Canadian Task Force for Preventive Health Care (CTFPHC) guidelines' quality assessment and comparison with other guidelines with similar scope

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Research Team

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Abbreviations and acronyms

AAA:	Abdominal Aortic Aneurism
AAFP:	American Academy of Family Physicians
AB-HS:	Alberta Health Service (Alberta Provincial Genitourinary Tumour Team)
ACP:	American College of Physicians
ACS:	American Cancer Society
BC:	British Columbia Guidelines
CASL:	Canadian Association for the Study of the Liver
CAR:	Canadian Association of Radiology
CCO/PEBC:	Cancer Care Ontario's Program in Evidence-based Care
CDC:	Centers for Disease Control and Prevention
CSVS:	Canadian Society of Vascular Surgery
CTFPHC:	Canadian Task Force on Preventing Health Care
CUA:	Canadian Urological Association
FIT:	Fecal immunochemical test
gFOBT;	guaiac fecal occult blood test
HCV:	Hepatitis C Virus
IDSA:	Infectious Diseases Society of America
TOP:	Toward Optimized Practice Clinical Practice Guidelines
USPSTF:	U.S. Preventive Services Task Force.
V&P:	Values and Preferences
Y:	Years

CTFPHC Guidelines Comparison Project

Introduction

The Strategy for Patient-Oriented Research (SPOR) Evidence Alliance is a Canada-wide alliance of researchers, healthcare providers, patients, policy makers and other knowledge users. The SPOR Evidence Alliance was established to provide national coordination and project management in support of knowledge synthesis, clinical practice guideline development, relevant knowledge translation, and patient-oriented research.

The Canadian Task Force on Preventing Health Care (CTFPHC) develops preventive health care guidelines for primary care practitioners on a variety of topics. The CTFPHC produces on average three guidelines per year, following a systematic methodology with input from task force members, patients, content experts and different stakeholders. The CTFPHC has requested the SPOR Alliance to perform a quality assessment and comparison of selected CTFPHC guidelines with guidelines from national or international organizations (non-CTFPHC) on specific topics.

Objective

The objective of this project was to compare a set of selected guidelines from the CTFPHC with national and international guidelines similar in scope, according to their characteristics and methodological quality to identify the potential factors behind the differences in the recommendations from both groups.

Methodology

This project involved four stages: 1) Guidelines' selection process; 2) Summary of guidelines' characteristics and main recommendations from guidelines; 3) Quality assessment of the guidelines (both CTFPHC and non-CTFPHC); and 4) Analysis of the differences between CTFPHC and non-CTFPHC guidelines.

Guidelines' selection process

The CTFPHC prioritized and requested an evaluation of the following guidelines:

- Colorectal cancer (2016) [1]
- Breast cancer (2018)[2]
- Cervical cancer (2013)[3]
- Prostate cancer (2014)[4]
- Lung cancer (2016)[5]
- Abdominal Aortic Aneurysms (2017)[6]
- Hepatitis C (2017)[7]

- Asymptomatic Bacteriuria in Pregnancy (2018)[8]
- Developmental delay (2016)[9]

Additionally, the CTFPHC was interested in evaluating and comparing their guidelines (CTFPHC) with guidelines similar in scope and settings (non-CTFPHC). As per request, our team developed a systematic search of guidelines that could be "matched" to the CTFPHC guidelines. We conducted focused literature searches in ECRI- National Guidelines' Clearinghouse, Pubmed and in Canadian and/or American specialty and professional societies related to each one of the nine topics of the CTFPHC topics. We selected and prepared a list of 88 guidelines as candidates to be compared with the CTFPHC guidelines trying to match as much as possible the scope and the date of publication. We categorized them in three categories: Canadian, US, and International Guidelines. Appendix 1 presents the full list of candidate guidelines.

The CTFPHC used the list candidate guidelines to conduct a survey among the Task Force members to select the most appropriate guidelines for comparison. This process was designed and conducted by the CTFPHC team. Finally, a list of 24 non-CTFPHC guidelines was selected and sent to our team. We, therefore, evaluated and compared the 9 CTFPHC guidelines with the selected comparators. In total, 33 guidelines were included in our analyses.

Summary of guidelines' characteristics and main recommendations

We reviewed all the documents related to the included guidelines (including appendices and/or supplementary files). Independently and in duplicate, two experienced reviewers extracted relevant information from each guideline such as: scope, year of publication, scope, use of GRADE approach to summarize the evidence and develop the recommendations from both guidelines' groups CTFPHC and Non-CTFPHC. We also extracted a summary of the evidence of effectiveness and the harms, and the additional considerations to develop the recommendations, such as values and preferences recommendations, costs/resources considerations, and feasibility and applicability considerations for each recommendation.

Quality assessment of the guidelines

We assessed the quality of the guidelines with the AGREE II instrument[10]. AGREE II is a validated instrument composed by 23 items grouped under 6 domains and one final item to evaluate the overall quality of the CPG. The domains are *Scope and Purpose* (3 items), *Stakeholder Involvement* (3 items), *Rigour of Development* (8 items), *Clarity of Presentation* (3 items), *Applicability* (4 items), and *Editorial Independence* (4 items). For each item, each appraiser scores based on the statement, using a Likert scale from 1 ((Strongly disagree) to 7 (Strongly agree). A score between 2 and 6 was assigned when the item did not meet the full criteria or considerations. A score was assigned depending on the completeness and quality of reporting, following AGREE II manual indications.

Each CPG was evaluated by two experienced assessors who independently provided their scores. When items' scores from both reviewers differed by 2 points or less in the Likert scale, we calculated the scores per domain following the recommendations by the AGREE collaboration. Namely, the domain scores were calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. When the difference among the scores assessors was 3 or more points, the disagreement was resolved by consensus. Final scores per domain were calculated, i.e., each CPG obtained 6 scores that ranged from 0 to 100%. All the assessments will be performed using the AGREE-PLUS online tool (http://www.agreetrust.org/resource-centre/agree-plus/).

For this project we selected a cut-off for high-quality CPGs of 60% or more, to determine the highest quality for each domain. Moreover, the cut-offs for low and moderate quality were set in <40%, and 40%-59%, respectively. Although to facilitate results presentation, we used a colour-coded display using green as high quality, yellow as moderate quality and red as low-quality guidelines.

Analysis of the differences between CTFPHC and non-CTFPHC guidelines

We present a narrative summary of the differences in recommendations, among the guidelines of the same scope based on the comparison descriptive analyses and the quality assessment. We performed a descriptive analysis trying to explain the differences in the recommendations, considering differences in terms of the characteristics of the guidelines (e.g., year of publication, organization,) use of GRADE, conflicts of interests), quality of the evidence that supports the recommendations, strength and direction of the recommendations, consideration of costs and resource implications, considerations of values and preferences, and the quality of the guidelines (AGREE scores, with emphasis on the rigor of development domain).

Results

Guidelines and comparators

We analyzed 9 CTFPHC guidelines and compared them to 24 non-CTFPHC guidelines (See table 1). Five of the CTFPHC guidelines are focused on the screening for the early detection of cancer (colorectal, breast, cervical, prostate and lung cancer). The screening for colorectal cancer guideline[1] was published in 2016 and was compared with three guidelines: the U.S. Preventive Services Task Force (USPSTF)[11], the Cancer Care Ontario/Program in Evidence Based Care (CCO/PEBC)[12], the Toward Optimized Practice Clinical Practice Guidelines from Alberta (TOP)[13], and the British Columbia Guidelines (BC-Guidelines)[14]. The screening for breast cancer guideline[2] was published in 2018 and was compared to three guidelines: the USPSTF[15], American Cancer Society (ACS)[16], and TOP[17]. The screening for cervical cancer guideline[3] was published in 2013 and was compared with the USPSTF[18], the TOP[19] and the American Academy of Family Physicians (AAFP)[20]

guidelines. Prostate cancer guideline[4] was published in 2014, and was compared with USPSTF[21], Canadian Urological Association (CUA)[22] and Alberta Health Services (AB-HS)[23]. Lastly, the screening for lung cancer guideline[5] was published in 2016 and it was compared with the USPSTF[24], the Cancer Care Ontario/Program in Evidence Based Care (CCO/PEBC)[25], and the Canadian Association of Radiologists (CAR)[26] guidelines.

The remaining four guidelines were focused on non-cancer screening, including the detection of infectious diseases (hepatitis C and asymptomatic bacteriuria), a vascular disorder (abdominal aortic aneurysm) and a neurocognitive disorder (developmental delay and the early detection of autism disorder). The screening for hepatitis C guideline[7] was published in 2017 and was compared with guidelines from the USPSTF[27], the Center for Disease Control and Prevention (CDC)[28], and the Canadian Association for the Study of the Liver (CASL)[29]. The screening for asymptomatic bacteriuria in pregnancy guideline[8] was published in 2018 and it was compared with the Infectious Diseases Society of America (IDSA) guideline[30]. The screening for abdominal aortic aneurysms guideline[6] was published in 2017 and it was compared with the USPSTF[31] and the Canadian Society for Vascular Surgery (CSVS)[32] guidelines. Lastly, the screening for developmental delay guideline[9] was published in 2016 and it was compared with the USPSTF[33] guideline only.

General characteristics of the guidelines and quality assessments

Guidelines' main characteristics are detailed in table 1. Additional guidelines information is provided in appendices. Appendix 2 presents each guideline recommendation with the evidence summary of effectiveness and harms, and the reported literature that supports the recommendations. Appendix 3 presents each guideline with the additional factors considered for developing the recommendations, values and preferences, costs and feasibility/acceptability issues.

Quality assessments per AGREE II domain are presented in appendix 4. In all the diseases/scopes, except for hepatitis C and breast cancer, the CTFPHC guideline was judged to be the highest quality guideline, based on the rigor of development domain. For hepatitis and breast cancer, the guidelines with the highest domain 3 scores were the CDC (90%) and the ACS (guidelines obtained a higher score in the mentioned domain).

Recommendations from each guideline are displayed and compared in table 2. For each CTFPHC guideline recommendation recommendations from non-CTFPHC guidelines are presented. Table 2 also presents the AGREE II scores per domain for each guideline. Color codes per domain show the three categories: high (green), moderate (yellow) and low quality (red).

Analysis of the differences in the recommendations among the guidelines

Table 2 presents each topic covered and the recommendations provided by the guidelines along with the quality assessment. The last two columns of the table display the similarities and differences among the guidelines per topic and the potential explanations for disagreements among them.

For colorectal cancer, 5 guidelines were analyzed (CTFPHC, USPSTF, CCO/PEBC, TOP and BC). The CCO/PEBC guideline did not consider screening in their scope and therefore, although its quality was assessed, it was not analyzed. We found that the guideline from CTFPHC was the best and the only one categorized as of high-quality. CTFPHC conducted a deeper analysis of the evidence (establishing differences in the strength of the recommendation by age subgroups and prioritizing direct over indirect evidence for gFOBT, to recommend this test as an alternative), and a systematic consideration of values and preferences and costs (which allowed the panel to recommend FIT as an additional alternative). Lower-quality guidelines (TOP and BC) did not provide a strength of recommendations and did not explicitly consider other factors to develop their recommendations. USPSTF was a moderate quality guideline with some differences with CTFPHC such as in the age subgroups, in the frequency of the recto-sigmoidoscopy and the recommendation of FIT. In summary, a higher quality guideline produced by the CTFPHC was found to be related to the considerations of factors to support the recommendation (Values and preferences and costs) and to a deeper analysis of the evidence (i.e., subgroups, and direct evidence).

In breast cancer, we found that three of the four guidelines (CTFPHC, USPSTF and ACS, not TOP) were judged to be of high quality. Guidelines agreed on not recommending screening in women <40 or 45y, and on recommending it for women aged 50-74y. Guidelines, however, differed in the age thresholds for the screening, in the strengths of some recommendations and in the frequency for screening. In summary, guidelines quality did not play a major role in explaining the differences among ACS, CTFPHC and USPSTF as the three of them were of high quality. The low certainty of the evidence supporting the breast cancer screening creates a scenario in which the recommendations may vary depending on additional contextual factors, in this case values and preferences, costs (efficiency) and feasibility played a role in explaining differences.

For cervical cancer screening, we analyzed four guidelines (CTFPHC, USPSTF, TOP and AAFP). The first three guidelines focused on screening while the AAFP guideline focused on diagnosis and treatment of cervical cancer. CTFPHC was the only one considered as of high quality (Score domain 3 was 75%), while the USPSTF was considered as moderate quality, and TOP as low quality. The three guidelines agreed on recommending screening for women 25-65y. Minor differences were found in younger ages, and in the strength of the recommendation. In summary, quality of guidelines cannot explain the differences among the guidelines, in part because the highest quality guideline (CTFPHC) is the least recent guideline, and we found that key evidence on women <30y was missed by this guideline, potentially influencing final guideline recommendations. Date of publication seems to be the main role in explaining differences among the guidelines.

For prostate cancer guidelines, we evaluated the CTFPHC and four more guidelines (USPSTF, ACP, CUA and Alberta). All but the CTFPHC were considered of moderate (USPSTF ACP and CUA) and low (Alberta) quality. Guidelines agreed on most of the recommendations, with some

disagreements in terms of strength of the recommendations and in age ranges. These differences can be explained by the quality of the guideline, the uncertainty of the evidence and the benefits/harms balance analysis. The high-quality guideline (CTFPHC) made an analysis of the benefits/harms (considered many false positives of the prostate-specific antigen and the harms derived from the biopsy derived from those false positives) and found no impact on mortality with screening (55-70y). Moreover, moderate quality guidelines (ACP and USPSTF) recommend individualized decisions according to patients' preferences. Lastly, low-quality guidelines (CUA and AB) relied more on the life expectancy rather than on the quality of the evidence.

The lung cancer screening guidelines (CTFPHC, USPSTF and CAR) provided similar recommendations with differences in their age limits and in when to stop the screening (CTFPHC suggests stopping after three negative results). The CCO/PEBC guideline suggested by the CTFPHC did not have recommendations for lung cancer screening, only diagnosis and treatment, and therefore it was not analyzed. CTFPHC and USPSTF guidelines were judged as of high quality; the CTFPHC guidelines had the highest quality scores, and CAR was judged as a low-quality guideline. The high agreement among guideline recommendations can be explained by two factors: high-quality evidence used by all the guidelines (NLST trial), and one guideline (CAR) used the other two guidelines (CTFPHC and USPSTF) as an evidence/information resource. In summary, guideline quality did not play a major role in explaining the differences in the recommendations. CTFPHC and USPSTF were of high quality and CAR, although of low quality, used information from CTFPHC and USPSTF to develop their recommendations. The lack of appropriate evidence to support certain decisions (e.g., when to stop screening) opened the scenario to heterogeneity (three consecutive screenings vs no limit), while introduction of indirect evidence (i.e., modelling studies) allowed some differences in age limits.

Regarding hepatitis C guidelines, we analyzed four guidelines (CTFPHC, USPSTF CDC and CASL). All guidelines (except USPSTF that was judged as a moderate-quality guideline), were judged as of high quality. We found that CTFPHC was the only one that recommended against screening of non-high-risk individuals. Differences among guidelines may partially explain differences in the recommendations for three reasons: the evidence's target (direct evidence in CTFPHC vs indirect in the rest), the evidence quality assessment (CTFPHC considering the low quality, vs the rest not considering the low quality), values/preferences, feasibility/acceptability, and costs considerations (only in CTFPHC), and the date (CTFPHC search on 2016, while USPSTF in 2020, considering treatment evidence).

The screening for abdominal aortic aneurysm was covered by three guidelines: CTFPHC, USPSTF and the CSVS guidelines. In general, recommendations are very similar. Quality varied among them. CTFPHC was the only high-quality guideline, while the USPSTF was judged as of moderate quality and the CSVS as a low-quality guideline. The USPSTF made different recommendations; they did not recommend screening in women with no smoking history. Guidelines' quality does not explain the differences in the recommendations. However, quality may

explain the differences in the strength in the recommendations. CTFPHC and to a lesser degree the USPSTF, acknowledge the uncertainty when considering the evidence and provide a "weak" or "B" recommendation; CSVC (low quality guideline), on the other hand, provides a strong recommendation.

For asymptomatic bacteriuria in pregnancy, we analyzed two guidelines (CTFPHC and IDSA). Both guidelines were considered high quality with the CTFPHC guideline having better scores. Both guidelines recommended screening pregnant women. Differences are related to the strength of recommendations and different evidence focus (CTFPHC considered direct evidence of effectiveness comparison of screening vs no screening, which was scarce and of low quality, while IDSA considered evidence from antibiotic treatment vs no treatment, not direct evidence of screening vs no screening). Thus, the higher quality guideline conducted a deeper evidence assessment explain the differences in the strength of the recommendations.

Lastly, for developmental delay we analyzed two guidelines (CTFPHC and USPSTF). Both were judged as high quality with CTFPHC having higher scores. Both guidelines had important differences including their scope, recommendations and the evidence that was considered. The CTFHC guideline's scope focused on screening to identify any developmental delay. Meanwhile, the USPSTF guideline is focused on detecting autism disorder. This, in turn, explains differences in the evidence considered: CTFPHC focused on evidence about screening while USPSTF focused on identifying tools focused exclusively on autism. In the end, CTFPHC recommend against (considering the low-quality evidence of the screening tool) and USPSTF did not provide a recommendation. In summary, the scope and purpose of the guidelines was the major factor to explain the differences in the recommendations.

Conclusions

Guidelines developed by the CTFPHC were found to be of high quality. In all the cases (nine topics), except for lung cancer and hepatis C screening guidelines, the CTFPHC was the highest quality guideline for a particular disease/scope. Our in-depth analysis of the guidelines and their recommendations considering their quality, the assessed evidence, the analysis of the benefits and harms balance, the considerations of values and preferences, costs and applicability and feasibility issues, among others, yielded some potential explanations to the identified differences.
The quality of the guidelines as defined by the AGREE instrument assessment may explain the differences in the recommendations between CTFPHC guideline and the non-CTFPHC guidelines, in 4 topics (Colorectal, prostate, abdominal aortic aneurism, asymptomatic bacteriuria in pregnancy). The rest of the topics either had minor differences in the recommendations, or the differences were mostly explained by other factors such as differences in the scope of the guideline (developmental delay), in the date of publication (cervical cancer), in the relative value given by guideline panels (Breast cancer), lack of evidence for some key decisions recommended and the use of indirect evidence (lung cancer) or a combination of factors (hepatitis C).

Table 1. General characteristics of guidelines

1.1. Colorectal cancer

Guidelines' organization/author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for colorectal cancer in primary care	2016	Mar 2016	Canada	Screening	Yes	Public Health Agency of Canada and the Canadian Institutes of Health Research	None declared.	https://www.cmaj.ca/content/cmaj/188/5/340.full.pdf
USPSTF	Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement	2002	Jun 2016	United States	Screening for asymptomatic patients over 50 years old for CRC	No	The USPSTF is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.	All authors have completed and submitted the ICMJE Form for Disclosure of	https://jamanetwork.com/journals/jama/fullarticle/2529486
CCO	Guideline for referral of patients with suspected colorectal cancer by family physicians and other primary care providers	2014	Aug 201	Canada/ Ontario	Family physicians and other primary care providers	No	The work of the PEBC is supported by the Ontario Ministry of Health and Long-Term Care through CCO, and the PEBC is editorially independent from its funding source.	None declared	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4131960/pdf/0600717.pdf
TOP	Colorectal cancer screening: clinical practice guideline. Edmonton, AB: Toward Optimized Practice.	2013	Jan 2020	Canada/ Alberta	Asymptomatic men and women of all ages	No	Cancer Control Alberta operating budget	Conflicts of interests disclosed following G-I-N principles	http://www.topalbertadoctors.org
BC Guidelines	Colorectal Screening for Cancer Prevention in Asymptomatic Patients	2013	Jun 2016	Canada	Detection of colorectal cancer and adenomas in asymptomatic patients, aged ≥ 19 years.	No	Not mentioned	Not mentioned	https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/colorectal_screening.pdf

1.2 Breast Cancer

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for breast cancer in women aged 40–74 years who are not at increased risk for breast cancer	2018	Jan 2017	Canada	This guideline updates the task force's previous recommendations for primary care providers on breast cancer screening for women aged 40 to 74 years who are not at increased risk of breast cancer.	Yes	The Public Health Agency of Canada.	None declared.	https://www.cmaj.ca/content/cmaj/190/49/E1441.full.pdf
USPSTF	Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement	2016	Feb 2016	United States	Asymptomatic women 40 years or older who do not have preexisting breast cancer or a previously diagnosed high-risk lesion and who are not at high risk for breast cancer because of a known underlying genetic mutation or a history of chest radiation	No	The USPSTF is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.	CoI disclosed	https://www.acpjournals.org/doi/10.7326/M15-2886
ACS	ACS Releases Guideline on Breast Cancer Screening // Breast Cancer Screening for Women at Average Risk. 2015 Guideline Update From the American Cancer Society	2015	Sept 2015	United States	Not mentioned	No	Not mentioned	Not mentioned	https://www.aafp.org/afp/2016/0415/p711.pdf https://jamanetwork.com/journals/jama/fullarticle/2463262
TOP	Breast Cancer Screening	2013	Not stated	Canada/ Alberta	Asymptomatic women of all ages	No	Not mentioned	Not mentioned	https://actt.albertadoctors.org/CPGs/Lists/CPGDocumentList/Breast-Cancer-Screening-CPG.pdf
BC-Guidelines	Colorectal Screening for Cancer Prevention in Asymptomatic Patients	2013	Jun 2016	Canada	Detection of colorectal cancer and adenomas in asymptomatic patients, aged ≥ 19 years.	No	Not mentioned	Not mentioned	https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/colorectal_screening.pdf

1.3 Cervical Cancer

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for cervical cancer	2013	Apr 2012	Canada	Screening for cervical cancer in Canada	Yes	Funding for the Canadian Task Force on Preventive Health Care is provided by the Public Health Agency of Canada and the Canadian Institutes of Health Research.	None of the members of the guidelines writing group (listed at the end of the article) have declared competing interests.	https://www.cmaj.ca/content/185/1/35
USPSTF	Screening for Cervical Cancer USPreventive Services Task Force Recommendation Statement	2018	Feb 2017	United States	Update the US Preventive Services Task Force (USPSTF) 2012 Recommendation on screening for cervical cancer.	Yes	The USPSTF is an independent, voluntary body. The US Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.	All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Two authors reported conflicts. One author reported grant from HPV vaccine manufacturer, one author received funding from government to promote HPV vaccination	https://jamanetwork.com/journals/jama/fullarticle/2697704
TOP	Cervical Cancer Screening Clinical Practice Guideline	2016	Not stated	Canada	The recommendations reflect the CTFPHC guidelines published in 2013 as well as cervical cancer screening approaches in other jurisdictions across Canada and elsewhere.	No	Not stated	No information	https://actt.albertadoctors.org/CPGs/Lists/CPGDocumentList/Cervical-Cancer-Screening-CPG.pdf#search=cervical
AAFP	Cervical Cancer: Evaluation and Management	2018	2017	USA	Not specified	No	Not stated	Author disclosure: No relevant financial affiliations.	https://www.aafp.org/afp/2018/0401/p449.html

1.4 Prostate Cancer

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for prostate cancer with the prostate-specific antigen test	2014	Aug 2014	Canada	Provide recommendations on screening for prostate cancer using the PSA test with or without digital rectal examination in men in the general population.	Yes	Funding for the Canadian Task Force on Preventive Health Care is provided by the Public Health Agency of Canada and the Canadian Institutes of Health Research	None of the authors (members of the guideline writing group) have declared competing interests.	https://www.cmaj.ca/content/186/16/1225
ACP	Screening for Prostate Cancer: A Guidance Statement From the Clinical Guidelines Committee of the American College of Physicians	2013	Aug 2012	United States	Guidance statement to critically review available guidelines to help guide internists and other clinicians in making decisions about screening for prostate cancer	No	Financial support for the development of this guideline comes exclusively from the ACP operating budget	CoIs disclosed. No relevant CoIs.	https://www.acpjournals.org/doi/full/10.7326/0003-4819-158-10-201305210-00633?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
Alberta Provincial Genitourinary Tumour Team	Prostate Cancer	2015	Dec 2014	Canada / Alberta	Guideline to describe the appropriate management and follow up strategies for prostate cancer.	No	No information	COI disclosure but relationships with industry although present, not descried in detail	https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-gu004-prostate.pdf
CUA	Canadian Urological Association recommendations on prostate cancer screening and early diagnosis	2017	Feb 2017	Canada	Provide guidance on the current best prostate cancer screening and early diagnosis practices and to provide information on new and emerging diagnostic modalities.	Yes	No information	The authors report no competing personal or financial interests	https://cuaj.ca/index.php/journal/article/view/4888
USPSTF	Screening for Prostate Cancer USPreventive ServicesTaskForce Recommendation Statement	2018	Jul 2017	United States	To update the 2012 USPSTF recommendation on prostate-specific antigen (PSA)– screening for prostate cancer and subsequent treatment of screen-detected prostate cancer.	Yes	The USPSTF is an independent, voluntary body. The US Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.	CoIs declared and handled following IMCJE policy.	https://jamanetwork.com/journals/jama/fullarticle/2680553

1.5 Lung Cancer

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for lung cancer	2016	Jan 2016	Canada	This guideline is intended to provide primary care providers and policymakers with guidance on screening for lung cancer, and replaces the previous 2003 Canadian Task Force on Preventive Health Care recommendations.	Yes	Funding for the Canadian Task Force on Preventive Health Care is provided by the Public Health Agency of Canada. The Cancer Risk Management Model has been made possible through a financial contribution from Health Canada, through the Canadian Partnership Against Cancer.	Competing interests: None declared.	https://canadiantaskforce.ca/guidelines/published-guidelines/lung-cancer/
USPSTF	Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement	2013	Dec 2012	United States	Focused on the evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) in improving health outcomes.	No	The USPSTF is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.	COIs declared	https://doi.org/10.7326/M13-2771
CCO/PEBC	Referral of Suspected Lung Cancer by Family Physicians and Other Primary Care Providers	2019	May 2018	Canada /Ontario	This report focuses on patients presenting to primary care with signs or symptoms of lung cancer. Screening studies were excluded because they include asymptomatic patients.	No	The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.	CoIs declared. One author declared receiving grant from CCO, and another author received a grant from BrachyVisionTM for lung cancer brachytherapy.	https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/216
CAR	Canadian Association of Radiologists: Guide on Computed Tomography Screening for Lung Cancer	2016	Not stated	Canada	These guidelines are meant to be recommendations based on the literature currently available, regarding the best practice to carry out lung cancer screening.	No	This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.	No information	http://dx.doi.org/10.1016/j.carj.2017.01.002

1.6 Hepatitis C

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on heptatitis C screening for adults	2017	Sept 2016	Canada	The recommendations are intended to provide clinicians and policymakers with guidance on screening asymptomatic Canadian adults for HCV	Yes	the Public Health Agency of Canada	Competing interest: none declared	https://www.cmaj.ca/content/cmaj/189/16/E594.full.pdf
USPSTF	Screening for Hepatitis C Virus Infection in Adults: U.S. Preventive Services Task Force Recommendation Statement	2020	Sept 2019	USA	To update its 2013 recommendation, the USPSTF commissioned a review of the evidence on screening for HCV infection in adolescents and adults.	No	US Preventive Services Task Force	CoI disclosed	https://jamanetwork.com/journals/jama/fullarticle/2762185
CDC	Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965	2012	Jul 2011	USA	Evaluate the effect of a birth-year based testing strategy versus the standard of care for identification of HCV infection b) HCV testing (versus no testing) among adults at average risk for infection who were born during 1945–1965	Yes	CDC	CoIs disclosed-No members' activities were restricted based on the information disclosed.	https://www.cdc.gov/mmwr/pdf/rr/rr6104.pdf
CASL	The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver	2018	Oct 2017	Canada	to assist physicians and other health care professionals in the management of adult patients with chronic HCV infection. it makes recommendations on the assessment, evaluation and management (treatment) in many specific scenarios and risk based considerations	No	Canadian Association for the Study of the liver	All members signed a commitment and competing interest statement. Individuals with relevant disclosure were not excluded form voting recommendations. Association´s executive evaluate the presence of commercial bias. No funding was provided to the panel	https://www.cmaj.ca/content/190/22/E677

1.7. Asymptomatic Bacteriuria in pregnancy

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for asymptomatic bacteriuria in pregnancy	2018	Oct 2017	Canada	provides patients, clinicians and policymakers with guidance on screening for asymptomatic bacteriuria in pregnancy	Yes	the Public Health Agency of Canada	competing interest: none declared	https://www.cmaj.ca/content/cmaj/190/27/E823.full.pdf
IDSA	Clinical Practice Guideline for the management of asymptomatic bacteriuria: 2019 update by the infectious disease society of America	2018	Jun 2017	USA	to provide evidence-based guidance on the screening and treatment of ASB in populations where ASB has been identified as common or potentially detrimental. Pregnant and non-pregnant women, child and other high-risk population for ABS	Yes	IDSA	CoI disclosed. Nine authors declared financial conflicts with industry one-time	https://www.idsociety.org/practice-guideline/asymptomatic-bacteriuria/

1.8 Abdominal Aortic Aneurysm

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for abdominal aortic aneurysm in primary care	2017	Jan 2017	Canada	This guideline presents recommendations on AAA screening in asymptomatic adults for primary care providers.	Yes	Public Health Agency of Canada.	No relevant financial CoIs declared No other competing interests were declared.	https://www.cmaj.ca/content/cmaj/189/36/E1137.full.pdf
CSVS	2018 Screening for abdominal aortic aneurysms in Canada: Review and position statement from the Canadian Society of Vascular Surgery	2018	Not stated	Canada	Not mentioned	Yes	Not mentioned	NONE (all authors)	https://vascular.ca/resources/Documents/Clinical-Guidelines/FINAL-2018-CSVS-Screening-Recommendations.pdf
USPSTF	Screening for Abdominal Aortic Aneurysm: U.S. Preventive Services Task Force Recommendation Statement	2014	Sept 2013	United States	These recommendations apply to asymptomatic adults aged 50 years or older.	No	The USPSTF is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.	COI disclosed; No relevant declared.	https://jamanetwork.com/journals/jama/fullarticle/2757234

1.9. Developmental Delay

Guidelines organization/ author	Title	Publication year	Date last search	Country/ province	Scope	Use of GRADE Yes/No	Funder	Conflicts of interests' disclosure	Link to the guideline
CTFPHC	Recommendations on screening for developmental delay	2016	Sep 2015	Canada	This guideline presents evidence-based recommendations for primary care providers on screening for developmental delay in children aged one to four years with no apparent signs of such delay in primary care settings.	Si	Funding for the Canadian Task Force on Preventive Health Care is provided by the Public Health Agency of Canada and the Canadian Institutes of Health Research. The views of the funding bodies have not influenced the content of the guideline.	Competing interests: None declared.	https://canadiantaskforce.ca/guidelines/published-guidelines/developmental-delay/
USPSTF	Screening for Autism Spectrum Disorder in Young Children	2016	Aug 2014	USA	This recommendation applies to children who have not been diagnosed with ASD or developmental delay and for whom no concerns of ASD have been raised by parents, other caregivers, or health care professionals.	No	The USPSTF is an independent, voluntary body. The US Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.	CoIs declared.	https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/autism-spectrum-disorder-in-young-children-screening

Table 2. Guidelines' quality and recommendations' analyses

Guidelines Organization	Target population	Recomendations	AGREE Domain scores						Analysis and differences among guidelines	Explanations
			1	2	3	4	5	6		
Screening for Colorectal Cancer										
CTFPHC 2016	Adults 60-74y	Recommends screening with FOBT (gFOBT or FIT) every two years or flexible sigmoidoscopy every 10 years. **(Strong recommendation)**	**100 %**	**58%**	**70%**	**97%**	**77%**	**67%**	Similarities All guidelines agree: Not Rec. screening in >75y All guidelines Rec. screening between 50-75y, not in <50y Differences: ***Screening method & frequency*** CTFPHC: FOBT (FIT or gFOBT) USPSTF: Any (FOBT or sigmoido-/colonoscopy) TOP & BC: FIT (not specified) Also, CTFPHC analyzed evidence about the frequency allowing the panel to recommend Sigmoidoscopy every 10y, while USPSTF recs is based on indirect evidence (modelling studies) ***Age groups:*** CTFPHC: Strong Rec. 60-74y; Weak Rec. 50-60y (subgroups based on effectiveness & safety evidence) USPSTF also Rec. individual decision in 76-85y Rest of guidelines Recs for 50-70 or 75y group, No subgroups in this group; and no recs in >75y ***Recommendations' strength*** CTFPHC: Different strengths by age subgroups (see above) USPSTF: Rec. "A" for 50-75y TOP, BC, USPSTF: No Rec. Strength ***Screening Frequency:*** CTFPHC: every/2y; USPSTF: Not stated; TOP & BC: 2y ***Evidence analysis:*** CTFPHC analyses differences: gFOBT and sigmoidoscopy with direct evidence on mortality. FIT no direct, but with better accuracy than gFOBT. No direct evidence head-to-head. ***Costs***: CTFPHC only one that considered, and found economic analyses that support FIT as cost-effective ***V/Preferences***: CTFPHC considered V&P; not the rest	Guidelines differed in their quality. CTFPHC and USPSTF were considered of high quality, while TOP and BC were judged as of low quality. Guidelines agreed on the age periods of recommendations: 50-70y or 75y period. However, there were differences in the recommendations for the other age ranges, strength and screening methods, seem to be explained by values/preferences, costs considerations, and evidence analyses as described below: -V&P were considered by CTFPHC, not by the other guidelines and may explain differences (not clear their influence, though). - Costs consideration by CTFPHC explain that in Canada FIT is considered and recommended (not by USPSTF) -Clear differentiation in Recs' strength by age groups due to benefit/harms evidence analyses per subgroups (CTFPHC), not in the rest of guidelines - Evidence supports the frequency (every 10y) for sigmoidoscopy (in CTFPHC, not analyzed in other guidelines) - Evidence shows FIT accuracy is better than gFOBT (all guidelines cover this) but no differences in the recommendations on these tests in two guidelines (USPSTF, CTFPHC) and recommendation of FIT, no gFOBT, in other two (BC and TOP). - CTFPHC was judged to be of high-quality, USPSTF of moderate quality and the rest of low quality - In summary a higher quality was found to be related to the considerations of additional factors to support the recommendation and to a deeper analysis of the evidence (i.e., subgroups, and direct evidence).
USPSTF 2016	Adults 50-75y	Recommends screening using FOBT, sigmoidoscopy, or colonoscopy in adults, beginning at age 50 years and continuing until age 75 years. The risks and benefits of these screening methods vary. **(A recommendation).**	**94%**	**33%**	**63%**	**92%**	**6%**	**92%**		
	Adults 76-85y	The decision to screen for colorectal cancer in adults aged 76 to 85 years should be an individual one, taking into account the patient's overall health and prior screening history **(C recommendation).**								
CCO/PEBC 2014	Adults	*NOTE: This guideline does not address colorectal cancer screening for asymptomatic patients.*	**83%**	**58%**	**45%**	**64%**	**17%**	**63%**		

TOP 2013	Adults 50-74y	Screening is recommended with the FIT Screen with FIT everyone to two years If the FIT result is positive, promptly refer for a colonoscopy. Use local CRC screening or endoscopist, depending on available resource **(Recommendations without strength)**	**33%**	**19%**	**23%**	**81%**	**19%**	**29%**		
BC 2016	Adults ≥19y	FIT every 2 years for average-risk individuals. Colonoscopy every 10 years is an acceptable alternative to FOBT for screening **(Recommendations without strength)**	**72%**	**3%**	**7%**	**75%**	**8%**	**0%**		
Screening for Breast Cancer										
CTFPHC 2018	Women 40-49y	Recommends not screening with mammography; the decision to undergo screening is conditional on the relative value a woman places on possible benefits and harms from screening **(Conditional recommendation).**	**86%**	**72%**	**78%**	**97%**	**98%**	**100%**	<u>Similarities.</u> ***Age*** Guidelines agree on not recommending in <40 or 45y Benefit/harms analysis (evidence) is in favor in >50y, and against, in <50y (both CTFPHC and USTSPF) ***Strength*** CTFPHC & USPSTF recommendations are conditional or "B". No strength provided in ACS, TOP. ***Frequency:*** -CTFPHC & USPSTF biennial <u>Differences</u> ***Ages*** - CTFHC: does no recommend in <50y -USPSTF recommends making individual decisions (personal preferences) in 40-50y - ACS: 40-45: offered as individual decision; 45-55y: Annual screening; ≥55y Biennial (no limit) -TOP: Recommends 50-74y; and individualized decisions for remaining age periods ***Frequency:*** -ACS annually, while the rest, biennial.	Guidelines agree on not recommending screening in women <40y, and on recommending it between in women 50-74y. Guidelines differ in the age thresholds, and in strengths. All guidelines (CTFPHC, USPSTF and ACS), except by TOP were judged to be of high quality. Some possible explanations to the differences among them can be: - Available evidence (of low to very low quality/certainty) provide some support to screening in 50-69y. This, plus other factors detailed below explain a conditional or B recommendation in favor of the screening I CTFPHC, USPSTF and ACS. TOP guideline has no clear evidence synthesis process but uses the CTFPCHC to inform their recommendations. - Benefit and harms balance analysis explain how CTFPHC do not recommend screening in women <50y, and USPSTF states that it should be an individual decision. Although both seem different recommendations, this scenario is common when evidence is of low certainty. Both are very close in the decision spectrum and differences are explained by differences in the values. CTFPHC gave more value to the potential harms (False positives of screening and very large number needed to screen), while USTFP gave more value to the small benefit (stating that patients need to give more value to this). - Differences in frequency may be due to more value put into lives gained than into efficiency in the ACS case, in comparison to the other guidelines which recommended biennial (CTFPHC, USPSTF). ACS authors used a
	Women 50-69y	Recommends screening with mammography every 2-3 years; the decision to undergo screening is conditional on the relative value that a woman places on possible benefits and harms from screening **(Conditional recommendation).**								
USPSTF 2016	Women 50-74y	Recommends biennial screening mammography for women aged 50 to 74 years. **(B recommendation)**	**69%**	**53%**	**75%**	**100%**	**46%**	**92%**		
	Women 40-49y	The decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years. **(C recommendation)**								
	Women ≥75y	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older. **(I statement)**								

ACS 2015	Women ≥40y	1.Women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 years. **(Strong Recommendation)**. 1a. Women aged 45 to 54 years should be screened annually. **(Qualified Recommendation)** **1b.** Women 55 years and older should transition to biennial screening or have the opportunity to continue screening annually. (**Qualified Recommendation)** 1c. Women should have the opportunity to begin annual screening between the ages of 40 and 44 years. **(Qualified Recommendation)** 2. Women should continue screening mammography as long as their overall health is good, and they have a life expectancy of 10 years or longer**. (Qualified Recommendation)** 3. The ACS does not recommend clinical breast examination (CBE) for breast cancer screening among average-risk women at any age. **(Qualified Recommendation**)	**100%**	**94%**	**89%**	**86%**	**38%**	**64%**		modelling article that showed that the screening would be more efficient when implemented biennial, but more lives gained when done annually. - V&P were considered by CTFPHC, and by ACS, not the rest of guidelines. In CTFPHC there was a literature review, while in ACS there were two patients' representatives in the panel. This could have influenced towards conditional Rec, in 50-74y, and no recommendation in other ages (CTFPHC). Patients' values analysis identified that some women may prefer not to screen considering the potential associated harms. In ACs the direct impact of values on the final decisions was not clearly explicit. USPSTF did not consider Values/preferences. - Costs not systematically considered in CTFPHC, but the screening was not considered a financial threat. No systematic costs analysis in the rest - the Feasibility factor moved the strength of recommendation from C to B (USPSTF) because of potential financial barriers; While in the CTFPHC guideline., the panel considered screening a feasible and acceptable intervention by women - In summary, guidelines quality did not play a major role in the differences among ACS, CTFPHC and USPSTF guidelines, as with some differences, the three of them were of high quality. The low certainty of the evidence supporting the screening creates a scenario in which the recommendations may vary depending on additional contextual factors, in this case values and preferences, costs (efficiency) and feasibility played a role in explaining differences
TOP 2013	Women ≤39y	Screening with mammography is not recommended **(No strength).**	**61**	**33%**	**10%**	**97%**	**10%**	**8%**		
	Women 40-49y	The balance of benefits and risks is not great enough to recommend routine screening. Consider woman's preference whether to start screening **(No strength).**								
	Women 50-74y	Screening recommended every two years **(No strength).**								
	Women ≥75y	Consider individual health factors and woman's preference to continue screening **(No strength).**								
Screening for Cervical Cancer										
CTFPHC 2013	Women <20y	Recommends not routinely screening for cervical cancer. **(Strong recommendation)**	**100%**	**17%**	**75%**	**63%**	**92%**	**83%**	<u>Similarities.</u> ***Age*** - CTFPHC & USTPF agree on recommending 25-69y - All guidelines agree on not recommending in <20y	Guidelines for cervical screening provide mostly similar recommendations. They all agreed on screening for women 25-65y. Minor differences were found in younger ages, and in the strength of the recommendation. Guidelines differ I their quality. CTFPHC was the only one considered as of high quality, USPSTF as with moderate quality and TOP as low quality.
	Women 20-24y	Recommends not routinely screening for cervical cancer. (**Weak recommendation)**								
	Women 25-29y	Recommends routine screening for cervical cancer every 3 years. **(Weak recommendation)**								
	Women 30-69y	Recommends routine screening for cervical cancer every 3 years **(Strong recommendation)**								

	Women ≥70y & good prior screening (i.e., 3 neg. Pap. in 10 years)	Recommends that routine screening may stop. For all other women 70 years of age or older, we recommend continued screening until 3 negative test results have been obtained**. (Weak recommendation)**							->70y, all guidelines, either do not recommend or recommend stopping. ***- Strength*** - Strong or "A" recommendation across the 30-70y age range. **V&P, costs, feasibility assessments** -There was not a systematic V&P, cost-effectiveness or feasibility assessments in any of guidelines <u>Differences</u> ***Age*** - USPSTF recommends screening in women 21-29y, CTFPHC does not recommend in <25y - TOP only in women >25y or sexually active (regardless of age) - >70y: not recommended (USPSTF), and only if 3 neg. results obtained (CTFPHC) ***Strength (different systems)*** - <30y CTFPHC: Weak while USPSTF recommends "A" - <20y strong recommendation against (CTFPHC) and "D" recommendation against (USPSTF) - TOP does not provide recs. strength ***Note: AAFP guideline scope did not include cervical cancer screening in its scope***	Potential explanations for disagreement can be explained by differences in evidence sources and date of publication -Effectiveness evidence to support screening in <25years is definitely lacking. USPSTF based its recommendation on modelling studies (indirect evidence). - Rest of Guidelines rely on the evidence of the balance benefit/harms in favor of the screening in women ≥25y, since in younger the higher rate of false positives (FP) leads to unnecessary colposcopies. - Differences in the strength of recommendation for women<30y (recommendation "A" by USTPF, and Weak by CTFPHC) may be explained by differences in the analyzed evidence /due to date of publication). CTFPHC found moderate quality of evidence of high number of false positives in the latter, while in USPSTF, authors analyzed evidence from trials and cohort studies indicating a significant risk of identifying CIN+3. This evidence was not captured by CTFPHC as it was almost all of it published between 2012-2018 (Ogilvie 2015,2017, 2018, Leinonen 2012, Canfell 2017, Zorzi 2017), after CTFPHC search dates. In summary, quality cannot explain the differences among the guidelines, in part because the highest quality guideline (CTFPHC) is the less recent guideline and we found that key evidence on women <30y was missed by this guideline, potentially influencing final guideline recommendation- Date of publication seems to be the main role in explaining differences
USPSTF 2018	Women <21y	Recommends against screening for cervical cancer **(D recommendation).**	**89%**	**28%**	**59%**	**94%**	**33%**	**100%**		
	Women 21-29y	Recommends screening for cervical cancer every 3 years with cervical cytology alone. **(A recommendation)**								
	Women 30-65y	Recommends screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing plus cytology (co-testing)								
	Women >65y + good prior screening, not at high risk	Recommends against screening for cervical cancer **(D recommendation)**								
TOP 2016	Women <21y	Do not screen **(No Strength)**	**67%**	**31%**	**17%**	**72%**	**27%**	**0%**		
	Women sexually active (Currently or past).	Screen asymptomatic average risk women who are or have ever been sexually active. Start after three years from onset of sexual activity or age 25, whichever is later. **(No Strength)**								
	Women ≥70 adequately screened and choose to stop	Do not screen **(No Strength)**								
AAFP 2018	Not applicable	*This guideline focuses on the diagnosis and treatment of cervical cancer, does not cover screening recommendations*	**0%**	**0%**	**14%**	**36%**	**0%**	**21%**		
Screening for Prostate Cancer										
CTFPHC 2019	Men <55y	Recommends not screening for prostate cancer with the prostate-specific antigen (PSA) test. **(Strong recommendation)**	**92%**	**44%**	**66%**	**94%**	**62%**	**71%**	<u>Similarities</u> - <50-55y and >70y, agreement among guideline not recommending the screening. Evidence shows small to no benefit in this age ranges - Guidelines did not explicitly consider costs or feasibility/acceptability issues in their development <u>Differences:</u> ***Recommendation:***	Guidelines agreed on most of the recommendations, with some disagreements in terms of strength of the recommendations and in age ranges. These differences can be explained by the quality of the guideline, the uncertainty of the evidence and the benefits/harms balance analysis as is described below. - High quality guideline (CTFPHC) makes analysis of the benefits/Harms, against the screening (large FP and harms) and found no impact on mortality with screening (55-70y).
	Men 55–69y	Recommends not screening for prostate cancer with the PSA test. **(Weak recommendation)**								
	Men ≥70y	Recommends not screening for prostate cancer with the PSA test**. (Strong recommendation; low-quality evidence).**								
USPSTF 2018	Men ≥70y	Recommends against PSA-based screening for prostate cancer **(D recommendation)**	**58%**	**33%**	**59%**	**6%**	**83%**	**50%**		
	Men 55-69y.	The decision to undergo periodic prostate-specific antigen (PSA)–based screening for prostate cancer should be an individual one. Clinicians should not screen men who do not express a preference for screening **(C recommendation)**								

ACP 2013	Men 50y and >69y, or life expect. <10y	Recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in **(No strength)**	**17%**	**19%**	**40%**	**8%**	**88%**	**17%**	- 55-69y CTF does not recommend (weak); USPSTF and ACP suggest individualized decision (informing patients about benefits and harms). ***Ages*** - CUA & Alberta-HS: recommend offering PSA to any men with life expectancy >10y, not very clear but seems to be for >55y only (CUA) and >50y (AB). Also suggest stop at 70y (recommendation C) - USPTD and ACP guidelines do not provide a recommendation against screening in men <50y ***Strength:*** - ACP and AB-HS do not provide strength - Most weak/low strength, except ACP that provides B, CTFPHC provide strong in <55 and >70y ***V&P*** - CTFPHC and USPSTF considered patients V&P, CU and AB-HS did not	-CTFPHC considers different levels of uncertainty across age ranges to provide different strengths. - AB-HS and CUA rely mostly on life expectancy to offer screening and suggest an individualized decision. - Moderate quality guidelines (ACP) do not use strength and rely in individualized decisions -Lower quality guidelines (CUA and AB-HS) provide recommendations that are not very clear on age ranges and rely more on life expectancy than in ages. In summary, the quality of the guidelines played a role in explaining the differences among the recommendations, with high quality guideline (CTFPHC), considering additional factors and balancing benefits and harms and conducting a more detailed assessment of the evidence.
	Men 50-69y	Recommends that clinicians inform men between the age of 50 and 69 years about the limited potential benefits and substantial harms of screening for prostate cancer. Recommends that clinicians base the decision to screen for prostate cancer using the prostate-specific antigen test on the risk for prostate cancer, a discussion of the benefits and harms of screening, the patient's general health and life expectancy, and patient preferences. Recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in patients who do not express a clear preference for screening. **(No strength).**								
CUA 2017	Men with life expectancy > 10 years	The CUA suggests offering PSA screening to men with a life expectancy greater than 10 years. The decision of whether or not to pursue PSA screening should be based on shared decision-making after the potential benefits and harms associated with screening have been discussed **(¡ Grade of recommendation: B)**	**83%**	**31%**	**32%**	**0%**	**17%**	**50%**		
	Men >50y or >45y + high risk	For men electing to undergo PSA screening, we suggest starting PSA testing at age 50 in most men and at age 45 in men at an increased risk of prostate cancer **(Grade of recommendation: C)**								
	Men electing to undergo PSA screening	Suggests that the age at which to discontinue PSA screening should be based on current PSA level and life expectancy. **a.**For men aged 60 with a PSA <1 ng/ml, consider discontinuing PSA screening **(Grade of recommendation: C).** b. For all other men, discontinue PSA screening at age 70 **(Grade of recommendation C)** c. For men with a life expectancy less than 10 years, discontinue PSA screening **Grade of recommendation: C).**								
AB-HS 2015	Men between the ages of 50 and 75 years with at least ten years life expectancy	Fit men between the ages of 50-75 years with at least ten years life expectancy should be made aware of the availability of PSA as a detection test for prostate cancer; they should also be aware of the potential benefits and risks of early detection so they can make an informed decision as to whether to have the test performed. **(No strength).**	**89%**	**33%**	**20%**	**23%**	**100 %**	**67%**		
Screening for Lung Cancer										
CTFPHC 2016	Adults 55-74y	Recommends screening for lung cancer among adults aged 55 to 74 years with at least a 30 pack-year smoking history, who smoke or quit smoking less than 15 years ago, with low-dose computed	**97%**	**94%**	**91%**	**100%**	**100%**	**92%**	<u>Similarities</u>	Guidelines had high similarities in the recommendations. CTFPHC and USPSTF guidelines were judged as of high quality,

		tomography (LDCT) every year up to three consecutive years. Screening should only be done in health care settings with access to expertise in early diagnosis and treatment of lung cancer. **(Weak recommendation).**							- All guidelines agree on recommending in high-risk individuals aged 55-75y and in the frequency: every year - All guidelines based their recommendation on the NLST trial (which studied population 55-74y) -CTFPHC and USPSTF agree on stopping after 15y without smoking -Although not directly interchangeable CTFPHC and USPSTF somehow agree on the strength of the recommendation (weak and "B") - All guidelines also agree on the method: Low dose CT <u>Differences:</u> ***Age:*** - Minor difference in the higher age limit: USPSTF set age limit in 80y, CTFPHC in 75y, and CAR did not set an age limit - CTFPHC recommends stopping screening with 3 consecutive negative results, while USPSTF every year until 15 years of the last smoking. ***Evidence and recommendations*** - CAR used a model for risk prediction & used recommendations and information from other CPGs (i.e., CTFPHC, USPSTF) - CTFPHC recommends against chest radiography and against screening in other populations. This, because they searched and analyzed chest radiography evidence which was of low quality and found no impact on cancer mortality and there are significant false positives. Rest of guidelines do not mention X-ray and do not recommend against other screening populations ***V&P*** - CTFPHC did a systematic review of V&P and conducted focal groups. -Rest of guidelines did not consider V&P ***Costs*** - CTFPHC: used a cost-effectiveness analysis (Coffin 2015) to support their recommendation; USPSTF: did not consider costs; CAR: did an economic model, from NLST data ***Note: CCO/PEBC guideline scope did not include lung cancer screening in its scope***	being CTFPHC the one with the highest quality scores. This high agreement among guidelines can be explained by two factors: a high-quality evidence used by all the guidelines (NLST trial) and that one guideline (CAR) used the other two guidelines (CTFPHC and USPSTF) as an evidence/information resource. Minor differences in age limit and in providing additional recommendations (e.g., X-ray) can be explained by several reasons, including V&P considerations (CTFPHC) and the scope of the evidence analyzed, as explained below. - Regarding the scope of the evidence, as described the NLST was the main evidence source. This trial analyzed adults 55-74y. However, USPSTF used modeling studies to predict the benefits and harms of screening programs that use different screening intervals. The model predicted benefits when screening is extended to 80y. - In terms of when to stop the screening the differences between CTFPHC and USPSTF are not directly related to the evidence. There is no evidence to determine the best time to stop. CTFPHC took a conservative approach and stopped after three negative results. Although not explicit, this difference might be explained by different developer values (Different values from CTFPHC and USPSTF panels as the former decided to be conservative, maybe giving more value to the balance benefit/harms and reducing irradiation) - Evidence and benefits/harms balance on chest radiography was considered by CTFPHC, which explains why this recommendation exists while USPSTF and CAR guidelines did not cover this (CAR guideline scope was specific about screening with LDCT) In summary, guidelines quality did not play a major role in explaining the differences. CTFPHC and USPSTF were considered of high quality and CAR, although of low quality, used information from CTFPHC and USPSTF (sort of a recommendations' endorsement) to develop their recommendations. The lack of appropriate evidence to support certain decisions (e.g., when to stop screening) open the scenario to some heterogeneity in the recommendations and the introduction of indirect evidence (i.e., modelling studies), allowed some differences in age limits (USPSTF). Considerations of V&P and costs, although varied and might be one of the main
	Adults, other ages, no risk factors for lung cancer	Recommends not screening all other adults, regardless of age, smoking history or other risk factors, for lung cancer with low-dose CT. **(Strong recommendation)**									
	All Adults	Recommends that chest radiography, with or without sputum cytology, not be used to screen for lung cancer. **(Strong recommendation, low-quality evidence).**									
USPSTF 2013	Adults 55-80y	Recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery**. (B Recommendation)**	**89%**	**14%**	**77%**	**97%**	**54%**	**96%**			
CAR 2017	Not specified	We recommend screening patients who have a 1.5% or higher risk of developing lung cancer over the next 6 years. We recommend routine annual screening for high-risk patients until such time as they no longer meet eligibility criteria. In addition, screening should be discontinued in those who develop health problems that substantially limit life expectancy or would preclude curative treatment. **(No strength).**	**100%**	**67%**	**48%**	**100%**	**65%**	**100%**			
CCO/PEBC 2019	Not applicable	This guideline does not provide recommendations for patients in a screening program.	**50%**	**67%**	**81%**	**25%**	**63%**	**42%**			

										differences between guidelines (CTFPHC systematically considered both, and USPSTF did not) did not explain the minor differences in the recommendations because both factors ended up supporting the final recommendation (in favor of screening)
Screening for Abdominal Aortic Aneurysm										
CTFPHC 2017	Men aged 65 to 80 years	Recommends one-time screening with ultrasonography for AAA **(Weak recommendation)**	**92%**	**81%**	**76%**	**97%**	**85%**	**92%**	Similarities - CTFPHC, USPSTF & CSVS recommend one time screening all men 65-80y with ultrasound - CTFPHC and USPSTF provide weak/low strengths/ CSVS provides strong recommendation -CTFPHC and CSV to women only if smokers or CV risk. Differences -USPSTF: recommends for men smokers and for no smokers to offer. Does not recommend to women (not conclusive, although it seems to be a negative recommendation) -CTFPHC considered V&P (local) and Cost-effectiveness analyses	CTFPHC was the only high-quality guideline, while the USPSTF was judged as of moderate quality and the CSVS as a low-quality guideline. In general, guidelines' recommendations are very similar. Differences are given by USPSTF guideline which does not recommend screening in women with no smoking history. Quality does not explain the differences in the recommendations (very similar). But it may explain the differences in the strength of the recommendations. CTFPHC, and in less degree the USPSTF, acknowledges the uncertainty when considering the evidence; CSVC (low quality guideline), provides a strong recommendation without a systematic evidence quality assessment. In summary, differences in the quality of the guidelines explain the differences in the strengths of the recommendations with a more conservative approach: weak or "B" recommendation from high-to-moderate quality guidelines vs. a strong recommendation from a low-quality guideline.
	Men older than 80 years	Recommends not screening for AAA **(Weak recommendation)**								
	Women 65-80 with history of smoking or CV disease	Suggests a one-time screening ultrasound **(Weak recommendation)**								
USPSTF 2014	Men 65 to 75 years	Recommends 1-time screening for AAA with ultrasonography who has ever smoked. Recommends that clinicians selectively offer screening for AAA who have never smoked **(B recommendation)**	**83%**	**22%**	**54%**	**97%**	**17%**	**93%**		
	Women aged 65 to 75 year	Concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for AAA in women who have ever smoked. Recommends against routine screening for AAA in women who have never smoked. **(C recommendation)**								
CSVS 2018	Men between 65-80 years of age	Recommends a one-time screening ultrasound **(Strong recommendation)**	**11%**	**14%**	**29%**	**86%**	**13%**	**96%**		
	Women 65-80y with smoking history/CV dis.	Suggests a one-time screening ultrasound **(Weak recommendation**								
Screening for Hepatitis C										
CTFPHC 2017	Adults	Recommends against screening for HCV in adults who are not at elevated risk **(Strong recommendation)**	**63%**	**46%**	**75%**	**100%**	**61%**	**72%**	Similarities -Recommendation only for high-risk individuals (CTFPHC, CDC and CASL) Differences ***Recommendations*** -USPSTF recommend screening in all adults ***Strengths*** -CTFPHC: strong against -CDC: strong in favor, CASL: 2A in favor - USPSTF B (in favor) ***V&P***	All guidelines (except USPSTF that was judged as a moderate-quality guideline) were judged as of high quality. Guideline differed significantly in the recommendations. Differences in evidence analyses may explain differences for three reasons: the evidence's target, quality assessment, date of publication/search, values/preferences analyses, costs considerations, feasibility, and acceptability Target: CTFPHC focused on direct evidence (Direct evidence comparing screening vs no screening, which was absent). Rest of
USPSTF 2020	Adults(18-79y)	For adults aged 18 to 79 years: **Grade B** Screen adults for hepatitis C virus (HCV) infection.	**61%**	**17%**	**50%**	**94%**	**14%**	**75%**		
CDC 2012	Adults	In addition to testing adults of all ages at risk for HCV infection, CDC recommends test: a) Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk **(Strong Recommendation, Moderate Quality of Evidence),** and b) All persons identified with HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed	**64%**	**58%**	**90%**	**95%**	**56%**	**88%**		

		by referral to appropriate care and treatment services for HCV infection and related conditions							- CTFPHC considered local patients' values and preferences (from literature and Local analysis); -USPSTF & CASL: V&P not considered; CDC: QoL measured for patients that had screening+ treatment (increased QoL), but no specific V/P analyzed ***Costs/resources*** -CTFPHC: one local BIA (AB); CASL: One CADTH CEA; CDC: 2 CEA, USPSTF did not consider ***Feasibility/Acceptability & Equity (FAE):*** - Considered by CTFPHC (support negative recommendation) - USPSTF: Nothing; CDC & CASL: No specific Analysis of the FAE considerations	guidelines on indirect evidence: Increase in prevalence, and evidence of diagnostic accuracy (Anti-HCV tests followed by HCV RNA assay). Quality assessment: CTPHC judged the evidence as low quality (accuracy); USPSTF didn't explicitly judged it and used the magnitude without quality assessment Date: CTFPHC date 2016 vs USPSTF 2019. USPSTF introduced more evidence of treatment efficacy to justify their decisions Values and preferences: Considerations of V/P and feasibility, acceptability, and equity analyses, may have also explained a negative recommendation in CTFPHC guideline (V/P analyses did not favor the screening) which was not considered by other guidelines Costs, Feasibility, equity, and acceptability. consideration in CTFPCH guideline played a role in the recommendation against. Large resources needed if implemented, and barriers for implementing the screening and treatment of detected cases (high treatment costs), and the possibility of increasing inequalities if recommended, influenced the panel to develop a negative recommendation. Lastly, acceptability would be low by some provinces' governments. These (Costs, values, feasibility, equity, acceptability) were not considered I the other guidelines In summary, quality of the guidelines may explain some differences (e.g., the differences between USPSTF a moderate quality guideline, vs CTFPHC, ahigh-quality guideline, due to lack of consideration of the former of key factors: values/preferences, costs, equity, acceptability, and feasibility)
CASL	Adults	To increase the identification of the large proportion of persons living with undiagnosed HCV, we recommend that screening be both risk-based and target the birth cohort of individuals born from 1945 to 1975, which currently encompasses the majority of persons chronically infected with HCV in Canada **(class of recommendation: 2a)**	**89%**	**95%**	**39%**	**95%**	**50%**	**25%**		
Screening for Asymptomatic Bacteriuria in pregnancy										

CTFPHC 2018	Pregnant women	Recommends screening pregnant women once during the first trimester with urine culture for asymptomatic bacteriuria **(Weak recommendation)**	**89%**	**75%**	**77%**	**100%**	**63%**	**100%**	Similarities ***Recommendation:*** CTFPHC/IDSA: Similar recommendation Differences ***Evidence of effectiveness*** CTFPHC: Low quality evidence of Screening vs no screening IDSA: Moderate quality evidence (Antibiotic vs placebo to prevent pyelonephritis & preterm birth) ***Harms*** CTFPHC: Analyzed for Screening-intervention (low Quality) IDSA: Analyzed for antibiotics in Patients with AB (not for screening) (Moderate Quality described, but Evidence source - Cochrane- seems Low) ***Strength:*** Weak (CTFPHC); Strong (USPSTF) ***V&P*** CTFPHC: Considered V&P(Local), in favor of screening; while IDSA only indirectly considered (panel views), in favor of screening. In both cases V&P supported screening. ***Costs/resources:*** CTFPHC: Costs' evidence sought, not found IDSA: Not explicitly considered	Both guidelines (CTFPHC and IDSA) were considered of high quality with CTFPHC having better scores. Both guidelines recommend screening pregnant women, and both were of high quality. Differences are related to the strength of recommendations and different considerations of evidence, and values - Differences in evidence assessment (effectiveness and harms); CTFPHC considered direct evidence of effectiveness comparison of screening vs no screening (Scarce and of very low quality), while IDSA considered evidence or antibiotic treatment vs no treatment of patients with antibiotics (considered as moderated although the original source, a Cochrane review, labeled the evidence as low to very low quality; i.e., there was a disagreement between the Cochrane review quality assessment and the guideline assessment). - Differences in recommendations strengths difference may be related to the differences in the focus of the evidence considered: CTFPHC considered direct evidence: Screening +treatment vs. IDSA considered as evidence the impact of antibiotic treatment on outcomes, not the evidence of the screening as an intervention) (see above). In summary, although both guidelines were of high quality, CTFPHC had better scores and did a deeper analysis of the evidence quality of a screening intervention while USTPF only analyzed the evidence of the antibiotic intervention. This explains the differences in the strength of both recommendations: CTFPHC (weak), IDSA (Strong)
IDSA 2018	Pregnant women	Recommends screening for and treating ASB **(Strong recommendation)**	**89%**	**67%**	**69%**	**95%**	**27%**	**46%**		
Screening for developmental delay											

CTFPHC 2016	Children 1-4y	Recommends against screening for developmental delay using standardized tools in children aged one to four years with no apparent signs of developmental delay and whose parents and clinicians have no concerns about development **(Strong recommendation; low quality evidence)**	**97%**	**92%**	**92%**	**100%**	**75%**	**96%**	Similarities. No similarities found Differences ***Recommendations*** -CTFPHC: Recommends against screening; USPSTF: Does not provide recommendation ***Strength*** -CTFPHC: Strong against; USPSTF: does not provide ***Evidence*** CTFPHC mod and low-quality evidence, with surrogate outcomes (identification), and with no difference in important outcomes (developmental delay and oral tests) Tools Diagnostic accuracy poor performance (high FP rates) (mainly: Ages and Stages Questionnaire -AQS) USPSTF: Did not identify evidence. Their search was focused only on specific tools for Autism disorder. ***Harms***. CTFPHC. High number of false positives, which could lead to anxiety and labelling USPSTF: Potential harms include misdiagnosis and the time, effort, and anxiety associated with further testing after a positive screening result ***V&P*** CTFPHC no V&P evidence USPSTF: Not considered ***Costs*** CTFPHC: not systematically addressed USTPF: Not evaluated for screening but for treatments	Both guidelines (CTFPHC and USPSTF) were judged as of high quality with CTFPHC having higher scores. Both guidelines have important differences including scope, recommendations and the evidence that was considered. - CTFHC's scope focused on Developmental delay screening, while USPSTF in detecting autism disorder. This, in turn, explains differences in the evidence considered to support the recommendation. CTFPHC focused on evidence about screening while USPSTF focused on autism-specific evidence. Evidence specific about screening tools to identify autism disorder which was not found. - Considering the low-quality evidence of no differences between screening vs not screening, the poor performance of the AQS test (high false positives rates) the CTFPHC decided not to recommend screening; Meanwhile, the USPSTF did not identify evidence for their scope, thus, they opted for not providing recommendation (I-Statement) In summary, guidelines quality did not explain the differences in the recommendations. The scope and purpose of the guideline is the major factor for explaining the differences in the recommendations
USPSTF 2016	Young children	Concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for ASD in young children for whom no concerns of ASD have been raised by their parents or a clinician**. (I statement)**	**94%**	**33%**	**75%**	**86%**	**58%**	**93%**		

Guidelines developers/organizations (Alphabetical order): AAFP: American Academy of Family Physicians; AB-HS: Alberta Health Service (Alberta Provincial Genitourinary Tumour Team); ACP: American College of Physicians; ACS: American Cancer Society; BC: British Columbia Guidelines; CASL: Canadian Association for the Study of the Liver; CAR: Canadian Association of Radiology; CCO/PEBC: Cancer Care Ontario's Program in Evidence-based Care; CDC: Centers for Disease Control and Prevention; CSVS: Canadian Society of Vascular Surgery; CTFPHC: Canadian Task Force on Preventing Health Care; CUA: Canadian Urological Association; IDSA: Infectious Diseases Society of America; TOP: Toward Optimized Practice Clinical Practice Guidelines; USPSTF: U.S. Preventive Services Task Force.
Abbreviations: AAA: Abdominal Aortic Aneurism; gFOBT; guaiac fecal occult blood test; FIT: fecal immunochemical test; HCV: Hepatitis C Virus; V&P: Values and preferences; Recs: Recommendations; Y: Years.

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