Script for Guideline on screening for chlamydia and gonorrhea in primary care for individuals not known to be at high risk

[Slide 1]

- The Canadian Task Force on Preventive Health Care
- Guideline on screening for chlamydia and gonorrhea in primary care for individuals not known to be at high risk

[Slide 2]

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

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- Task Force members who made up the working group for this guideline are: Ainsley Moore, Brenda Wilson, Donna Reynolds, Guylène Thériault, Brett Thombs, John Riva.
- Task Force spokespersons are: Ainsley Moore, Brenda Wilson, Donna Reynolds, Guylène Thériault
- Content experts were Jo-Anne Dillon, Ameeta Singh, Tom Wong, Anne Burchell. Content experts are external advisors to the working group and do not vote or have input on the direction or strength of recommendations.

[Slide 4]

- Overview of the Webinar
- Presentation
    - Background on chlamydia and gonorrhea
    - Methods of the CTFPHC
    - Recommendation
    - Results
    - Rationale for recommendations
    - Knowledge gaps and next steps
    - Conclusions
    - Questions and Answers

[Slide 5]

- Background

[Slide 6]

- Chlamydia and gonorrhea are the most common sexually transmitted infection in Canada. Rates have steadily increased since 2000.
- True prevalence is unknown, but reported rates in 15-29 year-olds were 1.0-1.9% for chlamydia and 0.2-0.3% for gonorrhea; rates among individuals over 30 years old were much lower, at <0.5% for chlamydia and <0.2% for gonorrhea.

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- Since these infections are commonly asymptomatic, underreporting is estimated at at least 70%, which means that the true rates for chlamydia are likely in the range of 5-7% in the 15-29 year age group.

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- This table outlines some of the main consequences of untreated chlamydia and gonorrhea, with the estimated likelihood of occurrence. Most of these data come from studies on untreated chlamydia, but studies on gonorrhea have shown, for example, that PID might be more likely.
- Chronic pelvic pain is defined as lasting longer than 6 months.

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- Screening could help reduce clinical complications by identifying those with chlamydia and gonorrhea and treating the infections. Given the high rate of asymptomatic infection (most infections are asymptomatic), they will only be identified through screening, and not through testing of those with symptoms.

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- National guidance exists from the Public Health Agency of Canada, but was last updated in 2010 for screening recommendations, and does not include recommendations on screening for gonorrhea. The Task Force identified a need for updated national guidance in this area based on a rigorous systematic review of potential harms, benefits, and patient values and preferences.

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- The population of interest is all sexually active individuals under 30 not KNOWN by the healthcare provider to be at high risk. Readers should refer to relevant national, provincial, or local guidance for the screening of individuals known to have specific high-risk behaviours (e.g., having multiple sexual partners, previous STIs, sex without condoms, although this will vary by jurisdiction), testing of individuals seeking care for symptoms, pregnant individuals, and for selection of appropriate antibiotic treatment, partner notification, re-testing, and forensic testing strategies.

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- Methods

[Slide 13]

- The Canadian Task Force on Preventive Health Care is an independent body of up to 15 clinicians and methodologists.
- The mandate is to develop evidence-based clinical practice guidelines that support primary care providers in the delivery of preventive healthcare.
- Ultimately the goal of the Task Force is to improve the health of Canadians by making sure that primary care providers have access to clinical prevention guidelines that are based on the best available evidence.

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- The Task Force works with Evidence Review and Synthesis Centres (ERSCs) who independently review the evidence.
- The ERSCs undertake a systematic review of the literature based on the analytical framework and prepare the final report and GRADE tables. GRADE: Grading of Recommendation, Assessment, Development and Evaluation.
- They also participate in working group and Task Force meetings (non-voting).

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- This infographic provides an overview of the TF guideline process and who provides critical input at the topic selection, evidence synthesis, guideline, and dissemination stages. This includes a variety of internal and external stakeholder (more detail on next slide).

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- The TF review process includes:
    - Internal review by the guideline working group and all other Task Force members
    - External review is undertaken at 3 key stages:
        - Protocol, systematic review(s) and guideline
- External stakeholder reviewer groups include:
    - Generalist and disease specific stakeholders
    - Academic peer reviewers
- CMAJ undertakes an independent peer review process to review guidelines before accepting for publication

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What are we grading?

1. Certainty of Evidence

Degree of confidence that the available evidence **correctly reflects the theoretical true effect** of the intervention or service

- *High, moderate, low, very low*

2. Strength of Recommendation

The balance between the **certainty of supporting evidence**; the certainty about the **balance between desirable and undesirable** effects; the certainty/variability in **values and preferences** of individuals; and the certainty about whether the intervention represents a **wise use of resources**

- *Strong and conditional*

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- The systematic review that informed this guideline will be published in the journal Systematic Reviews at the same time that the guideline is published.
- Reviews that inform Task Force guidelines can be found on the Task Force website, or through the journal's Task Force collection.

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KQ1: What is the effectiveness of screening compared with no screening for chlamydia and/or gonorrhea in non-pregnant sexually active individuals?

KQ2: What is the comparative effectiveness of different screening approaches for chlamydia and/or gonorrhea in non-pregnant sexually active individuals?

KQ3: What is the relative importance that people place on the potential outcomes from screening for chlamydia and/or gonorrhea?

KQ 1 and 2 outcomes

a. Chlamydia/gonorrhea infection transmission: hierarchy using (i) incidence [# new cases during follow up/#population or person-years], (ii) prevalence [# positive tests/# in population at follow up time point], then (iii) index case management (as reported; could include # cases receiving treatment/# cases or also include partner notification and/or retesting/# cases) [females and males]
b. Cervicitis [females]
c. Pelvic inflammatory disease [PID; females]
d. Ectopic pregnancy [females]
e. Chronic pelvic pain (≥6 months duration) [females]
f. Infertility: unable to conceive with unprotected sex for 12 months or longer [females and males]
g. KQ2 only: Repeat infection/reinfection (proportion having positive test ≥3 months after the index infection; measurement may not distinguish between infection due to new exposure following treatment, treatment failure/nonadherence, false positives, or lack of initial treatment)
h. Negative psychosocial impact (i.e., anxiety, sexual relationship distress including partner violence, stigmatization, blame) from screening procedure, or based on results a positive diagnostic test or presumptive diagnosis (i.e., regardless of test results in those with symptoms or considered at very high risk due to partner diagnosis)
i. Serious** adverse drug reaction from antibiotic treatment (e.g., anaphylaxis, QTc interval prolongation/cardiac arrhythmias, severe colitis from Clostridium Difficile, hepatic toxicity, thrombocytopenia, hemolytic anemia; requiring hospitalization)

KQ3 outcomes:

a. Utilities/health state valuations
b. Non-utility, quantitative information on relative importance of benefits and harms (e.g., willingness to be screened, screening uptake, relative ratings/rankings, preference weights, willingness to pay, probability trade-offs)
c. Qualitative information indicating relative importance between benefits and harms
All outcomes will only be in relation to the primary outcomes for KQ 1 and 2.

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Recommendation

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- The Task Force recommends opportunistic screening of sexually active individuals under 30 years of age who are not known to belong to a high-risk group, annually, for chlamydia and gonorrhea at primary care visits, using a self- or clinician-collected sample (Conditional recommendation; very low-certainty evidence).

- Providers should refer to relevant national, provincial, or local guidance for screening of individuals known to belong to specific high-risk groups (i.e., exhibit high-risk behaviours).

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- To implement this screening recommendation, clinicians in primary care settings are advised to identify individuals who are eligible for screening (sexually active individuals under 30 years of age), not seeking care for a possible STI, and to offer chlamydia and gonorrhea screening opportunistically (i.e., without requiring a separate screening visit, and not only during sexual health visits). Results from one RCT identified in our review suggest that patient acceptance of screening is high when offered.

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- As individuals at high risk of chlamydia and gonorrhea infection may not always readily self-identify or be easily identified by clinicians, this routine offer of screening applies to all sexually active individuals without clinician knowledge of their membership of a high-risk group.
- STIs are associated with shame, embarrassment and significant stigma, which could prevent patients from seeking screening and treatment. Routinely offering screening to all sexually active individuals has been suggested as one way to reduce stigma associated with STI testing.
- Those seeking testing or who are known to belong to a high-risk group should be managed following relevant national, provincial, or local guidance applicable to those populations. Sexual activity can be generally defined as ever having oral, vaginal or anal intercourse.
- Informed consent, which is required for STI testing, is an additional implementation consideration. The main issues to address are those of privacy, reporting of positive test results to local public health offices, and potential partner notification.
- Screening for sexually transmitted infection may cause feelings of embarrassment and anxiety for some patients. Offering screening requires sensitivity to stigmatization and fear of social disapproval, especially regarding gender, culture, behaviour and other vulnerabilities.

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- There was very little evidence on the most appropriate screening interval. The body of evidence in KQ1 (screening versus no screening) suggests that a reduction in PID may be attainable for females interested and/or accepting one screening test with 1-year follow-up. Also, the one trial in KQ1 that tested for CT at baseline in both study arms (freezing the samples in the control arm until study completion) found that while fewer females had PID in the screening versus control arm at 1-year follow-up, most episodes of PID (79%) in the study population occurred in females who tested negative for CT at baseline (i.e., within the one-year window).

- While we did not identify evidence that would allow recommendation of specific screening strategies, acceptability and uptake of screening may be improved by minimally invasive sample collection methods, of which self-collected vaginal swabs from females and urine samples from males are the most accurate (NAAT). Clinician-collected swabs are likely acceptable and feasible during certain encounters (e.g. Pap testing). Ultimately patient preference and clinical scenario will likely dictate the preferred sampling method. Clinicians are reminded to consider pharyngeal and rectal swabs if clinically warranted, although we did not identify any evidence to evaluate screening at these sampling sites.
- We did not have sufficient evidence to make recommendations on one type of test or sampling site versus another.
- In cases of actual or suspected child abuse, clinicians are directed to their local, provincial and territorial authorities (public health offices, child protection services, pediatricians and clinical experts), for STI testing, treatment, reporting and management.

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- Results

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- There were no studies that matched exactly how screening is done in primary care in Canada (an opportunistic offer of screening by clinicians directly to patients during clinic visits).
- Generally there were three categories of studies, those that examined an offer to screen regardless of uptake (via mailed invite, public education and screening encouragement, or clinic-level packages to influence physician screening), those that only examined the outcomes in those who underwent screening (acceptors), and one study that used an offer to screen in a population that was pre-selected by having them complete a pre-screening questionnaire on chlamydia risk and then accepted a primary care appointment offer, which would select for those individuals interested in screening.

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- *Offer to* screen, regardless of uptake
    - Meta-analysis of 2 RCTs (n = 141,362) found very low-certainty evidence for little to no difference in PID rate among females aged 16-29 over 1 to 3 years using an annual offer of chlamydia screening via self-collected vaginal samples (0.3 more in 1000 [95% confidence interval [CI] 7.6 fewer to 11 more]).
- *Offer to screen, pre-selected individuals interested in screening*

    - One RCT (n= 2,607) among females aged 18-34 (81% under age 24) pre-selected based on completing a pre-screening questionnaire on chlamydia risk and then accepting a primary care appointment offer (suggesting an interest in being screened), found low-certainty evidence that offering a single chlamydia screening via clinician-collected cervical swabs may reduce PID (15.4 fewer per 1,000 [95% CI 3.0 to 21.3 fewer], NNS= 65 [95% CI 47 to 333]).

- *Acceptors of screening*
    - Two RCTs and one CCT (n = 30,652) found low-certainty evidence that females aged 15-29 who complete a single chlamydia screen over 12-18 months via self-collected vaginal or urine samples may have a reduced risk for PID over 1 year (5.7 fewer per 1000 [95% CI 10.8 fewer to 1.1 more].

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- *Offer to* screen, regardless of uptake
    - One RCT (n = 15,459) found very uncertain effects on infertility and very low-certainty evidence for little to no difference in ectopic pregnancy rates for females aged 21 to 24 over 9 years from a single offer of chlamydia screening via self-collected vaginal samples (0.2 more in 1000 [95% CI 2.2 fewer to 3.9 more]).
    - Note that here we differentiate between 'very low-certainty evidence' and 'very uncertain effects.' In some cases, evidence was of such low certainty that we were not able to draw any conclusions on the outcome. In these cases (here and in remaining slides) we have used the wording 'very uncertain.'
    - Meta-analysis of 3 RCTs (n = 41,709) found low-certainty evidence for little to no difference in chlamydia transmission for individuals aged 15-29 years over 1 to 3 years from a single offer of chlamydia screening via self-collected vaginal or urine samples (5.4 fewer per 1000 [95% CI 21.0 fewer to 12.6 more).

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- No studies on the effects of chlamydia screening on cervicitis, chronic pelvic pain, or male infertility were identified.
- No studies were identified on the effects of gonorrhea screening on any of the outcomes of interest in a general risk population.

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- One RCT reported on adverse events from antibiotics resulting from chlamydia screening.

- Ten uncontrolled cohort studies reported on psychosocial harms from chlamydia screening.
- No studies examined harms of screening for gonorrhea.
- The single RCT that reported on adverse events from antibiotics did not report any adverse events (n = 37,543 tested; n = 4,574 diagnosed with chlamydia; number treated not reported; very low-certainty evidence).

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- Cohort studies on the harms of screening were synthesized narratively, and provided low or very low-certainty evidence.
- low- or very low-certainty evidence indicated that undergoing screening may lead to feelings of stigmatization (e.g., guilt, embarrassment, social disapproval) or anxiety about future infertility, sexuality, or risk of infection in a small to moderate proportion of individuals (50-400 per 1,000 individuals screened). This data relates to individuals undergoing screening, so the number of individuals affected in the entire eligible population is likely smaller.
- We did not identify data that described the exact duration or severity of these symptoms.

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- Some data was identified for KQ2, looking at home versus clinic sampling strategies. However the evidence was of very low certainty, and studies were carried out in a way that makes them of limited applicability to primary care. No other comparisons of different screening strategies were identified.
- The one RCT that provided a more direct estimate of transmission (incidence) was carried out via outreach settings in a high prevalence population. The evidence of effect on incidence was of very low certainty.
- Three RCTs measured treatment rates, which we accepted as a surrogate of transmission. These also used methods that are less applicable to primary care such as outreach or mail invitations. This evidence was also of very low certainty.
- Eligible comparisons in the systematic review were:

  KQ2: Any screening comparison differing from the intervention by the following factors:
  a. Universal vs. risk-based testing
  b. Health care setting only: sample collection location (i.e., clinic/health care setting vs. home)
  c. Outreach screening only: offered through street-based (e.g. mobile van) vs. other venues (e.g. bars, community services, bath houses, sporting events)
  d. Sample collection method (i.e., NAAT vs culture; invasive [urethral or cervical swab] vs non-invasive [urine or self-collected vaginal swab]; genital vs. genital and extragenital [e.g., as determined suitable])
  e. Sample collection personnel (i.e., self vs. health care provider)

f. Screening interval (i.e., one-time vs. annual vs. other)
g. Case management approaches (i.e., retesting cases, method for partner notification/treatment)
Studies from KQ1 may be used to help answer (indirectly) KQ2, for example when effectiveness appears to differ between different studies using different screening interventions compared with no screening.

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- Patient values and preferences

[Slide 34]

- The systematic review by Pillay et al., assessed studies that looked at the relative importance of benefits and harms to patients. This included studies of health utilities (a measure of preference for being in a particular state of health; four studies), as well as survey or qualitative studies where patients provided their preferences (ten studies).
- Studies of health state utilities suggested that utility values were similar across the various benefits of screening. These do not take into account the duration of the health state, and once we did that, it appeared that the avoidance of infertility and chronic pelvic pain may be more important to females than ectopic pregnancy, PID, or cervicitis (low-to-moderate certainty).
- Note that studies of health utilities did not provide any information about harms of screening (i.e., only touch upon relative importance of potential benefits of screening).

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- When considering benefits relative to harms, surveys and qualitative studies found that individuals considering screening (7 studies; n = 777) or undergoing screening (3 studies; n = 77) placed greater relative importance on potential reproductive health and transmission benefits compared to anxiety or stigma of screening (very low-certainty evidence).
- No studies considered patient values related to adverse events from medication.

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- The Task Force patient engagement process, carried by our Knowledge Translation team at St. Michael's Hospital, involves two phases of surveys and focus groups with members of the public.
- At the protocol stage, 16 sexually active participants (9 identified as female, and 7 identified as male) aged 24 to 38 years rated the importance of screening outcomes via online survey and participated in a focus group to share their rationale for their ratings.

- After the evidence review was completed, 17 different sexually active participants aged 24 to 38 years (13 participants identified as male, 3 identified as female, one identified as non-binary) rated the importance of screening outcomes via online survey, this time after being provided with a summary of systematic review results.
- The patient engagement study indicated that patients likely prioritize potential benefits of screening (all rated critical or important) over harms (all rated important) and have a strong preference to be screened; this was the case even when participants were presented with the evidence and its uncertainty.

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- The Task Force also considered whether the recommendation for screening would be feasible and acceptable to a variety of stakeholders, as well as whether the recommendation might impact health equity.
- The Task Force judged that a recommendation to screen for chlamydia and gonorrhea would likely be feasible and acceptable for a wide range of stakeholders, given:
    - Screening is currently part of usual primary care practice
    - Non-invasive sampling and effective treatments exist
    - Current Canadian clinical and laboratory practice is to combine testing for CT and NG using a single sample
    - One RCT in the systematic review reported screening was accepted 80% of the time that it was offered

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- Routinely offering screening to all sexually active individuals could improve health equity by reducing important barriers to screening, such as fear of disapproval or discrimination and feelings of stigmatization, through normalization.
- Additionally, since females carry most of the burden of clinical consequences of infection, screening of males (a reservoir of infection for females) may improve health equity for females.

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- Rationale for recommendation

[Slide 40]

- The indirectness (low applicability) of available evidence to inform opportunistic screening in Canada represents a major source of uncertainty.

- PID may be reduced for those accepting and undergoing chlamydia screening and for those interested in being screened who are offered it (low certainty), however it may not when chlamydia screening is offered via mailed invitation or clinic-level packages encouraging screening (very low certainty).
- The Task Force judged that the true benefit of chlamydia screening when offered directly by Canadian primary care practitioners, who are positioned to identify those eligible and to offer screening opportunistically, would likely lie within this observed range of screening effectiveness.

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- The Task Force placed a lower priority on the very uncertain evidence of no serious adverse effects of antibiotic treatment for chlamydia and gonorrhea and uncertain evidence for psychosocial harms of screening (anxiety, shame and stigma) that are likely to be experienced by a small proportion of those eligible for screening.

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- Overall, the potential benefits of screening for chlamydia and gonorrhea to reduce PID in females, albeit very uncertain, were judged to outweigh possible harms. Evidence suggests that most Canadian patients also prioritize the benefits over the harms of screening for chlamydia and gonorrhea, even when provided with the evidence and its uncertainty. Therefore, considering the balance of benefits and harms as well as evidence uncertainty, the task force provides a conditional recommendation in favour of opportunistic screening for chlamydia and gonorrhea in primary care for individuals under 30 years of age.

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- The recommendation to screen individuals under 30 years of age is based on almost all of the underlying evidence coming from studies of individuals under 30 years of age. Further, the rates of chlamydia and gonorrhea are increasing among those aged 25-29 years in Canada, with rates and total cases similar to those aged 15-19 years. Conversely, rates of chlamydia for those aged 30-39 are less than half those for individuals 15-19 and 24-29, and less than one quarter of those for individuals aged 20-24. Similarly, rates in those 40-59 are less than a quarter of those in individuals aged 30-39.
- Considering the properties of sexual networks, this recommendation to also screen sexually active males is intended to reduce chlamydia and gonorrhea infection and its negative consequences in females, through their role in the transmission of these infections (although there were no available studies informing this rationale).
- The recommendation to also screen for gonorrhea was made (despite the lack of available evidence) given that many gonorrhea cases are asymptomatic, up to 40% of those with gonorrhea may have concurrent chlamydia and current Canadian clinical and laboratory practice is to combine testing for

gonorrhea with chlamydia using a single sample (most commercial nucleic acid amplification test (NAAT) assays test for both organisms simultaneously with a single specimen). The incremental costs of screening for both chlamydia and gonorrhea (versus, for example, chlamydia alone) is uncertain but likely minimal, as many provincial schedules already include NAAT for chlamydia and gonorrhea together under a single price.

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- A conditional recommendation is used when:
    - The desirable effects probably outweigh the undesirable effects (conditional recommendation in favour of an intervention) or undesirable effects probably outweigh the desirable effects (conditional recommendation against an intervention) but appreciable uncertainty exists.

- This recommendation is conditional due to the low certainty of the available evidence.

[Slide 45]

- Knowledge gaps and next steps

[Slide 46]

- We did not identify any trials that carried out screening for chlamydia or gonorrhea in a manner consistent with how screening is offered directly to patients, opportunistically, in Canadian primary care. There was also limited evidence on health outcomes of screening for chlamydia or gonorrhea in men or their specific female partners (considering sexual networks).

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- Almost no studies included participants over the age of 30 (which may be due to the low prevalence in this population). Studies comparing the impacts of different screening intervals or different screening strategies in primary care settings on health outcomes are required.

[Slide 48]

- Knowledge translation (KT) tools

[Slide 49]

- Knowledge Translation

- A KT tool has been developed to **help clinicians and individuals understand** the chlamydia and gonorrhea screening guideline.
- After the public release, this tool will be **freely available** for download in both **French** and **English** on the website: http://canadiantaskforce.ca.

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- We have also developed an infographic to help patients better understand the processes involved in screening for chlamydia and gonorrhea.
- After the public release, this tool will also be **freely available** for download in both **French** and **English** on the website: http://canadiantaskforce.ca.
- We also have a social media campaign with images and videos that can shared on platforms used by those under 30 such as Instagram.
- Partner communications with spokespeople institutions (e.g. McMaster) to share on social media, do website article etc. to highlight faculty involvement. Also with endorsers who may want to communicate their endorsement and GL info to their stakeholders.

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- Conclusions

[Slide 52]

- Opportunistic screening for chlamydia and gonorrhea among sexually active individuals under 30 years of age confers uncertain but potentially important benefits, particularly for PID in females.
- Psychosocial harms of screening are anticipated to be relatively mild, and patients likely prioritize potential screening benefits over harms.
- The Task Force conditionally recommends in favor of screening sexually active individuals under 30 years of age not known to belong to a high risk group for chlamydia and gonorrhea at primary care visits. Informed consent is required for screening.

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

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- Questions & Answers
- Thank you