review due to differing eligibility criteria.[111] Of note, only results clearly from studies that met the eligibility criteria for this review were included in this synthesis. Nine papers reported the qualitative component of a mixed-methods study,[41,100,101,105,112,113,125,127,132] while four papers described survey designs that involved the collection of open-ended or qualitative data.[103,109,114,124] Many (n = 17) of the research studies reported a general "qualitative study" or interview study, without further mention of the theoretical or analytical approach. Twenty-five of the included primary research studies collected data using interviews and four studies used focus groups. Five studies collected data using open-ended questionnaires. One paper reported collecting secondary data from case interviews.

Fifteen studies reported experiences of pregnant persons and/or their partners and health care providers from the US,[103,106,112,115,116,118,130] with an additional 12 studies from the UK.[41,101,102,105,107,110,111,114,117,120,123,128] Two studies were conducted in Australia,[100,132] two in New Zealand,[109,122] two in Canada,[108,113] one in Spain[104] and one in Ukraine.[129] Details are provided in Appendix 14.

Quality assessment

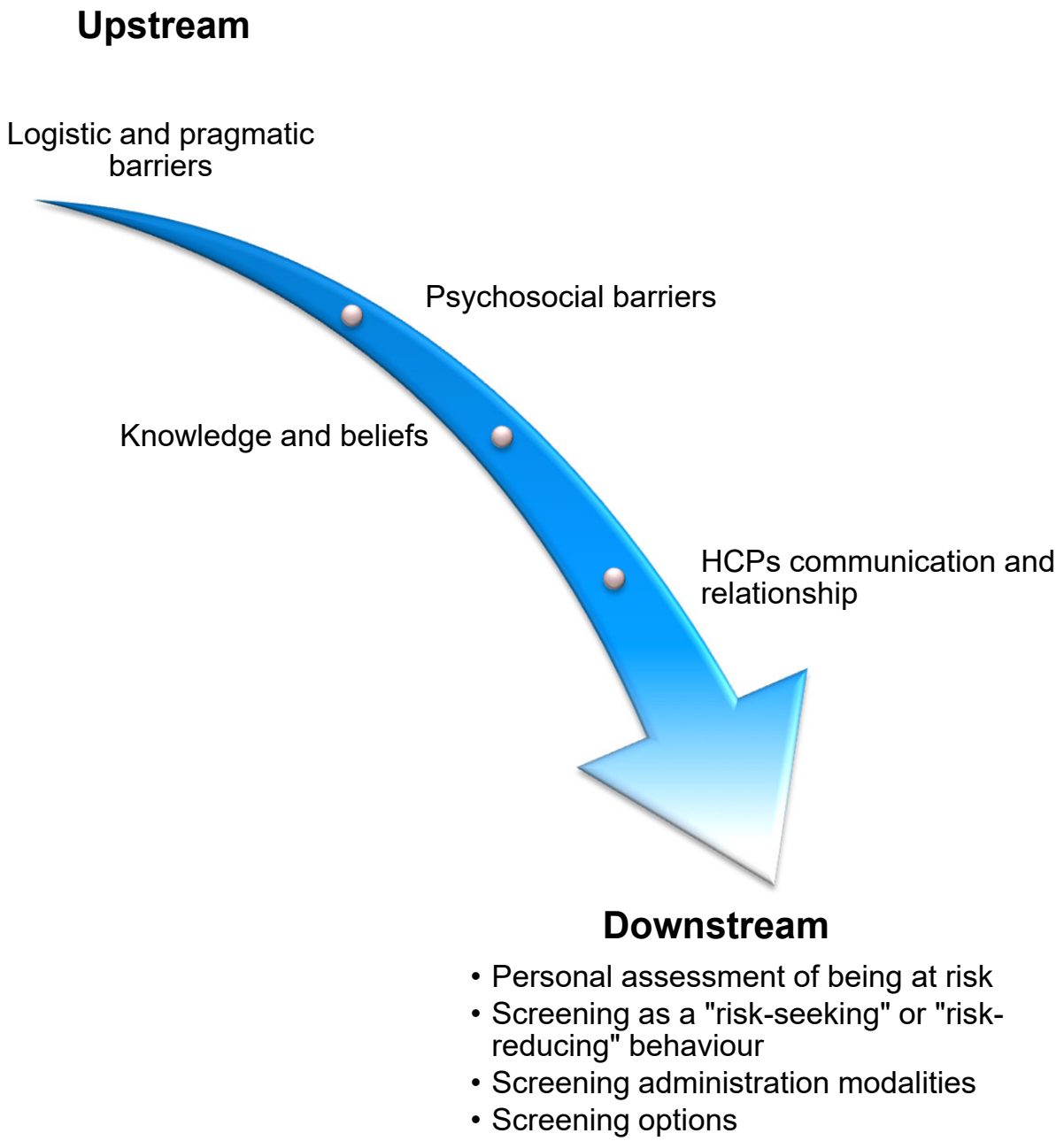
A narrative assessment of the major strengths and weaknesses of included papers, based on the CASP checklist for qualitative studies, the Critical Appraisal of a Survey for survey studies and CASP Systematic Review Checklist, is presented in Appendix 15.[3,96] The methodological quality of the included papers was mixed, but generally strong. Notably, only four studies considered the role of the researcher in the study,[104,120,121,132] thus the extent to which the findings may have been influenced by the researchers' own backgrounds or beliefs is unclear. Three of the papers failed to report whether the study had received ethics approval.[76,107,112] The survey studies generally lacked a rigorous analysis process for the collected qualitative data; one study noted coding the responses for emerging themes, but subsequently quantified the results.[124] However, most papers were clear about the research aims of the study, and the research reported was a valuable contribution to the current policy concern.

Thematic Analysis

The following sections explore the results of the thematic analysis. In accordance with the analytic plan, the analytic themes represent the meaning of those experiences and perspectives of pregnant persons with respect to undergoing screening for STIs (GC/CT, syphilis, herpes, HPV, and HIV), as well as their health care providers' perspectives on screening for STIs during pregnancy. As noted above, the studies included in this review primarily focused on pregnant persons' perspectives. Partners' perspectives were not represented in the included studies; whereas, health care providers' perspectives were represented to a small extent. The thematic analysis reflects this discrepancy of perspectives available in the literature.

A multilevel analytic structure (Figure 5) emerged during the analysis that describes a number of factors that act as opportunities or barriers to pregnant persons' decision-making about participation in STI screening. Two analytical themes emerged within the analysis: upstream and downstream factors that inform pregnant persons' decisions to engage with STI screening. Upstream factors situate pregnant persons' approach to screening within a wider framework of overarching conditions that directly and indirectly frame downstream factors, which in turn address pregnant persons' direct incentives and disincentives to screening. Upstream factors include logistic and pragmatic barriers to antenatal care, knowledge and beliefs, psychosocial barriers, and health care provider relationship and communication. Downstream factors include personal assessment of health and risk, screening as a "risk-seeking" or "risk-reducing" behaviour, screening administration modalities, and screening options. Each factor was discussed in turn, detailing how for each level — upstream and downstream — it could act as incentive or disincentive for screening. For example, a pregnant person's understanding of their own risk was reported to be closely related to their sense of motherhood and moral responsibility to protect their baby's health, as well as to their understanding of STIs and medical treatment. Some categories were more closely connected than others. These findings have implications for implementation of STI screening at the levels of policy, and for provider and patient education.

Figure 5: Multilevel Analytic Structure



Analytical Theme 1: Upstream Factors

The first analytical theme encompasses a set of factors that pregnant persons perceive to broadly encourage or discourage their decision to screen for STIs. These factors include logistic and pragmatic barriers to antenatal care, knowledge and beliefs, psychosocial barriers, and health care provider relationship and communication.

Logistic and Pragmatic Barriers to Antenatal Care

Logistic challenges acted as a strong disincentive to screening. A general lack of time was commonly reported by both health care providers[132] and by pregnant persons, which required the former to engage in time consuming administrative tasks (e.g., coordination of tests, results) and the latter to strike a balance between multiple priorities, such as family and work commitments, and prenatal care, including STI screening.[112,128,130,131]

Pregnant persons in American-based studies often mentioned health insurance and the cost of screening as a logistical barrier, although this topic was not prevalent in countries that cover costs of STIs screening through a universal health care system.[128,130,131] For these pregnant persons, the cost of STI screening was a strong reason to abstain from screening. Structural barriers, such as discontinuity in health care and insurance services, lack of prenatal clinics, and long wait times also limited pregnant persons' antenatal STI screening.[124,128,130,131]

Finally, in some studies pregnant persons and their prenatal care providers noted health care providers' lack of training in managing STIs.[131] Both pregnant persons and health care providers perceived the role of prenatal care providers and general practitioners as "diagnosing, but not managing" STI-positive pregnant persons, which they considered to be the work of specialists.[129,131,132] These providers would subsequently refer pregnant persons to clinics, where staff in turn complained about being overburdened, and long wait times ensued.[131] Overall, discontinuity in the delivery of care inhibited pregnant persons' and health care providers' STI screening behaviours.

Knowledge and Beliefs

Pregnant persons reported not having accurate or complete knowledge about STIs and reported that the lack of access to adequate and credible information about STIs and STI testing was a disincentive to screening. In the included studies, pregnant persons identified a lack of information on issues such as their source, transmission, treatment, health and social consequences, risk factors, practicalities of screening options (e.g., the time it takes to obtain and interpret test results, and the next steps after diagnosis), reliability of testing, the purpose of screening tests, and the risks for the fetus related to the treatment. In particular, they rarely acknowledged the link between screening and preventive care.[108,110,115,119,126,131,133] Social taboos surrounding discussions of sex and STIs and fear of stigma limited access to information;[123,131] whereas, too much information provided only in written form hindered pregnant persons' ability to retain information.[107] These pregnant people reported a need for education on the purpose for STI screening and information related to the procedure.[100,106,108,126] Pregnant persons and/or their partners and health care providers identified educational interventions or campaigns as important sources of information and motivation to participate in screening.[100,110,115,119] Even though they had access to informal sources of information, such as family, peers, and sexual education in school,[100,110,115,119] they also identified educational campaigns as significant motivators to screening; in particular, it enabled them to understand the different aspects of STIs and STI screening and to be more informed and confident in making health care decisions.[100,110,115,119]

Psychosocial Barriers

Some pregnant persons viewed their choice to undergo STI screening or not as driven by social and psychological factors. Stigma perceived to be associated with promiscuity and social isolation[120,121,133] was a major concern for the pregnant persons due to the nature of the transmission of the infection.[100,105,113] Negative moral connotations associated with STI screening and positive STI test results either in the health care setting, their community, or from broader society were commonly reported concerns that discouraged screening behaviour, regardless of the screening modality.[100,104,105,110,112,113,117,119-121,123,125,126,128,131-133] Psychosocial barriers also included pregnant persons' fear of disruption of their relationship with their partners, including fear of rejection, the partner leaving or abuse by the partner.[100,110,113,117,120,121,127,130] This stigma of relationship disruption was a significant barrier to accepting screening for STIs,[100,105,110,113,117,119-121,123,125-127,130-133] but was less of a concern for pregnant persons who were informed, more prepared, and who consciously prioritized protecting the health of their babies.[125]

Pregnant persons with high-risk lifestyles, such as commercial sex workers and drug users, reported fears and distress about social stigmatization and discrimination, both in health care settings and in the community, which ultimately influenced their decision to avoid screening.[112,120,131] Even though in some instances pregnant persons with high-risk life styles perceived motherhood as a motivating factor to reduce risky behaviours and reported the belief that all pregnant persons should be tested, they also reported feeling unwilling to pursue preventive care measures — such as STI screening — due to external factors beyond their control, such as the perceived stigma and discrimination associated with their lifestyle and their previous negative experiences within the health care and community setting.[112]

Similarly, teen pregnancy stigma represented a barrier for young pregnant persons to accessing STI screening during pregnancy. Seeking and undergoing STI screening would have disclosed their pregnancy status to family and the community, potentially exposing them to stigma and social isolation.[112,132]

Relationship and Communication With Health Care Providers

Health care providers' communication and interpersonal relationship style had a substantial effect on their relationship with pregnant persons, which in turn affected pregnant persons and/or their partners and health care providers' preferences about when and how to engage with the health care system, including participation in STIs screening during pregnancy.

When pregnant persons felt supported in making decisions about their health and the health of their child, they positively perceived recommendations for STI screening from their prenatal care provider.[105,107,119,121,123,126] Health care provider support contributed to the trust relationship between pregnant persons and provider, and when not present led to barriers in pregnancy care. Pregnant persons provided examples of experiences with health care providers related to STI screening that undermined trust: when they did not feel they were allowed to ask questions concerning their health,[122,123,126] not receiving timely test results in person,[107,122] experienced paternalistic attitudes when recommending or offering the test,[107,108,110,115,117,121,122,125,131] perceived their providers to hold negative beliefs about pregnant persons living with STIs,[100,121,126] experienced breaches of confidentiality,[121] and experienced physicians' abandonment of pregnant persons with high-risk lifestyles (such as sex workers and drug users).[116,126] A lack of trust with the health care providers also influenced pregnant persons' feelings of concern for their privacy and confidentiality, as some pregnant persons felt offended when offered the STI screening as they perceived the

offer as a judgment of promiscuity.[105,109] Overall, pregnant persons were less likely to participate in STI screening when they were not in a trusting relationship with their care provider,[121,126,127] or felt stigmatized or disrespected,[100,107,110,115,121,125,126] or when their autonomy in making informed decisions was eroded.[108,112,117] In one study, a small number (4) of health care providers reported similar concerns. In this study, health care providers believed that the lack of clear and open communication with pregnant persons hindered pregnant persons' acceptance of undergoing screening.[132] However, in the same study, most of the care providers also believed that providers' efforts and sense of "moral responsibility" in ensuring pregnant persons' engagement with STI screening was not sufficient to improve pregnant persons' participation in screening.[132] Ultimately, pregnant persons' reported previous negative experiences with the health care system and care providers as acting as a barrier to engaging with the health care system in general as well, not just the particular health care provider.[107,116,127]

However, when pregnant persons had a trusting relationship with their health care providers they were more likely to decide to undergo STI screening.[105,107,119,121-123,126] When pregnant persons were satisfied with the information received in a confidential way, they felt reassured and empowered,[105,107,119,121-123,126] and comfortable to share personal sexual history information with the provider.[100] An important feature of this positive experience was having the health care professional explain the screening procedure, which enabled pregnant persons to make informed decisions about participation and reduce anxiety and fear of the screening process and the results.[107,119,121,122,126]

Analytical Theme 2: Downstream Factors

The second analytical theme captures factors that directly incentivize and dis-incentivize pregnant persons' decisions of undergoing STIs at the individual level. Downstream factors include personal assessment of health and risk of having or contracting an STI, screening as a "risk-seeking" or "risk-reducing" behaviour, screening administration modalities, and screening options.

Personal Assessment of Health and Risk of Contracting or Having an STI

The way in which pregnant persons identify their own personal risk for contracting or having STIs, including beliefs and perceptions of vulnerability, as well as their related concepts of health and health care, influences their decisions and behaviours concerning screening practices.[100,106,108,110,112,113,117,119,125,126,131,133] Although these factors are interwoven with their knowledge of personal risk (i.e., general understanding of STIs and its risk factors, screening procedures, and the link with pregnancy), and how they see themselves in relation to these factors, there are specific elements that are enacted in the moment that pregnant persons make screening decisions.

Most pregnant persons were not always clear on why they should have undergone STI screening. Confusion mostly resulted from the lack of symptoms typically thought to be related to STI diseases and from pregnant persons' perceptions of health and their awareness of attending prenatal care.[41,76,100-103] Pregnant persons generally perceived themselves as being at low risk of contracting or having STIs.[105,113,118,125,131,132] As illustrated above, barriers to accessing information about infection and transmission, and about medical treatments and preventive measures against transmission of infection to the fetus, contributed to low levels of awareness of risk influencing pregnant persons' thoughts on whether screening should occur or not.[107,117,118,131,132] In one study, pregnant persons believed chlamydia to be a minor infection, "like herpes," and did not completely understand the consequences of the infection for them and for the fetus.[100] This low perception of risk

led pregnant persons to conceptualize health care as crisis management rather than preventive care, which for some, led to a refusal of screening.[118,125,131,132]

Opinions about why they should have undergone STI screening then reflected pregnant persons personal understandings of risk rather than physician-based recommendations. The appraisal of one's personal risk draws on pregnant persons' perceptions of their health status in relation to lifestyle behaviours, relationship status, and non-promiscuous sexual behaviours.[105,118,125,131,132] Pregnant persons reported a belief that long-term and monogamous relationships did not pose a risk of being infected by STIs.[113,118,119] Pregnant persons believed that having a long-term committed relationship with one partner signalled a risk prevention behaviour that did not warrant the need for STI screening.[107,113,118,121] However, pregnant persons in both long-term and short-term relationships were more likely to accept screening when there was a lack of trust in the relationship with their partner, showing that trust in particular influenced pregnant persons' thoughts on whether screening should occur or not.[118,119]

Screening as a "risk-seeking" or "risk-reducing" behaviour

Pregnant persons also assessed screening based on the way they framed the risks of undergoing STI testing and not only based on the personal assessment of the risk of contracting or having an STI. On one hand, pregnant persons defined screening as a "risk-seeking" behaviour when they framed STI testing as the traumatic experience of receiving positive test results. On the other hand, they framed STI screening as a "risk-reducing" behaviour when they felt empowered to take control over the uncertainty of the disease and its adverse health outcomes for themselves and mostly for the wellbeing of their baby.

In the first instance, pregnant persons reported framing screening based on the adverse outcomes of a positive test result, rather than emphasizing the benefits of screening. They perceived screening as a "risk-seeking" behaviour.[110] Stigma, feelings of guilt, and inability to cope with a positive result were perceived as factors adding stress to the pregnancy and the fetus, which discouraged pregnant persons from undergoing screening.[76,105,109,110,112,119,121,128] Most pregnant persons felt emotionally unprepared when receiving the diagnosis, reporting feelings of confusion, "shock," and "disbelief."[100,105-107,117,120-123,125,127-129] These pregnant persons described the disruptive effect and trauma that resulted from an antenatal diagnosis of STIs. In these instances, pregnant persons believed that knowing their positive results and status was disempowering.[105,110,112,119,121,128] For these pregnant persons, framing knowledge as disempowering meant focusing more on the adverse outcomes of receiving a positive test result.[110] Most participants ascribed these reactions to being emotionally and mentally unprepared to receive such diagnosis, and some reacted with denial.[106,107,110,120,127]

Other pregnant persons reacted more positively, seeking information from their health care providers as well as from other sources.[104,110,117,119] Partner support played an important role in mitigating the traumatic effects of the diagnosis.[105,120,127] Most of these pregnant persons expressed the desire to have been better informed before undergoing the test. When informed, pregnant persons defined knowledge as "empowering."[100,107,110,117,119,121,123,126] Knowledge helped to "mitigate" the confusion, fears, and adverse outcomes of positive test results[107,110,126] Knowing about screening benefits meant understanding the advantages of prevention and medical treatment both for the mother and the fetus.[100,107,110,117,119,121,123,126] With knowledge pregnant persons gained awareness and a "special sense of responsibility" to safeguard the baby's health.[105,107,110,112,115,117-119,125-127] Maternal responsibility framed pregnant persons' views of health and rationale for screening.[100,105,107,110,112,115,117-119,125-127] Protecting the health of the baby was the most important benefit and the "main motivating

factor in the acceptability of screening."[100,105,107,110,112,115,117-119,125-127] The sense of maternal responsibility gained with knowledge about STIs empowered some pregnant persons to take action in accepting STI screening, and to gain control over the risk of transmitting the infection to the child with appropriate prenatal care.[100,117,118,121,125,127] For those who based the risk assessment of screening on maternal responsibility as a pregnant person, they framed STIs screening as risk reducing.[100,105,107,110,112,115,117-119,125-127] If they understood screening and treatment to be safe during pregnancy,[115,118] pregnant persons reported feelings of reassurance that transcended any potential harm and concern about screening.[110,115,117-119] Unlike many other types of prenatal testing (where, for example, there might be risk of harm to the baby), some pregnant persons were concerned about the risk of *not* doing the screening and of missing an opportunity to minimize risks of infection for the baby, as opposed to the risk of the screening procedure.

Administration Modality of Screening

Pregnant persons reported voluntary screening within a framework of autonomous informed decision-making process as an incentive to participate in STI screening. Many pregnant persons believed in the need for routine universal prenatal STI screening, while allowing pregnant persons final control over this decision.[100,101,105,107,110,112,113,115,117,119,121,122,125-128] *Routine* screening refers to the established and regularly followed care process that does not require health care providers' assessment of risk for STI infection to offer a test to the patient. Many pregnant persons reported routine as easing access to STIs screening,[113] because it removed the fear of stigmatization and discrimination and normalized the testing practice.[100] As one study participant highlights: "Well you [get] tested for everything else, all these other things that can harm the baby, don't you? I mean there's a test for Hep B, HIV, all these other things that can harm the baby. I mean if chlamydia is an infection that can harm the baby, go for it. Why would you want to put your baby through any [potential harm]?"[100] Additionally, screening can be *universal*, that is, offered to all pregnant persons, or *targeted*, that is targeted to a specific subpopulation of patients identified as at high risk of contracting the STI, typically defined on the basis of behaviour, clinical, or demographic characteristics. Normalized universal routine practice removed stigma surrounding STI screening and provided an opportunity for pregnant persons who engaged in high-risk lifestyle behaviours to undergo testing that they otherwise would have missed because of stigma.[112,113,119,125,127] Pregnant persons also supported routinized universal STI screening because of the asymptomatic nature of STIs.[101] Pimenta et al.(2003) note that: "in the absence of symptoms, many respondents reported that they would not have been sufficiently motivated to seek out screening themselves."[101] Finally, universal routine screening complied with pregnant persons sense of maternal responsibility in protecting the health of the fetus.[100] Regardless of their relationship status, whether they had been tested previously for STIs, and had past distressful experiences with false-positive results, many pregnant persons supported routine STIs screening during pregnancy.[100,101,105,107,110,112,113,115,117,119,121,122,125-128] Health care providers in one study addressed this aspect, and reported instead that targeting young pregnant persons was appropriate, however they suggested extending the age range beyond the age of 25 to the age of 30.[102]

Studies presented contradictory findings about the mandatory or voluntary method of administrating routine testing. *Mandatory* screening requires care providers to offer and perform screening to all patients that seek care without the patient's explicit consent. This screening administration modality does not consider patients declining testing. *Voluntary* testing instead can be structured in two ways to allow patients to refuse screening. First, in the *opt-out* screening strategy, care providers perform STI screening after informing the

patient that the test will be performed and that the patient may decline or defer testing. Assent is inferred unless the patient declines testing. Second, in the *opt-in* screening strategy, care providers perform STI screening only after informing the patient that the test is recommended and after the patient's explicit and written consent to perform the screening.

Sense of maternal responsibility as opposed to value for individual autonomy and choice influenced pregnant persons' preferences for administering STI screening. Some pregnant persons were convinced of the need for health care providers to recommend testing, and for pregnant persons to participate in mandatory preventive screening programs to minimize risks for the fetus and for reasons of public health.[105,112,121,127] Other pregnant persons experienced mandatory screening as a loss of autonomy and right to choose, pointing out that tests should be a pregnant person's choice "but mandatory for the baby,"[112,127] thus offered and not demanded by health care providers. Based on the belief that autonomous individuals are placed in a better position to evaluate their best interests, these study participants valued pregnant persons' autonomy and right to choose independently from public health policies and health care providers' recommendations.[105,110,112,115,121,125-127,129] As such, these pregnant persons indicated voluntary opt-in testing as the preferred method to administer STIs testing.[105,110,112,115,121,125-127,129]

While some pregnant persons supported a voluntary routine STI screening policy to encourage high uptake and to minimize risks to the fetus, some questioned routine screening's compatibility with informed consent.[107,108,110,112,115,117,121,126] Several pregnant persons described routine screening as a "voluntary-compulsory sequence," reducing pregnant persons' awareness and understanding of the need for testing.[108,112,117] They perceived routine testing as eroding their autonomy in making informed decisions as it "was often equated with lack of choice."[108,112,117] Pretest communication between pregnant persons and health care providers focused on medical information, often omitting to inform them about opt-out options if policies were in place, and assuming that the health care provider would make treatment decisions in the patient's best interest.[107,108,110,112,115,117,121,125,126,129] Feeling pressured and confused, pregnant persons often reacted by accepting that their concerns would go unanswered and by consenting without thoughtful deliberation.[107,108,110,112,115,117,121,125,126,129]

Screening Options

Pregnant persons who engaged in screening did not mention physical discomfort, but indicated that urine screening procedures were preferable to cervical or vaginal swabs taken by care providers because they were less invasive and less embarrassing.[41,100,101] Some pregnant persons expressed preferences regarding the location of the testing because of stigma and confidentiality concerns. These pregnant persons preferred attending STI screening in hospitals or in clinics in towns rather than family practices to avoid privacy breeches and stigmatization within the community.[113,129]

Summary of Results from the Patients' Perspectives and Experiences Review

This review aimed to describe pregnant persons' experiences with GC/CT screening and their resultant perspectives on barriers, facilitators, and preferences for the same. Given the relatively small qualitative literature on GC/CT screening during pregnancy, we broadened the review to include other STI screening that is transferable or relevant to evidence-informed decisions regarding the optimal screening policy for CT and/or GC during pregnancy. Informed by the iterative and emergent nature of qualitative inquiry, broadening the review to include other STIs' screening, while focusing on those aspects of screening

that are transferrable across STIs, allowed us to draw on a more comprehensive, yet relevant, evidence base rather than focusing on the limited qualitative literature on CT and/or GC alone.

Our review outlines a number of factors related to STI screening that may impact pregnant persons' experiences and thus the participation in screening. We identified a multilayered thematic framework that situates incentives and disincentives to the STIs' screening within two connected levels of factors that inform pregnant persons' decisions to engage with STI screening: one upstream and another downstream. Upstream factors are broader social and systemic conditions that offer opportunities for or as barriers against STI screening for pregnant persons, which in turn have a cascade effect on downstream factors. Upstream factors include logistic and pragmatic barriers to antenatal care, knowledge and beliefs, psychosocial barriers, health care provider relationships and communication. Downstream factors encompass individual behavioural incentives or disincentives to screening, which include: personal assessment of health and risk, screening administration modalities, screening for risk-seeking and risk-reducing behaviour, and overall screening options.

Along the upstream-downstream continuum, many of these factors closely interact with and influence each other. Both upstream and downstream factors work synergistically at the individual level, incentivizing or deterring pregnant persons' acceptance and experience of STI screening. In this review, logistic upstream conditions create barriers to prenatal care. Pragmatic barriers, such as family and work commitments, lack of accessible clinical sites or, as reported in American-based studies, insurance policies that can limit pregnant persons' ability to access and participate in STI screenings. Psychosocial factors, such as social stigma and discrimination associated with STIs, also influence pregnant persons' willingness to seek STI screening. In most studies, pregnant persons and/or their partners perceived STIs as having a negative moral connotation and as being a self-inflicted problem that would not warrant empathetic understanding. Embarrassment, shame, and vulnerability were found to be strong deterrents of screening acceptance. These perceptions in turn can have a downstream cascade effect on pregnant persons' personal assessment of risk, which can shape pregnant persons' decision-making process for undergoing screening. This personal risk assessment was then seen to rest on the beliefs of many pregnant persons' in relation to their lifestyle behaviours, relationships status, and sexual activities. Whereas commercial sex workers and drug users often reported to perceive themselves as high-risk due to their lifestyle and sexual behaviours, other pregnant persons in long-term monogamous relationships tended to perceive themselves at a low-risk of STIs. Both the self-perceived high-risk and low-risk status can lead pregnant persons to abstain from screening, and fear social isolation and discrimination.

While pregnant persons assessed their personal risk of STIs in relation to their lifestyle behaviours, relationships status, and sexual activities, perceptions about the purposes and need for STI screening heightened pregnant persons' maternal responsibility to minimize the risks of infections for their neonate and to not miss an opportunity for screening. These pregnant persons reported relief and reassurance for the health of the infant as their prime motivators for screening. Pregnant persons' perceptions of the value of screening were also related to reassurances of the neonate's health after a negative screening result was received and for the hope of preventing risks of transmission in the case of positive results. As knowledge and awareness empowered pregnant persons to take action and gain control over the risk of infection and mother-to-child transmissions, education that focuses on the risk factors of STIs and mother-to-child transmission may improve acceptance to undergo STIs screening.

The potential of community stigma and isolation related to screening participation and sexual activity, and perceptions of health care providers' judgment and discrimination at the clinical encounter were reported to impede the choice to agree to STI screening during pregnancy. Many pregnant persons described that sensitive, clear communication from the health care provider that emphasizes the importance of STIs screening during pregnancy could improve participation. Effective patient–provider relationships also emerged as a potential strategy that pregnant persons felt could contribute to their decisions to accept prenatal STIs testing. Trust built on clear and confidential disclosure of information from the health care professional was reported to contribute to nurturing an effective relationship that mitigated feelings of embarrassment and fear of stigmatization.

Health care providers' clear communication and respect of pregnant persons' autonomy in making informed decisions was also a determining factor for screening acceptability. Generally, pregnant persons perceived routine universal prenatal STI screening as normalizing the STI screening practice and believed it to be the best method of screening administration. Opinions on the mandatory or voluntary nature of this routine screening diverged among pregnant persons, some preferring mandatory screening to voluntary prenatal STI screening policies. However, most pregnant persons believed in voluntary routine STI screening policies. Based on the belief that autonomous individuals are best placed to assess their best interests, our review found that pregnant persons believed that autonomous, well-informed, and deliberate decisions are factors that improve acceptability of STIs screening.

Discussion

Integration of Findings

This HTA report provides evidence to support decisions on CT and GC screening strategies across Canada. The report examines evidence across multiple areas: clinical, economic, and the perspectives and experiences of pregnant persons, partners, and health care providers. In this discussion, results are integrated across the various domains of this HTA as they relate to the policy question.

The clinical review suggests that screening at both entry into prenatal care and at another time point in pregnancy may result in better yields than screening at a single time point.[35,36,38,42,43] When screening is targeted (i.e., age-based or other risk factor-based), infections may be missed in pregnant persons who do not meet the screening criteria.[39] Furthermore, adherence to US-based targeted screening guidelines for CT and GC is lower than 40%, suggesting that even those pregnant persons who are deemed at risk for infection may not undergo the required testing.[35] A universal screening strategy was supported through a review of the literature regarding the perspectives of pregnant persons, which identified universal screening — in particular with an opt-out option — as a strategy that can minimize the stigma, embarrassment and shame associated with STI screening and that can act as disincentives to screening participation. While limited relevant literature was identified, the one study included in the qualitative evidence synthesis suggests that providers may instead believe that targeted screening of people based on age (i.e., people 30 years old or younger) is appropriate.[102] Although the results of the base-case economic analysis suggest that the financial investment in either universal or age-based targeted screening programs yields small incremental health improvements compared with a non-programmatic screening strategy when evaluated at up to 19 weeks postpartum, exploratory analyses of the economic evaluation suggested that strategies that entail universal screening in the third trimester (i.e., NNUM, TNUM, and UNUM) may be cost-effective when considering the impact of screening over a longer time horizon. The longer-term model incorporated a wider set of implications for both the pregnant person (i.e., PID, infertility) and the offspring (i.e., blindness, mortality) that, if left excluded from the analysis given the adoption of a narrower time horizon, may ignore some of the significant long-term quality of life and cost impact issues of managing the sequelae of infections. Further sensitivity analyses demonstrated the extent to which uncertainty has an impact on the economic findings; specifically, under a 19-week postpartum time horizon, the first trimester universal screening strategy (i.e., UNNM) was considered cost-effective at a willingness-to-pay threshold of $100,000 per QALY if there is a higher risk of CT or GC infection or if a causal link exists between CT and GC infections and adverse obstetric outcomes.

The evidence regarding the optimal type of specimen to use during screening is unclear. The literature suggests that pregnant persons who engaged in screening reported a preference for urine screening procedures, as compared with cervical or vaginal swabs taken by care providers, or self-collected vaginal samples, as this strategy was perceived as the least invasive and the least embarrassing.[41,100,101] Despite a reported preference, however, the comparative performance of testing using different specimens is unclear. Three non-randomized studies were included in the clinical review that compared the detection yield of urine samples, vaginal, and/or cervical specimens. All of the studies reported lower detection rates in urine samples compared with endocervical samples. Yet, the first found a statistically significant decrease for detection rates in urine samples compared with endocervical samples in persons between the ages of 20 and 35 years but

did not report the significance for persons 20 years or younger or persons between ages 36 and 40 years;[40] the second study reported that the difference across their population was not statistically significant;[37] and the third study did not report on statistical significance.[41] Given the uncertainty in diagnostic performance across specimens, patient preference may play a key role in determining a recommendation on specimen type when developing screening strategies.

Given the pragmatic barriers to accessing and participating in STI screening, such as family and work commitments; psychosocial factors, such as social stigma and discrimination; lack of accessible clinical sites; and complicated insurance policies, it is not surprising that 60% to 75% of pregnant persons across the US were not being screened for CT and GC in accordance with established targeted screening guidelines, which would potentially result in a number of undiagnosed infections.[35] Policies supporting universal, as opposed to targeted, screening for pregnant persons could limit these identified barriers and increase adherence rates.

Study Quality and Confidence in Results

Robust methodologies were employed across the various sections of this report. The protocol for this HTA was prepared a priori, with explicitly described methodology and is registered with PROSPERO.[29] The protocol was also reviewed by clinical context experts, peer reviewers, and stakeholders external to CADTH. The literature searches conducted by the information specialist were based on peer-reviewed search strategies. For both the clinical review and the review of perspectives and experiences, the selection of eligible citations, quality assessment of the included studies, and data extraction were independently conducted by two reviewers. Additionally, quality assessment was guided by tools broadly acknowledged within the evidence synthesis community.

Overall, the body of evidence in the clinical review.[34-43] was rated as having a high risk of bias, primarily due to concerns with regards to patient selection in nine of the ten included studies.[34-39,41-43] All the studies relied on retrospective reviews of medical records for the primary and secondary outcomes of interest, which are subject to convenience sampling, data inaccuracy and abstraction errors. In addition, they failed to provide sufficient information on inclusion/exclusion criteria and other clinical characteristics.[34-43] The lack of sufficient clinical and demographic information limits the ability to assess generalizability and also made it impossible to ascertain whether the infections identified at repeat screening were due to treatment failure or reinfection, and whether it was a repeat infection with the same sexual partner or new partner. As four of the clinical studies on which the conclusions on the screening approach were drawn were conducted in high-risk populations or populations of unknown risk profiles,[36,38,42,43] (of which only one took place in Canada[38]) caution is warranted when extrapolating the findings to populations with low prevalence, for example as might be the case in a universal screening strategy. All of the studies also failed to mention whether the pregnant persons belonged to other high-risk groups including sex workers, homeless persons, persons with a previous history of STIs, and persons with a history of drug misuse and abuse. As such, generalizability to the general population may be limited. Relatedly, five of the included studies performed subgroup analyses based on age, which is a known risk factor for CT and GC infections.[34,35,40,42,43] A variety of tests were used to determine detection yield across the studies and accuracy was disclosed in only two articles written about the same study.[42 43] Two studies reported confirming NAAT results either by duplicate testing[41] or a secondary test.[38] Given that the diagnostic accuracy parameters (sensitivity and specificity) of one test were disclosed to be less than 100%[42 43] and the paucity of information on the accuracy or verification of the remaining NAATs used,

confidence in the diagnostic yield results that are reported in this review may be tempered. The economic model reflects the most comprehensive economic analysis to date by assessing different screening strategies that varied by timing, frequency, and the approach to maternal CT and GC screening. Where possible, Canadian data sources were selected for the economic analysis and the model is expected to be broadly generalizable to a Canadian setting. It is important to note that there remains variability in clinical practice and management across Canada; where possible, appropriate sensitivity analyses were conducted.

However, clinical evidence gaps regarding the natural history and epidemiology of these infections, and the characteristics of different risks groups may have contributed to uncertainty in the economic analysis. Although the structure of the base-case model is consistent with existing medical science literature, it is recognized that such literature has been derived from older publications. For instance, there remains uncertainty on the true relationship between CT and GC infection and adverse obstetric outcomes. Furthermore, literature on the infection and reinfection risks across different subgroups of the Canadian pregnant population remains limited. As such, extensive sensitivity analyses were conducted. Notably, the economic model was found to be sensitive to higher-risk populations. The base case assumed that the primary benefit to screening is in the reduction of the vertical transmission risk to an infant in the immediate short-term, although this likely introduced additional uncertainty regarding the long-term generalizability of the base-case model itself. The base-case findings may not apply to decision-making contexts that consider longer-term consequences. Exploratory analyses of the model found that it was sensitive to the time horizon adopted as different conclusions on the costs-effectiveness of programmatic screening strategies were reached under a lifetime time horizon. Therefore, caution may be warranted in interpreting the findings from the base-case analyses.

The review of the perspectives and experiences of pregnant persons, their partners and health care providers empirically describes pregnant persons' experiences and perceptions of screening for STIs during pregnancy. The methodological quality of the included papers was mixed, but generally strong. Notably, only four studies considered the role of the researcher in the study,[104,120,121,132] thus the extent to which the findings may have been influenced by the researchers' own backgrounds or beliefs are unclear. Qualitative research in general provides theoretical and contextual insights into the experiences of limited numbers of people in specific settings. The results from individual primary qualitative research studies are not intended to be generalizable directly to populations, although meta-synthesis across a number of qualitative studies builds an increasingly robust understanding that is more likely to be transferable between settings. Qualitative insights often enlighten the understanding of experiences and are important for planning services across different settings. The findings of the studies reviewed here – and of this synthesis — generalize to the Canadian (or any specific) population, although are limited to the conditions included in the body of literature synthesized (i.e., STI screening). Informed by the iterative and emergent nature of qualitative inquiry, the focus of the review of perspectives and experiences was purposefully broad and included views on other STI screening, while focusing on those aspects that are transferrable across STIs. This broad approach allowed us to draw on a more comprehensive, yet relevant, evidence base in the absence of an opportunity to collect primary data, or to query people directly about issues that may be important to individual perspectives specifically regarding GC/CT, but that were not covered in the literature. Although this review does not focus exclusively on CT/GC screening, the inclusion of a related set of STIs has enabled this review to advance the conceptual understanding of the experience of undergoing CT/GC screening during pregnancy and to

enhance the depth and relevance of the analysis. In particular, the comparison and integration of screening experiences between STIs strengthened the experiences described in the studies that specifically addressed CT/GC

Directions for Future Research

While five studies in the clinical review provided outcome data for pregnant persons who received an initial screening as well as a repeated screening at another time point during their pregnancy,[35,36,38,42,43] no literature reported on the detection yield of other screening strategies. Future research for comparing detection yield between screening strategies could have included screening one group of pregnant persons in the first trimester only while screening a different group in the third trimester. Alternatively, given the challenge of conducting studies for all screening strategies of interest, there may be value toward developing linked evidence models that incorporate data on the diagnostic accuracy of tests with both the clinical decision-making impact of a test result and the subsequent effectiveness of the available treatment options in order to better understand the clinical utility of a screening test, and more broadly, of a screening program. Although such an exercise was performed as part of the economic evaluation, its focus was toward understanding the potential cost-effectiveness of different screening strategies.

Future clinical research could also be directed toward identifying and comparing outcomes of varying screening strategies specific to the Canadian setting, including assessing long-term outcomes of treating identified cases, and the overall prevalence of CT and GC. Furthermore, understanding the missed opportunities from a false screening test would be of value in evaluating the impact of screening. It remains uncertain the causal relationship between infection and adverse obstetric outcomes. Such research could further provide support to the existing economic model by informing model parameter values and assumptions. As noted previously, aspects of the natural history of the disease (e.g., rates of vertical transmission, impact of CT and GC on adverse obstetric outcomes) in the present economic model were informed by older literature and remains a limitation. Furthermore, such studies on clinical utility could be used to validate the predictive quality of the economic model.

Given that Canada is a low-prevalence society, further studies are required that explore the impact of differing screening strategies in low-prevalence populations, particularly with respect to false-positive results, the experiences and perspectives of sexual partners, and the screening strategies' cost-effectiveness. In addition, the economic evaluation highlighted that one of the areas of greatest uncertainty in the model remains the impact that screening has on a high-risk population. Future research that better characterizes the high-risk population in Canada may help to reduce this uncertainty. Specifically, more studies on the relationship between prevalence, incidence, and reinfection rates of CT and GC in high-risk groups could better inform the creation of model parameters for this subgroup.

Further studies are also required to explore the harms of varying screening strategies during pregnancy. The secondary outcome of interest in this review was the effect of differing screening strategies on the detection and treatment of adverse obstetric, gynecological or neonatal outcomes, and harms, although no related evidence was identified.

Understanding baseline screening rates for STIs during pregnancy across the provinces would allow for an assessment of the effectiveness of future changes to policies involving screening interventions. The challenges to collecting data on screening strategies, however, must be acknowledged. In particular, enrolling an adequate number of pregnant persons and/or their partners and health care providers to ensure sufficient statistical power to detect

differences in outcomes is challenging. Relatedly, the number of factors that influence screening behaviour, and outcomes, likewise suggests that a large number of participants will be needed to ensure the findings are generalizable to the population.

Finally, the absence of qualitative literature on GC/CT screening during pregnancy should not be interpreted as a lack of importance of GC/CT for pregnant persons, or that it is not relevant to their experiences or perspectives. Rather, the topic should be considered unexplored. A lack of primary research on pregnant persons' and their partners' perspectives on GC/CT screening can be ascribed mainly to the lack of awareness about the available screening benefits on pregnant persons' part. Unlike other types of prenatal testing that may involve risks of harming the fetus by performing the test, this screening seems to be mostly about the risk of *not* performing the tests, and seems to rest on health care providers' duty to not miss opportunities for screening. Therefore, pregnant persons' and their partners' perspectives on GC/CT screening represent an important area to explore in future research. Additionally, while some data were available in this review to assess the importance of health care providers' perspectives through pregnant persons' experiences (e.g., specifically for partners changing relationships, or dealing with desertion or abuse), it was not possible to explore these perspectives in depth. Therefore, health care providers' attitudes toward the value of this screening and investigating best practices for communicating with clients regarding screening is also an area of research that would be beneficial to explore further.

Conclusions and Implications for Decision- or Policy-Making

A limited number of studies were available from which to draw conclusions on screening for CT and GC. However, the findings that emerged from the clinical review, economic analysis, and PPE review offer complementary sets of conclusions that may inform policy decisions.

The clinical review of the evidence found that screening that targets high-risk pregnant persons will potentially result in a significant number of infections going undiagnosed. Furthermore, screening only at entry into prenatal care, will result in infections that develop at later points being missed. The findings suggest that universal screening at entry into prenatal care and at another time point during pregnancy will result in the highest detection yield. Although repeating screening and universal screening predictably yields additional cases of CT and GC, research is very limited on the impact of finding these cases as it remains unclear whether it could have any effect on the growing numbers of CT and GC cases. Regarding the selection of specimen, three studies suggested that there was a trend toward lower detection rates using urine samples. The evidence, however, is insufficient to make conclusive statements about the relative performance of various types of specimen. While it is important to note that pregnant persons in Australia and the UK who were offered screening preferred collecting urine specimen over endocervical or vaginal, further assessment may be needed to determine whether pregnant persons in Canada have a preference for specific sampling procedures. Given that universal screening is intuitively more costly than targeted screening, determining the optimal screening strategy requires consideration of the economic evidence.

The economic analysis found that the strategy of targeted screening for high-risk individuals or universal screening at entry into prenatal care only (strategy TNNM or UNNM) was dominated by other more efficient screening strategies. Excluding all prenatal visit screenings (strategy NNNM) was the least costly strategy but also was associated with the highest number of pediatric infections. It was considered the most likely cost-effective screening strategy for CT and GC infections in pregnant persons in Canada if one's willingness-to-pay threshold was under $2.3 million per QALY as programmatic screening before labour and delivery was found to offer small incremental QALY gains if the clinical impact associated with screening is to avert vertical transmission of the infection to the neonate and the time horizon of interest was up to the postpartum period. However, in an exploratory analysis that adopted a lifetime time horizon, universal screening at first and third trimester (strategy UNUM) was found to be a cost-effective screening strategy if one's willingness-to-pay threshold was under $11,468 per QALY. This exploratory analysis may be more reflective of the potential value of screening during pregnancy as the benefits may extend beyond the postpartum period.

The review of the perspectives and experiences of pregnant persons, their partners and health care providers outlines a number of factors related to STI screening that may impact pregnant persons' experiences and participation. Pregnant persons identified both upstream and downstream opportunities for or against pregnant persons' engagement with STI screening. In the upstream level, both pragmatic and psychosocial barriers influenced their decision to avoid screening, addressing stigma as a major deterrent to STI screening. At the individual level, a key aspect of a pregnant person's participation in STI screening is their sense of maternal responsibility. Ensuring the health of the baby was the most important benefit and one of the main driving factors for engaging in screening. A trusting and supportive relationship with the health care provider based on accessible and clear

communication could also improve participation in screening. However, pregnant persons also framed screening within a framework of autonomous informed decision-making processes, considering routine and universal voluntary opt-in screening policies as acting as an incentive for a pregnant person's participation in screening.

In summary, this HTA finds that universal screening at entry into prenatal care and at another time point during pregnancy provides the most health benefits. However, a trade off that exists between the expected costs and clinical benefits between different screening strategies was most sensitive to the potential harms associated with the outcomes of developing an infection. Although universal screening in first and third trimesters (strategy UNUM) was found to be the costliest strategy, it generated the greatest amount of health. The incremental gain in health associated with UNUM compared with other screening strategies was dependent on the potential magnitude of harm from undiagnosed CT and GC infections (e.g., high-risk populations, impact on obstetric adverse event, lifetime analysis) and the costs associated with managing such infections (e.g., cost of managing pediatric infection). Although the base-case analysis capturing up to the postpartum period would suggest that the magnitude of clinical benefit is marginal (i.e., ICUR of over $65 million per QALY gained), exploratory analysis found that UNUM may be the most likely cost-effective screening strategy at a willingness-to-pay threshold of $11,468 per QALY or greater when factoring a lifetime time horizon. The universal strategy also aligns with the perspectives and experiences of pregnant persons, their partners, and health providers, as it has the potential to minimize stigma and discrimination, important psychosocial factors that influence screening behaviours. Given the large proportion of pregnant persons who are not undergoing current screening guidelines, significant effort would be required to ensure that any new or updated guidelines are implemented accordingly.

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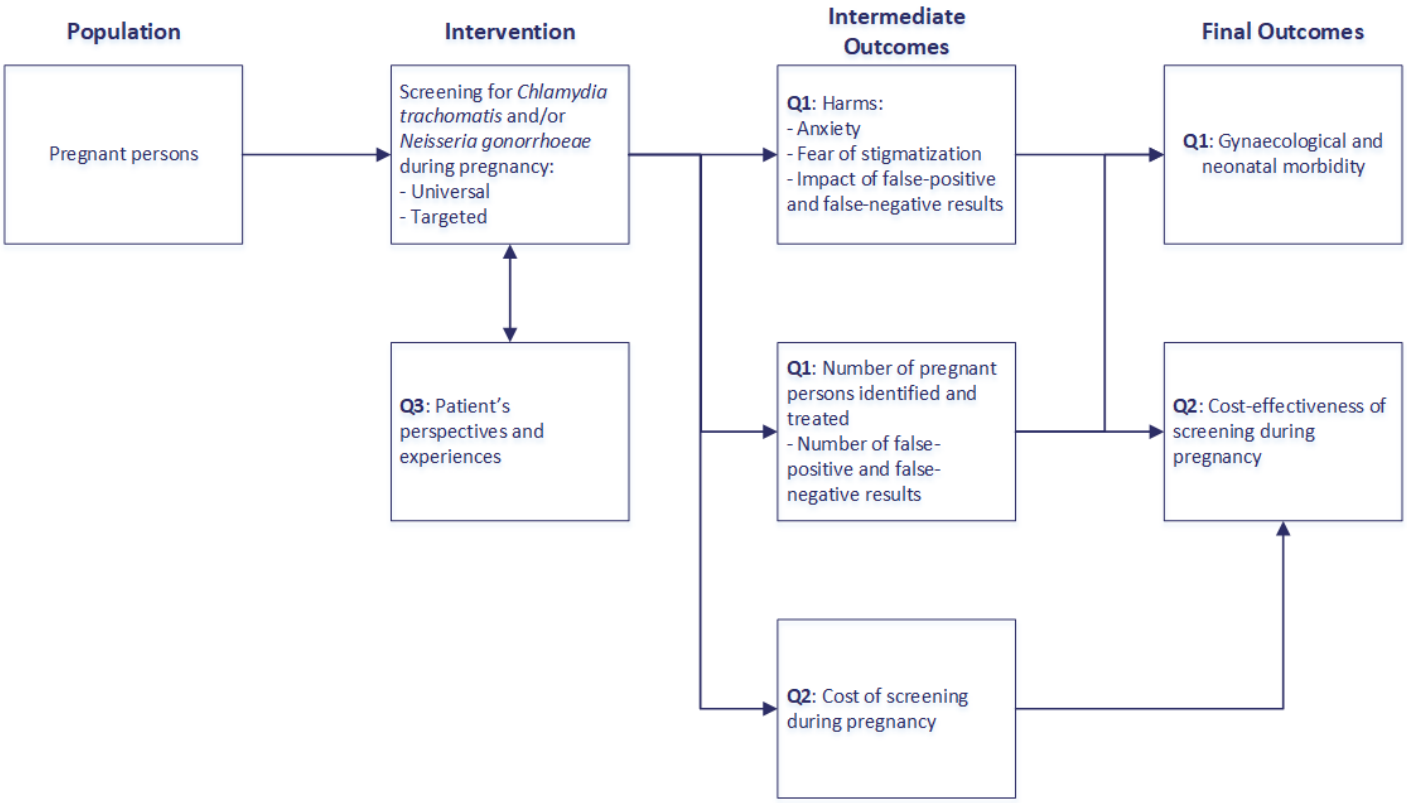
Appendix 1: Analytical Framework

Policy Question: How should Canadian health care providers screen pregnant persons for *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* — at what time(s) during pregnancy, using what specimen, with what frequency, and using a universal or a targeted approach?



CADTH

Appendix 2: Literature Search Strategy

Clinical Literature Search Strategy

OVERVIEW	
Interface:	Ovid
Databases:	Ovid Embase Ovid MEDLINE 1946 to Present Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations 1946 to present **Note:** Subject headings have been customized for each database. Duplicates between databases were removed in Ovid.
Date of search:	January 25, 2018
Alerts:	Monthly search updates until project completion.
Study Types:	No filters used
Limits:	Publication years 2003 forward English or French language Humans

SYNTAX GUIDE	
/	At the end of a phrase, searches the phrase as a subject heading
.sh	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
adj#	Adjacency within # number of words (in any order)
.ti	Title
.ab	Abstract
.kf	Author keyword heading word (MEDLINE)
.kw	Author keyword (Embase)
.pt	Publication type
medall	Ovid database code; Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

MULTI-DATABASE STRATEGY	
# Clinical Search Strategy – MEDLINE	
1	exp Prenatal Care/ or exp Pregnancy/ or exp Pregnant Women/ or exp Pregnancy Complications/
2	(pregnancy or pregnancies or pregnant or gestation or gestational or parous or gravid or gravidity or gravida or multigravid* or multiparous or nulliparous or primagravid* or prenatal or perinatal or maternity or maternal).ti,ab,kf.
3	1 or 2
4	exp chlamydiaceae/ or exp chlamydia/ or exp Chlamydiaceae Infections/ or exp chlamydia infections/
5	(Chlamydi* or C trachomatis or Chlamydiaceae* or Chlamydophila* or Trachoma*).ti,ab,kf.
6	exp Gonorrhea/ or exp Neisseria gonorrhoeae/
7	(Gonorrhea* or gonorrhoea* or gonorrhoeae* or Gonococc* or Neisseria*).ti,ab,kf.
8	4 or 5 or 6 or 7
9	exp Mass Screening/ or exp diagnosis/ or exp Monitoring, Physiologic/
10	(diagnosis or diagnostic or diagnose or diagnoses or diagnosing or diagnosed or monitoring or monitor or detect or detection or detecting or detected or test or tests or testing or assess or assessing or assessment or screen or screening or screened).ti,ab,kf.
11	((detection or screening) adj3 program*).ti,ab,kf.
12	exp Nucleic Acid Amplification Techniques/
13	(nucleic adj3 acid* adj3 (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
14	((NAT or NAAT or NABT or TMA or NASBA or NAP) and (techni* or test or tests or testing or analysis or anlyses or assay or assays)).ti,ab,kf.
15	(((DNA or RNA) adj3 amplifi*) and (techni* or test or tests or testing or analysis or analyses or probe or probes or assay or assays)).ti,ab,kf.
16	(transcription* adj3 mediat* adj3 amplifi* adj3 (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
17	(Ligase adj2 Chain* adj2 React*).ti,ab,kf.
18	(polymerase adj2 chain* adj2 react*).ti,ab,kf.
19	(Self-Sustain* adj2 Sequenc** adj2 Replicat*).ti,ab,kf.
20	(Nucleic Acid adj3 Sequenc* adj3 Amplifi*).ti,ab,kf.
21	Amplified Fragment Length Polymorphism Analysis.ti,ab,kf.
22	((LCR or PCR or RTPCR or RFLP or AFLP or RAPD or LCX or SDA or CTNRA) adj3 (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
23	((PCR or polymerase chain*) adj5 (multiplex or triplex or quantiplex or probe amplication or RAPD or random amplified polmorphic)).ti,ab,kf.
24	((DNA or RNA) adj5 (hybrid* or multiplex or triplex or quantiplex or probe amplification)).ti,ab,kf.
25	((DNA or RNA) adj3 amplifi*).ti,ab,kf.
26	(strand adj2 displacement* adj2 amplifi*).ti,ab,kf.
27	exp Culture Techniques/ or exp DNA, Bacterial/ or exp Cell Culture Techniques/ or exp Antibodies, Bacterial/an
28	(bacterial adj5 (culture or plate or cultures or plates or Thayer martin)).ti,ab,kf.
29	((vaginal or cervical or urine or genital) adj5 culture*).ti,ab,kf.
30	(McCoy adj3 culture*).ti,ab,kf.

MULTI-DATABASE STRATEGY	
# Clinical Search Strategy – MEDLINE	
31	(pathfinder adj3 chalymidia adj3 confirmat*).ti,ab,kf.
32	((amptima or hologic or genprobe or gen-probe or pelvo check or pelvocheck) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
33	((cobas or amplicor or cobas4800 or cobasamplicor) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
34	(hologic adj5 (combo2 or aptima)).ti,ab,kf.
35	((realtime CT NG or realtime CT or realtimeNG or realtimeCTNG or realtimeCT) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
36	((probetech or viper XTR or viperXTR or ProbeTecETQx or ProbeTech ET Qx or ProbeTecET Qx or ProbeTec ET or ProbetechCT* or Probetech CT or PACE or PACE2 or Light Cycler or Lightcycler) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
37	((genprobe or gen probe or APTIMA or APTIMAcombo or APTIMAGC or gonospot or gonostat) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
38	((genprobe or gen probe or APTIMA or APTIMAcombo or APTIMAGC) and (CT or NG or CTNG)).ti,ab,kf.
39	((probetech or viper XTR or viperXTR or ProbeTecETQx or PoobeTecET or ProbetechCT* or GenoQuick or AMPT or Accuprobe or hybrid capture) adj5 (CT or NG or CTNG)).ti,ab,kf.
40	(BD adj3 MAX adj3 (CT or GC or TV or CTGCTV or MCGT)).ti,ab,kf.
41	(BD adj2 (MAX or probetec or probe tec)).ti,ab,kf.
42	((Cepheid or intermedico) adj5 (xpert or genexpert or CT or NG or CTNG)).ti,ab,kf.
43	(xpert adj3 (CT or NG or CTNG)).ti,ab,kf.
44	Rapid Diagnostic System for Chlamydia*.ti,ab,kf.
45	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44
46	3 and 8 and 45
47	exp animals/
48	exp animal experimentation/ or exp animal experiment/
49	exp models animal/
50	nonhuman/
51	exp vertebrate/ or exp vertebrates/
52	or/47-51
53	exp humans/
54	exp human experimentation/ or exp human experiment/
55	or/53-54
56	52 not 55
57	46 not 56
58	limit 57 to yr="2003 -Current"
59	limit 58 to english language
60	58 and french.lg.

MULTI-DATABASE STRATEGY	
# Clinical Search Strategy – MEDLINE	
61	59 or 60

OTHER DATABASES		
PubMed	A limited PubMed search was performed to capture records not found in MEDLINE. Same MeSH, keywords, limits, and study types used as per MEDLINE search, with appropriate syntax used.	
Cochrane DARE through Wiley	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Cochrane Library databases.	
Cochrane Database of Systematic Reviews through Wiley	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Cochrane Library databases.	
Cochrane Central through Ovid	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions.	
CINAHL (EBSCO interface)	Same keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for EBSCO platform.	

Grey Literature

Dates for Search:	January 2-8, 2018
Keywords:	Included terms for chlamydia, gonorrhea, screening, and pregnancy
Limits:	Publication years 2003 to present; English or French language

Relevant websites from the following sections of the CADTH grey literature checklist *Grey Matters: a practical tool for searching health-related grey literature* (https://www.cadth.ca/grey-matters) were searched:

- Health Technology Assessment Agencies
- Health Economics
- Clinical Practice Guidelines
- Databases (free)
- Internet Search.

Patients' Preferences and Experiences Literature Search Strategy

OVERVIEW	
Interface:	Ovid
Databases:	Ovid MEDLINE 1946 to Present Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations 1946 to present **Note:** Subject headings have been customized for each database.
Date of search:	January 15, 2018 February 23, 2018
Alerts:	Monthly search updates until project completion
Study Types:	Qualitative studies, including surveys or questionnaires
Limits:	Please refer to each search strategy for limits Human-only

SYNTAX GUIDE	
/	At the end of a phrase, searches the phrase as a subject heading
.sh	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
adj#	Adjacency within # number of words (in any order)
.ti	Title
.ab	Abstract
.kf	Author keyword heading word (MEDLINE)
.kw	Author keyword (Embase)
.pt	Publication type
medall	Ovid database code; Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

MULTI-DATABASE STRATEGY	
Patients' Preferences and Experiences Search Strategy — MEDLINE — Strategy #1 – January 15, 2017	
1	exp Prenatal Care/ or exp Pregnancy/ or exp Pregnant Women/ or exp Pregnancy Complications/
2	(pregnancy or pregnancies or pregnant or gestation or gestational or parous or gravid or gravidity or gravida or multigravid* or multiparous or nulliparous or primagravid* or prenatal or perinatal or maternity or maternal).ti,ab,kf.
3	1 or 2
4	exp chlamydiaceae/ or exp chlamydia/ or exp Chlamydiaceae Infections/ or exp chlamydia infections/
5	(Chlamydi* or C trachomatis or Chlamydiaceae* or Chlamydophila* or Trachoma*).ti,ab,kf.
6	exp Gonorrhea/ or exp Neisseria gonorrhoeae/
7	(Gonorrhea* or gonorrhoea* or gonorrhoeae* or Gonococc* or Neisseria*).ti,ab,kf.

MULTI-DATABASE STRATEGY	
8	4 or 5 or 6 or 7
9	exp Mass Screening/ or exp diagnosis/ or exp Monitoring, Physiologic/
10	(diagnosis or diagnostic or diagnose or diagnoses or diagnosing or diagnosed or monitoring or monitor or detect or detection or detecting or detected or test or tests or testing or assess or assessing or assessment or screen or screening or screened).ti,ab,kf.
11	((detection or screening) adj3 program*).ti,ab,kf.
12	exp Nucleic Acid Amplification Techniques/
13	(nucleic adj3 acid* adj3 (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
14	((NAT or NAAT or NABT or TMA or NASBA or NAP) and (techni* or test or tests or testing or analysis or anlyses or assay or assays)).ti,ab,kf.
15	(((DNA or RNA) adj3 amplifi*) and (techni* or test or tests or testing or analysis or analyses or probe or probes or assay or assays)).ti,ab,kf.
16	(transcription* adj3 mediat* adj3 amplifi* adj3 (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
17	(Ligase adj2 Chain* adj2 React*).ti,ab,kf.
18	(polymerase adj2 chain* adj2 react*).ti,ab,kf.
19	(Self-Sustain* adj2 Sequenc** adj2 Replicat*).ti,ab,kf.
20	(Nucleic Acid adj3 Sequenc* adj3 Amplifi*).ti,ab,kf.
21	Amplified Fragment Length Polymorphism Analysis.ti,ab,kf.
22	((LCR or PCR or RTPCR or RFLP or AFLP or RAPD or LCX or SDA or CTNRA) adj3 (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
23	((PCR or polymerase chain*) adj5 (multiplex or triplex or quantiplex or probe amplication or RAPD or random amplified polmorphic)).ti,ab,kf.
24	((DNA or RNA) adj5 (hybrid* or multiplex or triplex or quantiplex or probe amplification)).ti,ab,kf.
25	((DNA or RNA) adj3 amplifi*).ti,ab,kf.
26	(strand adj2 displacement* adj2 amplifi*).ti,ab,kf.
27	exp Culture Techniques/ or exp DNA, Bacterial/ or exp Cell Culture Techniques/ or exp Antibodies, Bacterial/an
28	(bacterial adj5 (culture or plate or cultures or plates or Thayer martin)).ti,ab,kf.
29	((vaginal or cervical or urine or genital) adj5 culture*).ti,ab,kf.
30	(McCoy adj3 culture*).ti,ab,kf.
31	(pathfinder adj3 chalymidia adj3 confirmat*).ti,ab,kf.
32	((amptima or hologic or genprobe or gen-probe or pelvo check or pelvocheck) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
33	((cobas or amplicor or cobas4800 or cobasamplicor) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
34	(hologic adj5 (combo2 or aptima)).ti,ab,kf.
35	((realtime CT NG or realtime CT or realtimeNG or realtimeCTNG or realtimeCT) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
36	((probetech or viper XTR or viperXTR or ProbeTecETQx or ProbeTech ET Qx or ProbeTecET Qx or ProbeTec ET or ProbetechCT* or Probetech CT or PACE or PACE2 or Light Cycler or Lightcycler) and (techni* or test or tests or testing or

MULTI-DATABASE STRATEGY	
	analysis or analyses or assay or assays)).ti,ab,kf.
37	((genprobe or gen probe or APTIMA or APTIMAcombo or APTIMAGC or gonospot or gonostat) and (techni* or test or tests or testing or analysis or analyses or assay or assays)).ti,ab,kf.
38	((genprobe or gen probe or APTIMA or APTIMAcombo or APTIMAGC) and (CT or NG or CTNG)).ti,ab,kf.
39	((probetech or viper XTR or viperXTR or ProbeTecETQx or PoobeTecET or ProbetechCT* or GenoQuick or AMPT or Accuprobe or hybrid capture) adj5 (CT or NG or CTNG)).ti,ab,kf.
40	(BD adj3 MAX adj3 (CT or GC or TV or CTGCTV or MCGT)).ti,ab,kf.
41	(BD adj2 (MAX or probetec or probe tec)).ti,ab,kf.
42	((Cepheid or intermedico) adj5 (xpert or genexpert or CT or NG or CTNG)).ti,ab,kf.
43	(xpert adj3 (CT or NG or CTNG)).ti,ab,kf.
44	Rapid Diagnostic System for Chlamydia*.ti,ab,kf.
45	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44
46	3 and 8 and 45
47	"Surveys and Questionnaires"/
48	Health Care Surveys/
49	self report/
50	questionnaire*.ti,ab,kf.
51	survey*.ti,ab,kf.
52	or/47-51
53	exp Empirical Research/ or Interview/ or Interviews as Topic/ or Personal Narratives/ or Focus Groups/ or Narration/ or Nursing Methodology Research/
54	Interview/
55	interview*.ti,ab,kf.
56	qualitative.ti,ab,kf,jw.
57	(theme* or thematic).ti,ab,kf.
58	ethnological research.ti,ab,kf.
59	ethnograph*.ti,ab,kf.
60	ethnomedicine.ti,ab,kf.
61	ethnonursing.ti,ab,kf.
62	phenomenol*.ti,ab,kf.
63	(grounded adj (theor* or study or studies or research or analys?s)).ti,ab,kf.
64	(life stor* or women* stor*).ti,ab,kf.
65	(emic or etic or hermeneutic* or heuristic* or semiotic*).ti,ab,kf.
66	(data adj1 saturat$).ti,ab,kf.
67	participant observ*.ti,ab,kf.
68	(social construct* or postmodern* or post-structural* or post structural* or poststructural* or post modern* or post-modern* or feminis*).ti,ab,kf.

MULTI-DATABASE STRATEGY	
69	(action research or cooperative inquir* or co operative inquir* or co-operative inquir*).ti,ab,kf.
70	(humanistic or existential or experiential or paradigm*).ti,ab,kf.
71	(field adj (study or studies or research or work)).ti,ab,kf.
72	(human science or social science).ti,ab,kf.
73	biographical method.ti,ab,kf.
74	theoretical sampl*.ti,ab,kf.
75	((purpos* adj4 sampl*) or (focus adj group*)).ti,ab,kf.
76	(open-ended or narrative* or textual or texts or semi-structured).ti,ab,kf.
77	(life world* or life-world* or conversation analys?s or personal experience* or theoretical saturation).ti,ab,kf.
78	((lived or life) adj experience*).ti,ab,kf.
79	cluster sampl*.ti,ab,kf.
80	observational method*.ti,ab,kf.
81	content analysis.ti,ab,kf.
82	(constant adj (comparative or comparison)).ti,ab,kf.
83	((discourse* or discurs*) adj3 analys?s).ti,ab,kf.
84	narrative analys?s.ti,ab,kf.
85	(heidegger* or colaizzi* or spiegelberg* or merleau* or husserl* or foucault* or ricoeur or glaser*).ti,ab,kf.
86	(van adj manen*).ti,ab,kf.
87	(van adj kaam*).ti,ab,kf.
88	(corbin* adj2 strauss*).ti,ab,kf.
89	or/53-88
90	46 and 52
91	46 and 89
92	90 or 91
93	limit 92 to yr="2003 -Current"
94	limit 93 to english language
95	93 and french.lg.
96	94 or 95
97	exp animals/
98	exp animal experimentation/ or exp animal experiment/
99	exp models animal/
100	nonhuman/
101	exp vertebrate/ or exp vertebrates/
102	or/97-101
103	exp humans/
104	exp human experimentation/ or exp human experiment/

MULTI-DATABASE STRATEGY	
105	or/103-104
106	102 not 105
107	96 not 106
Patients' Preferences and Experiences Search Strategy — MEDLINE — Strategy #2 — February 23, 2018	
1	exp Prenatal Care/ or exp Pregnancy/ or exp Pregnant Women/ or exp Pregnancy Complications/
2	(pregnancy or pregnancies or pregnant or gestation or gestational or parous or gravid or gravidity or gravida or multigravid* or multiparous or nulliparous or primagravid* or prenatal or perinatal or maternity or maternal).ti,ab,kf.
3	1 or 2
4	exp chlamydiaceae/ or exp chlamydia/ or exp Chlamydiaceae Infections/ or exp chlamydia infections/
5	(Chlamydi* or C trachomatis or Chlamydiaceae* or Chlamydophila* or Trachoma*).ti,ab,kf.
6	exp Gonorrhea/ or exp Neisseria gonorrhoeae/
7	(Gonorrhea* or gonorrhoea* or gonorrhoeae* or Gonococc* or Neisseria*).ti,ab,kf.
8	exp Sexually Transmitted Diseases/
9	(STI or STIs or STD or STDs).ti,ab,kf.
10	Sexually transmitted*.ti,ab,kf.
11	(venereal adj3 (infection* or disease*)).ti,ab,kf.
12	exp Papillomavirus Infections/ or exp PAPILLOMAVIRIDAE/
13	(HPV* or hrHPV* or Papillomavirus* or Papilloma Virus*).ti,ab,kf.
14	exp HIV/
15	(Human Immunodeficiency Virus* or Human Immuno deficiency Virus* or AIDS or Acquired Immunodeficiency Syndrome* or Acquired Immuno deficiency Syndrome* or HIV or HTLV?III or LAVHTLV?III).ti,ab,kf.
16	exp Herpes Simplex/
17	(Herpes* or herpessymplex* or herpetic* or HSV?2 or HSV or HSVI).ti,ab,kf.
18	exp SYPHILIS/
19	(syphilis or chancre or neurosyphilis or syphilitic*).ti,ab,kf.
20	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21	exp Mass Screening/ or exp diagnosis/ or exp Monitoring, Physiologic/
22	(diagnosis or diagnostic or diagnose or diagnoses or diagnosing or diagnosed or monitoring or monitor or detect or detection or detecting or detected or test or tests or testing or assess or assessing or assessment or screen or screening or screened).ti,ab,kf.
23	((detect* or screening) adj3 program*).ti,ab,kf.
24	21 or 22 or 23
25	3 and 20 and 24
26	exp Empirical Research/ or Interview/ or Interviews as Topic/ or Personal Narratives/ or Focus Groups/ or exp Narration/ or Nursing Methodology Research/ or Narrative Medicine/
27	Interview/
28	interview*.ti,ab,kf.
29	qualitative.ti,ab,kf,jw.

MULTI-DATABASE STRATEGY	
30	(theme* or thematic).ti,ab,kf.
31	ethnological research.ti,ab,kf.
32	ethnograph*.ti,ab,kf.
33	ethnomedicine.ti,ab,kf.
34	ethnonursing.ti,ab,kf.
35	phenomenol*.ti,ab,kf.
36	(grounded adj (theor* or study or studies or research or analys?s)).ti,ab,kf.
37	(life stor* or women* stor*).ti,ab,kf.
38	(emic or etic or hermeneutic* or heuristic* or semiotic*).ti,ab,kf.
39	(data adj1 saturat$).ti,ab,kf.
40	participant observ*.ti,ab,kf.
41	(social construct* or postmodern* or post-structural* or post structural* or poststructural* or post modern* or post-modern* or feminis*).ti,ab,kf.
42	(action research or cooperative inquir* or co operative inquir* or co-operative inquir*).ti,ab,kf.
43	(humanistic or existential or experiential or paradigm*).ti,ab,kf.
44	(field adj (study or studies or research or work)).ti,ab,kf.
45	(human science or social science).ti,ab,kf.
46	biographical method.ti,ab,kf.
47	theoretical sampl*.ti,ab,kf.
48	((purpos* adj4 sampl*) or (focus adj group*)).ti,ab,kf.
49	(open-ended or narrative* or textual or texts or semi-structured).ti,ab,kf.
50	(life world* or life-world* or conversation analys?s or personal experience* or theoretical saturation).ti,ab,kf.
51	((lived or life) adj experience*).ti,ab,kf.
52	cluster sampl*.ti,ab,kf.
53	observational method*.ti,ab,kf.
54	content analysis.ti,ab,kf.
55	(constant adj (comparative or comparison)).ti,ab,kf.
56	((discourse* or discurs*) adj3 analys?s).ti,ab,kf.
57	(heidegger* or colaizzi* or spiegelberg* or merleau* or husserl* or foucault* or ricoeur or glaser*).ti,ab,kf.
58	(van adj manen*).ti,ab,kf.
59	(van adj kaam*).ti,ab,kf.
60	(corbin* adj2 strauss*).ti,ab,kf.
61	or/26-60
62	"Surveys and Questionnaires"/
63	Health Care Surveys/
64	self report/
65	questionnaire*.ti,ab,kf.

MULTI-DATABASE STRATEGY	
66	survey*.ti,ab,kf.
67	or/62-66
68	61 or 67
69	25 and 68
70	limit 69 to english language

OTHER DATABASES		
PubMed	A limited PubMed search was performed to capture records not found in MEDLINE. Same MeSH, keywords, limits, and study types used as per MEDLINE search, with appropriate syntax used.	
Cochrane DARE through Wiley	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Cochrane Library databases.	
Cochrane Database of Systematic Reviews through Wiley	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Cochrane Library databases.	
Cochrane Central through Ovid	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions.	
Scopus	Same keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Scopus database.	
CINAHL (EBSCO interface)	Same keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for EBSCO platform.	

Grey Literature

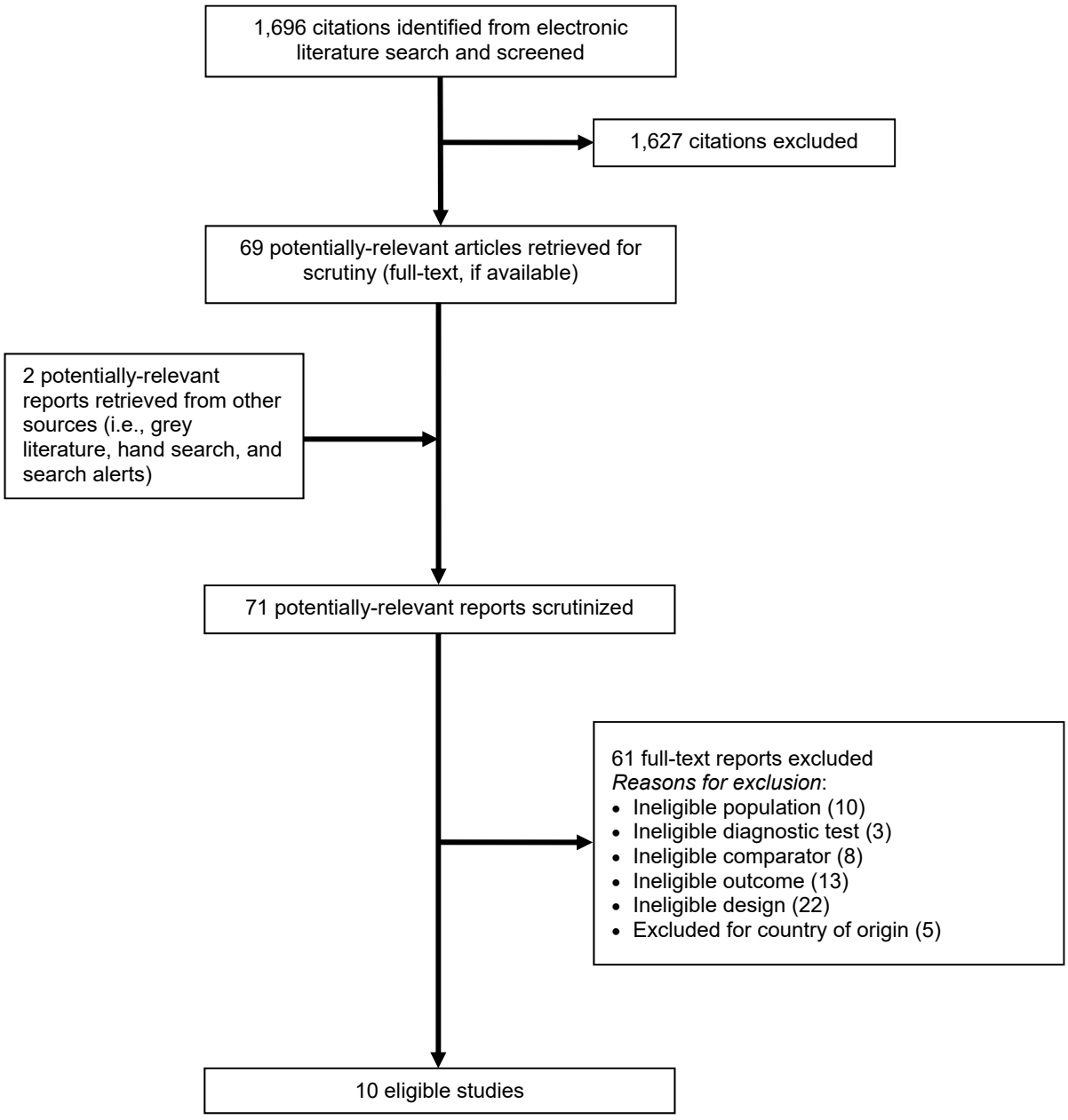
Dates for Search:	January 2-8, 2018
Keywords:	Included terms for chlamydia, gonorrhea, screening, and pregnancy
Limits:	Publication years 2003 to present; English or French language

Relevant websites from the following sections of the CADTH grey literature checklist *Grey Matters: a practical tool for searching health-related grey literature* (https://www.cadth.ca/grey-matters) were searched:

- Health Technology Assessment Agencies
- Health Economics
- Clinical Practice Guidelines
- Databases (free)
- Internet Search.

Appendix 3: Study Selection Flow Diagram — Clinical Review

Figure 6: PRISMA Flowchart of Selected Reports



Appendix 4: List of Included Studies — Clinical Review

1. Folger AT. Maternal Chlamydia trachomatis infections and preterm birth: The impact of early detection and eradication during pregnancy. *Matern Child Health J.* 2014;18(8):1795-1802.
2. Blatt AJ, Lieberman JM, Hoover DR, Kaufman HW. Chlamydial and gonococcal testing during pregnancy in the United States. *Am J Obstet Gynecol.* 2012;207(1):55.e51-58.
3. Berggren EK, Patchen L. Prevalence of chlamydia trachomatis and neisseria gonorrhoeae and repeat infection among pregnant urban adolescents. *Sex Transm Dis.* 2011;38(3):172-174.
4. Roberts SW, Sheffield JS, McIntire DD, Alexander JM. Urine screening for chlamydia trachomatis during pregnancy. *Obstetrics and gynecology.* 2011;117(4):883-885.
5. Aggarwal A, Spitzer RF, Caccia N, Stephens D, Johnstone J, Allen L. Repeat screening for sexually transmitted infection in adolescent obstetric patients. *JOGC.* 2010;32(10):956-961.
6. Silveira MF, Erbelding EJ, Ghanem KG, Johnson HL, Burke AE, Zenilman JM. Risk of chlamydia trachomatis infection during pregnancy: Effectiveness of guidelines-based screening in identifying cases. *Int J STD AIDS.* 2010;21(5):367-370.
7. Böhm I, Gröning A, Sommer B, Müller H-W, Krawczak M, Glaubitz R. A German chlamydia trachomatis employing semi-automated real-time PCR: Results and perspectives. *Journal of Clinical Virology.* 2009;46(S3):S27-S32.
8. Logan S, Browne J, McKenzie H, Templeton A, Bhattacharya S. Evaluation of endocervical, first-void urine and self-administered vulval swabs for the detection of chlamydia trachomatis in a miscarriage population. *BJOG.* 2005;112(1):103-106.
9. Miller JM, Maupin RT, Nsuami M. Initial and repeat testing for chlamydia during pregnancy. *J Matern Fetal Neonatal Med.* 2005;18(4):231-235.
10. Miller JM, Jr., Maupin RT, Mestad RE, Nsuami M. Initial and repeated screening for gonorrhea during pregnancy. *Sex Transmitted Dis.* 2003;30(9):728-730.

Appendix 5: List of Excluded Studies and Reasons for Exclusion — Clinical Review

Irrelevant Population (I.e., not Pregnant Persons)

O'Higgins AC, Jackson V, Lawless M, et al. Screening for asymptomatic urogenital Chlamydia trachomatis infection at a large Dublin maternity hospital: results of a pilot study. *Ir J Med Sci.* 2017;186(2):393-397.

Hoover KW, Tao G, Nye MB, Body BA. Suboptimal adherence to repeat testing recommendations for men and women with positive Chlamydia tests in the United States, 2008-2010. *Clin Infect Dis.* 2013;56(1):51-57.

Anschuetz GL, Asbel L, Spain CV, et al. Association between enhanced screening for Chlamydia trachomatis and Neisseria gonorrhoeae and reductions in sequelae among women. *J Adolesc Health.* 2012;51(1):80-85.

Andersen B, van Valkengoed I, Sokolowski I, Moller JK, Ostergaard L, Olesen F. Impact of intensified testing for urogenital Chlamydia trachomatis infections: a randomised study with 9-year follow-up. *Sex Trans Inf.* 2011;87(2):156-161.

Stevens MP, Tan SE, Horvath L, Fairley CK, Garland SM, Tabrizi SN. Absence of a Chlamydia trachomatis variant, harbouring a deletion in the cryptic plasmid, in clients of a sexually transmissible infection clinic and antenatal patients in Melbourne. *Commun Dis Intell Q Rep.* 2008;32(1):77-81.

Manhart LE, Marrazzo JM, Fine DN, Kerani RP, Golden MR. Selective testing criteria for gonorrhea among young women screened for Chlamydial infection: contribution of race and geographic prevalence. *J Infect Dis.* 2007;196(5):731-737.

Low N, Egger M, Sterne JA, et al. Incidence of severe reproductive tract complications associated with diagnosed genital chlamydial infection: the Uppsala Women's Cohort Study. *Sex Trans Inf.* 2006;82(3):212-218.

Church DL, Zentner A, Semeniuk H, Henderson E, Read R. Reasons for testing women for genital Chlamydia trachomatis infection in the Calgary region. *Can J Infect Dis.* 2003;14(1):35-40.

Macmillan S, McKenzie H, Templeton A. Parallel observation of four methods for screening women under 25 years of age for genital infection with Chlamydia trachomatis. *Eur J Obstet Gynecol Reprod Biol.* 2003;107(1):68-73.

Pimenta JM, Catchpole M, Rogers PA, et al. Opportunistic screening for genital chlamydial infection. I: acceptability of urine testing in primary and secondary healthcare settings. *Sex Trans Inf.* 2003;79(1):16-21.

Irrelevant Diagnostic Test (i.e., not NAAT for GC or CT and culture for CT)

Angelova M, Kovachev E, Tsankova V, Koleva I, Mangarova S. Role and Importance of Chlamydia Trachomatis in Pregnant Patients. *Open Access Macedonian Journal of Medical Sciences.* 2016;4(3):410-412.

Hood EE, Nerhood RC. The utility of screening for chlamydia at 34-36 weeks of gestation. *W V Med J.* 2010;106(6):10-11.

Ayuk PT, Dudley S, McShane H, Rees M, Mackenzie IZ. Efficacy of follow-up and contact tracing of women who test positive for genital tract chlamydia trachomatis prior to pregnancy termination. *J Obstet Gynaecol.* 2004;24(6):687-689.

No Relevant Comparator (I.e., not Comparative Clinical Study)

Reekie J, Roberts C, Preen D, et al. Chlamydia trachomatis and the risk of spontaneous preterm birth, babies who are born small for gestational age, and stillbirth: a population-based cohort study. *Lancet Infect Dis.* 2018.

Lazenby GB, Korte JE, Tillman S, Brown FK, Soper DE. A recommendation for timing of repeat Chlamydia trachomatis test following infection and treatment in pregnant and nonpregnant women. *Int J STD AIDS.* 2017;28(9):902-909.

Hill MG, Menon S, Smith S, Zhang H, Tong X, Browne PC. Screening for Chlamydia and Gonorrhea Cervicitis and Implications for Pregnancy Outcome. Are We Testing and Treating at the Right Time? *J Reprod Med.* 2015;60(7-8):301-308.

Tao G, Hoover KW, Nye MB, Body BA. Age-specific chlamydial infection among pregnant women in the United States: evidence for updated recommendations. *Sex Transmitted Dis.* 2014;41(9):556-559.

Mathur M, Robertson C, Caird L, Ho-Yen DO. Chlamydia infection among pregnant women and those seeking termination. *J Obstet Gynaecol.* 2007;27(4):409-412.

Barney OJ, Nathan M. A study of the prevalence of sexually transmitted infections and related conditions in pregnant women attending a sexual health service. *Int J STD AIDS.* 2005;16(5):353-356.

Grio R, Bello L, Smirne C, et al. Chlamydia trachomatis prevalence in North-West Italy. *Minerva Ginecol.* 2004;56(5):401-406.

Bachmann LH, Pigott D, Desmond R, et al. Prevalence and factors associated with gonorrhea and chlamydial infection in at-risk females presenting to an urban emergency department. *Sex Transmitted Dis.* 2003;30(4):335-339.

Irrelevant Outcome (i.e., not detection yield, clinical utility or harms)

Dahlberg J, Hadad R, Elfving K, et al. Ten years transmission of the new variant of Chlamydia trachomatis in Sweden: prevalence of infections and associated complications. *Sex Trans Inf.* 2018;94(2):100-104.

Ong JJ, Chen M, Hocking J, et al. Chlamydia screening for pregnant women aged 16-25 years attending an antenatal service: a cost-effectiveness study. *BJOG.* 2016;123(7):1194-1202.

Rours GI, Smith-Norowitz TA, Ditkowsky J, et al. Cost-effectiveness analysis of Chlamydia trachomatis screening in Dutch pregnant women. *Pathogens and Global Health.* 2016;110(7-8):292-302.

Lavoue V, Morcel K, Voltzenlogel MC, et al. Scoring system avoids Chlamydia trachomatis overscreening in women seeking surgical abortions. *Sex Transmitted Dis.* 2014;41(8):470-474

Krivochenitser R, Jones JS, Whalen D, Gardiner C. Underrecognition of cervical Neisseria gonorrhoeae and Chlamydia trachomatis infections in pregnant patients in the ED. *Am J Emerg Med.* 2013;31(4):661-663.

Gillespie P, O'Neill C, Adams E, et al. The cost and cost-effectiveness of opportunistic screening for Chlamydia trachomatis in Ireland. *Sex Trans Inf.* 2012;88(3):222-228.

Fjerstad M, Trussell J, Lichtenberg ES, Sivin I, Cullins V. Severity of infection following the introduction of new infection control measures for medical abortion. *Contraception.* 2011;83(4):330-335.

Chen MY, Fairley CK, De Guingand D, et al. Screening pregnant women for chlamydia: what are the predictors of infection? *Sex Trans Inf.* 2009;85(1):31-35.

Bernstein KT, Mehta SD, Rompalo AM, Erbelding EJ. Cost-effectiveness of screening strategies for Gonorrhea among females in private sector care. *Obstet Gynecol.* 2006;107(4):813-821.

French JI, McGregor JA, Parker R. Readily treatable reproductive tract infections and preterm birth among black women. *Am J Obstet Gynecol.* 2006;194(6):1717-1726; discussion 1726-1717.

Rours GI, Verkooyen RP, Willemse HF, et al. Use of pooled urine samples and automated DNA isolation to achieve improved sensitivity and cost-effectiveness of large-scale testing for Chlamydia trachomatis in pregnant women. *J Clin Microbiol.* 2005;43(9):4684-4690.

Chong S, Jang D, Song X, et al. Specimen processing and concentration of Chlamydia trachomatis added can influence false-negative rates in the LCx assay but not in the APTIMA Combo 2 assay when testing for inhibitors. *J Clin Microbiol.* 2003;41(2):778-782.

Pimenta JM, Catchpole M, Rogers PA, et al. Opportunistic screening for genital chlamydial infection. II: prevalence among healthcare attenders, outcome, and evaluation of positive cases.[Erratum appears in Sex Transm Infect. 2004 Apr;80(2):156]. *Sex Trans Inf.* 2003;79(1):22-27.

Irrelevant Study Design (i.e., not primary clinical study)

Shannon CL, Klausner JD. Keep Screening! Maternal Gonococcal Infection and Adverse Birth Outcomes. *Sex Transmitted Dis.* 2017;44(5):272-273.

Balendra A, Oakeshott P, Hayes K, Planche T, Hay PE. Chlamydia screening in an early pregnancy unit. *Sex Trans Inf.* 2016;92(3):231.

Gilbert L. Infections of concern during pregnancy: Prevention and interventions. *Med Today.* 2016;17(8):14-24.

Low N, Redmond S, Uuskula A, et al. Screening for genital chlamydia infection. *Cochrane Database Syst Rev.* 2016;9:Cd010866.

Anonymous. Chlamydia screening can prevent harm to newborns. *Australian Nursing & Midwifery Journal.* 2015;23(4):26.

Vermund SH. Screening for Sexually Transmitted Infections in Antenatal Care Is Especially Important Among HIV-Infected Women. *Sex Transmitted Dis.* 2015;42(10):566-568.

Hurt W, Peeling RW. What impact will new screening techniques have on the epidemiology of STIs worldwide? *Clinical Practice.* 2014;11(1):1-4.

Raychaudhuri M. False positive chlamydia results in pregnancy: should we retest them? *Sex Trans Inf.* 2013;89(8):665.

Curran G. Universal antenatal chlamydia screening by rural midwives. *Aust Nurs J.* 2012;19(7):30-32.

Kalwij SA. Opportunistic chlamydia screening in a general practice consultation. *BMJ.* 2011;343:d5108.

Gottlieb SL, Berman SM, Low N. Screening and treatment to prevent sequelae in women with Chlamydia trachomatis genital infection: how much do we know? *J Infect Dis.* 2010;201 Suppl 2:S156-167.

Kalwij S, Macintosh M, Baraitser P. Screening and treatment of Chlamydia trachomatis infections. *BMJ.* 2010;340:c1915.

Low N, Bender N, Nartey L, Shang A, Stephenson JM. Effectiveness of chlamydia screening: systematic review. *Int J Epidemiol.* 2009;38(2):435-448.

Moreno MA, Furtner F, Rivara FP. Advice for patients. Chlamydia screening: a routine test. *Arch Pediatr Adolesc Med.* 2009;163(6):592.

Lin KW, Ramsey L. Screening for chlamydial infection. *Am Fam Physician.* 2008;78(12):1349-1350.

Cheney K, Chen MY, Donovan B. Chlamydia trachomatis infection among antenatal women in Sydney. *Aust N Z J Public Health.* 2006;30(1):85-87.

Hope A. Chlamydia trachomatis among antenatal women in Sydney [3]. *Aust N Z J Public Health.* 2006;30(3).

Low N, Harbord RM, Egger M, et al. Screening for chlamydia [2] (multiple letters). *Lancet.* 2005;365(9470):1539-1540.

Quinlan JD. Sexually transmitted diseases in pregnancy. *Clinics in Family Practice.* 2005;7(1 SPEC. ISS):127-137.

Goold PC, Carlin EM. Chlamydia testing before termination of pregnancy. *Sex Trans Inf.* 2003;79(4):352.

Gray J, Huengsberg M, Mann M, et al. A multidisciplinary approach to chlamydia screening in women undergoing termination of pregnancy: how well are we doing? *Int J STD AIDS.* 2003;14(4):287-288.

Oakeshott P, Hay P. 10-Minute consultation: Cervical Chlamydia trachomatis infection. *Br Med J.* 2003;327(7420).

Country of Origin (i.e., not comparable to Canadian context)

Sethi S, Roy A, Garg S, Sree Venkatesan L, Bagga R. Detection of Chlamydia trachomatis infections by polymerase chain reaction in asymptomatic pregnant women with special reference to the utility of the pooling of urine specimens. *Indian Journal of Medical Research, Supplement.* 2017;146(Supplement):59-63.

Adachi K, Klausner JD, Xu J, et al. Chlamydia trachomatis and Neisseria gonorrhoeae in HIV-infected Pregnant Women and Adverse Infant Outcomes. *Pediatr Infect Dis J.* 2016;35(8):894-900.

Savitha S, Madhavan S, Vinoth Raja R. Incidence of chlamydial infection in women. *Journal of Pharmaceutical Sciences and Research.* 2009;1(1):26-33.

Kajaia D, Merabishvili N, Burkadze G. Pap testing and direct immunofluorescence for Chlamydia trachomatis infection in pregnant women. *Georgian Med News.* 2006(131):27-30.

Rastogi S, Das B, Salhan S, Mittal A. Effect of treatment for Chlamydia trachomatis during pregnancy. *Int J Gynaecol Obstet.* 2003;80(2):129-137.

Appendix 6 :Quality Assessment — Clinical Review

Table 45: Quality Assessment — Clinical Review

Author, Publication Year	Risk of Bias Domains						Justification
	Selection of Patients	Confounding Variable	Intervention (exposure) Measurement	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Outcome Reporting	
Folger, 2014[34]	High	High	Low	Low	Unclear	Low	• Study conducted in an urban county. May not be representative of the general population. • Data missing for inadequate antenatal care in both the intervention and comparator groups. • Due to incomplete data, BMI, birth spacing, and adequacy of antenatal care was not appropriately adjusted for. • 1,834 females were not included as they were not linked to the data set (47% of eligible patients); rate of spontaneous PTB higher in this population, which underestimates the effect estimate. • Potential selection bias due to convenience sampling from retrospective review of medical records. • Deterministic linking strategy used to join two separate databases; potential for bias due to misclassification of linked records. • Potential conflicts of interest not declared. • Assumed that patients were screened and treated in accordance with CDC guidelines, which could underestimate the number of females diagnosed with infections.
Blatt et al., 2012[35]	High	Low	Low	Low	Low	Low	• Possible selection bias toward those who sought medical care and agreed to be tested, underestimating the prevalence of infection. • The laboratory database lacked sufficient clinical data and therefore authors

Author, Publication Year	Risk of Bias Domains						Justification
	Selection of Patients	Confounding Variable	Intervention (exposure) Measurement	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Outcome Reporting	
							were unable to determine if the follow-up positive result was due to treatment failure or reinfection. • Conflict of interest as study funded by Quest Diagnostics and most study authors employees of Quest Diagnostics. • Patient characteristics and risk factors not reported; only a small percentage of those with a negative test received repeat testing; unable to ascertain the reasoning for testing or not testing, underestimating the prevalence of infection.
Berggren and Patchen, 2011[36]	High	Low	Unclear	Low	Low	Low	• No baseline demographic information provided to determine if sample is representative of the general population. • Secondary analysis of a prospective cohort study; adequate inclusion/exclusion criteria not specified and therefore there is potential selection bias. • Potential conflicts of interest not declared. • Unclear what percentage of sample tested using culture versus NAATs for CT and GC; CT for culture may underestimate the prevalence of infection.
Roberts et al., 2011[37]	High	Low	Low	Low	Low	Low	• Limited baseline demographic information provided to determine if sample is representative of the general population.
Aggarwal et al., 2010[38]	High	Low	Unclear	Low	High	Low	• Potential selection bias due to retrospective review of medical records; inclusion criteria not reported, possible convenience sampling. • The screening test utilized was not reported. • May not be generalizable to the adult pregnant population as adolescents

Author, Publication Year	Risk of Bias Domains						Justification
	Selection of Patients	Confounding Variable	Intervention (exposure) Measurement	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Outcome Reporting	
							are considered a high-risk group.
Silveira et al., 2010[39]	High	Low	Unclear	Low	Low	Low	• Potential selection bias due to retrospective review of medical records. • Black and Hispanic individuals were underrepresented in the study population. • The screening test utilized was not reported. • Potential conflicts of interest not reported.
Böhm et al., 2009[40]	Low	Low	Unclear	Low	Low	Low	• Although justification is not provided for the selected study date range, pregnant persons were enrolled in sequence, minimizing the possibility of selection bias. • Authors report that pooling multiple urine samples have nearly the same sensitivity and specificity as for individuals, specific details were NR. • Urine sample group was much smaller than cervical swab group; as prevalence rate was higher in the cervical swab group, the lack of demographic information raises concern of potential selection bias.
Logan et al., 2005[41]	High	Unclear	Low	Low	Low	Low	• No baseline demographic information provided to determine if sample is representative of the general population. • Fewer patients agreed to invasive endocervical swabs; due to lack of baseline demographic information there is a potential for selection bias. • The sources of funding or potential conflicts of interest were not reported. • Population limited to those potentially suffering a miscarriage' therefore, data may not be generalizable to all pregnant persons.
Miller, Maupin and Nsuami,	High	Low	Low	Low	Low	Low	• Population from an underserved area, may

Author, Publication Year	Risk of Bias Domains						Justification
	Selection of Patients	Confounding Variable	Intervention (exposure) Measurement	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Outcome Reporting	
2005[42]							have different CT rates in comparison with the general population and may not be generalizable. • Potential selection bias due to a retrospective review of medical records; inclusion/exclusion criteria were not reported; possible convenience sampling.
Miller et al., 2003[43]	High	Low	Low	Low	Low	Low	• Population from an underserved area, may have different GC rates in comparison with the general population and may not be generalizable. • Potential selection bias due to a retrospective review of medical records as inclusion/exclusion criteria not provided; possible convenience sampling. • Source of funding not reported.

CDC = Centers for Disease Control and Prevention; CT = *Chlamydia trachomatis;* GC = *Neisseria gonorrhoeae*; NAAT= nucleic acid amplification test; NR = not reported; PTB = preterm birth.

Appendix 7: Study Characteristics — Clinical Review

Table 46: Study Characteristics — Clinical Review

Author, Publication Year, Country, Funding Source	Study Design, Analytical Method	Patient Characteristics, Clinical Setting, Risk Factors Identified	Intervention Comparator(s)	Specimen, Screening Test	Study Period, Follow-up, Loss to Follow-up	Outcomes Measures	Subgroup Analyses
CT and/ or GC Infections							
Blatt et al. 2012[35] US Funded by Quest Diagnostics Potential conflicts of interest disclosed (authors employed and/or have equity interest in Quest Diagnostics)	Retrospective chart review Descriptive analysis, multivariate logistic regression analysis	761,315 and 730,796 pregnant adults and adolescents aged 16 to 40 years tested for CT and GC separately Clinical setting: Laboratory data from Quest Diagnostics Informatics Data Warehouse Risk factors:[a] Younger age (16 to 24 years) and race (African-American)	Intervention: Initial screening for CT and GC n = 761,315 and 730,796, respectively Comparator: Repeat screening for CT and GC at another point during pregnancy (including TOC for CT within 6 weeks of initial screen) n = 113, 275 and 104, 828	Specimen: NR Screening tests: (i) 70% — Strand displacement amplification (Beckman Dickinson and Co) (ii) 20% — DNA hybridization with chemiluminescent detection (Gen-Probe Inc.) (iii) 10% — Target capture, transcription-mediated amplification, dual-kinetic assay (Gen-Probe Inc.)	Study period: June 1, 2005 to May 30, 2008 Follow-up: NA Loss to follow-up: NA Not included in the analysis: Data unavailable for 647,589 and 638,982 females for CT and GC, respectively	Detection yield: (i) Number/per cent of positive CT and GC tests identified at initial and repeat testing Clinical Utility: (i) Number/per cent of individuals eligible for screening who obtained screening in accordance with recommendations	Guidelines-based screening by age: (i) CT – 16 to 25 years of age (ii) GC – 16 to 24 years of age
Berggren et al. 2011[36] US Funded by APHPA002026-04-00 US DHHS; the Summit Fund of Washington; the Alexander and Margaret Stewart Trust; and NICHD grant	Prospective cohort study (secondary analysis) Descriptive analysis	125 pregnant adolescents Age (range): 12 to 18 years Median age at delivery: 17 years Clinical setting: Urban academic	Intervention: Screening for CT and GC at entry to prenatal care n = 125 Comparator: Screening for CT and GC during the third trimester (~36 weeks of gestation)	Specimen: Endocervical[d] swab or urine samples Detection test: endocervical culture or urine NAAT	Study period: February 2003 to April 2005 Follow-up: 4 weeks for test-of-cure Loss to follow-up: NA Not included in the analysis: 30	Detection yield: (i) Number/per cent of positive CT and GC tests at initial and repeat testing Clinical Utility: (i) Number of CT and GC infections treated	None

Author, Publication Year, Country, Funding Source	Study Design, Analytical Method	Patient Characteristics, Clinical Setting, Risk Factors Identified	Intervention Comparator(s)	Specimen, Screening Test	Study Period, Follow-up, Loss to Follow-up	Outcomes Measures	Subgroup Analyses
number 1 T32 HD-30672-01		medical centre Risk factors: NR	n = 95				
Aggarwal et al. 2010[38] Canada No potential conflicts of interest	Retrospective chart review Descriptive analysis	211 adolescent pregnancies (including 10 adolescents with repeat pregnancies) Mean age: 16.1 years (range 13 to 18 years) Clinical Setting: Hospital-based Risk factors: NR	Intervention: Screening at first prenatal (i.e., baseline) visit for CT and GC[b] n = 211. Fourteen patients had their baseline screening during their third trimester Comparator: Screening for CT and GC during the third trimester n = 173 (excludes 14 who had their baseline screen during the third trimester)	CT: NAAT (strand displacement amplification assay) using cervical swab GC: Cervical culture with confirmation by immunofluorescence	Study period: January 2003 to December 2007 Follow-up: NA Loss to follow-up: NA Not included in the analysis: Data were unavailable for 11 adolescents	Detection yield: (i) Number/per cent of positive CT and/or GC tests at initial and repeat testing	None
Miller, Maupin, and Nsuami, 2005[42] US Funded in part by Louisiana Board of Regents Health Excellence Fund Grant (HEF (2001-06) 04)	Retrospective chart review Chi square test and *t*-test	752 pregnant adults and adolescents Mean age: NR Clinical setting: Community-based prenatal setting Risk factors:[a] Marital status (single), younger age, earlier in pregnancy, less parous, fewer prenatal visits, GC infection	Intervention: Screening for CT at entry into a prenatal program n = 752 Comparator: Screening for CT at entry and repeat screening at 34 weeks n = 752	Specimen: NR Screening test: Direct DNA assay (Gen-Probe, San Diego, CA)	Study Period: January 1998 to May 2000 Follow-up: NA Loss to follow-up: NA	Detection yield: (i) Number/per cent of positive CT tests Clinical utility: (i) Number of CT infections treated (ii) Number/ per cent of adverse neonatal outcomes: a. Gestational age at delivery (days) b. Birth weight (grams)	Age[e]: (i) ≤ 19 years (ii) ≥ 20 years

Author, Publication Year, Country, Funding Source	Study Design, Analytical Method	Patient Characteristics, Clinical Setting, Risk Factors Identified	Intervention Comparator(s)	Specimen, Screening Test	Study Period, Follow-up, Loss to Follow-up	Outcomes Measures	Subgroup Analyses
Miller et al., 2003,[43] US No disclosure of financial or competing interests	Retrospective chart review Chi square test and analysis of variance	751 pregnant persons Mean age : NR Clinical setting: Community-based prenatal setting Risk factors:[a] Younger age, CT infection	Intervention: Screening for GC at entry into a prenatal program n = 751 Comparator: Screening for GC at entry and repeat screening at 34 weeks n = 751	Specimen: NR Screening test: Direct DNA assay (Gen-Probe, San Diego, CA)	Study Period: January 1998 to May 2000 Follow-up: NA Loss to follow-up: NA	Detection yield: (i) Number/per cent of positive GC tests Clinical utility: (i) Number of GC infections treated (ii) Number/per cent of adverse neonatal outcomes: a. Gestational age at delivery (days) b. Birth weight (grams)	Age:[e] (i) ≤ 19 years (ii) ≥ 20 years
CT Infections Only							
Folger 2014[34] US No disclosure of financial or competing interests	Retrospective cohort study using linked public health databases Chi square and student's *t* tests, multivariate logistic regression using generalized estimating equations to calculate relative risk	3,354 pregnant adults and adolescents with live births and documented CT infections[b] during pregnancy Mean age: NR Clinical setting: Population-based; data retrieved from Hamilton County Public Health communicable disease records Risk factors: NR	Intervention: Early detection i.e., screening and treatment for CT at or before 20 weeks of gestation without subsequent detection n = 2,009 Comparator: Late detection i.e., screening and treatment for CT at or after 20 weeks of gestation or recurrent/persistent infection[c] n = 1,345	Specimen: NR Type of screening test: NR	Study period: 2006 to 2011 Follow-up : NR Loss to follow-up : NR	Clinical Utility: (i) Number/per cent of adverse maternal outcomes: a. Preterm birth b. Spontaneous preterm birth c. M/L preterm birth d. Spontaneous M/L preterm birth e. Very preterm birth f. Spontaneous very preterm birth (ii) Risk of preterm birth (iii) Number/per cent of adverse neonatal outcomes: a. Low birth weight b. Infant deaths c. Mean gestational age (weeks) d. Mean birth weight (grams)	Age: (i) < 20 years (ii) 20 to 29 years (iii) > 29 years

Author, Publication Year, Country, Funding Source	Study Design, Analytical Method	Patient Characteristics, Clinical Setting, Risk Factors Identified	Intervention Comparator(s)	Specimen, Screening Test	Study Period, Follow-up, Loss to Follow-up	Outcomes Measures	Subgroup Analyses
Roberts et al. 2011[37] US No potential conflicts of interest	Cross-sectional study McNemar's test and agreements reported by the κ statistic	2018 pregnant adults and adolescents Mean age (±SD): 26.9 ± 6.1 years Clinical Setting: Family planning and hospital obstetric clinic Risk factors: NR	Intervention: Screening of urine samples for CT at 35 to 37 weeks of gestation n = 2,018 Comparator: Screening of endocervical samples for CT at 35 to 37 weeks of gestation n = 2,018	Specimen: Urine samples and endocervical[d] tissue samples Detection test: NAAT (Aptima Combo 2 Assay, Tigris DTS system)	Study period: May 4 to September 2, 2009 Follow-up: N/A Loss to follow-up: None	Detection yield: (i) Number/per cent of positive CT tests	None
Silveira et al. 2010[39] US Author's postdoctoral scholarship funded by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)	Retrospective chart review Descriptive analysis	2,127 pregnant adults and adolescents with antenatal records who gave birth to a single baby at ≥ 20 weeks of gestation Mean age: NR Clinical Setting: Medical centre Risk factors:[a] Age (< 20 years), race (black), marital status (single), smoking, bacterial vaginosis, GC infection	Intervention: Routine screening for CT at any time point during pregnancy; inclusive population n = 2,104 Comparator: Screening for CT at any time point in pregnancy using USPSTF criteria (≤ 24 years old, single, and black or Hispanic) n = 2,104	Specimen: NR Diagnostic test: NAAT	Study period: July 2005 to February 2008 Follow-up: NA Loss to follow-up: NA Missing data: n = 23	Detection yield: (i) Number/per cent of positive CT cases	None
Böhm et al.2009[40] Germany No potential conflicts of interest	Retrospective cohort study Fisher's exact test	50,025 asymptomatic pregnant adults and adolescents Median age: 28 years Clinical setting: Specimens collected	Intervention: Screening for CT using cervical swabs n = 31,856 Comparator: Screening for CT using pooled urine	Specimen: NR Screening test: Semi-automated real-time PCR [*artus* C.Trachomatis Plus RG PCR Kit	Study period: April to December 2008 Follow-up: NA Loss to follow-up: NA	Detection yield: (i) Number/per cent of positive CT cases	Age: (i) ≤ 20 years (ii) 21 to 25 years (iii) 26 to 30 years (iv) 31 to 35 years (v) 36 to 40 years (vi) > 40 years (vii)

Author, Publication Year, Country, Funding Source	Study Design, Analytical Method	Patient Characteristics, Clinical Setting, Risk Factors Identified	Intervention Comparator(s)	Specimen, Screening Test	Study Period, Follow-up, Loss to Follow-up	Outcomes Measures	Subgroup Analyses
		by gynecologists, clinical setting unclear Risk factors: NR	samples n = 18,169	(Qiagen, Hilden, Germany)]			
Logan et al. 2005[41] UK No disclosure of financial or competing interests	Cross-sectional study Student's *t* test and Chi square test	207 adults and adolescents admitted for early pregnancy assessment with a positive pregnancy test, history of vaginal bleeding and were < 24 weeks pregnant Mean age (SD): 29.3 (5.9) years Clinical setting: hospital-based Risk factors: NR	Intervention: Screening for CT followed by semi-structured questionnaire n = 205 Comparator: Screening for CT by an alternate specimen n = 205	Specimen: Endocervical (n = 139)[d], self-collected vaginal (n = 205), or first-void urine (n = 205) samples Screening test: BD ProbeTec ET System	Study period: September to December 2001 Follow-up: NA Loss to follow-up: NA Missing data: Samples from two women leaked and were excluded	Detection yield: (i) Number/per cent of positive CT tests Clinical utility: (i) Number/per cent of women who declined screening (ii) Patient preference with screening strategy	None

CT = *Chlamydia trachomatis*; DHHS = Department of Health and Human Services; GC = *Neisseria gonorrhoeae*; M/L = moderate to late; NAAT = nucleic acid amplification test; NICHD = Eunice Kennedy Shriver National Institute of Child Health; NR = not reported; NS = non-significant; PCR = polymerase chain reaction; SD = standard deviation; STI = sexually transmitted infection; USPSTF = United States Preventive Services Task Force.

[a] The risk factors reported in the tables represent variables that were statistically significant.

[b] Patients with other STIs are not included in the report.

[c] Recurrent/persistent infection was defined as infections detected at or before 20 weeks of gestation and after 20 weeks of gestation, but at least seven days apart.

[d] The endocervix is the inner part of the cervix.[46]

[e] Subgroup analyses were also conducted on risk factors including sociodemographic characteristics, other STIs, and gynecological/obstetric factors but are not within the scope of this report.

Appendix 8: GRADE Assessment

Table 47: GRADE Assessment of the Evidence for Detection Yield: Initial Versus Repeat Screening (Impact of Repeat Screening)

Quality Assessment							Summary of Findings		
Number of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Impact	Certainty	Importance
Outcome: Number and Per cent of Positive Infections									
5	Retrospective chart review[35,38,42,43] (4) Prospective cohort study [secondary analysis][36] (1)	Serious limitations[a]	No serious inconsistency[b]	Serious indirectness[c]	No serious imprecision[d]	Undetected	Repeat screening resulted in higher detection yield in high-risk populations than one-time screening at entry into prenatal care.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection in all included studies.

[b] The wide range of prevalence can be attributed to heterogeneity in patient population.

[c] All included studies reported outcomes for screening once (i.e., at entry into prenatal care) versus screening at another time. There is serious risk of indirectness because the (cumulative) impact of repeat screening had to be determined by extrapolating data from the studies to calculate the proportion of all infections detected in the same population at a second time point (relative to the proportion of all infections detected at entry to prenatal care).

[d] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals.

Table 48: GRADE Assessment of the Evidence for Detection Yield: Universal Versus Targeted Risk, Factor-Based Screening

Quality Assessment							Summary of Findings		
Number of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Impact	Certainty	Importance
Outcome: Number and Per cent of Positive Infections									
1	Retrospective chart review[39] (1)	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision	Undetected	Universal screening at least once in pregnancy is recommended for all pregnant persons.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection in the one included study.

[b] A single study provided data for the outcome; therefore, inconsistency was not identified.

Table 49: GRADE Assessment of the Evidence for Detection Yield: Endocervical Versus Urine Versus Vaginal Sample Screening

Quality Assessment							Summary of Findings		
Number of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Impact	Certainty	Importance
Outcome: Detection Yield: Number and Per cent of Positive Infections									
3	Cross-sectional study (2)[37,41] Retrospective cohort study (1)[40]	Serious limitations[a]	Serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	Urine samples may have decreased test performance in comparison to cervical and vaginal samples.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection in the two of the three included studies.

[b] Due to a wide range of reported values that cannot be explained by a specific source of heterogeneity.

[c] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals in two of the three studies.

Table 50: GRADE Assessment of the Evidence for Clinical Utility: Initial Versus Repeat Screening

Quality Assessment							Summary of Findings		
Number of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Impact	Certainty	Importance
Outcome: Clinical Utility: Adherence to Guidelines-Based Screening									
1	Retrospective chart review (1)[35]	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	A large percentage of females are not being screened in accordance with guidelines.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection in the one included study.

[b] A single study provided data for the outcome, therefore inconsistency was not identified.

[c] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals.

Table 51: GRADE Assessment of the Evidence for Clinical Utility: Early Detection Versus Late Detection

Quality Assessment							Summary of Findings		
Number of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Impact	Certainty	Importance
Outcome: Clinical Utility: Number and Per cent of Preterm Births									
1	Retrospective cohort study (1)[34]	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was no statistically significant difference in the rates of preterm births in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical
Outcome: Clinical Utility: Number and Per cent of Spontaneous Preterm Births									
1	Retrospective cohort study (1)[34]	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was no statistically significant difference in the rates of spontaneous preterm births in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical
Outcome: Clinical Utility: Number and Per cent of Moderate-to-late Preterm Births									
1	Retrospective cohort study (1)[34]	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was no statistically significant difference in the rates of moderate-to-late preterm births in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical
Outcome: Clinical Utility: Number and Per cent of Moderate-to-late Spontaneous Preterm Births									
1	Retrospective cohort study (1)[34]	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was no statistically significant difference in the rates of moderate-to-late spontaneous preterm births in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical
Outcome: Clinical Utility: Number and Per cent of Very Preterm Births									
1	Retrospective cohort study (1)[34]	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was no statistically significant difference in the rates of preterm births in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical
Outcome: Clinical Utility: Number and Per cent of Spontaneous Very Preterm Births									
1	Retrospective cohort study (1)[34]	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was no statistically significant difference in the rates of spontaneous preterm births in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection in the included study.

[b] A single study provided data for the outcome, therefore inconsistency was not identified.

[c] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals.

Table 52: GRADE Assessment of the Evidence for Clinical Utility: Early Detection Versus Late Detection

Quality Assessment							Summary of Findings		
Number of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication Bias**	**Impact**	**Certainty**	**Importance**
Outcome: Proportion with Low Birth Weight									
1	Retrospective cohort study[34] (1)	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was no statistically significant difference in the proportion of neonates born with low birth weight in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical
Outcome: Infant Mortality									
1	Retrospective cohort study[34] (1)	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	There was a statistically significant, but clinically insignificant difference in mortality of neonates born to mothers in the early detection versus late detection group.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection in the included study.

[b] A single study provided data for the outcome, therefore inconsistency was not identified.

[c] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals.

Table 53: GRADE Assessment of the Evidence for Clinical Utility: Detection and Treatment at Initial Versus Repeat Screening

Quality Assessment							Summary of Findings		
Number of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication Bias**	**Impact**	**Certainty**	**Importance**
Outcome: Mean Gestational Age									
3	Retrospective cohort study[34] (1) Retrospective chart review[42,43] (2)	Serious limitations[a]	Serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	The findings suggest that infection with CT or GC has no impact on mean gestational age.	⨁◯◯◯ Very Low	Important
Outcome: Mean Birth Weight									
3	Retrospective cohort study[34] (1) Retrospective chart review[42,43] (2)	Serious limitations[a]	Serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	The findings suggest that infection with CT or GC has no impact on mean birth weight.	⨁◯◯◯ Very Low	Important

[a] Due to high risk of bias related to patient selection all the included studies.

[b] Due to heterogeneity in the intervention and comparators.

[c] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals for one included study.

Table 54: GRADE Assessment of the Evidence for Clinical Utility: Endocervical Versus Urine Versus Vaginal Sampling

Quality Assessment							Summary of Findings		
Number of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication Bias**	**Impact**	**Certainty**	**Importance**
Outcome: Preference for Specimen Sampling									
1	Cross-sectional study[41] (1)	Serious limitations[a]	No serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	Non-invasive sampling with either urine or self-collected vaginal swabs is preferred to cervical sampling.	⨁◯◯◯ Very Low	Important

[a] Due to high risk of bias related to patient selection in the included study.

[b] A single study provided data for the outcome, therefore inconsistency was not identified.

[c] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals.

Table 55: GRADE Assessment of the Evidence for Clinical Utility: Endocervical Versus Urine Versus Vaginal Sampling

Quality Assessment							Summary of Findings		
Number of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication Bias**	**Impact**	**Certainty**	**Importance**
Outcome: Number of Females Declining Screening									
1	Cross-sectional study[41] (1)	Serious limitations[a]	No Serious inconsistency[b]	No serious indirectness	No serious imprecision[c]	Undetected	Approximately a quarter of women declined screening for CT infection during pregnancy.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection in the included study.

[b] A single study provided data for the outcome, therefore inconsistency was not identified.

[c] Imprecision cannot be assessed, as results were not reported as a point estimate with a 95% confidence interval.

Table 56: GRADE Assessment of the Evidence for Clinical Utility: Initial Versus Repeat Screening

Quality Assessment							Summary of Findings		
Number of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Impact	Certainty	Importance
Outcome: Number of Females Treated for Infection									
3	Retrospective chart review[42,43] (2) Prospective cohort study [secondary analysis][36] (1)	Serious limitations[a]	No Serious inconsistency	No serious indirectness	No serious imprecision[b]	Undetected	100% of CT and GC infections detected at entry and repeat screening were treated.	⨁◯◯◯ Very Low	Critical

[a] Due to high risk of bias related to patient selection all the included studies.

[b] Imprecision could not be assessed, as results were not reported as point estimates with 95% confidence intervals.

Table 57: GRADE Assessment of the Evidence for Harms

Quality Assessment							Summary of Findings		
Number of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Impact	Certainty	Importance
Anxiety: No evidence identified									
Fear of stigmatization: No evidence identified									
Adverse pregnancy outcomes (e.g., miscarriage): No evidence identified									
Negative impact of false positives and false negatives: No evidence identified									

Appendix 9: Study Characteristics — Economic Literature

Table 58: Study Characteristics — Economic Literature

Characteristic	Rours, 2016	Ditkowsky, 2017	Ong, 2016
Country	Netherlands	US	Australia
Study Population	All pregnant women in the Netherlands	Pregnant women aged 15 to 24 in a higher burden setting	Pregnant women aged 16 to 25 in antenatal clinics
Perspective	Societal	Third-party payer	Third-party payer
Time Horizon	Unclear, beyond one-year	1 Year	1 Year
Study Type	Cost-utility analysis	Cost-benefit analysis	Cost-utility analysis
Decision Problem	To analyze the cost-effectiveness of antenatal CT screening.	To determine the cost- benefit of screening all pregnant women aged 15 to 24 for CT infection compared with no screening.	To determine the cost-effectiveness of screening all pregnant women aged 16 to25 years for chlamydia compared with selective screening or no screening.
Interventions Assessed	Screening until 1,000 CT cases identified versus not (26,605 women if prevalence is 3.9%), unclear screening implementation; "assumed screening to be incorporated in existing routine antenatal care of testing for HIV, syphilis, and other infections. We included the use of NAATs to test urine specimens for CT"	Screening all pregnant women versus not, unclear at which time point this would occur	Screening all pregnant women versus selective screening (subsets of teenagers aged 16 to 19 years, or people with more than one sexual partner) versus not at all
Modelling Approach	Decision tree	Decision tree	Decision tree
Health Outcomes	Maternal: Pelvic inflammatory disease, chronic pelvic pain, tubal infertility Obstetric: Preterm delivery, ectopic pregnancy Pediatric: Conjunctivitis, pneumonia	Maternal: Pelvic inflammatory disease Obstetric: Preterm delivery, pregnancy aborted Pediatric: Conjunctivitis, pneumonia	Maternal: Pelvic inflammatory disease, postpartum endometritis Pediatric: Conjunctivitis, pneumonia, low birth weight
Findings	Antenatal screening for CT is dominant compared with no antenatal screening.	Prenatal screening for CT resulted in increased expenditures, but reduced morbidity to women-infant pairs.	Screening all pregnant women was likely to be cost-effective compared with no screening and selective screening.
Uncertainty Analyses	Varied test costs; prevalence; screening in whole population versus pregnant women only	Altered screening rates	Altered CT prevalence

CT = *Chlamydia trachomatis;* NAAT = nucleic acid amplification test.

Note: A number of other economic evaluations were identified assessing screening strategies for CT and GC that had a broader focus on the general population rather than pregnant persons specifically in which incorporated neonatal infections from vertical transmission.[134-140] Of note, the most commonly included neonatal infections within these models were neonatal conjunctivitis and pneumonia.

Appendix 10: Diagnostic Test Accuracy Meta-Analysis Methodology

The pooled diagnostic test accuracy, sensitivity, and specificity, were based on the statistics in the contingency tables of diagnostic test accuracy (DTA) studies included in 2014 United States Preventive Services Task Force (USPSTF) recommendation for *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) screening.[14] Only statistics for the female population in NAAT versus NAAT studies[141-145] were extracted for the purposes of this health technology assessment. The data were imported to R environment (v3.4.2)[146] and RStudio (1.0.143).[147] A bivariate random-effects model available within the mada package was used for the meta-analysis.[148,149]The pooled sensitivities and specificities were reported with 95% CIs along with the characteristics of SROC curves, including theta, lambda, and beta parameters.

Meta-Analysis of CT NAATs

There were 17 arms from four studies for meta-analysis: Gaydos et al. 2013,[141] Schoeman et al. 2012,[142] Taylor et al. 2011,[143] and Van Der Pol et al. 2012.[144] The arms are summarized by sample collection method and reference tests in Table 59 and Table 60. Based on the numbers of combinations, it was possible to pool the DTA data based on endocervical samples and reference tests that included Aptima Combo 2 (AC2) test.

Table 59: Summary of CT NAAT Devices and Sample Collection Method

Index Test	Clinician-Collected Vaginal	Endocervical	FCU	Self-Collected Vaginal
AC2	0	3	2	1
ACT	1	1	1	1
Amplicor	1	1	1	1
c4800	0	1	1	0
CT/GC Qx	0	1	1	0
CTQ	0	1	1	0
PTCT	0	1	1	0
Xpert	0	1	1	1

AC2 = Aptima Combo 2; ACT = Aptima *Chlamydia trachomatis* test; Amplicor = Roche cobas Amplicor test; c4800 = Roche cobas 4800 CT and NG test; CTQ = Becton Dickinson ProbeTec CT Qx amplified DNA assay on the Viper system; CT/GC Qx = Becton Dickinson ProbeTec CT and NG Qx amplified DNA assay; FCU = first-catch urine; PTCT = Becton Dickinson ProbeTech ET CT amplified DNA assay.

Table 60: Summary of CT NAAT Devices and Reference Tests

Index Test	AC2, CT/GC Qx	AC2, PTCT	AC2, PTGC	Aptima CT	Vulture
AC2	2	2	0	2	0
ACT	0	0	0	0	4
Amplicor	0	0	0	0	4
c4800	2	0	0	0	0
CT/GC Qx	2	0	0	0	0
CTQ	0	2	0	0	0
PTCT	0	2	0	0	0
Xpert	0	0	3	0	0

AC2 = Aptima Combo 2; ACT = Aptima *Chlamydia trachomatis* test; Amplicor = Roche cobas Amplicor test; c4800 = Roche cobas 4800 CT and NG test; CTQ = Becton Dickinson ProbeTec CT Qx amplified DNA assay on the Viper system; CT/GC Qx = Becton Dickinson ProbeTec CT and NG Qx amplified DNA assay PTCT = Becton Dickinson ProbeTech ET CT amplified DNA assay; PTGC = Becton Dickinson ProbeTech ET amplified DNA assay for CT and NG.

All arms were merged to derive pooled DTA using a bivariate random-effects model. The pooled sensitivity was 0.93 (95% CI, 0.91 to 0.946). The pooled specificity was 0.996 (95% CI, 0.994 to 0.998). The SROC curve and its parameters are presented in Figure 7 and Table 61.

Figure 7: CT NAAT SROC Curve

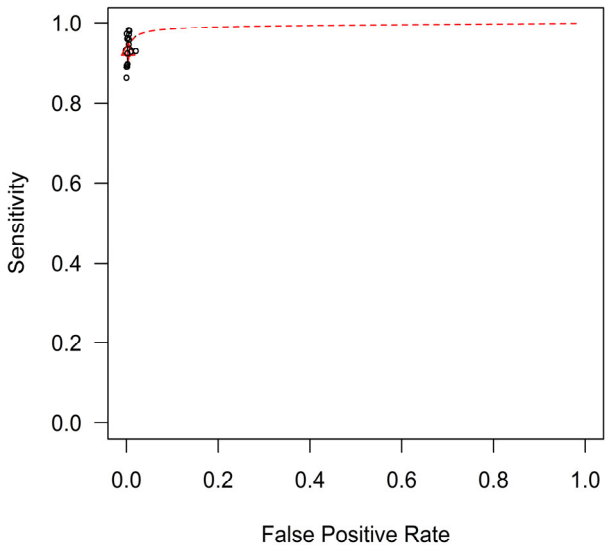


Table 61: CT NAAT SROC Curve Parameters

Parameter	Mean	Variance
Theta	–0.024	0.2007
Lambda	7.5826	0.2548
Beta	0.755	Not applicable

Meta-Analysis of GC NAATs

There were 15 arms from three studies for meta-analysis: Gaydos, et al., 2013,[141] Van Der Pol et al. 2012,[144] and Van Der Pol et al. 2012.[145] The arms are summarized by sample collection method and reference tests in Table 62 and Table 63. Based on the numbers of combinations, it was possible to pool the DTA data based on endocervical samples and reference tests that included the AC2 test.

Table 62: Summary of GC NAAT Devices and Sample Collection Method

	Endocervical	FCU	Self-Collected Vaginal
AC2	2	2	0
c4800	1	1	0
CT/GC Q^x	1	1	0
GCQ	1	1	0
PTNG	1	1	0
Xpert	1	1	1

AC2 = Aptima Combo 2; c4800 = cobas 4800 CT and NG test; CT/GC Q^x = Becton Dickinson ProbeTech CT and NG Q^x amplified DNA assay; FCU = first-catch urine; GCQ = Becton Dickinson ProbeTec NG Q^x amplified DNA assay on Viper system; PTNG = Becton Dickinson ProbeTech ET NG amplified DNA assay.

Table 63: Summary of GC NAAT Devices and Reference Tests

	AC2 , CT/GC Qx	AC2 , PTGC	AC2, PTNG
AC2	2	0	2
c4800	2	0	0
CT/GC Q^x	2	0	0
GCQ	0	0	2
PTNG	0	0	2
Xpert	0	3	0

AC2 = Aptima Combo 2; c4800 = cobas 4800 CT and NG test; CT/GC Q^x = Becton Dickinson ProbeTech CT and NG Q^x amplified DNA assay; GCQ = Becton Dickinson ProbeTec NG Q^x amplified DNA assay on Viper system; PTGC = Becton Dickinson ProbeTech ET for CT and NG; PTNG = Becton Dickinson ProbeTech ET NG amplified DNA assay.

All arms were merged to derive pooled DTA using a bivariate random-effects model. The pooled sensitivity was 0.917 (95% CI = 0.87 to 0.948). The pooled specificity was 0.998 (95% CI = 0.996 to 0.999). The SROC curve and its parameters are presented in Figure 8 and Table 64.

Figure 8: GC NAAT SROC Curve

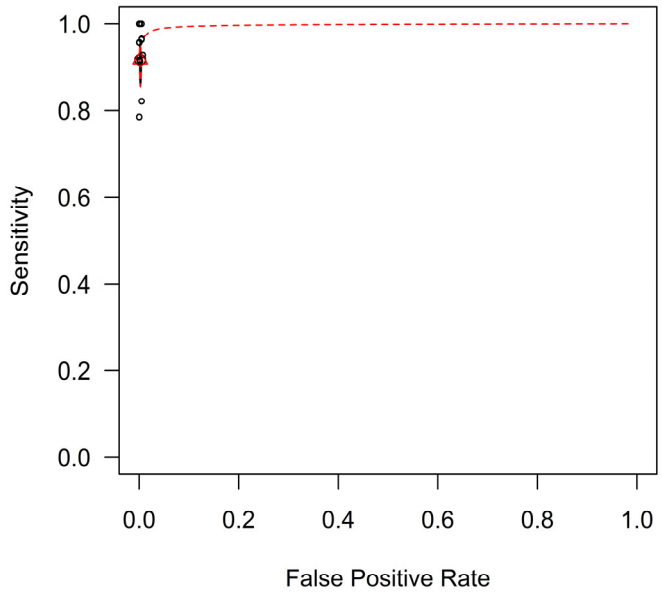


Table 64: GC NAAT SROC Curve Parameters

Parameter	Mean	Variance
Theta	–1.073411	0.0797126
Lambda	7.961082	1.173086
Beta	0.3803803	Not applicable

Appendix 11: Obstetric Outcome Case Definitions

Table 65: Obstetric Outcome Case Definitions

Obstetric Outcome	ICD10CA Case or CCI Procedure Code(s)
Term Birth	CCI labour and delivery intervention codes that focus on delivery in description - 5MD50AA, 5MD50GH, 5MD51ZZ, 5MD52KV, 5MD53JD, 5MD53JE, 5MD53KH, 5MD53KJ, 5MD53KK, 5MD53KL, 5MD53KM, 5MD53KN, 5MD53KP, 5MD53KS, 5MD54KH, 5MD54KJ, 5MD54KK, 5MD54KL, 5MD54KM, 5MD54KN, 5MD54NE, 5MD54NF, 5MD55KH, 5MD55KJ, 5MD55KK, 5MD55KL, 5MD55KM, 5MD55KN, 5MD55KQ, 5MD55KR, 5MD56AA, 5MD56GH, 5MD56NL, 5MD56NM, 5MD56NN, 5MD56NP, 5MD56NQ, 5MD56NR, 5MD56NU, 5MD56NV, 5MD56NW, 5MD56PA, 5MD56PB, 5MD56PC, 5MD56PD, 5MD56PE, 5MD56PF, 5MD56PG, 5MD56PH, 5MD56PJ, 5MD60AA, 5MD60CB, 5MD60CC, 5MD60CD, 5MD60CE, 5MD60CF, 5MD60CG, 5MD60JW, 5MD60JX, 5MD60JY, 5MD60JZ, 5MD60KA, 5MD60KB, 5MD60KC, 5MD60KD, 5MD60KG, 5MD60KT, 5MD60RA, 5MD60RB, 5MD60RG, 5MD60RH
Preterm Birth	ICD10CA Code O60.101 - Preterm spontaneous labour with preterm delivery, with or without mention of antepartum condition; O60.301 - Preterm delivery without spontaneous labour, with or without mention of antepartum condition.
Extremely Preterm Birth	Assumed same as preterm birth.
Stillbirth	ICD10CA Codes O36.421, O36.423, O36.431, O36.433, O36.491, O36.493: Maternal care for intrauterine death.
Term Birth	ICD10CA Codes Z37.000, Z37.001 - Single live birth; Z38.000, Z38.001, Z38.010, Z38.011 - Singleton, born in hospital.
Preterm Birth	ICD10CA Code P07.3 — Other preterm infants.
Extremely Preterm Birth	ICD10CA Code P07.2 — Extremely immaturity.

ICD10CA = International Statistical Classification of Diseases and Related Health Problems, tenth revision, Canada; CCI = Canadian classification of health interventions.

Appendix 12: Complete Economic Analysis Results

Table 66: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Probabilistic Base Case)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.73**	**561,663,682**	**0.00**	**0**	**Reference**
NNTM	**113,489.83**	**561,899,189**	**0.10**	**235,506**	**2,328,518**
TNNM	113,489.79	561,911,193	–0.03	12,004	Dominated
TNTM	113,489.84	562,420,549	0.01	521,361	Extendedly Dominated
NNUM	**113,490.15**	**562,780,969**	**0.32**	**881,780**	**2,775,685**
UNNM	113,490.08	562,812,279	–0.07	31,310	Dominated
TTTM	113,489.84	562,922,472	–0.31	141,503	Dominated
TNUM	**113,490.15**	**563,302,330**	**0.01**	**521,361**	**63,774,285**
UNTM	113,490.12	563,321,635	–0.04	19,305	Dominated
TTUM	113,490.16	563,804,252	0.00	501,922	Extendedly Dominated
UTTM (Current Strategy)	113,490.12	563,823,557	–0.03	521,228	Dominated
UNUM	**113,490.18**	**565,220,444**	**0.03**	**1,918,114**	**65,154,327**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 67: Pediatric Cost-Effectiveness Analysis Results per 100,000 Pregnant Persons (Probabilistic Base Case)

Strategy	Total					Incremental					ICER ($ Per Pediatric Infection Prevented[a])
	GC Conjunctivitis	CT Conjunctivitis	CT Pneumonia	Pediatric Infections[a]	Cost ($)	GC Conjunctivitis	CT Conjunctivitis	CT Pneumonia	Pediatric Infection Prevented[a]	Cost ($)	
NNNM	**80.4**	**276.7**	**132.0**	**489.1**	**561,663,682**	**0.0**	**0.0**	**0.0**	**0.0**	**0**	Reference Strategy
NNTM	**69.1**	**234.1**	**111.7**	**414.8**	**561,899,189**	**11.4**	**–42.6**	**–20.3**	**74.3**	**235,506**	3,171
TNNM	72.2	248.5	118.5	439.1	561,911,193	3.1	14.3	6.8	–24.3	12,004	Dominated
TNTM	68.6	230.7	110.0	409.3	562,420,549	–0.4	–3.4	–1.6	5.5	521,361	Extendedly Dominated
NNUM	**27.7**	**100.4**	**47.9**	**176.0**	**562,780,969**	**–41.3**	**–133.7**	**–63.8**	**238.9**	**881,780**	3,692
UNNM	40.5	129.5	61.8	231.8	562,812,279	12.7	29.2	13.9	–55.8	31,310	Dominated
TTTM	68.5	229.7	109.5	407.8	562,922,472	40.8	129.3	61.7	–231.8	141,503	Dominated
TNUM	**27.3**	**96.9**	**46.2**	**170.5**	**563,302,330**	**–0.4**	**–3.4**	**–1.6**	**5.5**	**521,361**	94,679
UNTM	36.9	111.7	53.3	202.0	563,321,635	9.6	14.8	7.1	–31.5	19,305	Dominated
TTUM	27.2	95.9	45.8	168.9	563,804,252	–0.1	–1.0	–0.5	1.6	501,922	Extendedly Dominated
UTTM (Current Strategy)	36.8	110.8	52.8	200.4	563,823,557	9.5	13.8	6.6	–29.9	521,228	Dominated
UNUM	**25.8**	**84.5**	**40.3**	**150.7**	**565,220,444**	**–1.5**	**–12.4**	**–5.9**	**19.8**	**1,918,114**	96,807

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICER = incremental cost-effectiveness ratio.

[a] Accounts for GC conjunctivitis, CT conjunctivitis, and CT pneumonia in aggregate.

Table 68: Cost-Utility Analysis Results per 100,000 Pregnant Persons (High-Risk Pregnant Population)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,486.17**	**563,876,964**	**0.00**	**0**	**Reference**
TNNM	113,486.77	563,918,824	0.60	41,860	Extendedly Dominated
NNTM	113,486.80	563,923,939	0.63	46,975	Extendedly Dominated
UNNM	**113,489.00**	**564,065,420**	**2.83**	**188,456**	**66,565**
NNUM	**113,489.08**	**564,101,229**	**0.07**	**35,808**	**481,855**
TNTM	113,486.86	564,374,285	–2.22	273,057	Dominated
UNTM	113,489.09	564,520,882	0.02	419,653	Extendedly Dominated
TNUM	113,489.14	564,551,575	0.06	450,346	Extendedly Dominated
TTTM	113,486.87	564,814,116	–2.21	712,887	Dominated
UTTM (Current Strategy)	113,489.10	564,960,712	0.02	859,483	Extendedly Dominated
TTUM	113,489.15	564,991,405	0.07	890,176	Extendedly Dominated
UNUM	**113,489.36**	**566,206,134**	**0.28**	**2,104,905**	**7,446,073**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 69: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Alternate CT Reinfection Rate)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.73**	**561,663,682**	**0.00**	**0**	**Reference**
NNTM	**113,489.83**	**561,899,149**	**0.10**	**235,467**	**2,326,666**
TNNM	113,489.79	561,911,172	–0.03	12,023	Dominated
TNTM	113,489.84	562,420,524	0.01	521,375	Extendedly Dominated
NNUM	**113,490.15**	**562,780,413**	**0.32**	**881,264**	**2,766,816**
UNNM	113,490.08	562,811,932	–0.07	31,518	Dominated
TTTM	113,489.84	562,922,450	–0.31	142,037	Dominated
TNUM	**113,490.16**	**563,301,788**	**0.01**	**521,375**	**64,103,497**
UNTM	113,490.12	563,321,283	–0.04	19,495	Dominated
TTUM	113,490.16	563,803,714	0.00	501,926	Extendedly Dominated
UTTM (Current Strategy)	113,490.12	563,823,209	–0.03	521,421	Dominated
UNUM	**113,490.18**	**565,220,122**	**0.03**	**1,918,334**	**66,664,513**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 70: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Low Pediatric Infection Rates)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,490.38**	**561,307,532**	**0.00**	**0**	**Reference**
TNNM	113,490.38	561,591,512	0.00	283,980	Dominated
NNTM	113,490.38	561,594,970	0.00	287,438	Dominated
TNTM	113,490.38	562,119,085	0.00	811,553	Dominated
TTTM	113,490.38	562,621,785	0.00	1,314,254	Dominated
UNNM	113,490.38	562,637,560	0.00	1,330,028	Dominated
NNUM	113,490.38	562,655,954	0.00	1,348,422	Dominated
UNTM	113,490.38	563,165,133	0.00	1,857,601	Dominated
TNUM	113,490.38	563,180,069	0.00	1,872,538	Dominated
UTTM (Current Strategy)	113,490.38	563,667,833	0.00	2,360,301	Dominated
TTUM	113,490.38	563,682,770	0.00	2,375,238	Dominated
UNUM	113,490.38	565,108,067	0.00	3,800,535	Dominated

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 71: Cost-Utility Analysis Results per 100,000 Pregnant Persons (High Pediatric Infection Rates)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,488.80**	**562,199,711**	**0.00**	**0**	**Reference**
NNTM	**113,489.05**	**562,353,412**	**0.24**	**153,701**	**631,368**
TNNM	113,488.96	562,392,422	–0.08	39,011	Dominated
TNTM	113,489.07	562,868,519	0.02	515,107	Extendedly Dominated
NNUM	**113,489.81**	**562,974,312**	**0.76**	**620,900**	**811,956**
UNNM	113,489.64	563,065,056	–0.17	90,745	Dominated
TTTM	113,489.07	563,368,651	–0.74	394,339	Dominated
TNUM	**113,489.83**	**563,489,419**	**0.02**	**515,107**	**26,155,405**
UNTM	113,489.75	563,541,153	–0.08	51,734	Dominated
TTUM	113,489.84	563,989,551	0.01	500,132	Extendedly Dominated
UTTM (Current Strategy)	113,489.75	564,041,285	–0.08	551,866	Dominated
UNUM	**113,489.90**	**565,385,013**	**0.07**	**1,895,594**	**26,724,631**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 72: Cost-Utility Analysis Results per 100,000 Pregnant Persons (High-Risk Pregnant Population and High Pediatric Infection Rates)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	**113,487.24**	**565,098,963**	**0.00**	**0**	**Reference**
UNNM	113,487.06	565,129,006	-0.18	30,044	Dominated
TNUM	113,487.39	565,504,618	0.15	405,655	Extendedly Dominated
UNTM	113,487.28	565,515,506	0.04	416,544	Extendedly Dominated
TTUM	113,487.40	565,939,693	0.16	840,730	Extendedly Dominated
UTTM (Current Strategy)	113,487.29	565,950,581	0.05	851,619	Extendedly Dominated
NNTM	113,481.76	566,671,770	–5.48	1,572,807	Dominated
TNNM	113,481.69	566,690,925	–5.55	1,591,962	Dominated
UNUM	**113,487.92**	**566,994,344**	**0.68**	**1,895,382**	**2,782,785**
TNTM	113,481.90	567,077,425	–6.02	83,081	Dominated
NNNM	113,480.25	567,106,831	–7.67	112,487	Dominated
TTTM	113,481.92	567,512,500	–6.00	518,156	Dominated

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 73: Cost-Utility Analysis Results per 100,000 Pregnant Persons (2016 Birth Mothers Age Distribution)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,589.38**	**561,652,129**	**0.00**	**0**	**Reference**
NNTM	**113,589.45**	**561,806,334**	**0.07**	**154,205**	**2,322,042**
TNNM	113,589.42	561,814,368	–0.02	8,034	Dominated
TNTM	113,589.45	562,147,800	0.01	341,466	Extendedly Dominated
TTTM	113,589.45	562,476,516	0.01	670,182	Extendedly Dominated
NNUM	**113,589.79**	**562,771,600**	**0.35**	**965,267**	**2,790,917**
UNNM	113,589.73	562,798,796	–0.06	27,196	Dominated
TNUM	**113,589.80**	**563,113,067**	**0.01**	**341,466**	**63,722,858**
UNTM	113,589.76	563,132,228	–0.04	19,162	Dominated
TTUM	113,589.80	563,441,782	0.00	328,716	Extendedly Dominated
UTTM (Current Strategy)	113,589.76	563,460,944	–0.03	347,877	Dominated
UNUM	**113,589.83**	**565,211,056**	**0.03**	**2,097,989**	**65,171,945**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 74: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Low Screening Cost)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.73**	**560,546,454**	**0.00**	**0**	**Reference**
NNTM	**113,489.83**	**560,559,816**	**0.10**	**13,362**	**132,109**
TNNM	113,489.79	560,578,722	–0.03	18,907	Dominated
NNUM	**113,490.15**	**560,630,598**	**0.32**	**70,783**	**222,811**
UNNM	113,490.08	560,683,619	–0.07	53,021	Dominated
TNTM	113,489.84	560,708,114	–0.31	77,515	Dominated
TNUM	**113,490.15**	**560,778,896**	**0.01**	**148,298**	**18,140,233**
UNTM	113,490.12	560,813,010	–0.04	34,114	Dominated
TTTM	113,489.84	560,853,266	–0.32	74,370	Dominated
TTUM	113,490.16	560,924,049	0.00	145,152	Extendedly Dominated
UTTM (Current Strategy)	113,490.12	560,958,163	–0.03	179,266	Dominated
UNUM	**113,490.18**	**561,324,659**	**0.03**	**545,763**	**18,538,415**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 75: Cost-Utility Analysis Results per 100,000 Pregnant Persons (High Pediatric Infection Hospitalization)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	**113,490.18**	**561,324,659**	**0.00**	**0**	**Reference**
NNTM	113,489.83	563,650,358	–0.32	119,241	Dominated
NNNM	113,489.73	563,733,752	–0.42	202,635	Dominated
TNNM	113,489.79	563,769,533	–0.35	238,416	Dominated
UNNM	113,490.08	563,780,118	–0.07	249,001	Dominated
TNUM	**113,490.15**	**564,026,795**	**0.01**	**495,678**	**60,632,673**
TNTM	113,489.84	564,146,036	–0.32	119,241	Dominated
UNTM	113,490.12	564,156,622	–0.04	129,827	Dominated
TTUM	113,490.16	564,521,361	0.00	494,566	Extendedly Dominated
TTTM	113,489.84	564,640,602	–0.32	613,808	Dominated
UTTM (Current Strategy)	113,490.12	564,651,188	–0.03	624,393	Dominated
UNUM	**113,490.18**	**565,852,348**	**0.03**	**1,825,554**	**62,010,243**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 76: Cost-Utility Analysis Results per 100,000 Pregnant Persons (GC Culture Investigation)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.73**	**561,690,712**	**0.00**	**0**	**Reference**
NNTM	**113,489.83**	**561,922,435**	**0.10**	**231,722**	**2,291,103**
TNNM	113,489.79	561,934,261	–0.03	11,826	Dominated
TNTM	113,489.84	562,444,213	0.01	521,779	Extendedly Dominated
NNUM	**113,490.15**	**562,790,251**	**0.32**	**867,816**	**2,731,729**
UNNM	113,490.08	562,820,792	–0.07	30,541	Dominated
TTTM	113,489.84	562,946,521	–0.31	156,270	Dominated
TNUM	**113,490.15**	**563,312,030**	**0.01**	**521,779**	**63,825,423**
UNTM	113,490.12	563,330,744	–0.04	18,715	Dominated
TTUM	113,490.16	563,814,337	0.00	502,308	Extendedly Dominated
UTTM (Current Strategy)	113,490.12	563,833,052	–0.03	521,023	Dominated
UNUM	**113,490.18**	**565,231,691**	**0.03**	**1,919,662**	**65,206,898**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 77: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Pediatric Ophthalmologist)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.73**	**561,693,074**	**0.00**	**0**	**Reference**
NNTM	**113,489.83**	**561,924,141**	**0.10**	**231,066**	**2,284,619**
TNNM	113,489.79	561,937,582	–0.03	13,442	Dominated
TNTM	113,489.84	562,445,183	0.01	521,043	Extendedly Dominated
NNUM	**113,490.15**	**562,791,512**	**0.32**	**867,372**	**2,730,329**
UNNM	113,490.08	562,826,270	–0.07	34,758	Dominated
TTTM	113,489.84	562,947,015	–0.31	155,503	Dominated
TNUM	**113,490.15**	**563,312,555**	**0.01**	**521,043**	**63,735,397**
UNTM	113,490.12	563,333,871	–0.04	21,316	Dominated
TTUM	113,490.16	563,814,386	0.00	501,832	Extendedly Dominated
UTTM (Current Strategy)	113,490.12	563,835,703	–0.03	523,148	Dominated
UNUM	**113,490.18**	**565,229,525**	**0.03**	**1,916,971**	**65,115,481**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 78: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Treatment for Mothers of Infants with Conjunctivitis or Pneumonia)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.73**	**561,768,872**	**0.00**	**0**	**Reference**
NNTM	**113,489.83**	**561,988,436**	**0.10**	**219,564**	**2,170,891**
TNNM	113,489.79	562,005,634	–0.03	17,197	Dominated
TNTM	113,489.84	562,508,634	0.01	520,197	Extendedly Dominated
NNUM	**113,490.15**	**562,818,762**	**0.32**	**830,325**	**2,613,714**
UNNM	113,490.08	562,862,212	–0.07	43,450	Dominated
TTTM	113,489.84	563,010,224	–0.31	191,462	Dominated
TNUM	**113,490.15**	**563,338,959**	**0.01**	**520,197**	**63,631,989**
UNTM	113,490.12	563,365,212	–0.04	26,253	Dominated
TTUM	113,490.16	563,840,549	0.00	501,590	Extendedly Dominated
UTTM (Current Strategy)	113,490.12	563,866,802	–0.03	527,843	Dominated
UNUM	**113,490.18**	**565,252,887**	**0.03**	**1,913,928**	**65,012,137**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 79: Cost-Utility Analysis Results per 100,000 Pregnant Persons (100% Prenatal Visit Screening Participation)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.72**	**561,670,179**	**0.00**	**0**	**Reference**
NNTM	**113,489.85**	**561,972,498**	**0.13**	**302,319**	**2,328,518**
TNNM	113,489.81	561,987,908	–0.04	15,410	Dominated
TNTM	113,489.86	562,641,767	0.01	669,269	Extendedly Dominated
NNUM	**113,490.26**	**563,104,437**	**0.41**	**1,131,939**	**2,775,685**
UNNM	113,490.17	563,144,629	–0.09	40,192	Dominated
TTTM	113,489.86	563,286,083	–0.39	181,647	Dominated
TNUM	**113,490.27**	**563,773,706**	**0.01**	**669,269**	**63,774,283**
UNTM	113,490.22	563,798,488	–0.05	24,782	Dominated
TTUM	113,490.27	564,418,022	0.00	644,316	Extendedly Dominated
UTTM (Current Strategy)	113,490.23	564,442,804	–0.04	669,098	Dominated
UNUM	**113,490.31**	**566,235,983**	**0.04**	**2,462,277**	**65,154,325**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 80: Cost-Utility Analysis Results per 100,000 Pregnant Persons (25% Third Trimester Rescreening of Pregnant Persons With a Previous Positive Test)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	124,180.37	614,571,979	0.00	0	**Reference**
NNTM	**124,180.48**	**614,829,670**	**0.11**	**257,691**	**2,328,518**
TNNM	124,180.45	614,840,683	–0.04	11,014	Dominated
TNTM	124,180.49	615,400,142	0.01	570,472	Extendedly Dominated
NNUM	**124,180.83**	**615,794,513**	**0.35**	**964,843**	**2,775,685**
UNNM	124,180.76	615,818,692	–0.08	24,179	Dominated
TTTM	124,180.50	615,949,345	–0.34	154,832	Dominated
TNUM	**124,180.84**	**616,364,986**	**0.01**	**570,472**	**63,774,285**
UNTM	124,180.80	616,378,151	–0.04	13,166	Dominated
TTUM	124,180.84	616,914,189	0.00	549,203	Extendedly Dominated
UTTM (Current Strategy)	124,180.81	616,927,354	–0.04	562,369	Dominated
UNUM	**124,180.87**	**618,463,785**	**0.03**	**2,098,799**	**65,154,327**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 81: Cost-Utility Analysis Results per 100,000 Pregnant Persons (0% Third Trimester Rescreening of Pregnant Persons With a Previous Positive Test)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**124,180.37**	**614,571,979**	**0.00**	**0**	**Reference**
NNTM	**124,180.48**	**614,829,670**	**0.11**	**257,691**	**2,328,518**
TNNM	124,180.45	614,835,379	–0.04	5,710	Dominated
TNTM	124,180.49	615,400,142	0.01	570,472	Extendedly Dominated
UNNM	124,180.75	615,793,493	0.27	963,823	Extendedly Dominated
NNUM	**124,180.83**	**615,794,513**	**0.35**	**964,843**	**2,775,685**
TTTM	124,180.50	615,949,345	–0.34	154,832	Dominated
UNTM	124,180.80	616,358,256	–0.03	563,742	Dominated
TNUM	**124,180.84**	**616,364,986**	**0.01**	**570,472**	**63,774,285**
UTTM (Current Strategy)	124,180.80	616,907,459	–0.04	542,473	Dominated
TTUM	124,180.84	616,914,189	0.00	549,203	Extendedly Dominated
UNUM	**124,180.87**	**618,463,785**	**0.03**	**2,098,799**	**65,154,327**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 82: Cost-Utility Analysis Results per 100,000 Pregnant Persons (100% Third Trimester Rescreening of Pregnant Persons With a Previous Positive Test)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**124,180.37**	**614,571,979**	**0.00**	**0**	**Reference**
NNTM	**124,180.48**	**614,829,670**	**0.11**	**257,691**	**2,328,518**
TNNM	124,180.45	614,856,595	–0.04	26,925	Dominated
TNTM	124,180.49	615,400,142	0.01	570,472	Extendedly Dominated
NNUM	**124,180.83**	**615,794,513**	**0.35**	**964,843**	**2,775,685**
UNNM	124,180.76	615,894,291	–0.07	99,778	Dominated
TTTM	124,180.50	615,949,345	–0.34	154,832	Dominated
TNUM	**124,180.84**	**616,364,986**	**0.01**	**570,472**	**63,774,285**
UNTM	124,180.81	616,437,838	–0.04	72,852	Dominated
TTUM	124,180.84	616,914,189	0.00	549,203	Extendedly Dominated
UTTM (Current Strategy)	124,180.81	616,987,041	–0.03	622,055	Dominated
UNUM	**124,180.87**	**618,463,785**	**0.03**	**2,098,799**	**65,154,327**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 83: Cost-Utility Analysis Results per 100,000 Pregnant Persons (100% Preterm and Extremely Preterm Screening)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.76**	**561,889,866**	**0.00**	**0**	**Reference**
NNTM	**113,489.86**	**562,130,283**	**0.10**	**240,417**	**2,506,849**
TNNM	113,489.82	562,141,805	–0.03	11,523	Dominated
TNTM	113,489.86	562,652,020	0.01	521,737	Extendedly Dominated
NNUM	**113,490.16**	**563,029,265**	**0.30**	**898,983**	**2,980,497**
UNNM	113,490.09	563,059,177	–0.07	29,912	Dominated
TTTM	113,489.87	563,153,992	–0.29	124,727	Dominated
TNUM	**113,490.17**	**563,551,003**	**0.01**	**521,737**	**68,025,233**
UNTM	113,490.13	563,569,392	–0.03	18,390	Dominated
TTUM	113,490.17	564,052,975	0.00	501,973	Extendedly Dominated
UTTM (Current Strategy)	113,490.13	564,071,365	–0.03	520,362	Dominated
UNUM	**113,490.19**	**565,470,503**	**0.03**	**1,919,501**	**69,703,076**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 84: Cost-Utility Analysis Results per 100,000 Pregnant Persons (0% Screening of Pregnant Persons Without Screening History at Presentation for Term Labour)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,407.01**	**561,030,111**	**0.00**	**0**	**Reference**
NNTM	**113,407.16**	**561,486,701**	**0.14**	**456,591**	**3,211,120**
TNNM	113,407.12	561,488,598	–0.03	1,897	Dominated
TNTM	113,407.16	562,008,059	0.01	521,358	Extendedly Dominated
TTTM	113,407.17	562,510,074	0.01	1,023,373	Extendedly Dominated
UNNM	113,407.52	563,174,262	0.36	1,687,561	Extendedly Dominated
NNUM	**113,407.59**	**563,190,445**	**0.43**	**1,703,744**	**3,947,489**
UNTM	113,407.56	563,693,723	–0.03	503,277	Dominated
TNUM	**113,407.60**	**563,711,803**	**0.01**	**521,358**	**64,075,668**
UTTM (Current Strategy)	113,407.56	564,195,738	–0.03	483,935	Dominated
TTUM	113,407.60	564,213,818	0.00	502,015	Extendedly Dominated
UNUM	**113,407.63**	**565,628,781**	**0.03**	**1,916,978**	**65,511,390**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 85: Cost-Utility Analysis Results per 100,000 Pregnant Persons (100% Screening of Pregnant Persons Without Screening History at Presentation for Term Labour)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,407.41**	**563,694,389**	**0.00**	**0**	**Reference**
NNTM	**113,407.47**	**563,712,224**	**0.06**	**17,835**	**$299,167**
TNNM	113,407.44	563,734,215	–0.03	21,991	Dominated
NNUM	**113,407.67**	**563,782,618**	**0.20**	**70,395**	**$349,055**
UNNM	113,407.61	563,861,254	–0.07	78,636	Dominated
TNTM	113,407.48	564,233,581	–0.19	450,963	Dominated
TNUM	**113,407.68**	**564,303,976**	**0.01**	**521,358**	**$64,075,676**
UNTM	113,407.65	564,360,621	–0.03	56,645	Dominated
TTTM	113,407.48	564,735,596	–0.20	431,620	Dominated
TTUM	113,407.68	564,805,991	0.00	502,015	Extendedly Dominated
UTTM (Current Strategy)	113,407.65	564,862,636	–0.03	558,660	Dominated
UNUM	**113,407.71**	**566,220,954**	**0.03**	**1,916,978**	**$65,511,390**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 86: Cost-Utility Analysis Results per 100,000 Pregnant Persons (0% Screening of Infants with Mothers Who Are GC-Positive at Presentation for Labour)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.71**	**561,669,247**	**0.00**	**0**	**Reference**
NNTM	**113,489.82**	**561,901,424**	**0.10**	**232,178**	**2,238,298**
TNNM	113,489.78	561,914,127	–0.03	12,703	Dominated
TNTM	113,489.83	562,421,169	0.01	519,745	Extendedly Dominated
NNUM	**113,490.14**	**562,772,695**	**0.33**	**871,271**	**2,673,384**
UNNM	113,490.07	562,807,006	–0.07	34,310	Dominated
TTTM	113,489.83	562,921,826	–0.32	149,131	Dominated
TNUM	**113,490.15**	**563,292,440**	**0.01**	**519,745**	**63,775,830**
UNTM	113,490.12	563,314,048	–0.04	21,608	Dominated
TTUM	113,490.15	563,793,098	0.00	500,658	Extendedly Dominated
UTTM (Current Strategy)	113,490.12	563,814,705	–0.03	522,265	Dominated
UNUM	**113,490.18**	**565,204,571**	**0.03**	**1,912,131**	**64,971,171**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 87: Cost-Utility Analysis Results per 100,000 Pregnant Persons (100% Effective Vertical Transmission Prevention Treatment)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,407.61**	**562,293,358**	**0.00**	**0**	**Reference**
NNTM	**113,407.67**	**562,547,482**	**0.07**	**254,124**	**3,872,647**
TNNM	113,407.64	562,559,443	–0.03	11,961	Dominated
TNTM	113,407.68	563,068,678	0.01	521,196	Extendedly Dominated
NNUM	**113,407.89**	**563,483,041**	**0.22**	**935,559**	**4,258,452**
UNNM	113,407.83	563,514,525	–0.07	31,485	Dominated
TTTM	113,407.69	563,570,422	–0.21	87,382	Dominated
TNUM	**113,407.90**	**564,004,237**	**0.01**	**521,196**	**60,486,081**
UNTM	113,407.87	564,023,761	–0.04	19,524	Dominated
TTUM	113,407.91	564,505,981	0.00	501,744	Extendedly Dominated
UTTM (Current Strategy)	113,407.87	564,525,505	–0.03	521,268	Dominated
UNUM	**113,407.93**	**565,922,484**	**0.03**	**1,918,247**	**65,186,460**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 88: Cost-Utility Analysis Results per 100,000 Pregnant Persons (0% Effective Vertical Transmission Prevention Treatment)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,407.27**	**562,477,542**	**0.00**	**0**	**Reference**
NNTM	**113,407.40**	**562,694,970**	**0.14**	**217,428**	**1,598,394**
TNNM	113,407.37	562,706,870	–0.03	11,900	Dominated
TNTM	113,407.41	563,216,521	0.01	521,551	Extendedly Dominated
NNUM	**113,407.82**	**563,524,744**	**0.41**	**829,775**	**2,006,843**
UNNM	113,407.75	563,555,609	–0.07	30,865	Dominated
TTTM	113,407.41	563,718,626	–0.40	193,882	Dominated
TNUM	113,407.83	564,046,296	0.01	521,551	Extendedly Dominated
UNTM	113,407.79	564,065,260	–0.03	540,516	Dominated
TTUM	113,407.83	564,548,401	0.01	1,023,657	Extendedly Dominated
UTTM (Current Strategy)	113,407.79	564,567,365	–0.02	1,042,621	Dominated
UNUM	**113,407.86**	**565,964,381**	**0.04**	**2,439,637**	**65,769,734**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 89: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Younger Than 25 Years Subgroup)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**122,922.90**	**614,662,833**	**0.00**	**0**	**Reference**
NNUM	**122,923.42**	**615,868,858**	**0.52**	**1,206,025**	**2,327,685**
UNNM	122,923.25	615,930,354	–0.17	61,496	Dominated
UNUM	**122,923.46**	**618,538,529**	**0.04**	**2,669,671**	**63,946,120**
UUUM	**122,923.48**	**621,108,593**	**0.01**	**2,570,064**	**214,670,689**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 90: Cost-Utility Analysis Results per 100,000 Pregnant Persons (25 Years and Older Subgroup)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**124,522.19**	**614,547,290**	**0.00**	**0**	**Reference**
NNUM	**124,522.63**	**615,774,304**	**0.44**	**1,227,013**	**2,775,918**
UNNM	124,522.58	615,801,166	–0.05	26,862	Dominated
UNUM	**124,522.67**	**618,443,467**	**0.04**	**2,669,163**	**65,105,665**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 91: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Exploratory Analysis: Strategy UTUM Included as a Comparator)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,489.73**	**561,663,682**	**0.00**	**0**	**Reference**
NNTM	**113,489.83**	**561,899,189**	**0.10**	**235,506**	**2,328,518**
TNNM	113,489.79	561,911,193	–0.03	12,004	Dominated
TNTM	113,489.84	562,420,549	0.01	521,361	Extendedly Dominated
NNUM	**113,490.15**	**562,780,969**	**0.32**	**881,780**	**2,775,685**
UNNM	113,490.08	562,812,279	–0.07	31,310	Dominated
TTTM	113,489.84	562,922,472	–0.31	141,503	Dominated
TNUM	**113,490.15**	**563,302,330**	**0.01**	**521,361**	**63,774,285**
UNTM	113,490.12	563,321,635	–0.04	19,305	Dominated
TTUM	113,490.16	563,804,252	0.00	501,922	Extendedly Dominated
UTTM	113,490.12	563,823,557	–0.03	521,228	Dominated
UNUM	**113,490.18**	**565,220,444**	**0.03**	**1,918,114**	**65,154,327**
UTUM	**113,490.19**	**565,722,366**	**0.00**	**501,922**	**214,095,828**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 92: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Exploratory Analysis: CT and GC Infection Impact Adverse Obstetric Outcomes)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNNM	**113,486.92**	**561,859,113**	**0.00**	**0**	**Reference**
TNNM	113,488.70	561,998,166	1.78	139,053	Extendedly Dominated
NNTM	113,488.21	562,010,591	1.29	151,477	Extendedly Dominated
TNTM	113,489.02	562,489,102	2.09	629,988	Extendedly Dominated
UNNM	**113,495.35**	**562,500,445**	**8.43**	**641,331**	**76,111**
NNUM	113,492.51	562,612,095	–2.83	111,650	Dominated
TTTM	113,489.16	562,983,990	-6.18	483,545	Dominated
UNTM	**113,495.66**	**562,991,380**	**0.32**	**490,935**	**1,554,224**
TNUM	113,493.32	563,090,606	–2.35	99,226	Dominated
UTTM (Current Strategy)	113,495.81	563,486,268	0.15	494,888	Extendedly Dominated
TTUM	113,493.47	563,585,494	–2.20	594,114	Dominated
UNUM	**113,496.30**	**564,850,954**	**0.64**	**1,859,574**	**2,905,194**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Table 93: Pediatric Cost-Effectiveness Analysis Results per 100,000 Pregnant Persons (Exploratory Analysis: CT and GC Infection Impact Adverse Obstetric Outcomes)

Strategy	Total					Incremental					ICER ($ Per Pediatric Infection Prevented[a])
	GC Conjunctivitis	CT Conjunctivitis	CT Pneumonia	Pediatric Infections[a]	Cost ($)	GC Conjunctivitis	CT Conjunctivitis	CT Pneumonia	Pediatric Infection Prevented[a]	Cost ($)	
NNNM	**86.0**	**277.4**	**132.3**	**495.8**	**561,859,113**	**0.0**	**0.0**	**0.0**	**0.0**	**0**	**Reference**
TNNM	76.8	249.0	118.8	444.6	561,998,166	–9.2	–28.4	–13.6	51.2	139,053	Extendedly Dominated
NNTM	**73.9**	**234.8**	**112.0**	**420.6**	**562,010,591**	**–12.2**	**–42.7**	**–20.4**	**75.2**	**151,477**	**$2,014**
TNTM	73.3	231.3	110.3	414.9	562,489,102	–0.6	–3.5	–1.7	5.7	478,511	Extendedly Dominated
UNNM	41.6	129.6	61.8	233.0	562,500,445	–32.2	–105.2	–50.2	187.5	489,854	Extendedly Dominated
NNUM	**29.7**	**100.7**	**48.0**	**178.4**	**562,612,095**	**–44.2**	**–134.0**	**–63.9**	**242.2**	**601,504**	**$2,484**
TTTM	73.2	230.3	109.8	413.3	562,983,990	43.5	129.6	61.8	–234.9	371,895	Dominated
UNTM	38.1	111.8	53.3	203.3	562,991,380	8.5	11.1	5.3	–24.9	379,285	Dominated
TNUM	**29.1**	**97.2**	**46.4**	**172.7**	**563,090,606**	**–0.6**	**–3.5**	**–1.7**	**5.7**	**478,511**	**$84,002**
UTTM (Current Strategy)	38.0	110.9	52.9	201.7	563,486,268	8.9	13.6	6.5	–29.0	395,662	Dominated
TTUM	29.0	96.2	45.9	171.1	563,585,494	–0.1	–1.0	–0.5	1.6	494,888	Extendedly Dominated
UNUM	**27.1**	**84.7**	**40.4**	**152.2**	**564,850,954**	**–2.0**	**–12.5**	**–6.0**	**20.5**	**1,760,348**	**$85,815**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICER = incremental cost-effectiveness ratio.

[a] Accounts for GC conjunctivitis, CT conjunctivitis, and CT pneumonia in aggregate.

Table 94: Obstetric Outcomes Cost-Effectiveness Analysis Results per 100,000 Pregnant Persons (Exploratory Analysis: CT and GC Infection Impact Adverse Obstetric Outcomes)

Strategy	Total					Incremental					ICER ($ Per Adverse Obstetric Outcome Prevented[a])
	Preterm Birth	Extremely Preterm Birth	Stillbirth	Adverse Obstetric Outcomes[a]	Cost ($)	Preterm Birth	Extremely Preterm Birth	Stillbirth	Adverse Obstetric Outcomes Prevented[a]	Cost ($)	
NNNM	**7,301.0**	**459.5**	**806.4**	**8,566.8**	**561,859,113**	**0.0**	**0.0**	**0.0**	**0.0**	**0**	**Reference**
TNNM	7,293.4	458.9	804.8	8,557.1	561,998,166	–7.6	–0.6	–1.5	9.7	139,053	Extendedly Dominated
NNTM	7,291.4	459.5	805.7	8,556.5	562,010,591	–9.6	0.0	–0.7	10.3	151,477	Extendedly Dominated
TNTM	7,291.2	458.9	804.7	8,554.8	562,489,102	–9.8	–0.6	–1.7	12.0	629,988	Extendedly Dominated
UNNM	**7,265.3**	**456.9**	**799.3**	**8,521.4**	**562,500,445**	**–35.7**	**–2.6**	**–7.1**	**45.4**	**641,331**	**$14,133**
NNUM	7,259.4	459.5	803.4	8,522.3	562,612,095	–5.9	2.6	4.2	–0.9	111,650	Dominated
TTTM	7,291.1	458.8	804.5	8,554.4	562,983,990	25.8	1.9	5.2	–33.0	483,545	Dominated
UNTM	**7,263.1**	**456.9**	**799.1**	**8,519.1**	**562,991,380**	**–2.2**	**0.0**	**–0.2**	**2.3**	**490,935**	**$209,783**
TNUM	7,259.2	458.9	802.4	8,520.6	563,090,606	–3,9	2.0	3.4	–1.5	99,226	Dominated
UTTM (Current Strategy)	7,263.1	456.8	798.9	8,518.8	563,486,268	0.0	–0.1	–0.2	0.3	494,888	Extendedly Dominated
TTUM	7,259.2	458.8	802.3	8,520.2	563,585,494	–4.0	1.9	3.2	–1.2	594,114	Dominated
UNUM	**7,258.5**	**456.9**	**798.8**	**8,514.1**	**564,850,954**	**–4.6**	**0**	**–0.3**	**4.9**	**1,859,574**	**$375,869**

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICER = incremental cost-effectiveness ratio.

[a] Accounts for preterm birth, extremely preterm birth, and stillbirth in aggregate.

Table 95: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Exploratory Analysis: Lifetime Time Horizon)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	**8,504,789.66**	**572,443,916**	**0.00**	**0**	**Reference**
TNUM	**8,504,808.26**	**572,644,155**	**18.60**	**200,238**	**10,764**
TTUM	8,504,813.66	573,054,138	5.40	409,983	Extendedly Dominated
UNUM	**8,504,874.79**	**573,407,114**	**66.53**	**762,959**	**11,468**
UNTM	8,504,721.49	574,206,701	–153.30	799,587	Dominated
UTTM (Current Strategy)	8,504,726.89	574,616,684	–147.91	1,209,570	Dominated
UNNM	8,504,625.44	575,381,434	–249.35	1,974,321	Dominated
NNTM	8,504,083.08	584,501,401	–791.72	11,094,288	Dominated
TNTM	8,504,101.68	584,701,640	–773.11	11,294,526	Dominated
TTTM	8,504,107.08	585,111,622	–767.72	11,704,509	Dominated
TNNM	8,504,005.63	585,876,373	–869.16	12,469,259	Dominated
NNNM	8,503,861.19	588,345,061	–1,013.60	14,937,947	Dominated

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

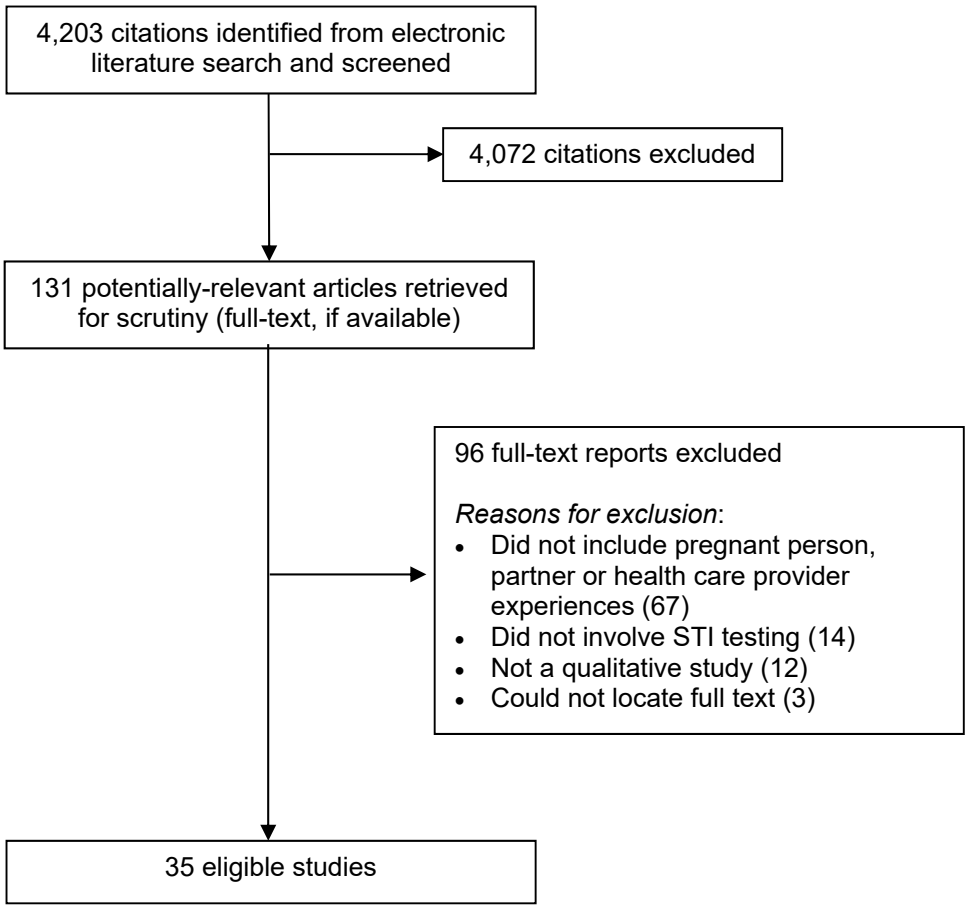
Table 96: Cost-Utility Analysis Results per 100,000 Pregnant Persons (Exploratory Analysis: Lifetime Time Horizon and Partner Treatment)

Strategy	Total		Incremental		ICUR ($ Per QALY Gained)
	QALYs	Costs ($)	QALYs	Costs ($)	
NNUM	**12,063,343.03**	**572,938,618**	**0.00**	**0**	**Reference**
TNUM	**12,063,361.63**	**573,196,669**	**18.60**	**258,051**	**13,871**
TTUM	12,063,367.03	573,663,615	5.40	466,946	Extendedly Dominated
UNUM	**12,063,428.16**	**574,171,682**	**66.53**	**975,013**	**14,655**
UNTM	12,063,274.86	574,760,680	–153.30	588,998	Dominated
UTTM (Current Strategy)	12,063,280.25	575,227,626	–147.91	1,055,944	Dominated
UNNM	12,063,178.81	575,876,568	–249.35	1,704,887	Dominated
NNTM	12,062,636.45	584,879,380	–791.72	10,707,698	Dominated
TNTM	12,062,655.05	585,137,431	–773.11	10,965,749	Dominated
TTTM	12,062,660.44	585,604,377	–767.72	11,432,695	Dominated
TNNM	12,062,559.00	586,253,320	–869.16	12,081,638	Dominated
NNNM	12,062,414.56	588,691,920	–1,013.60	14,520,238	Dominated

CT = *Chlamydia trachomatis*; GC = *Neisseria gonorrhoeae*; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Appendix 13: Study Selection Flow Diagrams — Patients' Preferences and Experiences Review

Figure 9: PRISMA Flowchart of Selected Reports



Appendix 14: Study Characteristics — Patients' Preferences and Experiences Review

Table 97: Study Characteristics — Patients' Preferences and Experiences

First Author, Publication Year, Setting	Research Objective	Reported Study Design or Analytic Approach	Patient Characteristics
HIV			
Alvarez-Del Arco, 2018, Spain[104]	To analyze elements shaping the desire for procreation among women living with HIV, and to specifically investigate the impact of HIV.	Qualitative study	Of 20 HIV-positive women, 11 had children
Baxter, 2000, UK [105]	To examine the attitudes of a group of pregnant women to the routine offer of the HIV test during pregnancy.	Qualitative study	Of 12 pregnant women, 6 had accepted the test and 6 did not
Blake, 2008, US[106]	To describe personal experiences of women in obtaining HIV testing and health care services in east Texas.	Secondary qualitative data analysis	Of 64 women, 23 were HIV-positive while 41 were high-risk HIV negative.
Boyd, 1999, UK[107]	To investigate the opinions of a sample drawn from a general population of pregnant women within the context of an HIV test offer.	Qualitative study, with reference to grounded theory analysis	29 pregnant women
Bulman, 2013, Canada[108]	To obtain an increased understanding of the information women receive about HIV/AIDS during the opt-out screening process and to advance the policy related dialogue around best practices in HIV screening within the province of Newfoundland and Labrador.	Qualitative descriptive study	12 pregnant women
Chambers, 2001, New Zealand[109]	To assess current attitudes and practice toward antenatal HIV risk assessment, as well as HIV testing and barriers toward implementation of among midwives, general practitioners, and obstetricians.	Survey	100 midwives 293 general practitioners 14 obstetricians
De Zulueta, 2007, UK[110]	To explore pregnant women's responses to routine HIV testing, their reasons for declining or accepting the test, and assess how far their responses fulfill standard criteria for informed consent.	Qualitative cross-sectional survey	32 pregnant women

First Author, Publication Year, Setting	Research Objective	Reported Study Design or Analytic Approach	Patient Characteristics
Evans, 2016, UK (included studies from US, Canada and UK)[111]	To explore nurses' and midwives' views and experiences of the provision and management of provider-initiated HIV testing and counselling.	Systematic review of qualitative evidence, data were pooled using a pragmatic meta-aggregative approach	21 publications from 18 research studies Nurses and midwives; studies where the sample included different cadres of health care providers if more than 50% were nurses or midwives.
Fielder, 2005, US[112]	To examine the attitudes and health beliefs among drug users about mandatory HIV testing of newborns and about voluntary versus mandatory testing of pregnant women; to examine to what extent negative experiences and stigmatization affected attitudes toward HIV testing.	Mixed-methods, "Qualitative Focus Group Study"	For Qualitative Component: 25 HIV-infected and uninfected, drug-using men and women. Does not report pregnancy status, but participants refer to having had children in the findings.
Gahagan, 2011, Canada[113]	To explore the various individual and structural barriers and facilitators to HIV counselling and testing experienced among a sample of adult women and men living in Nova Scotia.	Mixed-methods study	For Qualitative Component: 30 women 19 men 1 transgender person Does not report pregnancy status, but "several participants interviewed had been tested for HIV while they were pregnant."
Jones, 2004, UK[114]	To explore the reasons women gave when they declined HIV testing.	Survey/Audit	2,138 pregnant women
Katz, 2001, US[115]	To describe the experience of screening for HIV in pregnancy from the perspective of pregnant women.	Descriptive study, analyzed using a combination of grounded theory and content analysis	32 pregnant women
Kelly, 2001, US[116]	To examine the experience of testing and receipt of positive HIV test results by pregnant women in Texas who were tested after the mandatory perinatal testing law went into effect.	Interview study	29 HIV-positive pregnant women
Kelly, 2012, UK[117]	To understand the uniqueness of the experience of testing HIV positive from the perspective of pregnant women.	Qualitative study	4 pregnant women
Kelly, 2012, US[117]	To investigate how women who were being tested for HIV during their pregnancies were evaluating, conceptualizing, and negotiating their risk of infection.	Qualitative component of mixed methods, analyzed in accordance to grounded theory method	30 pregnant women

First Author, Publication Year, Setting	Research Objective	Reported Study Design or Analytic Approach	Patient Characteristics
Lee King, 2014, US[119]	To explore women's perspectives to inform comprehensive perinatal HIV testing communication.	Qualitative descriptive research design, analyzed using content analysis	Of 37 pregnant women, 32 were HIV-negative while 5 were HIV-positive (separate focus groups)
Lingen-Stallard, 2016, UK[120]	To explore women's experiences of receiving a positive HIV test result following antenatal screening.	Phenomenology	13 women who had received a positive HIV diagnosis in an antenatal HIV testing programme
Mawn, 1998, US[121]	To include the voices of laywomen at risk for or living with HIV in the ongoing debate on prenatal and newborn HIV screening.	Phenomenology	Of 33 women, 16 were HIV-positive
McAllister, 2013, New Zealand[122]	To investigate the impact on women, and their health care providers, of initial-reactive HIV test results that required retesting in the New Zealand antenatal HIV screening programme.	Qualitative study, analyzed using thematic analysis	19 general practitioners 11 midwives 7 pregnant women
McLeish, 2016, US[123]	To explore the experiences of women living with HIV in England who received or gave Mentor Mother (trained mother-to-mother) volunteer peer support during pregnancy and early motherhood.	Qualitative descriptive study, theoretically informed by phenomenology	12 HIV-positive pregnant women
Meyerson, 2014, US[124]	To identify the extent to which community health centres in Indiana implement routine HIV testing.	Community participatory research	28 community health centres reporting
Njie-Carr, 2012, US[125]	To describe and explore African-American and African-Caribbean women's knowledge, attitudes, beliefs, feelings, and interpersonal experiences related to participating in voluntary counselling and testing (VCT), disclosing their HIV status and their decisions related to pregnancy care and parenting practices.	Qualitative study	Of 23 women, 20 were pregnant and 3 were parenting an infant who was less than 12 months old.
Rothpletz-Puglia, 2012, US[126]	To solicit women's opinions about the process of routine prenatal HIV testing to identify strategies for routine testing that will address women's concerns, increase their level of comfort with testing, and	Exploratory study	Of 25 women, 24 were non-pregnant and one had given birth within the last year.

First Author, Publication Year, Setting	Research Objective	Reported Study Design or Analytic Approach	Patient Characteristics
	support universal prenatal HIV testing		
Simpson, 2007, US[127]	To elicit the personal perspectives of a unique group of women who first learned of their HIV diagnosis during pregnancy and to report their views of the benefits and the negative consequences of laws that mandate HIV testing for pregnant women.	Survey	Of 22 pregnant women, 11 were HIV-positive and 11 were HIV-negative.
Treisman, 2014, US[128]	To explore the following research question: How do United Kingdom-based African women perceive, make sense of, and manage a diagnosis of HIV during pregnancy, and after delivery?	Qualitative investigation, analyzed using interpretive phenomenological analysis	12 pregnant women
Tripathi, 2013, Ukraine[129]	To explore women's and providers' experiences of HIV testing during antenatal care, with a focus on consent, counselling, and confidentiality.	Qualitative study	25 health providers who conduct HIV testing of pregnant women. Of 60 pregnant women, 15 were HIV-positive.
Williams, 1990, US[76]	To investigate knowledge about perinatal transmission of HIV and perceptions of the childbearing role among women at risk of AIDS.	Content analysis	21 women
Syphilis			
DiOrio, 2018, US[130]	To understand the etiology of congenital syphilis through qualitative examination of case mother characteristics and behaviour.	Qualitative methods	23 pregnant women
Kroeger, 2018, US[131]	To elicit perspectives of providers and community members in Caddo Parish, Louisiana, on the persistence of congenital syphilis in the community.	Qualitative interviews	69 participants: 58 females and 11 males
Chlamydia			
Bilardi, 2010, Australia[100]	To determine the acceptability of screening pregnant women 16 to 25 years old for chlamydia as part of routine antenatal care.	Qualitative component of mixed methods	100 pregnant women, 69 who had tested negative for chlamydia and 31 positive for chlamydia.
Logan, 2005, UK[41]	To compare, in parallel, different approaches of opportunistically screening women with bleeding in early	Cross-sectional study	207 pregnant women

First Author, Publication Year, Setting	Research Objective	Reported Study Design or Analytic Approach	Patient Characteristics
	pregnancy for Chlamydia trachomatis.		
Perkins, 2003, UK[102]	To assess the feasibility and acceptability of opportunistic screening, both to the target population and to the health care professionals participating in the programme.	Qualitative evaluation component of mixed methods	13 general practitioners, 14 practice nurses, 15 practice receptionists, and 11 practice managers
Pimenta, 2003, UK[101]	To determine the acceptability of opportunistic screening for Chlamydia trachomatis in young people in a range of health care settings.	Qualitative evaluation component of programme evaluation	For qualitative component: 24 women and one man
Chlamydia and Gonorrhea			
Hack, 2009, US[103]	To discern whether there were any specific patterns of treatment or triggers during the examination that emergency physicians use when selecting to treat or not treat patients.	Survey	145 emergency physicians
General STIs			
Bar-Zeev, 2014, Australia[132]	To assess adherence to antenatal guidelines by clinicians and identify factors affecting the quality of antenatal care delivery to remote dwelling Aboriginal women.	Retrospective cohort study, interview component	27 health providers

Appendix 15: Quality Assessment of Included Studies – Patients' Perspectives and Experiences Review

Table 98: Quality Assessment of Included Studies — Patients' Perspectives and Experiences

First Author	Strengths	Weaknesses
Alvarez-del Arco, 2018[104]	Specifically describes characteristics of the research team, e.g., experience and training, and gender composition. Ethics approval sought Theoretical framework underlying analysis. In-depth description of the analysis process. Includes implications for health providers and policy-makers.	Data saturation was discussed among researchers although resource limitations did not allow for increasing the number of interviews.
Bar-Zeev, 2014[132]	Recruitment continued until data saturation had been reached in the analysis. Qualitative and quantitative data sources were used to corroborate findings around the issue of the quality of care. Ethics approval.	Qualitative part of a mixed-methods study: no explanation of how the qualitative component adds to the quantitative part. Appears to be a single author analysis, under supervision of another author; no description of initial independent coding.
Baxter, 2000[105]	Qualitative and questionnaire data obtained to gain a wider perspective. Ethics approval sought.	Relatively small sample size (n = 12), no mention that saturation was obtained. Only one researcher analyzed most interviews (independent person checked and confirmed coding of one transcript). Researcher has not clearly justified the selection of research methodology based on her research objective.
Bilardi, 2010[100]	Two authors reviewed the transcripts separately before meeting to discuss codes and emergent and recurrent themes, with a third author reviewing 10% of the transcripts independently to confirm coding and themes. Ethics approval sought. High participation rate (100 women of the 101 invited).	Interviews were relatively short (approximately 10 to 15 minutes) and lacked the depth of conventional qualitative interviews, as the women were limited for time. Relationship between researcher and participants has not been adequately discussed.
Blake, 2008[106]	Independent analysis by multiple researchers.	Structured qualitative focus groups (collected as part of quality improvement project). Use of focus groups versus interviews for sensitive topics. Unclear how many researchers participated in the analysis process.
Boyd, 1999[107]	Included comparison between interviewees and refusers. The transcripts were analyzed independently by two researchers to enhance the dependability of the analysis.	No mention of ethics approval or consent.

First Author	Strengths	Weaknesses
Bulman, 2013[109]	The researcher has clearly justified the research design . Ethics approval sought. Includes recommendations for practice and future research.	Low response rate and relatively small sample, no mention that saturation was obtained (all those who were interested and eligible participated) (n = 12).
Chambers, 2001[109]	Steps were taken to ensure rigour and trustworthiness; e.g., the questionnaire was reviewed by a nurse scholar.	Descriptive questionnaire study, no qualitative analysis of open-ended questions leading to analysis of limited depth. Although a trustworthy survey, the research question would likely have been better addressed by a qualitative study.
de Zulueta, 2007[110]	Compares demographic variables of refusers versus interviewees. Theoretical framework underlying analysis.	Use of interpreter for non-English speaking women, for sensitive and nuanced subject matter.
DiOrio, 2018[130]	No particular strengths to note; study was deemed poor quality.	Unclear interview data collection procedure. Poor description of analytical procedure.
Evans, 2016[111]	Systematic review Includes recommendations for practice and for research.	Half of included studies were from developing countries excluded from the current synthesis.
Fielder, 2005[112]	Focus group data used to clarify responses from longitudinal cohort study. Inclusion of males with the rationale that a male partner may be involved in a woman's decision to access prenatal care and/or obtain an HIV test.	Female focus groups conducted by single researcher. Use of focus groups versus interviews for sensitive topics. No mention of ethics approval or consent.
Gahagan, 2011[113]	Ethics approval sought. Representation from various populations and communities was sought (Indigenous, African-Nova Scotian, Caucasian and Immigrant populations, urban and rural participants). Combination of quantitative and qualitative data sources. Clear description of the role of the qualitative component.	Unclear how many individuals analyzed the data, and whether they did so independently.
Hack, 2009[103]	Questionnaire is likely to be valid and reliable.	Questionnaire study, no qualitative analysis of open-ended questions leading to analysis of limited depth.
Jones, 2004[114]	No strengths to report.	This was an audit study, with no qualitative analysis of open-ended questions leading to an analysis of limited depth.
Katz, 2001[115]	Ethics approval sought. Mechanisms to ensure credibility (3 participants validated themes) and fittingness (discussing findings with health care professionals). Included comparison between interviewees and refusers.	Unclear if analysis was independent.
Kelly, 2001[116]	Ethics approval.	Unclear if analysis was independent and/or done by multiple researchers.
Kelly, 2012[118]	Theoretical framework underlying analysis. Rich case study analysis, e.g., repeat	Relatively small sample (4 case studies), with no mention of data saturation or justification for a

First Author	Strengths	Weaknesses
	interview model used. Ethics approval. All members of the research team independently read and coded a selection of the original transcripts Clear explanation of the study's relevance to clinical practice.	small sample size.
Kelly, 2012b[117]	Three authors independently read and coded all interview transcripts. Ethics approval sought.	Non-testers not included. Use of focus groups for sensitive topic (focus groups were constructed to oversample Hispanic and African-American women due to the difficulty in recruiting, arranging for, and completing individual interviews with prenatal patients from these populations).
Kroeger, 2018[131]	Study includes both women and providers. Ethics approval sought. Entire team coded interviews. Description of the relevance of the study findings in the context of the subsequent policy actions taken by the state to mitigate barriers in the pathways to congenital syphilis prevention.	No weaknesses to note.
Lee King, 2014[119]	Ethics approval sought. Use of data-derived codes from one focus group applied systematically across focus group data. Two interpreters reviewed the original interpretation for accuracy and completeness.	Use of focus groups versus interviews for sensitive topics. Use of interpreters. Unclear if analysis was independent.
Lingen-Stallard, 2016[120]	Ethics approval sought. Nondirective and flexible approach to in-depth interviews allowing discussions to be participant-led, providing more relevance and depth. At the end of each interview, women were given contact details relevant to their interview (e.g., health professionals, counsellor support workers). Field notes were made during and following the interviews, and they included women's reactions such as laughter, crying, eye contact, facial expression, and signs of discomfort. The researchers, all midwives, were integral to the analysis process, acknowledging their influence on the interpretation.	Relatively small sample (n = 13), with no mention of data saturation or justification for a small sample size.
Logan, 2005[41]	Ethics approval sought.	Limited qualitative analysis (lack of description of data analysis).
Mawn, 1998[121]	Ethics approval sought. Study included acknowledgement of the investigator's own experiences and assumptions about the phenomenon of the study. Clear description of domain and theme	No weaknesses to note.

First Author	Strengths	Weaknesses
	development.	
McAllister, 2013[122]	Three researchers conducted analysis, using cross-checking of coding strategies and seeking agreement of a coding scheme. Ethics approval sought. Inclusion of both pregnant persons and health care providers. Thematic saturation among the small sample of women participants reached due to the relative homogeneity in feelings expressed.	Relatively small sample of pregnant persons (n = 7) compared with the number of included health care providers (n = 30); however with justification as data saturation was obtained. Interviews were relatively short (approximately 10 minutes) and lacked the depth of conventional qualitative interviews, to fit the schedules of women and providers.
McLeish, 2016[123]	Paper includes researcher demographics (white, UK-born, women with children) and notes that they worked reflexively, sensitive to the role as "outsider" researcher. Ethics approval. Each researcher independently analyzed the transcript to ensure validity of the analysis. Relatively small number of participants (n = 12)(even though authors described reaching data saturation).	Unable to compare refusers and participants due to recruitment process
Meyerson, 2014[124]	This study was deemed exempt from ethics review.	Qualitative data from questionnaire were "coded textually for emerging themes," but were subsequently quantified, leading to an analysis with limited depth.
Njie-Carr, 2012[125]	Theoretical framework underlying analysis. Ethics approval sought. Both qualitative and quantitative data sources were used. Recruitment continued until data saturation (n = 23). Interview guide was reviewed by a nurse scholar with an area of expertise is women, maternal, and child health. Four investigators independently conducted analysis. Clear description of implication for midwifery practice.	No weaknesses to report
Perkins, 2003[102]	Relatively long, in-depth interviews (approximately 1.0 to 1.5 hours) — in two waves of interviews, at the beginning and the end of the screening pilot. Ethics approval sought. Two researchers conducted initial coding independently. Diverse sets of participants (13 general practitioners, 14 practice nurses, 15 practice receptionists, and 11 practice managers). Includes implications for policy and practice.	No weaknesses to report.
Pimenta, 2003[101]	Qualitative and quantitative data sources were used. Ethics approval sought.	Very superficial description of the analysis ("The open coding method of content analysis was used to identify themes that related to the main study aims.")

First Author	Strengths	Weaknesses
Rothpletz-Puglia, 2012[126]	Ethics approval sought.	Use of focus groups versus interviews for sensitive topic. Analysis was conducted by only one investigator.
Simpson, 2007,[127]	Ethics approval sought. Includes implications for policy and practice. Contrasts perspectives of those who tested positive and those who tested negative.	Analysis was largely conducted by one investigator (second investigator reviewed categorization of themes).
Treisman, 2014[128]	Ethics approval sought.	Relatively small sample (n = 12), although authors note that it was a "purposive, carefully situated" sample. Analysis was conducted largely by one investigator (with other 2 researchers conducting an independent audit process on transcripts).
Tripathi, 2013[129]	Ethics approval sought. Transcript coding and initial analysis were done in the original language. Study includes both women and providers.	No weaknesses to report.
Williams, 1990[76]	Purposive sampling. Field testing of interview guide and review by experts.	Analysis conducted by a single investigator. No mention of ethics approval or consent.