Canadian Task Force on Preventive Health Care

Procedure Manual

October 2011

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Preface

The first draft of this manual, which is based on the methods manual of the United States Preventive Services Task Force[1] and the GRADE handbook,[2] was drafted in 2010 by Professor John Feightner (past chair of the Canadian Task Force on Preventive Health Care [CTFPHC]) in his role as a consultant to the Public Health Agency of Canada (PHAC). The manual was then edited by the chair and vice-chair of the Task Force, and members of the Office of the Task Force, and was subsequently reviewed by the members of the task force's methods group, as well as by the full task force. As part of its mandate, the methods group will periodically review and update the manual.

Section 1: Overview of structure and processes

1.1 Function

The Canadian Task Force on Preventive Health Care (CTFPHC) is an independent panel composed primarily of clinicians and methodologists that makes recommendations for clinical preventive actions based on rigorous, systematic review and synthesis of evidence conducted by the Evidence Review and Synthesis Centre (ERSC). The CTFPHC makes recommendations directly to its key constituency of primary care providers, but its work is also directly relevant to other health care professionals, developers of preventive programs, policy-makers and Canadian citizens. It uses standardized methodology and transparent processes to review and synthesize evidence, to weigh the balance of benefits and harms, and to make recommendations. The CTFPHC also develops and fosters linkages between primary care and community or public health programs that support clinical preventive services, as well as linkages to enhance the dissemination and uptake of its recommendations. Finally, the CTFPHC works with researchers to advance the evidence base supporting preventive care.

The recommendations of the CTFPHC are aimed at improving clinical practice and promoting public health. The CTFPHC provides recommendations about primary and secondary preventive services targeting clinically relevant conditions. The services must be provided in primary care settings or available through primary care referral. Primary prevention is the prevention of a target condition in healthy patients and takes the form of activities such as counselling and chemoprevention. Secondary prevention is directed to asymptomatic individuals with risk factors for a condition or preclinical disease (but not clinically evident disease).

1.2 Governance

The CTFPHC has independent decision-making authority in all aspects of its scientific mission, including the following activities:

- final decisions about topics to be covered
- setting of standards and expectations for review and synthesis of the evidence
- development and public declaration of its recommendations

The CTFPHC is accountable to the PHAC's chief public health officer (CPHO) to adhere to its own standards and procedures for reviews and recommendations and to fulfill negotiated expectations for productivity. It is also commits to the public that it will follow an explicit and transparent process for generating clear recommendations for clinical preventive actions, based on rigorous systematic review and synthesis of relevant evidence.

Notably, the Office of the CTFPHC within the PHAC is responsible for supporting the operations of the task force and assisting it in developing strategies that will facilitate the uptake of recommendations.

1.3 Overview of roles

1.3.1 Role of the CTFPHC

The CTFPHC is responsible for prioritizing the topics that will be reviewed and works with the Office of the CTFPHC to define the analytic framework and scope of each topic. The task force works closely with the ERSC and the Office of the CTFPHC in the preparation of evidence reviews and the development of recommendations for each topic. The task force is also primarily responsible for leading knowledge translation and dissemination activities and assists

PHAC and other key stakeholders in designing and implementing an evaluation strategy to assess the impact of the task force's products.

1.3.2 Role of the Office of the CTFPHC

The Office of the CTFPHC within PHAC supports the CTFPHC in all of its activities. A scientific research manager is assigned for each topic, and this person coordinates and supports the development of the evidence reviews and recommendations for the topic. A scientific research manager also serves as the cochair of the various working groups of the CTFPHC.

1.3.3 Role of the ERSC

The ERSC conducts the evidence reviews that are used as the basis for the recommendations of the CTFPHC. The ERSC follows documented methods for its reviews of topics specified by the CTFPHC and follows the methods of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group[2] in assessing the evidence.

1.4 Membership

The Office of the CTFPHC will periodically solicit nominations for new members, including the chair and vice-chair, by contacting appropriate stakeholder groups and through other appropriate channels. Both new and previous nominations will be considered. Nominations may also be submitted by current members of the task force. Once one or more individuals have been nominated, the task force appoints a selection committee composed of two current members of the task force, one representative of PHAC and one external representative appointed on a rotating basis by the chair and vice-chair of the task force. The selection committee reviews the qualifications of each nominee in relation to the required qualifications for selection (Table 1) and makes its recommendations for appointments to the task force, which votes on the recommendations. The CPHO then appoints new members approved through the voting process.

Table 1: Qualifications for appointment to the CTFPHC*

Recognition in field of expertise, nationally and internationally
Knowledge and experience in critical appraisal of peer-reviewed publications
Knowledge and experience in evidence review methods
Knowledge and experience in applying evidence to decision-making or policy-making
Expertise in disease prevention and health promotion
Demonstrated ability to collaborate with peers
No conflict of interest (including financial or intellectual conflicts) that would impair the integrity of the CTFPHC
Expertise in methodology (e.g., medical decision-making, clinical epidemiology, health economics)

Note: CTFPHC = Canadian Task Force on Preventive Health Care.
*Adapted from the procedure manual of the US Preventive Services Task Force.[1]

1.4.1 Selection of chair and vice-chair

The selection committee makes a recommendation for the chair of the CTFPHC to the CPHO, who appoints the chair. In turn, the chair makes a recommendation for vice-chair, based on discussions with the CPHO, and the CPHO appoints the vice-chair.

1.4.2 Selection of members

For the inaugural membership of the CTFPHC, the selection committee made recommendations for individual members to the CPHO, who subsequently appointed the new members. When

additional members are needed, the selection committee will make recommendations, on the basis of the criteria listed in Table 1. Individuals recommended for membership must be ratified by a majority vote of current members of the task force and are then appointed by the CPHO.

1.4.3 Terms of service

The CTFPHC consists of 12 to 16 individuals. The initial term for each member, including the chair and the vice-chair, is three years, with a possible one-year extension. The extension of terms will be staggered, to ensure continuity of membership over time and overlap of terms.

1.5 Quorum and voting

A quorum for official votes is two-thirds of the members, including the chair. Voting follows the procedures of the US Preventive Services Task Force.[1] Major decisions about procedures and methods, recommendations, clinical practice statements and the selection of new members all require a vote. Votes are taken by hand or voice, or by proxy, and voting can be done electronically if necessary (i.e., if a quorum is not available during an in-person meeting). Members with a potential conflict of interest related to the topic of a particular vote recuse themselves and do not vote.

1.6 Conflict of interest

Before each meeting, each member of the CTFPHC discloses any information that might prevent him or her from discussing and voting on a specific topic, by completing the PHAC Declaration of Affiliations and Interests Form and Checklist (Appendix I). The Office of the CTFPHC and the chair and vice-chair of the task force review the disclosures and recommend whether or not the member will be allowed to participate in the discussion. Members may recuse themselves from specific discussions but are still required to disclose any potential conflict. In addition to completion and review of the Declaration of Affiliations and Interests Form, PHAC requires a review of the actions taken in relation to the disclosure, to ensure that the objectives of the CTFPHC are achieved.

1.6.1 Process for disclosure

Before each meeting, every member of the CTFPHC and of the ERSC completes the PHAC Declaration of Affiliations and Interests Form to report any potential conflicts of interest (e.g., financial, business or professional, intellectual). Disclosure is required for each new topic, and disclosures must be updated to reflect any changes that have occurred since an initial disclosure. Completed forms are kept on file at PHAC. Outside experts who are asked to comment on the recommendations and documents prepared by the task force are also required to complete disclosure forms, which are kept on file at PHAC.

Although PHAC's intention is to keep personal information confidential, they will comply with all applicable laws pertaining to privacy and confidentiality in dealing with member information.

1.6.2 Process for determining appropriate actions

The Office of the CTFPHC reviews the disclosure forms in consultation with the chair or vice-chair of the task force to recommend the appropriate course of action, if any (see Table 2 for possible actions).

Table 2: Possible actions following disclosure of potential conflict of interest[1]	
Action	**Description**
No action	No recusal necessary
Disclosure of information to CTFPHC only	Member may discuss and vote on the topic and may serve as discussion leader
Recusal from topic lead, disclosure of information to CTFPHC	Member may discuss and vote on the topic, but may not lead the discussion
Recusal from all participation, disclosure of information to CTFPHC	Member may not lead or participate in discussion or vote on the topic and will not be present for discussion and voting. Recusal will be noted with published recommendations.
Recusal from all participation in CTFPHC	Member no longer participates on CTHPHC activities

Note: CTFPHC = Canadian Task Force on Preventive Health Care.

In making recommendations for action, the office of the CTFPHC and the chair and vice-chair of the task force will consider the transparency, integrity and acceptability of CTFPHC recommendations and products. The recommended action will be reported to the member and kept on file. Even if the recommended action is to allow the member to participate in discussions and vote on the topic, the member may withdraw from discussions or voting on a topic at any time if he or she feels it is appropriate to do so.

1.7 Public activities

The members of the CTFPHC are encouraged to discuss, disseminate and defend the recommendations of the task force in public forums.

1.7.1 Dealing with the media

Responses to media inquiries are coordinated through PHAC. The chair, vice-chair or other members of the task force may make comments or statements to the media at the discretion of the chair and vice-chair.

1.7.2 Expert testimony

Members of the CTFPHC may provide expert testimony on topics that have been considered by the task force. Any member of the task force who, within the previous five years, has provided expert testimony or who has reviewed a case related to a topic to be considered by the CTFPHC must disclose these activities through the disclosure process described in section 1.6.1. To avoid potential financial conflicts of interest, members of the CTFPHC should refrain from accepting more than $10 000 per year for testimony or review.

1.8 Authorship

Authorship for journal articles or other documents for public dissemination is assigned in accordance with the recommendations of the International Committee of Medical Journal Editors (http://www.icmje.org/ethical_1author.html). Other contributors who do not meet the criteria for authorship may be acknowledged.

During the preparation of articles and other documents, the authors must provide feedback on drafts within one week, to meet the time constraints of the CTFPHC.

1.9 External linkages

The CTFPHC and PHAC collaborate to identify appropriate stakeholder groups and related organizations to ensure effective and meaningful external linkages for the task force. These external linkages take several forms and serve a variety of functions, including the following:

- expert and peer review of protocols, drafts of reviews, final syntheses of evidence, and final reports and recommendations
- feedback on reviews and recommendations for specified topics
- enhancement of knowledge transfer
- suggestions of topics that might be reviewed

External linkages are developed with formal organizations (e.g., professional societies), government-related organizations and, in certain cases, selected groups of practitioners. These organizational linkages are intended primarily to represent end-users who use the CTFPHC recommendations in their day-to-day practice. External linkages may also be made with organizations that are in a position to enhance knowledge transfer and uptake of CTFPHC recommendations.

1.10 Review of CTFPHC reports and recommendations

Documents prepared by the CTFPHC are reviewed externally at several points during the development process. In particular, the CTFPHC solicits reviews of its preliminary documents (protocols, evidence reports and guidelines), as well as the draft recommendations, by stakeholder organizations and individual peer reviewers. Figure 1 shows the key steps in the guideline-development process at which input is solicited.

Peer reviewers and stakeholder organizations that participate in the review of documents related to a particular topic are identified jointly, on the basis of their scientific, clinical, or topic specific expertise, by the CTFPHC working group responsible for the topic and the ERSC. Each potential reviewer (individual peer reviewer and organizational reviewer) is asked to declare potential conflicts of interest using the standard declaration form (as described in section 1.6.1;) and must sign a confidentiality agreement (Appendix II). Actions related to declared conflicts, including disqualification of potential reviewers, are managed by the chair of the working group and/or the chair of the CTFPHC in accordance with the conflict of interest guidelines of the CTFPHC, as detailed in section 1.6. Potential reviewers are advised at the time of invitation that their participation will be acknowledged on the CTFPHC website and in technical documents published by the CTFPHC. Review occurs at various steps in the process of developing recommendations, as described in subsequent sections of this manual.

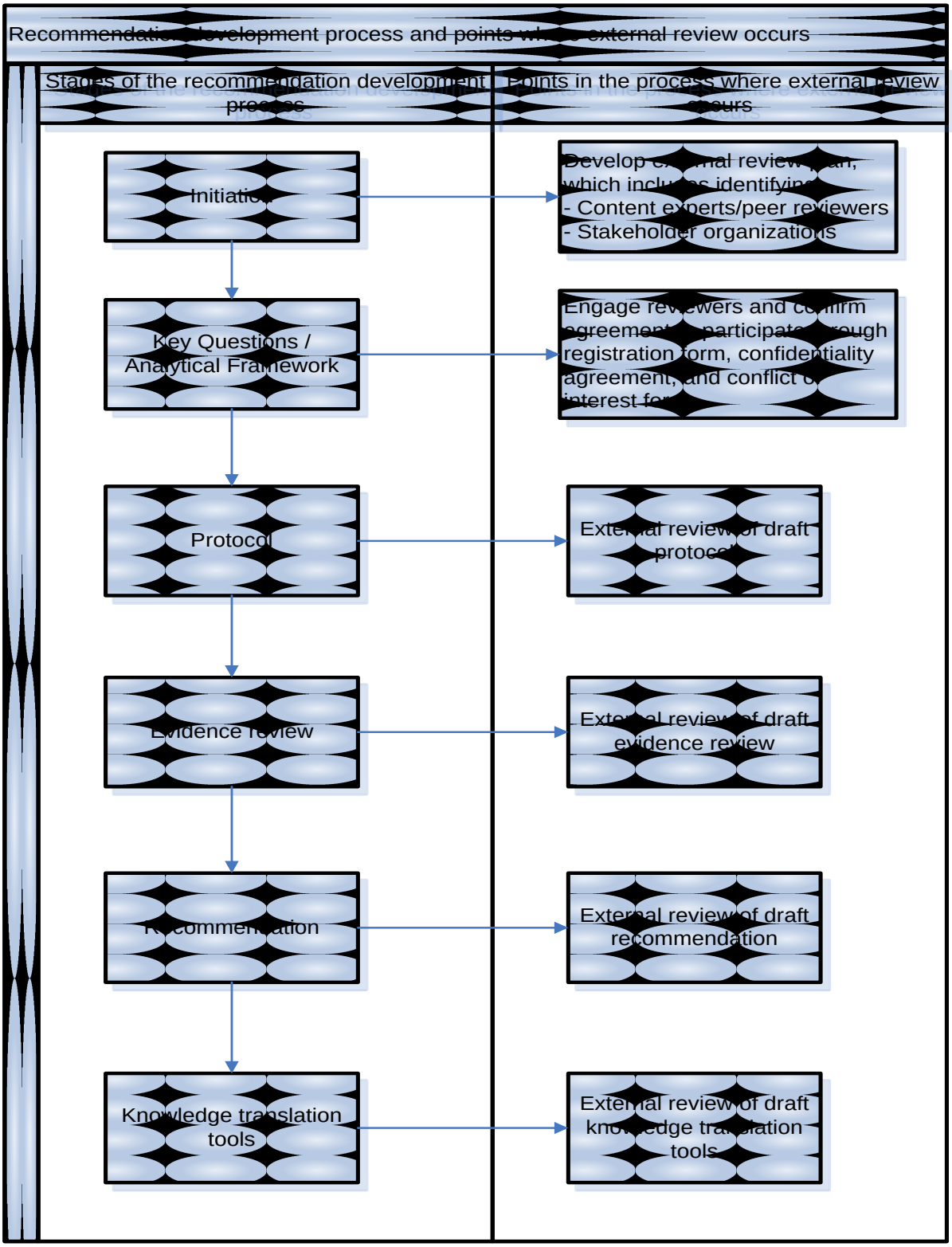

Figure 1: Process and timelines for review of guidelines, highlighting the points at which external review occurs.

The working group for the topic prepares a written response to each round of peer review, in the form of a summary document. The working group must respond to each comment raised during the peer review, although the responses may be brief (for example, "This comment was considered, but no action was taken"). At the time of publication of the guideline, all comments received from registered stakeholders and the TF response addressing each comment are made public on the TF website. Before publication, the responses may be made available to outside organizations at the discretion of the chair and/or vice-chair of the CTFPHC (for example, responses may be shared with a scholarly journal that is considering publication of a document prepared by the task force). The review comments and the working group's responses are shared with the entire CTFPHC for them to consider when reviewing the final versions of the guideline and its products.

Review occurs at three steps in the development of a guideline: the protocol, the draft synthesis report (i.e., review of the evidence) and the guideline itself.

- **Protocol:** The CTFPHC as a whole and any topic-specific partners are asked to comment on and provide approval of the key questions and analytic framework for the topic before these items are sent to the ERSC. The key questions and analytic framework are revised in accordance with these comments, and final versions are submitted to the ERSC for development of the protocol. The protocol, once developed, undergoes formal peer review.
- **Draft synthesis report (review of evidence):** The draft synthesis report is reviewed, revised and approved by the topic working group. It is then sent to three to six content experts and to the CTFPHC's federal partner organizations, according to the task force's partnership strategy. Some or all of these reviewers may have participated in the review of the protocol, described in the previous paragraph. The draft synthesis report and all of the reviewers' comments are then presented and discussed at a meeting of the CTFPHC. If no meeting is scheduled, dissemination and discussion take place by email.
- **Draft guideline (recommendations):** Following approval of the draft synthesis report (evidence review) by the CTFPHC, the assigned scientific research manager and the lead member of the topic working group draft recommendations based on the evidence. The recommendations are approved by the entire task force and are then sent to external peer reviewers for additional review.

To facilitate stakeholder engagement in the review process, a "Guide for Reviewers" is distributed to all individuals and organizations participating in the review. The first section of the guide reviews the mandate and the structure of the CTFPHC, the second describes opportunities for stakeholder participation, and the third provides specific guidance for stakeholders about how to review TF products (see Appendix VII for a copy of the Guide for External Reviewers).

Section 2: Overview of the guideline-development process

This section describes the steps taken by the CTFPHC in developing its recommendations, as illustrated in Figure 2. Working groups with responsibility for topic prioritization, methods, knowledge translation, and performance indicators have been formed to assist in this process (see Appendix III).

2.1 Selection of topics

2.1.1 Phase 1: Generating a topic list

Topics are identified by members of the task force, stakeholders, practitioners, PHAC, the ERSC, other organizations and individuals. The CTFPHC may also solicit topic nominations (see Appendix IV for notice used to solicit nominations).

The Office of the CTFPHC periodically updates the list of topics to be considered for new reviews and review updates in the coming year. This list includes all nominated topics and any additional topics identified through a scan of the current preventive health literature (Appendix V) or input from stakeholders.

To be included on the list of candidate topics, a topic must fall within the scope of the CTFPHC, i.e., the topic must be related to primary or secondary prevention in the primary care setting of a disorder or condition with a substantial health burden. In addition, effective treatment must be available for any condition selected for review, to ensure that any resources invested in screening can be related to the effectiveness of treatments.

2.1.2 Phase II: Generating a short list of topics

Using a modified Delphi process members of the topic prioritization working group select a short list of candidate topics according to the following criteria:

- Timing of most recent review: Priority is given to topics that have not been examined by the CTFPHC within the past five years and also to topics that have been examined by other organizations within the past two years, since such topics are considered good candidates for endorsement or adaptation.
- Availability of new evidence: Priority is given to topics for which new or controversial evidence, which might lead to a change in existing recommendations, has emerged since the last time the topic was reviewed by the CTFPHC.
- Input from primary care practitioners: Priority is given to topics that will address the needs of primary care practitioners. Input on such topics is obtained through an annual survey administered by the College of Family Physicians of Canada.

Each member of the topic prioritization working group selects from the master list the topics that he or she thinks best reflect these criteria. These individual lists are combined to create the short list. If this process does not reduce the number of topics to a manageable number (20–30), then the members of the topic prioritization working group discuss the list and come to a consensus about the final short list.

2.1.3 Phase III: Final selection of topics

The members of the topic prioritization working group examine and subjectively rank the short list according to the following criteria:

- Disease burden (prevalence, mortality, comorbidity, quality of life) and expected effectiveness of the preventive service in decreasing that burden

- Potential impact of recommendations in clinical practice
- Interest of the public or care providers
- Variation in care and potential for preventive service to decrease that variation
- Sufficiency of evidence
- New evidence, especially high-quality evidence in a stable field (i.e., an area where the evidence and state of knowledge are not changing rapidly)

In the ranking process, all criteria are considered equally (i.e., the criteria are not weighted). The prioritization process takes into account the requirement that the topics for each year should cover various disease types, populations, and types of services (screening, prevention). Topics are classified according to whether they will be the subject of new reviews, updates, endorsements, partnerships or adaptations.

The mean rankings for the topics are calculated and sent to the members of the prioritization working group, who repeat the ranking process. If the second round of ranking indicates that the members agree on the top 10 topics, the process is complete. If this round of ranking does not indicate consensus on the top 10 topics, the prioritization working group discusses the ranking results until they reach a consensus. The list of 10 potential topics and their respective priorities are then presented to the CTFPHC as a whole for discussion and approval.

Although the results of this formal process generally drive the timing of guideline development, the task force occasionally reprioritizes certain topics to take advantage of scientific developments or timely opportunities for partnerships.

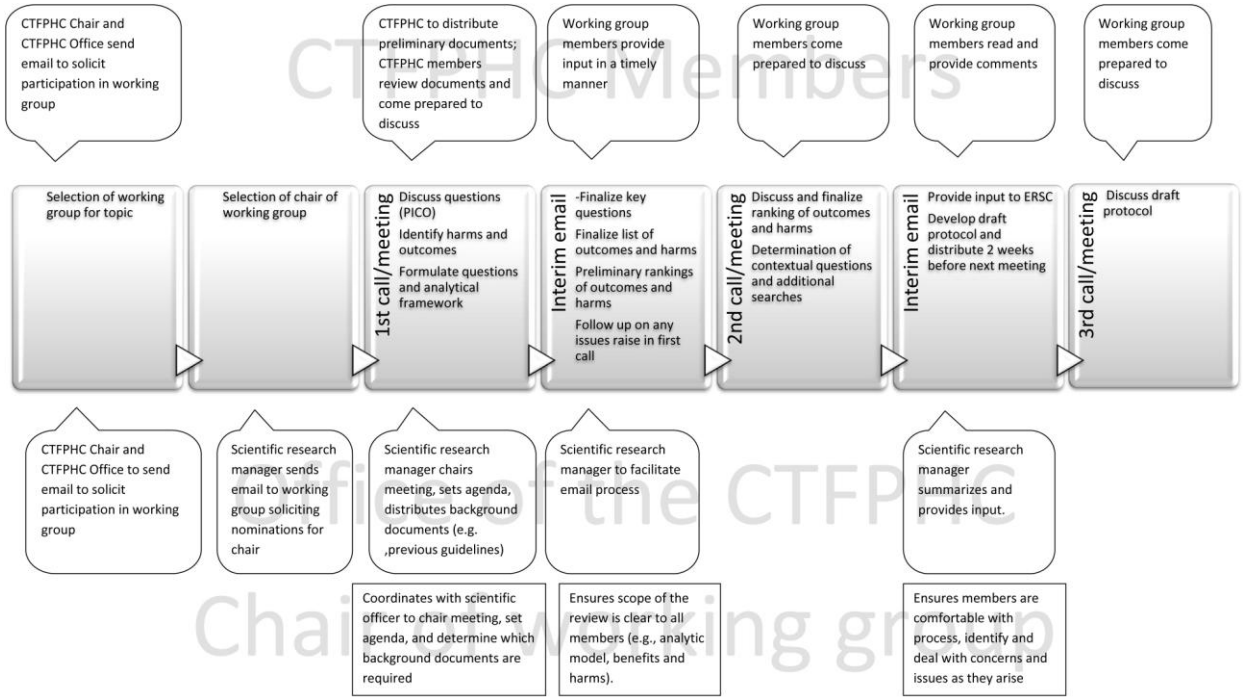

Figure 2A. Steps in the process of reviewing evidence and preparing recommendations (part 1). CTFPHC = Canadian Task Force on Preventive Health Care, ERSC = Evidence Review and Synthesis Centre, PICO = populations, interventions, comparators and outcomes.

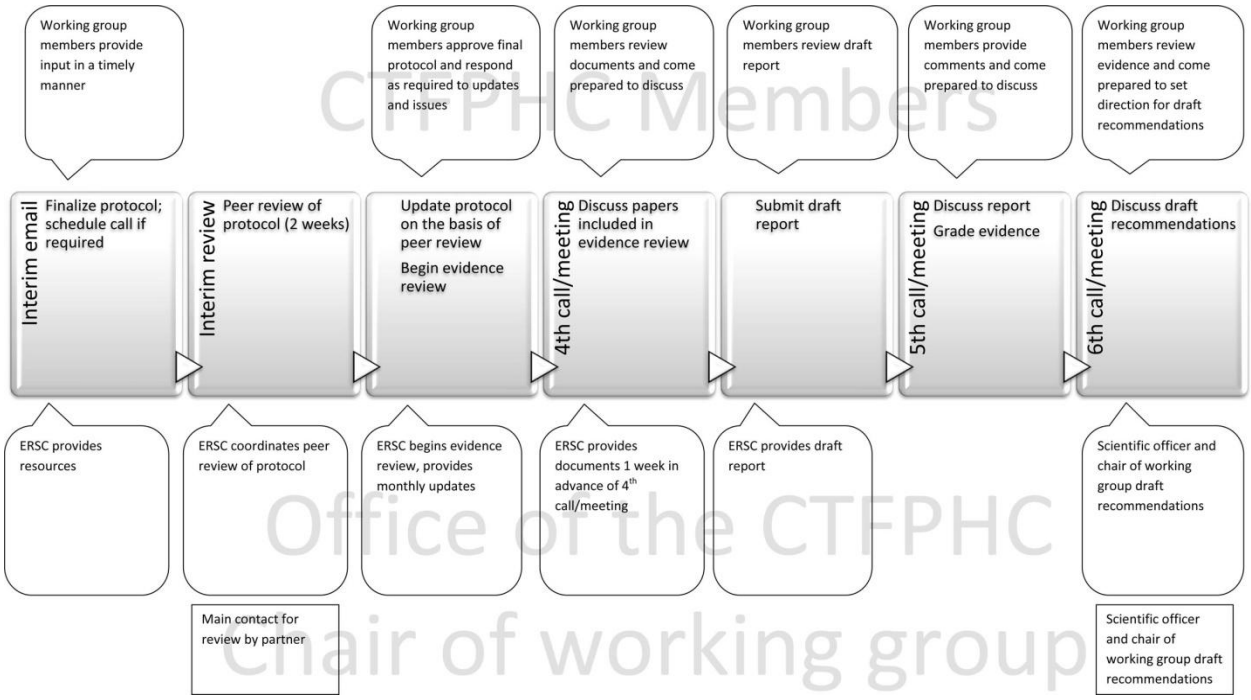

Figure 2B. Steps in the process of reviewing evidence and preparing recommendations (part 2). ERSC = Evidence Review and Synthesis Centre.

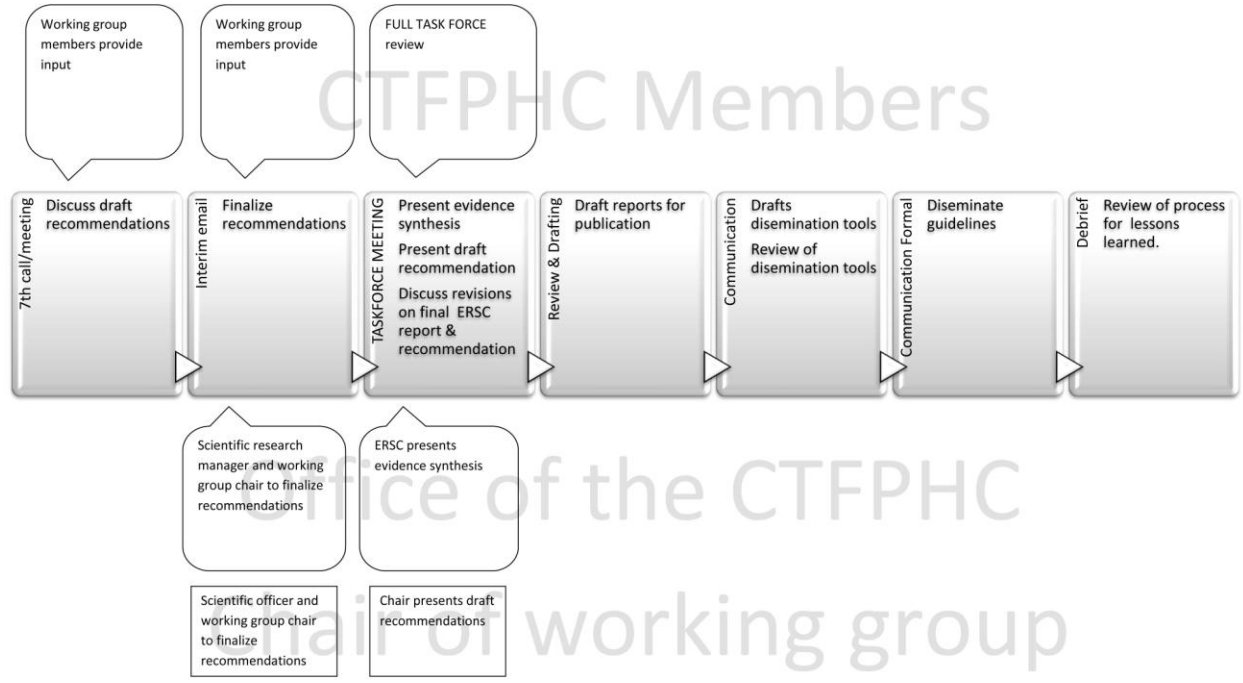

Figure 2C. Steps in the process of reviewing evidence and preparing recommendations (part 3). ERSC = Evidence Review and Synthesis Centre.

2.1.4 Topic working groups

For every topic selected by the CTFPHC, a topic working group is formed. This working group consists of two to five CTFPHC members who volunteer to join the working group (one of whom is selected as chair), a scientific research manager from the Office of the CTFPHC and members from the ERSC, as well as from partner organizations, if any such organizations are involved for the particular topic. The responsibilities of the members of topic working groups are described in Appendix VI.

2.2 Development of analytic framework and key questions

The topic working group develops the analytic framework and key questions, which define the scope and focus of the review and influence the associated workload. The CTFPHC as a whole and partner organizations (if applicable) review and approve these documents. (See Appendix VII: Guide for External Reviewers and Appendix VIII: Guide for Internal Reviewers).The chair or cochair of the working group then sends the analytical framework and key questions to the ERSC and they begin the review.

2.3 Development, review and approval of protocol

The ERSC and its clinical experts develop a protocol based on information received from the working group and the scientific research manager. The protocol contains information about the literature search, the analytic framework, the research questions (key and contextual), and the project schedule. The working group reviews and discusses the protocol and revises it if necessary.

The protocol is also sent to all members of the CTFPHC for approval and comment (within two weeks). The protocol is then reviewed by three to six peer reviewers who are experts in the topic area. If a partner organization is involved, that organization also reviews the protocol. Comments received from task force members, peer reviewers and partners (if applicable) are incorporated into the protocol. The final protocol is then approved first by the working group and then by the broader CTFPHC. (See Appendix VII: Guide for External Reviewers, Appendix VIII: Guide for Internal Reviewers and Appendix IX: Protocol Template).

2.4 Draft evidence review

The ERSC conducts a systematic review of the available evidence according to the final, approved protocol. At a predetermined midpoint in this process, the ERSC may prepare an interim review, consisting of the summary tables recommended by the GRADE Working Group,[2] for distribution to and discussion by the CTFPHC, to resolve any issues of concern that have arisen. Upon completion of the review process, the ERSC distributes the draft evidence review, including GRADE tables, to the topic working group. After approval by the working group, the ERSC also sends the draft evidence review to at least three peer-reviewers. Potential reviewers may be suggested by the ERSC, the CTFPHC or the Office of the CTFPHC. In addition, the chair and selected members of the CTFPHC are asked to provide feedback on the draft evidence review. (See Appendix X: Evidence Review Template).

2.5 Final evidence review

The chair of the working group, the PHAC scientific research manager and the ERSC edit the evidence review on the basis of feedback received from peer reviewers, partner organizations, and CTFPHC members. (See Appendix VII: Guide for External Reviewers for details on the external review process). The ERSC prepares for the topic working group a summary of reviewer comments, information about how the comments were addressed and a revised

version of the report. At this point an updated literature search is conducted to capture any new evidence that was published since the original search was undertaken. The evidence review is finalized once the members of the working group and the CTFPHC have reviewed and approved the revisions. At this point, members of the ERSC can prepare and submit a manuscript for publication in the scientific literature. Publication should be coordinated with the release of the recommendations.

2.6 Draft recommendations

While the draft evidence review is undergoing peer review, the chair of the working group and the scientific research manager discuss potential recommendations and clinical considerations arising from the evidence. They then draft the recommendations and share them with the topic working group. Once the topic working group has approved the recommendations, they are then shared with the entire CTFPHC, as described below.

2.6.1 CTFPHC vote on draft recommendations

During a meeting or virtual meeting of the CTFPHC, the ERSC presents the findings of the evidence review, and the working group presents the draft recommendations. Members of the task force discuss the evidence review and recommendations and may propose changes to the wording of the recommendations. The CTFPHC votes on the draft recommendations. The timeline from approval of the protocol to presentation of the draft recommendations to the CTFPHC is usually 9 to 15 months.

2.6.2 External review of draft recommendations

Following the discussion and voting during a meeting of the CTFPHC, the chair of the topic working group or the scientific research manager revises the recommendations and shares the revised version with all members for the CTFPHC for approval. The approved statement of recommendations is then sent to external peer reviewers for comment. (See Appendix VII: Guide for External Reviewers and Appendix VIII: Guide for Internal Reviewers).

2.7 Approval of final recommendations

Comments provided by peer reviewers are shared with the topic working group and the scientific research manager, who decide whether any changes are required. If substantial revisions are required or if the recommendations are controversial, the entire CTFPHC may be asked to review and discuss the comments. If no substantial revisions are required, the CTFPHC approves the final recommendations at its next meeting or by email if no meeting is scheduled. If substantial revisions are deemed necessary, the working group makes the changes and brings the recommendations back to the entire CTFPHC for approval.

2.8 Release of recommendations and evidence review

CTFPHC recommendation statements will be published in the peer-reviewed literature. An agreement has been reached with the *Canadian Medical Association Journal* giving the journal right to first refusal to publish the recommendations, with the option of also publishing a manuscript prepared from the evidence review. The recommendations should be released within nine months from the time of the CTFPHC vote described in section 2.6.1. Evidence reports and recommendations are published on the CTFPHC website in accordance with arrangements with the journal publishing the recommendations for a particular topic. All materials intended for publication or release are submitted to PHAC and the CPHO for information at least four weeks before any public announcement or release.

Section 3: Categories of CTFPHC recommendation statements

The CTFPHC's work on each topic depends on how the particular topic is to be handled. Active recommendations, as well as a list of topics that the task force is working on, are posted at the CTFPHC website (http://www.canadiantaskforce.ca). Activities related to active topics include updates of previous recommendations and endorsement or adaptation of guidelines from other organizations. Inactive topics are those that the CTFPHC has considered but has decided not to address, because they are no longer relevant to clinical practice, are not relevant to the primary care setting or for primary care providers, have a low burden in terms of public health or are otherwise determined to be beyond the scope of the CTFPHC.

The CTFPHC considers seven types of active topics:

- new (de novo) topics (i.e., topics that have not previously been addressed by the CTFPHC)
- topics for updates (i.e., topics that the CTFPHC has addressed in the past)
- topics to be addressed in partnership with another guideline organization (new or updated)
- topics for which guidelines by other major guideline organizations will be considered for endorsement
- topics for which guidelines by other major guideline organizations will be considered for adaptation
- topics for which existing CTFPHC recommendations will be reaffirmed
- topics that will be referred to other major guideline organizations performing evidence-based reviews

Each type of active topic has a defined process and timeline (Table 3A), along with specific resource requirements for associated activities and formats for documents arising from those activities (Table 3B). Additional detail about each type of active topic is provided below.

3.1 New (de novo) topics

Subsequent sections of this manual describe the processes for developing protocols (section 4), preparing evidence reviews (section 5) and making recommendations (section 6) related to new topics.

3.2 Topics for updates

The processes for preparing updates for active topics are similar to those for new topics, as described in sections 4, 5 and 6 of this manual.

3.3 Topics addressed in partnership

Topics to be addressed in partnership are those for which the CTFPHC has an opportunity to collaborate with an authoritative organization with a record of high-quality work. Working groups for such topics will include members from both the CTFPHC and the partner organization. The processes for preparing materials for topics to be addressed in partnership are similar to those for new topics, as described in sections 4, 5 and 6 of this manual.

3.4 Topics for endorsement

Topics for which the CTFPHC may consider endorsing an existing guideline are those that have been addressed recently by a major guideline organization. Before the CTFPHC provides its endorsement, the members of the task force appraise the guideline using an appraisal instrument such as the Appraisal of Guidelines for Research and Evaluation instrument (AGREE II)[3] and review the guideline in detail, according to the process shown in Figure 3. Ideally, and with appropriate permission from and facilitation by the partner organization, such a

review occurs before public dissemination of the guideline. If the guideline is deemed acceptable without changes, the task force endorses the guideline. If the members of the task force decide that the guideline cannot be endorsed in its original form, they may recommend the guideline for adaptation (see section 3.5).

3.5 Topics for adaptation

Topics for which the CTFPHC may consider adaptation of an existing guideline are those that have been addressed recently by a major guideline organization, but the task force has decided, after appraisal using an accepted instrument (such as AGREE II),[3] not to endorse the complete guideline (see section 3.4). The task force adapts the recommendations using an accepted instrument such as ADAPTE[4] and reviews the resulting adapted guideline in detail before approval and release.

Identification of an eligible* guideline for potential endorsement by:

- Office of the CTFPHC (literature scan)
- Member of CTFPHC
- Partner
- Suggestion from guideline-producing organization

Notify topic prioritization working group

Does the topic meet the CTFPHC's criteria for relevance†?

NO → Stop process: topic shelved; may be re-evaluated later

YES

Step 1: Formation of topic-specific endorsement working group

- 1 PHAC scientific research manager or officer
- 1 external content expert
- 2 or 3 CTFPHC members

Assisted by:

- ERSC
- Guideline liaison

Step 2: **Content review‡**

Step 3: Process review§
Endorsement working group assesses guideline-development process (AGREE II)

Evidence of high-quality content?

NO → Stop process: no endorsement. Can guideline be adapted? Updated? New guideline needed?

YES

Step 4: Endorsement working group liaises with guideline-producing organization

Evidence of high-quality process?

NO → Stop process: no endorsement. Can guideline be adapted? Updated? New guideline needed?

YES

Any gaps?

YES → Endorse with caveat that identified gaps will be addressed by CTFPHC

NO

CTFPHC endorsement posted at CTFPHC website, providing web link to the guideline

***Eligibility:**

- Identification of original guideline-development group and original funding source
- Focus on prevention: Is the guideline aligned with the CTFPHC mandate?
- Currency and Timing of guideline publication: preference for not-yet -released guidelines (window of acceptable endorsement needs to be determined)
- Application and relevance to Canadian context: rural, Aboriginal, immigrant, other populations unlikely to be covered by non-Canadian guideline-development groups
- Content review by clinical experts

†Criteria for relevance:

- Disease burden and expected effectiveness of preventive service in decreasing the burden
- Potential impact of recommendation on clinical practice
- Public or provider interest in the topic
- Variation in care and potential for preventive service to decrease that variation
- Sufficiency of evidence
- New evidence
- Degree of alignment with CTFPHC key questions

‡Content review:

- How strong and comprehensive is the evidence base for the guidelines?
- Have new systematic reviews been conducted or recent existing reviews included as part of the evidence base?*
- If the guideline is an adaptation of other guidelines, these questions need to be asked of the original guidelines as well as the adapted guideline
- Look at significant references: landmark studies, most recent available, external expert input
- Grading system used: consistent with the standards used by the CTFPHC?
- Are there clear recommendations for primary care practitioners?
- Comprehensiveness at covering topic: Are all aspects covered?
- Are appropriate primary and secondary outcomes defined?
- Consistency of content with related guidelines on same topic

§Process review: APPLICATION of AGREEII

NOTE: If the guideline is adapted from other guidelines, the AGREEII tool should be applied to all reference guidelines if the information is not available by the current guideline developers.
Domain 1. Scope and Purpose is concerned with the overall aim of the guideline, the specific health questions and the target population (items 1–3).
Domain 2. Stakeholder Involvement focuses on the extent to which the guideline was developed by the appropriate stakeholders and represents the views of its intended users (items 4–6).
Domain 3. Rigour of Development relates to the process used to gather and synthesize the evidence and the methods to formulate and update the recommendations (items 7–14).
Domain 4. Clarity of Presentation deals with the language, structure and format of the guideline (items 15–17).
Domain 5. Applicability pertains to the likely barriers to and facilitators of implementation, strategies to improve uptake and resource implications of applying the guideline (items 18–21).
Domain 6. Editorial Independence is concerned with the formulation of recommendations not being unduly biased with competing interests (items 22 and 23).

Figure 3: Process for review and appraisal of an existing guideline developed by another major organization, with a view to endorsement by the Canadian Task Force on Preventive Health Care (CTFPHC). AGREE II = Appraisal of Guidelines for Research and Evaluation (updated version), ERSC = Evidence Review and Synthesis Centre, PHAC = Public Health Agency of Canada.

3.6 Topics referred to other groups performing evidence-based reviews

If the CTFPHC deems that another organization is better suited to developing recommendations for a specific topic, the task force may refer the topic to that organization. Topics for referral to other organizations are ones for which the CTFPHC has developed recommendations in the past and that the task force would like to keep active. The organization being considered for referral must be an appropriate source of guidelines, must follow and document the methods used for conducting evidence reviews and must have a process for updating recommendations.

The process for referral of a topic consists of the following steps:

1. review of the previous evidence review and recommendations of the CTFPHC
2. identification of an organization that is making evidence-based recommendations on the topic
3. identification (by the Office of the CTFPHC) of recommendations and evidence review methods of the other organization
4. preparation (by the Office of the CTFPHC) of a summary of the topic, rationale for why it has been chosen as a topic for referral, reference to existing recommendations on the topic prepared by the identified organization, statement about differences in methods between the CTFPHC and the identified organization, and a statement that the previous CTFPHC evidence review will not be updated
5. presentation and discussion of the summary at a meeting of the CTFPHC and voting by members on whether to refer the topic
6. posting of the topic summary on the CTFPHC website with a link to the other organization's recommendation statement, once it has been completed
7. reconsideration of the topic by the CTFPHC every five years

Table 3A: Overview of the processes and timelines for active topics

Category of topic	Definition	Method of identifying topic	Method of evidence review	Time from topic identification to vote	Frequency of consideration
New	Topic never previously reviewed by the CTFPHC	Reframing of previous topic, Federal Register, nomination from CTFPHC	Full evidence review	12–16 mo	3 yr after publication of previous recommendations
Update (full or targeted, based on evidence review)	Topic reviewed previously by CTFPHC; decision to update because topic is a priority and is within the scope of the CTFPHC or because there is a compelling reason to prepare an updated statement; intensity of update depends on amount of new evidence, status of old evidence, complexity of topic and controversies	Topic prioritization working group	Evidence review: a) entire analytic framework or b) targeted to critical key gaps	6–16 mo	3 yr after publication of previous recommendations
Partnership	Topic that is addressed in partnership with another organization (new or updated)	Topic scan by CTFPHC, discussions with potential partner organization	Full evidence review	12–16 mo	3 yr after publication of previous recommendations

Table 3A: Overview of the processes and timelines for active topics					
Category of topic	**Definition**	**Method of identifying topic**	**Method of evidence review**	**Time from topic identification to vote**	**Frequency of consideration**
Endorsement	Topic that is being addressed by another major guideline organization (ideally while preparation of recommendations is still in progress)	Topic prioritization working group	Appraisal and discussion of evidence review and guideline prepared by other organization	3 mo	1 yr after original publication and periodically thereafter
Adaptation	Topic not previously reviewed by the CTFPHC, for which another organization has prepared a guideline	Topic prioritization working group	Appraisal of quality of other organization's guideline with accepted appraisal instrument	6 mo	3 yr after publication of previous recommendations
Reaffirmation	Topic with a well-established, evidence-based standard of practice; decision to reaffirm because topic is a priority and is within the scope of the CTFPHC or because there is a compelling reason to make a statement; recommendations are changed only in the presence of a very high level of new evidence	Topic prioritization working group	Brief literature search and consultation with experts and partners to identify high-level evidence	3 mo	3 yr after publication of previous recommendations
Referral to another organization	Topic of importance for which the CTFPHC decides that another organization is in a better position to make accurate and timely recommendations	Topic prioritization working group	Discussion by CTFPHC and with experts	3 mo	Every 4–5 yr

Note: CTFPHC = Canadian Task Force on Preventive Health Care.

Table 3B: Overview of the resources and format for active topics					
Category of topic	**Staff and resources**	**Use of experts**	**Format of documents**	**Web format and documents**	**Approval process and presentation at meeting (CTFPHC)**
New	ERSC, Office of the CTFPHC, CTFPHC Several full evidence reviews	At several steps	Full RS and evidence report	Active topic: RS and evidence report	Full presentation, full vote
Update (full or targeted, based on evidence review)	ERSC or Office of the CTFPHC with CTFPHC members Targeted literature search (i.e., limited number of critical key questions)	At several steps	Full RS and evidence update	Active topic: RS and evidence report	Full presentation, full vote
Partnership	ERSC, Office of the CTFPHC, CTFPHC	At several steps	Full RS and evidence report	Active topic: RS and evidence report	Full presentation, full vote
Endorsement	Office of the CTFPHC and CTFPHC (one member designated as lead) Review of recent recommendations of other organization, brief literature search of new high-level evidence and discussion with experts	Presentation of other organization's review with comments	Endorsement RS, link to other organization's RS	Active topic: endorsement RS, previous RS or report, summary of new evidence	Full presentation at meeting, full vote or electronic vote

Table 3B: Overview of the resources and format for active topics					
Category of topic	**Staff and resources**	**Use of experts**	**Format of documents**	**Web format and documents**	**Approval process and presentation at meeting (CTFPHC)**
Adaptation	Office of the CTFPHC and CTFPHC	At several steps	Adapted RS	Active topic: adapted RS	Full presentation at meeting, full vote or electronic vote
Reaffirmation	Office of the CTFPHC and CTFPHC (one member designated as lead) Brief literature search of new high-level evidence and discussion with experts	During monitoring process (to identify new evidence)	Reaffirmation RS: brief, modified RS with summary statement of recommendation and evidence, updated clinical considerations, description of search method and statement of no substantial new findings	Active topic: reaffirmation RS, previous RS or report, summary of new evidence	Full presentation at meeting, full vote or electronic vote
Referral to another organization	Office of the CTFPHC and CTFPHC Review and discussion of recommendations produced by other organizations	During identification of recommendations from other organizations	Statement about the referral, with reference to website of other organization and date stamp	Active topic	Full vote at meeting or electronic vote; periodic monitoring only after decision to refer has been made

Note: CTFPHC = Canadian Task Force on Preventive Health Care, ERSC = Evidence Review and Synthesis Centre, RS = recommendation statement.

Section 4: Development of a review protocol

For each topic that is deemed suitable for a new or updated review, a working group is created, consisting of two to five members of the CTFPHC, members from the ERSC and a PHAC scientific research manager. The chair of the working group and the assigned PHAC scientific research manager collaborate to prepare the work assignment (a formal statement of the work required and the type of review to be conducted) for the topic. The working group is also responsible for clearly defining the scope of the topic for the ERSC research team that will prepare the evidence review. The ERSC assigns a team and a lead investigator. In addition, with support from the chair of the working group and the scientific research manager, the ERSC prepares the protocol on the basis of the work assignment. The working group reviews the protocol and then sends it for external peer review. After updating to reflect the peer reviewers' comments, the draft protocol is presented to the CTFPHC for approval, and the protocol is finalized by the working group and the ERSC. Final approval is given by the chair of the working group and the chair and/or vice-chair of the CTFPHC. Further details about preparation and approval of the protocol are provided in the sections below. Development of a protocol can take up to four months.

4.1 Types of reviews

To address the key questions associated with a topic, the ERSC undertakes a series of evidence reviews. Several approaches are used to ensure efficiencies:

- a full evidence review (the most common approach) to address each key question in the analytic framework; existing high-quality evidence reviews may be used if they are relevant to the research questions
- targeted evidence reviews for a limited number of key questions in the analytic framework that address critical gaps in knowledge, for which established or current evidence may not be available (common approach for updates)
- staged reviews to address key questions in the analytic framework that must be answered before a full review can proceed (used as a means of informing the CTFPHC that there is sufficient evidence to proceed with other questions in the analytic framework)

4.2 Appropriate approach to the reviews

The working group determines the level of evidence (i.e., the acceptable study design) needed to develop recommendations. For updated reviews, the following process is used to determine the appropriate approach:

- review of the previous CTFPHC recommendations to determine their relevance for the current review
- examination of the scope, questions, limitations and gaps of the previous evidence review
- identification of current evidence

4.3 Method for developing a protocol

The ERSC uses the protocol template (Appendix IX) to prepare the protocol. The following sections outline the main steps in preparing the protocol.

4.3.1 Identify the questions

Each recommendation should answer a key question, so the first step in developing the protocol is to identify these key questions. Each key question should specify the target population, the intervention, its comparator, and the outcomes, as well as relevant temporal characteristics (e.g., the timing and duration of the intervention). The types of evidence that will be used to examine each key question should also be considered, although they need not be specified in

the questions themselves. The mnemonic used to summarize these characteristics is PICOT, for population, intervention, comparator, outcomes, timing. See section 4.3.3.2 for examples of well-constructed key questions.

4.3.2 Select outcomes and rank their importance

The topic working group identifies and ranks all clinically important patient outcomes using a modified-Delphi method. Rankings are based on the GRADE approach.[2] Each member of the topic working group will rank the outcomes, and the median ranking (rounded up if necessary) will be used in the review. Outcomes ranked 1 to 3 are of limited importance, those ranked 4 to 6 are important, and those ranked 7 to 9 are critical. Critical outcomes are of decisive or essential importance; in addition, information about such outcomes is indispensable, and these outcomes are likely to determine a decision about care. Important outcomes are meaningful, consequential and significant, and they may influence a decision about care. Such outcomes should be included in a GRADE summary-of-findings table, but inclusion of a particular important outcome may depend on the number of other important outcomes. Outcomes of limited importance are of little consequence or significance, are unlikely to influence a decision and are not included in a summary-of-findings table. When ranking outcomes, the working group typically adopts the patient's perspective. Critical and important outcomes are included in the GRADE evidence profile, but only critical outcomes are considered for the recommendations.

The CTFPHC and its working groups use three main principles in ranking outcomes:

1. The judgments are based on values; the values of those who are affected (i.e., patients) should be used wherever possible.
2. The judgments are relative, not absolute (i.e., the importance of each outcome is considered in relation to other relevant outcomes for the specific care decision that is being considered).
3. The relative importance of an outcome depends on the likelihood that it will be affected by the intervention (e.g., the outcome of death is crucial to most people, but it is of limited or no importance in decisions about many interventions).

4.3.3 Create analytic framework

The working group uses an analytic framework to illustrate the key and contextual questions that the literature review must answer to determine whether the proposed preventive service will safely prevent clinically relevant adverse outcomes. The analytic framework links interventions and outcomes to help structure the evidence review.

Analytic frameworks do not incorporate all factors associated with the clinical preventive service. Furthermore, they are not decision algorithms and do not incorporate all possible outcomes.

In an analytic framework, actions (such as the performance of a screening test) are depicted by arrows, and outcomes (such as decreased morbidity) are depicted by rectangles (see template in Figure 4). An analytic framework distinguishes between clinically relevant outcomes (those that are perceived by the patient) and intermediate outcomes, including surrogate outcomes and clinical correlates (which cannot be perceived by the patient). All clinical relevant outcomes must be specified. The CTFPHC considers intermediate outcomes only when evidence about clinically relevant outcomes is lacking. In this situation, the intermediate outcomes must be specified. Use of intermediate outcomes may lead to a downgrading of the quality of the evidence in the final evidence review. The association of intermediate outcomes to the final outcome is depicted with a dashed line.

Whenever cause-specific and all-cause mortality are available, they should be used as outcomes in the analytic framework.

4.3.3.1 Conventions

The analytic framework specifies populations, actions and outcomes (Figure 4).

- The **population** consists of the patients for whom the proposed preventive service is intended.
- The **actions** link the population to the outcomes (or they may link the outcomes directly) and may include screening and treatment. The name of each action appears in a label above its respective arrow. Adverse events, which are considered to be "actions" and which are denoted by curved arrows, can also be included in the framework.
- Clinically relevant or intermediate **outcomes** result from actions or from previous outcomes. Clinically relevant outcomes are depicted as rectangles with square corners, whereas intermediate outcomes are depicted as rectangles with rounded corners.

Each arrow is associated with a key question that must be addressed by the evidence review, and all of the key questions are listed with the analytic framework.

Figure 4 illustrates the template for an analytic framework that will guide the ERSC or PHAC staff researchers in conducting a literature review for the CTFPHC. The framework shows, in order, the population identified for study (i.e., persons at risk), the activities to be studied (i.e., screening and early detection), the intermediate and ultimate health outcomes being sought, and the desired association between them. Adverse effects of screening are shown as ovals below the main flow. Each element in the flow chart is related to one of the key questions.

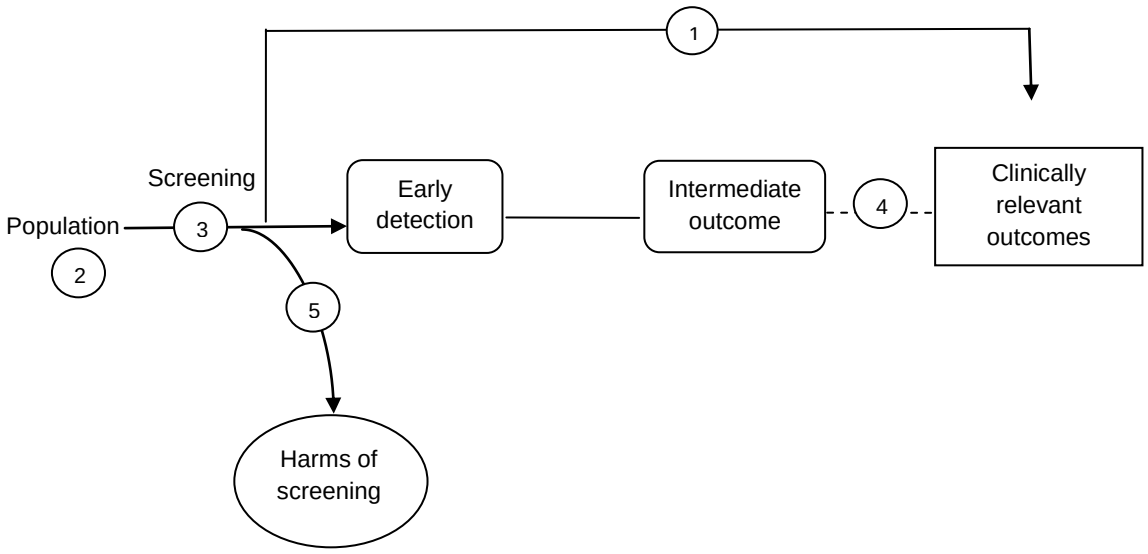

Figure 4. Template for an analytic framework. The circled numbers relate to examples of numbered key questions shown in the text.

The analytic framework may be revised over the course of the project, depending on the findings of the evidence review.

4.3.3.2 Key questions

The key questions are associated with the analytic framework and serve to focus and guide the evidence review. They specify the population, interventions and outcomes for the topic under consideration and are critical to conducting the literature search and the evidence review and to developing the recommendations. Key questions for an updated review may focus on a limited aspect of the topic and may be used to examine gaps in the evidence for the previous review, or they may be used to examine new evidence published since the previous review.

The following are templates for well-constructed key questions relating to the template in Figure 4:

1. What is the evidence that screening for X in patient population Y reduces morbidity and mortality?
2. Can a group at high risk for X be identified on clinical grounds?
3. What is the evidence that accurate (i.e., sensitive and specific) screening tests are available for condition X?
4. How strong is the association between intermediate outcomes and clinically relevant outcomes for condition X?
5. What are the harms of screening test X for patient population Y?

Questions on the appropriate interval of screening and special considerations for high risk groups should also be included as key questions. Subquestions may be included if they are directly related to the main key question. If the subquestion is not part of the main key question, this should be its own key question.

4.3.3.3 Contextual questions

Contextual questions (identified by the topic working group) are not associated with the analytic framework, but the CTFPHC requires responses to these questions as context for the recommendations. The contextual questions, which are not addressed with formal evidence reviews, may relate to risk factors, prevalence, cost-effectiveness, equity, patient values and preferences, comorbidities, and performance measures. Treatment of the condition should only be considered in the background section of the systematic review as it is outside of the CTFPHC's scope.

Contextual questions often included in the evidence review are:

1. What is the cost-effectiveness of <intervention> for <disease/condition in <population>?
2. What are the patient values and preferences for <intervention> for <disease/condition>?
3. What process and outcome performance measures or indicators have been identified in the literature to measure and monitor the impact of <intervention> for <disease/condition>?
4. What is the optimal screening interval for <intervention> for <disease/condition>?
5. What risk assessment tools are identified in the literature to assess the risk of <disease/condition>?
6. What is the evidence for a higher burden of disease, a differential treatment response, differential performance of <intervention>, or barriers to implementation of <intervention> for <disease/condition> in subgroups? Subgroups include: Aboriginal population, rural or remote populations, or other ethnic populations.

4.3.4 Perform preliminary scan of evidence

The ERSC conducts a preliminary scan of the literature during the protocol-development phase to determine the volume of literature related to the key questions. Searches for English-language publications are conducted in the Cochrane Database of Systematic Reviews and MEDLINE. Retrieval of articles is limited to systematic reviews, meta-analyses, randomized controlled trials and controlled clinical trials. For questions about harms, cohort and case–control studies are also included. The ERSC also searches the resources of major guideline-producing organizations to identify ongoing, planned or completed reviews that may be relevant to the topic.

4.3.5 Check previous CTFPHC recommendations

If the project is an update of a previous CTFPHC review and recommendations, the current protocol and evidence review cites the previous recommendations, analytic framework, key questions, findings and conclusions. Any limitations of the previous review should be included.

4.3.6 Consult content experts

The ERSC may contact content experts for advice on the protocol and methodology. Topic experts must complete the conflict of interest form (Appendix I) and must sign a confidentiality agreement (Appendix II).

4.3.7 Send protocol to peer reviewers

The protocol must be reviewed by three to six content experts before it is finalized. The ERSC develops a list of potential peer reviewers for review and approval by the PHAC scientific research manager. The ERSC then coordinates the peer review. Once comments have been received and incorporated into the protocol, a summary of the comments and action taken are presented to the working group for approval.

4.3.8 Seek approval of protocol from CTFPHC

The final protocol is presented to the CTFPHC for approval.

Section 5: Development of evidence reviews

This section describes the CTFPHC process for developing its evidence reviews.

5.1 Inclusion and exclusion criteria

The inclusion and exclusion criteria used in selecting articles for the evidence review are documented in the protocol and the review itself.

In the case of an update, the inclusion or exclusion of studies that were considered in the previous CTFPHC review will depend on the topic and the extent to which the new key questions were addressed in the previous review. More specifically, the topic working group must determine if the key questions in the current review were appropriately addressed in the previous review and then decides whether to exclude the studies or to include them (i.e., review them again if the current questions are different or the methods used in the current and previous reviews differ).

To reduce duplication of effort, primary studies that were included in other high-quality evidence reviews relevant to the current review may be excluded and the results of the other evidence reviews used in the current review (see also section 5.9).

5.1.1 Study design

The levels of evidence used for a review, which are determined in part by study design, vary by topic. The following is a general hierarchy for evidence based on study design:

1. systematic reviews of randomized controlled trials
2. randomized controlled trials (RCTs)
3. systematic reviews of nonrandomized controlled trials
4. nonrandomized controlled trials
5. observational studies with controls (prospective and retrospective cohorts, case–control studies, studies with before-and-after designs)
6. observational studies without controls (cross-sectional, case series)
7. ecological studies and surveys

Because the Task Force is focusing on the best quality evidence that is available to answer a particular questions evidence to answer key questions about the benefits of interventions is limited to studies with the first five designs, whereas searches for evidence of harms can be extended to all study types. Evidence to answer contextual questions can be even broader. Only published data may be included as evidence, and abstracts on their own are not sufficient. Modeling studies are considered when there is insufficient data from the first five study designs to answer the key questions. Modeling data can be useful to study the cost effectiveness of interventions, the age at which to start or stop screening and to help to determine appropriate screening intervals. These data should be used with caution if they are the only data available to address the clinical effectiveness of an intervention. When modeling studies are used to answer key questions, a separate process must be followed to select and appraise these studies. This process is outlined in Appendix XI. Modeling studies used to answer contextual questions are not subject to the modeling assessment process and are examined in the same manner as any other contextual questions (see section 5.10). The decision to include modeling studies is made by the working group.

Once the key and contextual questions have been developed, the topic working group determines, on the basis of their own knowledge and input from the ERSC's technical experts,

which study designs would be most appropriate to answer each of the research questions. At this point, members of the working group can determine whether they would like to focus exclusively on systematic reviews and RCTs or whether they will expand the search to include observational and modeling studies. The group may also decide on a staged approach to the search, whereby they first collect data from RCTs and make the decision about whether supplemental observational or modeling data are needed once the RCT data have been reviewed. In such cases, the process and criteria for supplementing the RCT data should be documented in advance.

The topic working group should come to a consensus, based on a clear rationale, about the study designs that will be admissible for the review and should document these decisions. For example, in an examination of the impact of harms, the working group may decide to include large cohort studies, as these are more likely than RCTs to detect effects. Decisions about inclusion criteria that are based on study design should be sent to the methods working group for discussion, and input from technical experts should be sought as required.

If a decision is made to include observational studies, the working group may decide to limit the amount of observational data collected on the basis of sample size, study design or other relevant criteria. A minimum sample size of 1000 is suggested for inclusion of observational data.

In addition, the topic working group may consider the following questions when deciding whether to include observational data:

- Are there sufficient high-quality RCTs to answer the key questions?
- In cases where a staged approach to the search is being employed, would the addition of new data from observational studies change the conclusions of the review or the guideline recommendation?
- Are the findings from RCTs homogeneous, or are there inconsistencies in the results that observational data might help to address?
- What are the costs and benefits of including observational data (i.e., this substantially increase the workload with little additional benefit to the review)?
- For the topic under consideration, is it important to be as comprehensive as possible by collecting all of the available evidence? Such a comprehensive approach may be necessary if study results vary widely or the topic is particularly controversial.
- Is the key question better answered with observational studies?
- Are certain types of observational studies (e.g., cohort or large-sample studies) better suited to answer the research question than other types of observational or RCT designs?
- Are the observational data current?
- Would the inclusion of observational data change the strength of the evidence that will form the basis of the recommendation? For example, the GRADE Working Group recommends that if the quality of evidence differs across critical outcomes and the outcomes point in different directions — toward benefit and toward harm — the lowest-quality evidence for any of the critical outcomes determines the overall quality of the evidence. This means that if both RCT and observational data are used for an outcome, the overall data quality would be low.[2]

The selected approach should be documented a priori in the protocol (to reduce the potential for bias) and should be explained in the final review. Any changes that are made to the search parameters after the review is under way should also be documented. The process should be transparent, defensible and reproducible.

5.2 Literature search

Once the protocol has been finalized (as described in section 4), an ERSC librarian, with input from the topic working group, develops the search strategy to identify systematic reviews and meta-analyses on the topic. The search begins with the Cochrane Database of Systematic Reviews and MEDLINE. Other databases, such as EMBASE and topic-specific databases, are also searched if needed. The search timeframe is not limited unless the review is an update, in which case the search is limited to three months before the final date of searching for the previous review. Languages are limited to English and French.

The databases of ClinicalTrials.gov and the National Institutes of Health Computer Retrieval of Information on Scientific Projects may also be searched to identify trials in progress that may be relevant to the topic. When the first draft of the evidence review is complete, one update of the search is conducted to identify any studies that have been completed in the interim.

The search will also include terms to identify any relevant modeling studies or studies related to risk assessment tools. Any identified studies on modeling or risk assessment tools will be set aside by the ERSC and will be used if the working group decides this information is required for the evidence review.

A search of the grey literature should also be conducted to identify relevant Canadian data that has been disseminated from high-quality governmental and nongovernmental organizations such as the PHAC, the Canadian Institutes for Health Research, Statistics Canada and the Canadian Agency for Drugs and Technologies in Health. This type of information is incorporated into the review as contextual information and is not assessed with the GRADE system.

5.2.1 Documentation of search strategy

The search strategy is documented in the final evidence review. If an updated search is conducted after completion of the draft evidence review (see section 5.2, above), it is also documented in the search strategy.

5.2.2 Database of included and excluded articles

For all articles identified during the literature search or by other search methods, the ERSC enters information in a database, recording the source of the citation, whether the study will be included or excluded, reasons for inclusion or exclusion, and any other relevant information.

5.3 Selection of articles

The ERSC applies the a priori inclusion and exclusion criteria to the results of the literature search to identify articles suitable for the evidence review. There are two rounds of screening. Level 1 screening involves review of the title and abstract of each article. Either two reviewers screen all titles and abstracts independently, or one reviewer screens the titles and abstracts and the other confirms the decision to include or exclude. On the basis of this review, all citations are coded as “included” or “excluded.” Any studies that are screened in by only one of the two reviewers at this stage are automatically selected for level 2 screening.

The articles selected during level 1 screening then undergo level 2 screening by at least two additional reviewers. This screening involves review of the full text of each article, and each article is again coded as “included” or “excluded.” Studies that are screened in at this stage

must be coded to specify the key question addressed, and excluded studies are coded with the reason for exclusion.

5.4 Abstraction of data

Data from the included articles may be abstracted using a specific form (see Appendix XII) or may be inserted into evidence tables. Abstracted data include, but are not limited to, information related to the key question, as well as details of the study design, the population studied, the intervention, results, study quality, and generalizability. Data are abstracted either by two reviewers working independently or by one reviewer with confirmation by the other reviewer. Disagreements are resolved by a third party, as required.

5.5 Critical appraisal

The ERSC uses the GRADE process to assess the internal and external validity of each included study.

5.5.1 Quality of evidence

As defined by the GRADE Working Group, the quality of evidence is the "extent to which our confidence in an estimate of the effect is adequate to support a particular recommendation."[2] The CTFPHC considers the quality of evidence related to all critical and important outcomes when developing its guidelines.

The GRADE Handbook[2] provides information about assessing the quality of evidence, which is the basis for the system used by the CTFPHC. The ERSC, in consultation with the topic working group, first grades the quality of evidence for each outcome of importance to patients and then determines the overall quality of evidence across all outcomes. The quality of evidence for an individual outcome can be affected by a number of factors (some of which are described in the subsections below), and judgment is used to determine the overall classification of quality. In both cases, the quality of evidence is classified according to the GRADE system[2] into one of four grades: high, moderate, low or very low. If the CTFPHC's confidence in an effect is unlikely to be influenced by additional research, the grade is high, whereas a low grade indicates that the CTFPHC is uncertain of the effect. Moderate and low grades are used for effects that are likely (moderate) or very likely (low) to be influenced by further research. The GRADE Handbook provides additional information about factors affecting the quality of the evidence.[2]

- **Study design:** In general, the GRADE approach considers RCTs as representing stronger evidence than observational studies. However, the limitations of specific RCTs or the strengths of specific observational studies may affect the quality of evidence from these studies. The GRADE Handbook[2] provides further information about grading evidence on the basis of study design.
- **Risk of bias:** The GRADE approach includes an assessment of risk of bias.[2] Limitations of RCTs that may result in bias include, but are not limited to, lack of allocation concealment or blinding, lack of reporting of loss to follow-up, lack of adherence to intention-to-treat analysis and incomplete reporting of outcomes. The limitations of observational studies include, but are not limited to, inappropriate eligibility criteria, inaccurate measurement of outcomes, lack of control of confounders and incomplete follow-up. The CTFPHC considers a study's limitations and potential bias when rating the quality of evidence and reporting the risk of bias for outcomes (Appendix XIII).
  When case-control and cohort studies are included in the review, the ERSC will complete the Newcastle-Ottawa Scale[5] to assesss their risk of bias. This information is used to determine if the "limitations" component of the GRADE quality assessment should be downgraded. Once complete, the ERSC in conjunction with the chair and the scientific

manager assess whether the limitations are considered to be negligible (no down grading), serious (downgrade by one), or very serious (downgrade by two). The remainder of the GRADE quality assessment categories (inconsistency, indirectness, imprecision and publication bias) can be completed as they are for randomized control trials.

- **Inconsistency across studies:** Differences in results across studies (heterogeneity) may occur because of differences in the populations studied, the interventions applied or the outcomes evaluated. Therefore, any assessment of the quality of the evidence should consider heterogeneity.
- **Indirectness of evidence:** Indirect comparisons or use of indirect populations, interventions, comparators or outcomes will affect the quality of the evidence. Indirect comparisons are used when the two interventions of interest are not compared directly, but rather are both compared to another intervention. The two interventions can then be compared indirectly. Indirectness can also occur when the population, intervention, comparator or outcome being investigated varies from the evidence available in the literature (eg: use of evidence from a different population than the population of interest).
- **Imprecision of evidence:** Results with wide confidence intervals are imprecise and carry less weight than more precise results. The precision of results should therefore be considered in the assessment of the quality of the evidence. The GRADE Handbook[2] provides additional information about imprecision in dichotomous and continuous outcomes and its role in the assessment of quality of evidence.
- **Publication bias:** When assessing the quality of evidence, the CTFPHC considers the potential that there has been selective publication of studies resulting in publication bias.
- **Large effect sizes:** The quality of evidence associated with observational studies can be upgraded if the studies are of high quality and have no limitations, and the effect size is large (relative risk [RR] < 0.5 or RR > 2) or very large (RR < 0.2 or RR > 5).
- **Plausible confounding:** Confounding that may cause an increase or decrease in the effect is considered when the quality of evidence is assessed. The assessment of quality may be upgraded for studies with confounding, on the basis that if only very ill patients receive an intervention and recover, then it is likely that the actual effect of the intervention is greater than the data suggest.
- **Dose–response effect:** The presence of a dose–response effect is considered in assessments of the quality of evidence. Such an effect may support the conclusion that the intervention has an effect. The assessment of quality may be upgraded for studies with a dose–response effect.

5.5.2 Overall quality of evidence across outcomes

When assessing the overall quality of the evidence, the CTFPHC considers only critical outcomes. The lowest-quality evidence determines the overall quality for studies with different results (benefit or harm) for critical outcomes. The highest-quality evidence determines the overall quality in cases where all studies have the same result for a particular critical outcome. The quality of evidence for all critical outcomes is combined to determine the overall quality of evidence for each recommendation.

5.5.3 External validity of the evidence base

The assessment of external validity is based on the generalizability of the results to patients receiving the preventive service in Canada (populations), to primary care provided throughout Canada (settings) and to all primary care providers (providers).

- **Population:** Particular characteristics of the study population (such as age, comorbidities, sex and ethnicity) may affect the study results and, in turn, the generalizability to other populations. Applicability of the results to other populations who may experience a greater or lesser benefit from the intervention should be considered, as well as the potential for

lower adherence to the intervention in the real-world setting than was the case in the study setting.
- **Setting:** The setting of a study may affect the generalizability of its results to all primary care settings. As such, the effects of the intervention in a real-world setting may be over- or under-estimated by the results of the study.
- **Providers:** The providers of the intervention in a study may differ from the providers of care in various primary care settings. In particular, training and skill levels may affect the generalizability of results to all primary care providers.

5.6 Summary of the evidence

The main results of the evidence review are reported in a summary-of-findings table (for an example, see Appendix XIV). This type of table, described in detail in the GRADE Handbook,[2] includes outcomes, assumed risk, corresponding risk, relative magnitude of effect, number of participants, number of studies, overall quality rating and additional comments as appropriate. Where possible, the CTFPHC provides both relative and absolute measures of effect in the summary-of-findings tables. These tables are completed regardless of whether a meta-analysis is appropriate and even if only one study is included in the review.

Evidence tables are also prepared, reporting information related to the key questions, the grade of evidence and the results. The Number Needed to Screen (NNS) is also calculated and added to the evidence table. NNS is calculated using the relative risk method: first a weighted relative risk (RR) must be calculated and then the number of lives saved per million ((1-RR) multiplied by control group event rate per million) is calculated. Finally the number needed to screen (1,000,000/lives saved per million) is calculated. In general, meta-analyses using relative measures (such as the relative risk) are associated with less heterogeneity than meta-analyses of absolute measures (such as the risk difference). When there is variation in control event rates, using the relative risk method is preferred.

All calculations and presentation of data in the evidence set are rounded to four decimal places.

5.7 Applicability of the evidence

5.7.1 Definition of primary care

CTFPHC recommendations are specific to interventions used in primary care or interventions to which the patient is referred by a primary care provider; therefore, the evidence should be applicable in the primary care setting. The CTFPHC uses the same definition of primary care as the US Institute of Medicine:[6]

> Primary care is the provision of integrated, accessible health care services by clinicians who are accountable for addressing a large majority of personal health care needs, developing a sustained partnership with patients, and practicing in the context of family and community. This definition acknowledges the importance of the patient clinician relationship as facilitated and augmented by teams and integrated delivery systems (p. 31).[6]

5.7.2 Applicability in relation to key questions

The CTFPHC considers the applicability of the findings to the key questions. The evidence is assessed to determine if any clinically important differences in the results are relevant to those expected in the Canadian primary care setting. This assessment should consider the following possibilities:
- whether the evidence suggests that the intervention will be effective in the Canadian primary care setting

- whether the benefit that was achieved in the studies would be similar to the benefit that would be achieved in the Canadian primary care setting
- whether the harms that occurred in the studies would be similar to the harms that would occur in the Canadian primary care setting
- whether the relation between benefits and harms in the studies would be similar to the relation between benefits and harms in the Canadian primary care setting
- whether the effort needed to provide the interventions would be possible in the Canadian primary care setting
- whether the intervention is feasible for Canadian patient populations and primary care providers in terms of time, effort and cost
- whether it is feasible to extrapolate from the data in the reported studies to the larger asymptomatic Canadian population

5.7.3 Relative importance of efficacy and effectiveness

Because recommendations of the CTFPHC are intended for widespread implementation throughout Canada, the task force considers both efficacy (benefit in the ideal setting) and effectiveness (benefit in the usual setting) when determining the potential overall benefit of an intervention. Some jurisdictions have more resources than others, so the CTFPHC attempts to provide recommendations suitable for a variety of settings.

5.8 Other considerations for evidence assessments

5.8.1 Ecologic evidence

Ecologic evidence is data at the level of a population, rather than an individual. Such evidence is reported as population averages. Comparisons of outcomes in ecologic studies may be in the form of comparisons between different populations at a single time point or comparisons over time within the same population. Ecologic studies are often used to estimate the effect of geographic differences. An “ecologic fallacy” occurs when conclusions from an ecologic study are drawn at the level of individuals, rather than at the aggregate ecologic level.

Because of potential biases, the CTFPHC generally does not use ecologic evidence to determine the effectiveness of an intervention. However, the task force may consider such evidence for use as background information, for example, if other guideline groups have used well-known ecologic evidence in their recommendations or if an ecologic study has yielded substantive results.

If the CTFPHC decides to include ecologic evidence in a review, the study must be appraised. The criteria for the appraisal might include how the outcomes, exposure or confounder were measured; whether adjustments were made for confounders; and whether the populations and interventions are comparable to and relevant for those in the primary care setting.

5.8.2 Mortality as an outcome

The CTFPHC considers both all-cause mortality and cause-specific mortality (when such data are available) in developing its recommendations.

In situations where the condition of interest commonly causes death, the CTFPHC may consider all-cause mortality, rather than cause-specific mortality, as a final health outcome. Any difference in the effect of the intervention between all-cause mortality and cause-specific mortality should also be considered. Such differences may be attributed to there being a benefit of the intervention for the condition of interest but an increase in mortality related to other

conditions. Alternatively, the difference may occur because there is a decrease in cause-specific mortality but no change in all-cause mortality, which would indicate a potential harm of the intervention for patients with other conditions. Differences between all-cause and cause-specific mortality may also occur if the condition of interest is rare or if the population is subject to other causes of mortality, in which case the intervention has little or no effect on all-cause mortality.

Methodologic issues may contribute to differences between all-cause and cause-specific mortality. Accurately ascertaining the cause of death for participants in clinical studies is potentially difficult, and deaths may be attributed to a chronic condition even in cases where the condition did not contribute to the death. Conversely, when physicians know that their patients are involved in a study (as is the case for some interventions where blinding is impossible) and are uncertain of the actual cause of death, they may be reluctant to attribute the death to the condition of interest. This could lead to a false reduction in cause-specific mortality and a false increase in all-cause mortality. Moreover, participants enrolled in the active intervention arm of a trial may be followed more closely before death than those in the passive, no-intervention arm, which may mean that selected information about those in the intervention arm is available even to the external adjudicators of cause of death. This in turn may lead to biased estimates of cause-specific mortality.

5.8.3 Relative versus absolute risk reduction

The CTFPHC is interested in reducing the risk for both populations and individuals, although its focus is on individuals seen in primary care practices. Therefore, the CTFPHC considers both relative and absolute risk reduction, with an emphasis on the latter.

5.9 Incorporating other evidence reviews in CTFPHC reviews

The CTFPHC may incorporate high-quality evidence reviews or meta-analyses into its reviews to address all or some of the key questions or to serve as the evidence base for a specific time period. An existing review could also be used as a reference, to confirm the findings of the current CTFPHC review.

To assess the methodologic quality of evidence reviews, the CTFPHC uses the AMSTAR measurement tool.[7] The previous review must be relevant to one or more of the key questions being addressed in the CTFPHC review. It must also report the relevant study designs, populations, settings, interventions, comparators and outcomes. The CTFPHC considers the publication date of the previous review to determine its relevance and to determine if updated searches are required.

5.10 Incorporating evidence for contextual questions

5.10.1 Subgroup analysis

The CTFPHC may develop certain recommendations for specific populations. As such, evidence reviews may incorporate appropriate subgroup analyses. The task force analyzes the evidence for the subgroups to determine the quality and feasibility of including information about the subgroups.

In addition, the CTFPHC attempts to assess whether its guidelines have particular implications for the equitable delivery of preventive services to specific subgroups. To inform this issue, the task force considers the following questions:

- How does the burden of disease (especially mortality) for the subpopulation differ from the burden of disease for the population as a whole?

- Is there reason to believe that the screening tool may not perform as well for the subpopulation as for the population as a whole (e.g., because of language or cultural barriers, education level, genetic variation, providers' adherence in the delivery of screening)?
- How do the effectiveness and harms of the preventive intervention or treatment differ for subpopulations (e.g., because of language or cultural barriers, socioeconomic barriers, genetic differences, patient preferences or physicians' adherence to treatment recommendations)?
- Are there unique implementation issues for the subpopulation?

If the topic working group reaches consensus that the answer to one or more of these questions is Yes for any particular subgroup, this triggers targeted searches for evidence to address the issues. The searches will identify any subgroups for which there are literature to support differential burden, effectiveness, harms or implementation issues, so specific subgroups do not need to be identified in advance. The decision to include recommendations for specific subgroups in the final guideline is based on evidence from these searches. Of note, the clinical benefits and harms of the intervention in different subgroups will be captured in the key question, and therefore a separate contextual question is not required.

Subgroups that are routinely considered for examination include Aboriginal peoples, remote or rural dwellers, women, children and adolescents, elderly people, immigrant populations and ethnic subgroups in Canada. The working group may consider other subgroups at its discretion.

5.10.2 Consideration of resource use

The cost effectiveness of interventions is addressed by adding a contextual question on costs to all searches. Modeling studies may be appropriate to answer these questions. Section 6.2 discusses how the CTFPHC incorporates information on expected costs and resource use related to specific recommendations.

5.10.3 Consideration of values and preferences in the target population

A search of the literature is performed to determine the values and preferences of the target population in relation to the intervention in question. The CTFPHC uses this information to incorporate patients' preferences into the formulation of their recommendations.

5.10.4 Consideration of concomitant medical conditions

During the literature review, concomitant medical conditions are considered by means of the following questions:

- What is the population being studied?
  - general population
  - primary care population (from practices)
  - secondary or tertiary care population (from specialized care settings)
- Did the study report patients' characteristics?
- Did the study report specifically on comorbidities, either those associated with the condition of interest or unrelated comorbidities?
- Were specific subgroup analyses performed for patients with particular comorbidities?
- Are the benefits of the study of importance for all subgroups?
- Are there any elements that could compromise the generalizability of the results to the primary care population that will be the target of the guidelines?

Expedited searches are conducted to answer contextual questions. In these expedited searches, the ERSC searches selected databases to identify evidence reviews published in the past five years that present evidence relating to the identified subgroups. This search is supplemented by a search of key journals and websites for additional primary studies disseminated in the past two years (i.e., potentially too recent to have been included in published reviews). For these expedited reviews, the ERSC uses Canadian data sources wherever possible. The list of journals and databases to be searched is determined by the working group, with input from the ERSC and clinical and content experts. Input on this list is usually solicited when the protocol is sent for external review (see section 4.2.7).

Evidence used to address contextual questions does not require quality assessment and may be examined by only one reviewer.

Section 6: Development of recommendations

The process for reviewing evidence and developing recommendations that is described here is based on guidance in the GRADE Handbook.[2]

6.1 Application of the GRADE approach in formulating recommendations

When developing recommendations, the CTFPHC must first, in accordance with the GRADE approach, agree on the critical and important outcomes to be reviewed (see section 4.2.2). In addition, the task force must agree on the evidence to be included and the assessment of its quality; as such, the CTFPHC should review and discuss the evidence review (see section 5). The factors used in determining the strength of the recommendations (as discussed in section 6.2) should be considered in the development of recommendations. Voting may be needed to reach agreement on a recommendation and its strength. The results of such voting may be reported in the final guideline documents.

6.2 Strength of recommendations

In accordance with the GRADE guidelines, recommendations are classified as strong or weak.

A recommendation is rated as strong if the CTFPHC determines that the benefit of the intervention outweighs its harms or vice versa. A recommendation is rated as weak if the CTFPHC determines that the benefits of the intervention probably outweigh its harms or the harms probably outweigh the benefits.[2]

When determining the strength of a recommendation, the CTFPHC considers the baseline risk of the outcome, the effect size of the intervention and the precision of the effect. The quality of the evidence, the costs, patients' values and preferences and the balance between benefits and harms are also considered. Further information about the strength of recommendations can be found in the GRADE Handbook.[2]

6.3 Incorporating cost and resource use into recommendations

The cost of an intervention and associated use of resources may also be considered in the development of recommendations. When considering costs, the CTFPHC usually takes the perspective of the health care payer or the societal perspective. The quality of evidence about costs and resource use should also be considered.

The CTFPHC uses evidence profiles for resource use to determine if the benefit of an intervention is worth the incremental costs.

The GRADE Working Group does not recommend inclusion of cost-effectiveness or cost-utility modeling,[2] but these approaches may be used to help inform decisions of the CTFPHC. Further information about incorporating costs and resources into recommendations is provided in the GRADE Handbook.[2]

6.4 Wording of recommendations

Each recommendation should specify the target population and the intervention and should provide indicators to help users interpret the strength of the recommendation. Details on wording are described in the GRADE Handbook.[2]

6.5 Symbolic representation of recommendations

The CTFPHC uses GRADE symbols to represent the quality and strength of recommendations.[2]

6.6 Other considerations for recommendations

Factors such as age, risk of the condition, and benefits and harms of the intervention may be considered in recommendations about starting and stopping screening. If sufficient evidence is available, a recommendation on the interval for a screening test will be specified. The manual of the US Preventive Services Task Force further describes factors that should be considered when recommending start and stop times or intervals for screening.[1]

Section 7: Development of performance indicators

Evaluation is an important component in the process of developing and implementing clinical practice guidelines. Within the Knowledge to Action Cycle[8], two aspects of evaluation are identified: monitoring knowledge use and evaluating outcomes. The first component focuses on knowledge translation, the uptake of guidelines and actions to implement and integrate them into practice. The second step, evaluating outcomes, is focused on the resulting impact that the implementation of the guidelines has on the quality of patient care and outcomes of the patients receiving that care. The information gathered from these indicators will inform opportunities for quality improvement initiatives, contribute to public reporting activities, and may be included in accreditation requirements.

The methodology to identify appropriate performance indicators to measure quality of care involves a number of steps. For the CTFPHC, these steps will occur concurrently with the process of developing the recommendations. Table 4 outlines the high-level process the CTFPHC will undertake to identify appropriate performance indicators as a guideline is being developed.

Table 4: CTFPHC Process for Development of Performance Indicators

Development of CPG Recommendations (High level steps)	Development of Performance Indicators
Topic selection for CPG	Select goals for performance measurement within the topic area
Development key questions and contextual questions for search	Develop contextual questions regarding performance indicators
Systematic search of the evidence to address research questions	Search for performance indicators
Appraisal of evidence	Appraisal of performance indicators
Develop consensus-based recommendations	Develop consensus-based indicators
Implementation plan	Measurement plan
Consultation on draft	Consultation on indicators
Writing summaries	Create data definition templates
Evaluation, revision and updates to recommendations	Regular review and update of performance indicators

Note: CPG = clinical practice guideline; PM = Performance Measurement

7.1 Wording of the contextual question, the process, and the output

Performance indicators will be addressed in the contextual questions. The suggested wording for the contextual question is "What process and outcome performance measures or indicators have been identified in the literature to measure and monitor the impact of *intervention* for *disease/condition?*" Additional sub-questions can be added if deemed important to address sub-groups of the population. The final output is a list of outcome and process indicators to be included in the guideline and knowledge transfer tools. The indicators include primary and secondary, long-term and short-term or immediate indicators, and harms.

Figure 5 illustrates the process that is followed to produce the indicators for each guideline and identifies the group responsible for each task.

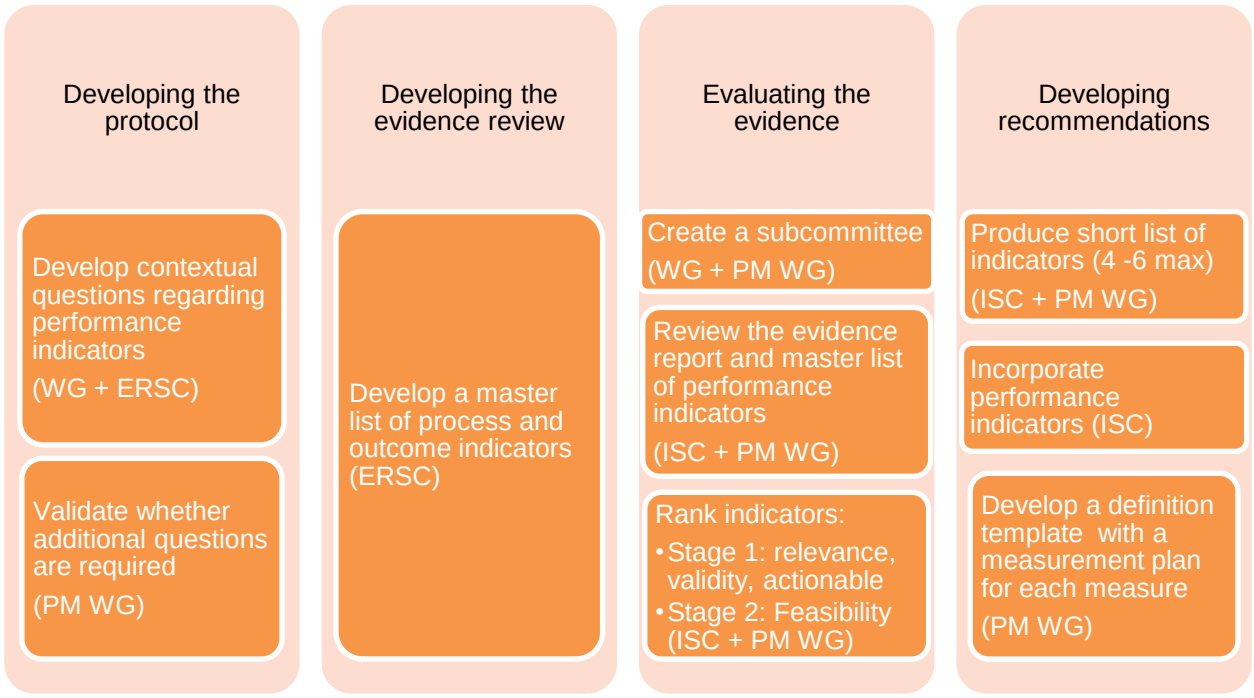

Figure 5: Process for performance indicators; WG= Working Group; PM WG= Performance Measurement Working Group; ERSC= Evidence Review and Synthesis Centre; Indicators Sub-Committee = ISC

While the evidence is being evaluated, the PM WG will consult with the WG Chair to create a Subcommittee dedicated to producing the guideline indicators. The indicators subcommittee (ISC) will be composed of the WG Chair, one other WG member, and the Chairs of the Performance Measurement WG.

The indicators subcommittee will perform the following tasks:

1. Review the evidence report and master list of indicators produced by ERSC
2. Identify indicators and references missing – if any
3. Rank Indicators (stage 1 and stage 2 as described in section 7.2 of this chapter)
4. Produce a short list of indicators (4 – 6 maximum)
5. Incorporate performance indicators into the recommendation statement before it is sent out to the TF for review and approval

7.2 Ranking of performance indicators

Performance indicators will be evaluated based on preset criteria[9]. This evaluation will be done in two stages and include the following criteria:

Stage 1:

- **Relevance:** Extent to which the measure is relevant to the organization's goals.
- **Validity:** Extent to which the measure has been shown to capture what it was intended to measure.
- **Actionable:** The information gained from collecting the indicator has clearly defined actions that can be undertaken to improve the quality of care provided in the context of the measurement environment.

Stage 2:

- **Feasible:** The availability of the data to measure the indicator and the balance between the cost of obtaining the data and the benefit of having the data to inform improvement initiatives.

Other criteria that could be used to assess the indicators are:

- **Targets Improvement in the Health of Populations:** Extent to which the measure addresses areas where performance improvement is likely to have a significant impact on the health of specified populations.
- **Precisely Defined and Specified:** Extent to which the measure is standardized with explicit pre-defined requirements for data collection and for calculation of the measure value or score.
- **Reliable:** Ability of the measure to identify consistently the events it was designed to identify across multiple participating health care organizations over time.
- **Can be Interpreted:** Extent to which the measure rationale and results are easily understood by users of the data including providers and consumers.
- **Under Provider Control:** Extent to which the provider has the ability to influence the processes and/or outcomes being measured.

7.3 Performance indicator definition template

A performance indicator definition template will be completed by the Performance Measurement Working Group for each performance indicator included with the recommendation statement (1 page each). The purpose of this is to increase standardization and consistency in measurement of indicators. This will enable interpretation of results and potential comparability across providers.

The definition template includes two sections:

1. Operational Definition
    - Title of indicator
    - Operational definition
    - Rationale statement
    - Case definitions for cohort (ICD10 codes where available)
    - Numerator and denominator
    - Risk adjustment factors
    - Additional analytical notes
2. Measurement Considerations
    - Data source and data collection methods
    - Frequency of reporting considerations (e.g., monthly, quarterly, annually)
    - Access to data

Operational definitions and measurement plans will normally be completed within four weeks of the working group signing off on the recommendations and before it goes out to the task force for review and approval.

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Appendix I: Declaration of affiliations and interests form and checklist

Public Health Agency of Canada
Office of the Canadian Task Force on Preventive Health Care

Declaration of Affiliations and Interests Form

Name: _____

I have reviewed my current activities and those of recent years, particularly as they relate to the attached *Affiliations and Interests Checklist*. I have also considered the activities of my spouse and immediate family members in so far as they could be viewed to affect my impartiality.

I would like to bring the following to the attention of the Public Health Agency of Canada as well as to the other members of the Canadian Task Force on Preventive Health Care:

I hereby certify that I am not in a position of real, potential or apparent conflict of interest except as disclosed above.

I undertake to inform the Public Health Agency of Canada's Office of the Canadian Task Force on Preventive Health Care of any changes in circumstances that may place me in a position of real, potential or apparent conflict of interest.

Signature _____ Date _____

Public Health Agency of Canada
Office of the Canadian Task Force on Preventive Health Care

Affiliations and Interests Checklist

In reviewing your activities (and those of your spouse and immediate family members) to determine whether they affect your impartiality or create a real, potential or apparent conflict of interest, among other things, consider the following:

- Investments in a business enterprise (Other than mutual funds or Registered Retirement Savings Plans that are not self-directed);
- Participation as investigator in clinical trials of relevance to the Committee's mandate;
- Previous, present and potential Contracts, Grants and/or Contributions;
- Pending negotiations regarding potential contracts;
- Honoraria and other sources of personal income;
- Advice to or close association with international organizations;
- Gifts and hospitality of significant value;
- Travel sponsorship;
- Promotion of a product(s) of relevance to the Committee's mandate;
- Publications;
- Public statements;
- Lobbying activities;
- Membership in special interest groups;
- Expert testimony in court;
- Access to confidential information;
- Any interest or activity which may create a reasonable apprehension of bias.

If for any reason you feel you cannot sign this statement as worded, or if you have further questions, please contact the PHAC Task Force Office at **613-957-9429.**

Appendix II: Confidentiality agreement

Name: _____

1. The PEER-REVIEWER acknowledges that information which is confidential and/or commercially sensitive ("Confidential Information") may be disclosed to the PEER-REVIEWER.
2. The PEER-REVIEWER acknowledges that they shall (and shall procure that all persons associated with them, whether as directors, employees or otherwise):
   (a) keep all the documents and information that the PEER-REVIEWER may receive from the Public Health Agency of Canada (PHAC) in the course of carrying out his responsibilities as a PEER-REVIEWER, or that the Canadian Task Force on Preventive Health Care (Task Force) may develop while performing its mandate, strictly confidential;
   (b) not use any Confidential Information for any purpose other than those indicated by PHAC or the Task Force;
   (c) not disclose any Confidential Information to any third party without the prior written consent of PHAC or the Task Force, and in the event that such disclosure is permitted, the PEER-REVIEWER shall procure that said third party is fully aware of and agrees to be bound by these undertakings.
3. No Waiver of Privilege - The PEER-REVIEWER acknowledges that the Confidential Information is the property of PHAC and the Task Force (and as some cases may allow, a third party), and that none of the latter intend to and do not waive, any rights, title or privilege they may have in respect of any of the Confidential Information.
4. Specific Exclusions - The PEER-REVIEWER's obligation to protect Confidential Information hereunder does not apply to Confidential Information which, even if it may be marked "confidential", in the following circumstances:
   (a) IN PUBLIC DOMAIN - the information was legally and legitimately published, or otherwise part of the public domain (unless due to the disclosure or other violation of this Confidentiality Agreement by the PEER-REVIEWER);
   (b) ALREADY KNOWN TO THE PEER-REVIEWER - the information was already in the possession of the PEER-REVIEWER at the time of its disclosure to the PEER-REVIEWER and was not acquired by the PEER-REVIEWER, directly or indirectly, from PHAC;
   (c) THIRD PARTY DISCLOSES - the information becomes available from an outside source who has a lawful and legitimate right to disclose the information to others;
   (d) INDEPENDENTLY DEVELOPED - the information was independently developed by the PEER-REVIEWER without any of the Confidential Information being reviewed or accessed by the PEER-REVIEWER.
5. The PEER-REVIEWER acknowledges that there are no conflicts of interest or if there are, that they are indicated on the attached CONFLICT DISCLOSURE form.

Signature of Individual/Peer-reviewer…… Date ……

Print Name ……..

Appendix III: Functional working groups

Topic prioritization working group

The topic prioritization working group assists the Canadian Task Force on Preventive Health Care (CTFPHC) in selecting topics to consider for guideline development, according to the process outlined in section 2.1 of the Procedure Manual. Criteria for topic selection were developed and are applied to ensure transparency, reproducibility and objectivity in the topic-selection process. On the basis of these criteria, the working group solicits and considers input from the CTFPHC and its partners about which topics should be addressed. Topic priorities are re-examined every 6 months.

The working group has also developed criteria to determine which of the following guideline types should be used for a given topic:

- **Endorsement** (pick pending guidelines from high-quality partners and get a head start on appraising them; endorse without changes if acceptable)
  example: US Preventive Services Task Force guideline on prostate cancer
- **Update** (take a guideline that the CTFPHC itself has produced in the past and update its literature search and recommendations; there are not too many of these now, but the number will grow)
  example: screening for breast cancer
- **Adaptation** (use components of an existing clinical practice guideline from a high-quality organization; update literature search if needed; modify recommendations to fit CTFPHC views and context)
  example: screening for dyslipidemia
- **Partner** (jointly produce a guideline with a high-quality partner)
  example: hypertension guidelines, with Canadian Hypertension Education Program
- **De novo** (new topics that neither CTFPHC nor anyone else has tackled lately and for which no clinical practice guidelines are pending from major organizations)

The topic prioritization working group is led by a member of the CTFPHC or the Office of the CTFPHC and is composed of other interested individuals from the CTFPHC and a representative of the Evidence Review and Synthesis Centre (ERSC).

Methods working group

The methods working group assists the CTFPHC in maintaining the highest methodologic standards in guideline development. The output from the working group ensures that CTFPHC guidelines and the methods used to produce them are methodologically sound, scientifically defensible, reproducible and well documented.

The working group is responsible for the ongoing review and updating of the CTFPHC Procedure Manual, which documents the methods used by the ERSC, the CTFPHC and the Office of the CTFPHC to develop reviews and recommendations for clinical preventive services. According to a regular schedule, the working group will identify areas where modifications, expansions or updates are required.

In addition, the methods working group addresses important scientific and methodologic issues as they arise, including but not limited to reviewing the existing tools for appraising (e.g., Appraisal of Guidelines for Research and Evaluation instrument [AGREE II][3]) and adapting (e.g., ADAPTE[4]) guidelines developed by other organizations, integrating performance measurement into the guidelines process and making recommendations about the types of studies to include in the evidence reviews. All decisions related to methodologic issues will be documented in the Procedure Manual.

The methods working group is led by a member of the CTFPHC and is composed of other interested individuals from the CTFPHC, a representative of the ERSC and a representative from the Office of the CTFPHC.

Knowledge transfer and exchange working group

The knowledge transfer and exchange (KT&E) working group assists the CTFPHC in implementing and evaluating the task force's knowledge transfer initiatives.

Members of the KT&E working group also participate in the activities of the topic prioritization and methods working groups to provide input on knowledge translation issues and to ensure that knowledge translation is considered in all aspects of guideline development. Other key responsibilities of this working group include the following:

- updating the CTFPHC on emerging best practices for knowledge translation
- evaluating the need for changes in approaches to knowledge translation over time
- collaborating with stakeholders to determine the best way to implement and disseminate the final guidelines
- considering the implications of CTFPHC guidelines for the health care system and for patients with multiple morbidities, and incorporating these considerations into the knowledge translation strategy
- designing and implementing pilot studies of guideline implementation
- collaborating with the CTFPHC performance measures and evaluation working group to determine the impact of CTFPHC documents

The KT&E working group is led by a member of the CTFPHC or another qualified individual designated by the chair and is composed of other CTFPHC members and a representative from the Office of the CTFPHC.

Performance measurement working group

The performance measurement working group assists the CTFPHC in identifying performance indicators for the evaluation of their clinical guidelines and builds on the CTFPHC's mandate and goals. The output from the working group allows the guidelines to be assessed by those practitioners who implement the guidelines and by groups interested in undertaking surveillance activities related to the guidelines. Such performance measures assess whether "things are being done", "how well things are being done", and 'how timely things are being done'. These indicators can be measures of system, program or clinical performance and can measure

immediate, short-term, or long-term targets. Indicators identified by the CTFPHC will mostly address process and outcomes of care.

Members of the performance measurement working group are involved at each one of the stages of the guideline development process. In the early stages, the working group assists topic-specific working groups in drafting contextual questions, which will be used by the ERSC to search best available evidence for key process and outcome indicators. In subsequent stages, the list of performance indicators produced by the ERSC is reviewed by the working group to identify an initial set of potential indicators. Working group members then facilitate discussions with the individual topic groups to rank the most relevant indicators.

The working group members will develop and complete a data dictionary to provide clear and consistent operational definitions and inclusion/exclusion criteria for each indicator to increase consistency and standardization in measurement across practitioners. After the guideline is disseminated, the working group helps to ensure that indicators remain current and relevant.

The performance measurement working group is led by a member of the CTFPHC and is composed of other interested individuals from the CTFPHC, a representative of the ERSC and a representative from the Office of the CTFPHC.

Appendix IV: Solicitation of nominations for topics for the Canadian Task Force on Preventive Health Care (CTFPHC)

AGENCY: Public Health Agency of Canada

ACTION: Solicit new topic nominations

The CTFPHC invites nominations for topics to review and develop recommendations for primary care. Topics should be for primary or secondary prevention. Recent or current topics reviewed by the CTFPHC are attached.

The CTFPHC is an independent panel of experts that develops evidence-based recommendations on interventions for primary or secondary prevention in asymptomatic individuals, including screening, counselling and preventive treatment.

Individuals, organizations, evidence-based practice centres or the CTFPHC can nominate topics, which will then be reviewed and prioritized by the CTFPHC. The following criteria will be used to consider topics:

- Disease burden (prevalence, mortality, comorbidity, quality of life) and expected effectiveness of the preventive service in decreasing that burden
- Potential impact of recommendations in clinical practice
- Interest of the public or care providers
- Variation in care and potential for preventive service to decrease that variation
- Sufficiency of evidence
- New evidence, especially high-quality evidence in a stable field (i.e., an area where the evidence and state of knowledge are not changing rapidly)

Topics will be prioritized that have the potential to impact clinical practice. Topics previously reviewed by the CTFPHC will also be considered. To nominate a topic, please describe in no more than 500 words the topic and the rationale for conducting a review. Rationale will include the relevance of the topic to the primary care setting, whether the intervention is for primary or secondary prevention, the public health importance, summary of new evidence, and the potential impact of the review. Citations and supporting information can be included which does not count toward the 500-word limit.

Nominations for topics can be submitted to:
Office of the Canadian Task Force on Preventive Health Care
785 Carling Avenue, Address Locator 6807B
Room 713B1
Ottawa, Ontario K1A 0K9
or to info@canadiantaskforce.ca

The CTFPHC solicits nominations to create a balanced portfolio of topics. Topics will be selected based on the criteria described here, the CTFPHC prioritization process, and the current expertise of the CTFPHC.

Dated:

Director:
Notice is released with a current list of topics and topics in progress.

Appendix V: Literature surveillance

Surveillance of the literature should be conducted by the Office of the Canadian Task Force on Preventive Health Care (CTFPHC) every four to eight weeks to identify literature related to primary or secondary prevention in the primary care setting. Topics being reviewed by the CTFPHC or topics previously reviewed should be searched, and any findings that could affect current or past recommendations should be shared with the CTFPHC.

Appendix VI: Role and responsibilities of the Canadian Task Force on Preventive Health Care topic working groups and the topic working group leads

Each topic working group consists of two to five members of the Canadian Task Force for Preventive Health Care (CTFPHC), a scientific research manager from the Public Health Agency of Canada and members from the Evidence Review and Synthesis Centre. In the case of a partnership with an external organization, one or two members of that organization will also be appointed as members of the working group.

Working group members are expected to actively participate in all aspects of the guideline-development process, including developing the questions and analytic framework, reviewing the evidence and drafting the guidelines. This involves attending regular conference calls and providing prompt feedback as required.

A chair is assigned for each group. The Office of the CTFPHC asks for a volunteer from the working group members. The chair of the working group has the following responsibilities:

- Work with the scientific research manager (who will cochair the working group) to set the agenda and chair meetings of the working group. The chair will be responsible for ensuring that the work proceeds according to the predetermined timelines.
- Liaise with the scientific research manager to provide updates about the work and to coordinate meetings.
- Play a leadership role to ensure that the scope of the review is clear for all working group members (e.g., the analytic model, benefits and harms).
- Ensure that working group members are comfortable with the process in which they are engaging, and attempt to identify and deal with concerns and issues as they arise.
- Lead the process of assessing the evidence on each key question according to the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.[2]

The scientific research manager will lead the drafting of the recommendations in close collaboration with the chair of the topic working group. The chair of the topic working group will present the recommendations, along with a proposal regarding the certainty and grading of the evidence and recommendations, at a meeting of the CTFPHC.

<u>Teleconference calls</u>

- The Office of the CTFPHC will schedule calls for the working group, taking into consideration the chair's schedule. The chair should respond promptly to requests about calls from the Office of the CTFPHC or members of the working group.
- For each call, the chair and at least one other member of the working group must be available.
- Working group members who cannot attend a call may provide comments, before or after the call, to the chair, the scientific research manager or all working group members.

Appendix VII: Guide for External Reviewers

The purpose of this document is to facilitate stakeholder engagement in the work done by the Canadian Task Force on Preventive Health Care (CTFPHC).

The first section in this document reviews the mandate and the structure of the CTFPHC, the second section describes opportunities for stakeholder participation, and the third section provides specific guidance for stakeholders about how to review TF products.

1. CTFPHC Overview

1.1 The mandate of the Canadian Task Force on Preventive Health Care

The Canadian Task Force on Preventive Health Care (CTFPHC) develops and disseminates clinical practice guidelines for primary and preventive care, based on systematic analysis of scientific evidence. Recommendations for primary or secondary prevention in asymptomatic individuals are developed based on the highest quality evidence that is available, and include interventions aimed at screening, counselling and preventive treatment. Task Force recommendations are specific to interventions used in primary care or interventions to which the patient is referred by a primary care provider; therefore, the evidence should be applicable in the primary care setting.

1.2 Guideline Topic Selection

Periodically throughout the year, the CTFPHC drafts a list of topics, including new topics and updates, to be considered for the upcoming year. This list includes all nominated topics and any additional topics identified through a scan of current preventive health literature. Topics can be nominated by Task Force members, members of stakeholder organizations, health practitioners, and the general public. In order to be included in the list of candidate topics, topics must fall within the scope of the Task Force.

Once the initial list is generated, members of the Topic Prioritization Working Group select a short list of candidate topics and rank the topics following preset criteria to identify and prioritize the top ten. After the results are calculated, these are presented to the CTFPHC for approval of the guideline topics to work on next.

1.3 How the CTFPHC determines the scope of a guideline

Each recommendation answers a key question, and thus the first step in developing a recommendation is to identify these key questions. Each key question specifies the target population, the intervention, its comparator, and the outcomes, as well as relevant temporal characteristics (e.g., the timing and duration of the intervention).

The Task Force uses additional contextual questions to address whether its guidelines have particular implications for the equitable delivery of preventive services to specific subgroups such as Aboriginal populations, women or the elderly. A search of the literature is also performed to determine the values and preferences of the target population in relation to the intervention in question. The Task Force uses this information to incorporate patients' preferences into the formulation of their recommendations. Information on expected costs and use of resources related to specific recommendations and on concomitant medical conditions is also considered when formulating recommendations. In sum, the key and contextual questions define the scope of the guideline to be developed and help set limits for evidence review.

1.4 How the CTFPHC produces Recommendation Statements

The Task Force uses an analytic framework to formulate the key and contextual questions that the literature review must answer to determine whether the proposed preventive service will safely prevent clinically relevant adverse outcomes.

Using the analytical framework as a guiding document, the Task Force develops a protocol and undertakes different types of systematic reviews of the literature to identify the best available evidence to inform its recommendations. The analytic framework also links interventions and outcomes to help structure the evidence review. Outcomes form the basis of the systematic reviews, with a separate review conducted for every outcome that is deemed to be clinically relevant and important for patients. The systematic reviews include new reviews, updates of past reviews, endorsement of guidelines from other organizations and partnerships with other groups to increase efficiency and avoid duplication.

The evidence identified through the systematic review is then assessed according to the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. GRADE provides the Task Force with a systematic approach to ranking the quality of its evidence and the strength of its recommendations.

Once the systematic review is completed, the recommendation statement is drafted. The systematic review of the literature and the recommendation statement are distributed to external expert reviewers for comments. The CTFPHC updates the document to incorporate or address the comments received. The final guideline is formally approved by the entire Task Force, after due consideration of any contentious issues. Once the final version of the guideline product is produced it is submitted to a peer-reviewed journal for publication and dissemination to primary care healthcare practitioners. Depending on the topic of the guideline, the Task Force might deem appropriate to develop and disseminate patient tools in addition to the clinical guidelines.

The process to develop recommendation statements is rigorous, transparent and based on the latest methods for practice guideline development. A quality improvement process is in place and methods are continuously being refined to reflect advances in the field.

1.5 Key principles of guidelines developed by the CTFPHC:

The CTFPHC recommendation statements are guided by the following principles:

- aim to improve the quality of care for patients
- assess how well different primary care prevention interventions work
- set out the clinical care that is suitable for most patients with a specific condition
- are not an in depth critical appraisal of the whole literature around the topics
- take account of the views of those who might be affected by the guideline (including primary care and public health professionals, health service managers, and government bodies)
- are based on the best available research evidence and expert consensus
- are developed using a 'best practice' standard process, and standard ways of analysing the evidence
- make it clear how each recommendation was decided
- are advisory rather than compulsory, but should be taken into account by primary care healthcare professionals when planning care for individual patients
- are easily accessible to primary health care providers

1.6 Groups involved in developing TF clinical guidelines

The development of TF preventive clinical guidelines involves the following groups:

- The Canadian Task Force on Preventive Health Care (CTFPHC)
- The Task Force Office (TFO)

- The Evidence Review and Synthesis Centre (ERSC)
- Topic-Specific Working Groups (WGs)
- Expert/ peer reviewers
- Stakeholder organizations

2. Opportunities for Participation

Individuals and organisations can contribute by reviewing and providing critical comments on the evidence review process and emerging clinical guideline statement at various stages during its development process:

- Stage 1: analytical framework and protocol
- Stage 2: evidence review
- Stage 3: recommendation statement
- Stage 4: knowledge translation tools

The comments from reviewers help improve the quality of the guidelines. While the TF appreciates the important value added by reviewers, and encourages participation from individuals and organizations to garner critical expert feedback, there is also a need for rules of engagement to ensure maintenance of the independence of the Task Force. Such rules of engagement and specific review instructions are described in the sections that follow.

3. Rules of Engagement and Review Instructions

3.1 Rules of Engagement

Reviewers' involvement is confirmed through a registration form before any Task Force materials are provided. Only one registration form is required per organization, which has to be signed by the organization representative, whereas each individual expert reviewer is asked to sign a registration form (See Appendix A for a copy of the registration form). All individuals participating in the review (representing an organization or their personal view) are also asked to sign a confidentiality agreement and a conflict of interest form as part of the registration process (See Appendix B for a copy of the conflict of interest form and Appendices C and D for a copy of the confidentiality agreements for organizational reviewers and individual expert reviewers).

Once stakeholder organizations and individuals are registered, the TF distributes a draft of the guideline product(s) to the individual expert reviewer or to the representative of the stakeholder organization. It is critical to CTFPHC that person(s) participating in the review on behalf of the stakeholder organizations have a good understanding of the guideline topic. Only one set of comments are expected from each stakeholder organization.

Other considerations reviewers should keep in mind before providing feedback on guideline products are the following:

- Guidelines apply to the Canadian context as a whole, so they will not address the needs of specific provinces or municipalities.
- Guidelines are generally published within 18 months of the commencement of the development process to ensure that information is up to date at publication. For some larger topics, the key questions and contextual questions have been restricted to what can realistically be covered in that timeframe.

3.2 Upon receiving a confidential copy of the guideline product(s)

Please note the TF will not consider comments that are not prepared according to these instructions, or that arrive after the deadline. The Scientific Officer (who will distribute the guideline products) can answer questions on submitting comments.

Review instructions for stakeholder organizations:

- Decide who within your organization will be participating in the review and select a representative.
- Have the representative sign the Registration Form (Appendix A), the Conflict of Interest Form (Appendix B) and the Confidentiality Agreement for Organizational Reviewers (Appendix D)
- Ask all other reviewers within your organization to complete and sign the Conflict of Interest Form (Appendix B) and the Confidentiality Agreement for Organizational Reviewers (Appendix D).
- Send a scanned copy of all signed forms to the email address provided, indicating who the organizational representative is and adding the organisation's name to the subject of the email, or via fax to the phone number provided.
- Circulate the draft within your organisation making it clear that it is for consultation and asking recipients to respond to the organisation's stakeholder contact (rather than responding directly to CTFPHC)
- Prepare the response and return it to the CTFPHC, remembering to:
    - collate the comments into one response from stakeholder's organisation using the form provided (do not make changes to the draft document)
    - include the name of organisation in the response
    - return the response by the closing date
- Send comments electronically to the email address provided, adding the organisation's name to the subject of the email
- The TF will acknowledge the Stakeholder organization, but does not have the resources to acknowledge or respond to comments from several individuals within a registered stakeholder organisation.
- All comments received from registered stakeholders will be made public on the TF website, so do not include confidential information (such as information about individual patients).
- Make sure that comments are constructive and clearly worded.

Review instructions for expert reviewers:

- Sign the Registration Form (Appendix A), the Conflict of Interest Form (Appendix B) and the Confidentiality Agreement for Individual Expert Reviewers (Appendix C)
- Review the document(s), prepare response and return it to the CTFPHC, remembering to:
    - collate comments using the form provided (do not make changes to the draft document)
    - include contact information in response
    - return the response by the closing date
- Send comments electronically to the email address provided
- Keep in mind all comments received will be made public on the TF website, so do not include confidential information (such as information about individual patients)
- Make sure that comments are constructive and clearly worded

3.3 What happens after stakeholders provide comments?

The CTFPHC updates the document to reflect the comments received and prepares a formal response to comments. The draft guideline product(s) is/are presented to the CTFPHC for approval. Once the final version of the guideline product is produced, a copy of the final version is distributed to stakeholder organizations and individuals that participated in the review, along with a copy of the response to comments that will be posted to the CTFPHC website.

Lastly, the Task Force would like to acknowledge the reviewers' critical contribution and will ask for permission to have the name of the organization and individual experts that participated in the review listed in the acknowledgments of the final guideline and synthesis review that will be posted on the

CTFPHC website. Those that agree to be acknowledged will be asked to confirm their agreement via email.

APPENDIX A TO THE GUIDE FOR EXTERNAL REVIEWERS

REGISTRATION FORM FOR ORGANIZATIONS AND EXPERT REVIEWERS

THIS FORM was completed on _____
BY THE CANADIAN TASK FORCE ON PREVENTIVE HEALTH CARE (TASK FORCE)
AND
INSERT NAME OF ORGANIZATION or OF EXPERT REVIEWER:
_____

Background and Purpose

This Registration Form is to document the established engagement of INSERT NAME OF ORGANIZATION or EXPERT REVIEWER: _____ (Hereinafter referred to as the "STAKEHOLDER") by the Canadian Task Force on Preventive Health Care (Hereinafter referred to as the "TASK FORCE") in the Task Force guideline development and dissemination process.

Task Force Mission

The Task Force mission is to develop clinical practice guidelines that support primary care providers in delivering preventive health care. The Task Force is mandated to develop and disseminate clinical practice guidelines for primary and preventive care, based on systematic analysis of scientific evidence.

Non-Committal Declaration

This form is to establish a record involvement with the production of the TASK FORCE's GUIDELINE NAME: _____. The TASK FORCE reserves the right to determine the degree to which the STAKEHOLDER is involved in the guideline development and dissemination process. By completing this form the STAKEHOLDER is providing acknowledgement that they have been engaged in the guideline development and dissemination process. This document does not establish a commitment or endorsement of any form by the STAKEHOLDER to the TASK FORCE or the GUIDELINE NAME: _____ at present or at any time henceforth. The STAKEHOLDER reserves the right to abstain from any future involvement with the TASK FORCE or the GUIDELINE NAME_____.

Objectives

Specific purposes of this document:

- To provide the TASK FORCE with a record of stakeholder engagement
- To provide the STAKEHOLDER with a record of involvement with the TASK FORCE.

THIS FORM executed in two copies as of the last written date below:

SIGNED on behalf of the Canadian Task Force on Preventive Health Care

Title_____, Name_____

Signature_____, Date_____

SIGNED on behalf of _____

Title_____, Name_____

Signature_____, Date_____

APPENDIX B TO THE GUIDE FOR EXTERNAL REVIEWERS

Declaration of Affiliations and Interests Form and Checklist

Office of the Canadian Task Force on Preventive Health Care

Declaration of Affiliations and Interests Form

Name: _____

I have reviewed my current activities and those of recent years, particularly as they relate to the attached *Affiliations and Interests Checklist*. I have also considered the activities of my spouse and immediate family members in so far as they could be viewed to affect my impartiality.

I would like to bring the following to the attention of the Public Health Agency of Canada as well as to the other members of the Canadian Task Force on Preventive Health Care:

I hereby certify that I am not in a position of real, potential or apparent conflict of interest except as disclosed above.

I undertake to inform the Public Health Agency of Canada's Office of the Canadian Task Force on Preventive Health Care of any changes in circumstances that may place me in a position of real, potential or apparent conflict of interest.

Signature _____ Date _____

Office of the Canadian Task Force on Preventive Health Care

Affiliations and Interests Checklist

In reviewing your activities (and those of your spouse and immediate family members) to determine whether they affect your impartiality or create a real, potential or apparent conflict of interest, among other things, consider the following:

- Investments in a business enterprise (Other than mutual funds or Registered
- Retirement Savings Plans that are not self-directed);
- Participation as investigator in clinical trials of relevance to the Committee's mandate;
- Previous, present and potential Contracts, Grants and/or Contributions;
- Pending negotiations regarding potential contracts;
- Honoraria and other sources of personal income;
- Advice to or close association with international organizations
- Gifts and hospitality of significant value;
- Travel sponsorship;
- Promotion of a product(s) of relevance to the Committee's mandate;
- Publications;
- Public statements;
- Lobbying activities;
- Membership in special interest groups;
- Expert testimonies in court;
- Access to confidential information;
- Any interest or activity which may create a reasonable apprehension of bias.

If for any reason you feel you cannot sign this statement as worded, or if you have further questions, please contact the Task Force Office at **613-957-9429.**

APPENDIX C TO THE GUIDE FOR EXTERNAL REVIEWERS

Confidentiality Agreement for Individual Expert Reviewers

Expert Reviewer: _____

1. The EXPERT REVIEWER acknowledges that information which is confidential and/or commercially sensitive ("Confidential Information") may be disclosed to the EXPERT REVIEWER.
2. The EXPERT REVIEWER acknowledges that they shall (and shall procure that all persons associated with them, whether as directors, employees or otherwise):
   (a) keep all the documents and information that the EXPERT REVIEWER may receive from the Public Health Agency of Canada (PHAC) in the course of carrying out his responsibilities as a EXPERT REVIEWER, or that the Canadian Task Force on Preventive Health Care (Task Force) may develop while performing its mandate, strictly confidential;
   (b) not use any Confidential Information for any purpose other than those indicated by PHAC or the Task Force;
   (c) not disclose any Confidential Information to any third party without the prior written consent of PHAC or the Task Force, and in the event that such disclosure is permitted, the EXPERT REVIEWER shall procure that said third party is fully aware of and agrees to be bound by these undertakings.
3. No Waiver of Privilege - The EXPERT REVIEWER acknowledges that the Confidential Information is the property of PHAC and the Task Force (and as some cases may allow, a third party), and that none of the latter intend to and do not waive, any rights, title or privilege they may have in respect of any of the Confidential Information.
4. Specific Exclusions - The EXPERT REVIEWER's obligation to protect Confidential Information hereunder does not apply to Confidential Information which, even if it may be marked "confidential", in the following circumstances:
   (a) IN PUBLIC DOMAIN - the information was legally and legitimately published, or otherwise part of the public domain (unless due to the disclosure or other violation of this Confidentiality Agreement by the EXPERT REVIEWER);
   (b) ALREADY KNOWN TO THE EXPERT REVIEWER - the information was already in the possession of the EXPERT REVIEWER at the time of its disclosure to the EXPERT REVIEWER and was not acquired by the EXPERT REVIEWER, directly or indirectly, from PHAC;
   (c) THIRD PARTY DISCLOSES - the information becomes available from an outside source who has a lawful and legitimate right to disclose the information to others;
   (d) INDEPENDENTLY DEVELOPED - the information was independently developed by the EXPERT REVIEWER without any of the Confidential Information being reviewed or accessed by the EXPERT REVIEWER.
5. The EXPERT REVIEWER acknowledges that there are no conflicts of interest or if there are, that they are indicated on the attached CONFLICT DISCLOSURE form.

Signature of EXPERT REVIEWER ……. Date ……

Print Name …….

APPENDIX D TO THE GUIDE FOR EXTERNAL REVIEWERS

Confidentiality Agreement for Organizational Reviewers

Organization:_____

Organizational Reviewer:_____

1. The ORGANIZATION acknowledges that information which is confidential and/or commercially sensitive ("Confidential Information") may be disclosed to the ORGANIZATIONAL REVIEWER.
2. The ORGANIZATIONAL REVIEWER acknowledges that they shall (and shall procure that all persons associated with them, whether as directors, employees or otherwise):
   (a) keep all the documents and information that the ORGANIZATIONAL REVIEWER may receive from the Public Health Agency of Canada (PHAC) in the course of carrying out his responsibilities as a ORGANIZATIONAL REVIEWER, or that the Canadian Task Force on Preventive Health Care (Task Force) may develop while performing its mandate, strictly confidential;
   (b) not use any Confidential Information for any purpose other than those indicated by PHAC or the Task Force;
   (c) not disclose any Confidential Information to any third party without the prior written consent of PHAC or the Task Force, and in the event that such disclosure is permitted, the ORGANIZATIONAL REVIEWER shall procure that said third party is fully aware of and agrees to be bound by these undertakings.
3. No Waiver of Privilege - The ORGANIZATIONAL REVIEWER acknowledges that the Confidential Information is the property of PHAC and the Task Force (and as some cases may allow, a third party), and that none of the latter intend to and do not waive, any rights, title or privilege they may have in respect of any of the Confidential Information.
4. Specific Exclusions - The ORGANIZATIONAL REVIEWER's obligation to protect Confidential Information hereunder does not apply to Confidential Information which, even if it may be marked "confidential", in the following circumstances:
   (a) IN PUBLIC DOMAIN - the information was legally and legitimately published, or otherwise part of the public domain (unless due to the disclosure or other violation of this Confidentiality Agreement by the ORGANIZATIONAL REVIEWER);
   (b) ALREADY KNOWN TO THE ORGANIZATIONAL REVIEWER - the information was already in the possession of the ORGANIZATIONAL REVIEWER at the time of its disclosure to the ORGANIZATIONAL/REVIEWER and was not acquired by the ORGANIZATIONAL REVIEWER, directly or indirectly, from PHAC;
   (c) THIRD PARTY DISCLOSES - the information becomes available from an outside source who has a lawful and legitimate right to disclose the information to others;
   (d) INDEPENDENTLY DEVELOPED - the information was independently developed by the ORGANIZATIONAL REVIEWER without any of the Confidential Information being reviewed or accessed by the ORGANIZATIONAL REVIEWER.
5. The ORGANIZATIONAL REVIEWER acknowledges that there are no conflicts of interest or if there are, that they are indicated on the attached CONFLICT DISCLOSURE form.

Signature …… Date ……

Print Name …….

Organization/Title …….

Appendix VIII: Guide for Internal Reviewers

The purpose of this document is to facilitate the internal review (by Task Force members) of the recommendation statement and related products (e.g. evidence review, knowledge translation tools, etc.). The first section describes the general internal review process, the second section outlines generic review rules that, in principle, apply to all documents/products to be reviewed, and finally, the third section provides information on what TF members can expect in response to their feedback.

1. Internal review process

The internal review of TF preventive clinical guidelines and related products involves the following groups:

- The Canadian Task Force on Preventive Health Care (CTFPHC)
- Topic-Specific Working Groups (WGs)
- The Task Force Office (TFO)
- The Evidence Review and Synthesis Centre (ERSC)

TF members contribute to the recommendation development process by reviewing and providing critical comments on the evidence review and emerging clinical guideline statement at various stages:

- Stage 1: key questions and analytical framework
- Stage 2: protocol
- Stage 2: evidence review
- Stage 3: recommendation statement
- Stage 4: knowledge translation tools

The comments received from TF members help improve the quality of recommendations and related products.

2. Rules of engagement and review instructions

Rules of engagement are established to ensure all comments are addressed systematically and, as part of an internal quality control process, to maintain an audit trail of decisions reached. Such rules of engagement and specific review instructions are as follows:

a. **Required reviews:** TF products normally undergo two levels of review: documents are first reviewed by WG members and then by all TF members. A document can only be considered to be final after all TF members have had the opportunity to review and comment on it and a formal response to their comments has been provided. To ensure the timely review of documents, if reviewers do not comment within a reasonable timeframe or by the deadline provided, the lack of comment will be considered an agreement to proceed with the next phase of the review.

   There are situations where only the review and approval of certain TF members will be required. In those cases, the decision and rationale will be documented in a change request form as it is considered a deviation from the standard process.

b. **Time for review:** as a general rule, TF members will be given one week to review documents. However, in practice, the time for review might have to be adjusted. For example, when reviewing a lengthy document or to meet specific timelines.

- **Instructions for reviewers:**
  - Review the document(s), prepare response, and send comments electronically to the email address provided when distributing the document.

- Provide feedback in two ways:
  - Option 1: Incorporate comments in a separate table provided for that purpose (see Appendix A columns A, B, C, and D). Please note all lines in the document distributed for review will be numbered for ease of reference. Please enter your initials in column B, reference the line number in column C, and add your comment in column D.
  - Option 2: Incorporate feedback throughout the document by inserting comment boxes and referencing the line number in question. Please avoid making additions, deletions, and/or changes to the wording in the draft document.

    Note: Option 1 is the preferred option since it facilitates the identification and collation of comments from different reviewers. Also, it facilitates analysis when more than one comment relates to the same issue and/or there is a difference of opinion amongst reviewers.

- Return the response by the closing date.
- Keep in mind comments received will be shared with all TF members, so please verify that comments are clearly worded.

If reviewers have questions regarding the review process, they can contact the Scientific Manager or Officer who distributed the documents.

3. What Reviewers can expect in response to their feedback

The Scientific Manager (SM) updates the document to reflect the comments received and works with the WG Chair to prepare a formal response to comments (Responses to comments are entered in Column D of Appendix A). In the case of the evidence review, the ERSC works with the SM and the WG Chair to prepare to the response to comments. The revised product(s) is/are presented to the WG Chair and the SM for approval.

Once approved by the WG Chair and the SM, a copy of the document is distributed to all TF members. TF members then review and comment on the documents. A version is only deemed to be final once all TF members have had the opportunity to review and approve it. To ensure the timely completion of documents, if TF members do not respond within a reasonable timeframe or by the deadline provided, the lack of response will be considered an approval.

TF= Task Force
WG = Working Group
ERSC=Evidence Review Center
SM = Scientific Manager

Appendix A
Insert Working Group Name
Reviewer Form

Please enter line number from the document associated with your comment, and add your comment to the “reviewer comment” column.

Report: Screening for Diabetes draft report **Feedback Submitted by: May 11, 2011**				
A	**B**	**C**	**D**	**E**
#	**Reviewer Initials**	**Line # in doc**	**Reviewer Comment**	**Response to Comments**
MAJOR COMMENTS				
1.				
2.				
3.				
4.				
5.				
6.				
MINOR COMMENTS				
7.				
8.				
9.				

Appendix IX: Protocol template

This template is used to develop the protocol for an evidence review for the Canadian Task Force on Preventive Health Care (CTFPHC). The protocol is completed on the basis of information gathered during calls of the topic working group, including the chair, cochair (a Public Health Agency of Canada [PHAC] scientific research manager) and the Evidence Review and Synthesis Centre (ERSC). The protocol should focus on the key questions, contextual questions, inclusion and exclusion criteria, literature search, and analytic framework. Information to add context to the topic should be included in the background section, whereas information needed to add context to the recommendation can be included as contextual questions (Section 4.3.3.3).

Project Title:

ERSC Project Lead Investigator:
ERSC Project Staff:

CTFPHC Working Group Chair:
CTFPHC Working Group Members:

PHAC Scientific Research Manager:
PHAC Scientific Officer:

Section I. Purpose and Background

Purpose

Describe the purpose of the report (used by CTFPHC to develop recommendations), and address whether the project is new, an update, etc.

Condition Background (maximum of two pages)

The background section of the protocol (and evidence review) should provide the context for the topic, including the condition, risk factors, rationale for screening, treatments or interventions, and current clinical practice. The background section should not exceed two pages.

Condition definition.
Defines the condition

Prevalence and burden of the condition.
Include the prevalence of the condition in subpopulations and overall, and discuss any information about differences in prevalence in subpopulations if relevant.
Include the population primarily affected by the condition, and if there are primary and secondary causes of the condition. The burden of the condition should also be included in this section.

Etiology and natural history.

Include information on the causes of the condition and consequences if untreated. Information about the primary and other causes of the condition are discussed. Discuss differences in natural history if they exist.

Risk factors.
Discuss the risk factors for the condition and if those at high risk can be identified. Information about the prevalence of the conditions in populations at high risk and differences between populations at high and low risk can be included. Any information about how to assess the risk factors should also be discussed.

Rationale for screening and screening strategies.
Describe the rationale for the intervention and how the condition is detected. Information about different ways to detect the condition and any information about issues with timing of detection can be included. A discussion about which strategies are currently recommended or practiced, how these strategies are used in practice, and any issues with current screening strategies can be included.

Interventions/treatment.
Describe the interventions used for the condition. This should be included in the background section, and not as a contextual question. Relevance and validity of different treatment methods are included. Information about how treatment outcomes can be assessed, timing of treatment, timeframe of treatment to determine success of treatment and other outcomes to assess treatment effectiveness can be described. Patient preferences for treatment may also be included if applicable to the topic.

Current clinical practice.
Describe the current clinical practice and any factors that should be considered when discussing the clinical preventive service. The usage of the clinical preventive service can be included.

Section II. Previous Review and CTFPHC Recommendations
For updated topics, describe the previous review, the results and recommendations. The questions used in a previous CTFPHC review can be included, and describe any limitations to the previous review.

Section III. Recommendations from Other Guideline Developers and Current State
This section can describe recommendations from other guideline development groups, such as the USPSTF, SIGN, NICE, and other relevant organizations. Recommendations currently being followed by the Provinces and Territories, and any other contextual information to describe why the guideline is being updated should be included.

Section IV. Scan of New Evidence since Previous Recommendation (see Section IV for search strategy)
For updated topics, report the new evidence identified from a scoping search. If ongoing studies were identified in the previous review, these should be discussed.

Section V. Review Approach
If the topic is an update, information about how the review will be updated (new systematic review, updated, focused or staged) and if all key questions from the previous review will be updated (key questions for which there is no new evidence may not be updated).

Analytic Framework and Key Questions

The analytic framework, key questions and contextual questions are reported in this section. Standard contextual questions include:

1. *What is the cost-effectiveness of <intervention> for <disease/condition in <population>?*
2. *What are the patient values and preferences for <intervention> for <disease/condition>?*
3. *What process and outcome performance measures or indicators have been identified in the literature to measure and monitor the impact of <intervention> for <disease/condition>?*
4. *What is the optimal screening interval for <intervention> for <disease/condition>?*
5. *What risk assessment tools are identified in the literature to assess the risk of <disease/condition>?*
6. *What is the evidence for a higher burden of disease, a differential treatment response, differential performance of <intervention>, or barriers to implementation of <intervention> for <disease/condition> in subgroups? Subgroups include: Aboriginal population, rural or remote populations, or other ethnic populations.*

Literature Search

Describe databases, time periods and any other relevant information about the search strategy.

Inclusion and Exclusion Criteria

Report all information about the population, intervention, comparator and outcomes included and excluded. Study designs and settings included and excluded, language and date limits, and any other information on inclusion and exclusion criteria should be described. The data abstraction and article screening forms should be included.

Section VI. Planned Timeline

The project schedule with deliverables and milestones is listed.

Section VII. Reviewers

A list of individual peer reviewers and organizational reviewers who will be contacted to review the protocol is reported.

Section VIII. Plan to Update the Search

Outline the plan to update the search prior to publication of the systematic review and to identify key studies that are in progress or have been published since the search was conducted.

References Cited

Generate the list of references used in developing the protocol.

Appendix X: Evidence Review Template

Project Title
[Level 1 Title: Times New Roman, Bold, Size 24]

Date
[Level 6 Title: Times New Roman, Size 12]

MERSC Group Authors
McMaster University
Hamilton Ontario Canada

CTFPHC Leads:

PHAC Scientific Officer:

Working Task Force Members:

Task Force Members:

Abstract [Level 2 Title: Times New Roman, Bold, Size 18]

Background: [Level 5 Title: Times New Roman, Bold, Size 12]

Purpose:

Data Sources:

Study Selection:

Data Abstraction:

Results:

Data Synthesis:

Limitations:

Conclusions:

Table of Contents

Abbreviations/ Glossary

Chapter 1: Introduction [Tables included throughout body of text]

Purpose [Level 3 Title: Times New Roman, Bold, Size 16]

Condition Background

Definition [Level 4 Title: Times New Roman, Bold, Size 14]

Prevalence and burden of disease

Etiology and natural history

Consequences if left untreated

Risk Factors

Rationale for Screening

Screening Strategies

Interventions/Treatments

Current Clinical Practice

Previous Review and CTFPHC Recommendations

Chapter 2: Methods

Analytic Framework and Key Questions

Search Strategies

Study Selection

External Review

Quality Assessment, Data Abstraction and Analysis

Chapter 3: Results

Summary of the Literature Search

Results for Key Questions

Key Question 1a:

Key Question 1b:
Key Question 1c:
Key Question 2a:
Key Question 2b:
Key Question 2c:
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Contextual Question 1:
Contextual Question 2:
Contextual Question 3:
Contextual Question 4:

Discussion

Limitations
Future Research

Conclusion

Reference List

Figure 1: Analytic Framework and Key Questions
Figure 2: Search Results
Figure 3: Search Results

Table: Characteristics of Included Studies
Table: Risk of Bias Table
Evidence Sets
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Evidence Set 2:
Evidence Set 3:
Evidence Set 4:
Appendix 1: Search Strategies for Cervical Cancer Screening
Appendix 2: Grey Literature Search
Appendix 3: List of Reviewers (Protocol)
Appendix 4: List of Reviewers (Review)
Appendix 5: Tools
Appendix 6: List of Excluded Studies
Acknowledgements:

Appendix XI: Process to incorporate and quality assess modeling studies that address key questions

Objective

The following process is designed for use when modeling studies are being used to answer Key Questions for a CTFPHC systematic review. If the working group decides that modeling data are to be considered, the ERSC conducts a search of the literature to identify modeling studies that can be used to answer the questions.

Background

The current GRADE approach emphasizes the need to determine the quality of evidence supporting the clinically important benefits and harms attributable to use of an intervention. Randomized Controlled Trials (RCTs) or meta-analysis of RCTs remain the gold standard in terms of evidence for benefits. RCT may provide high quality of evidence for harms, but given the rarity of harms, it is now recognized that prospective observational studies may be the best source of evidence for uncommon or rare harms. Identifying evidence relevant for patient important outcomes remains the central goal.

In the field of clinical prevention, an intervention may include several components applied in sequence (such as screening followed by treatment in identified cases), and, due to slow progress of a disease, may include intermediate outcomes rather than clinically important final outcomes. While in an ideal world a RCT for benefits and a prospective cohort for harms would provide the highest quality of evidence for screening interventions, these may not be available for the general population or subgroups within a population. In addition, guideline developers may also have questions concerning the frequency of screening, and the cost effectiveness of screening. Developing de novo models or micro-simulations, or using evidence from published models, may provide an important source of new evidence.

A TF working group may choose to incorporate evidence from modeling and CEA studies to inform the estimate of benefits and harms of a preventive intervention or to inform the resource use related to an intervention. When modeling and CEA studies are sought to help inform the benefits and harms of an intervention for a general population of subgroups of a population, then the evidence centre will use the 6-step process described herein to systematically search, appraise and judge the quality of the CEA/modeling study.

The results of a CEA/modeling study will be incorporated into the evidence review only if it is considered to be methodologically rigorous (“well done” or “very well done”). At this stage, the working group will then need to assign a GRADE quality rating in collaboration with the evidence centre related to the evidence for benefits and harms related to patient important outcomes.

STEP 1:

The ERSC screens the papers identified in the search for “applicability” before completing the Drummond checklist

Step 1: Applicability Appraisal			
		Study 1	Study 2
Applicability criteria	1. Is the study population appropriate for the guideline?		

Applicability criteria	2. Are the interventions appropriate for the guideline (e.g. screening)?		
Applicability criteria	3. Overall judgement of applicability: Directly applicable/Partially applicable/Not applicable		

Overall judgment of the applicability of the economic evaluation to the clinical guideline:[1]
• **Directly applicable** – the study meets all applicability criteria, or fails to meet one or more applicability criteria but this is unlikely to change the conclusions about cost effectiveness.
• **Partially applicable** – the study fails to meet one or more applicability criteria, and this could change the conclusions about cost effectiveness.
• **Not applicable** – the study fails to meet one or more applicability criteria, and this is likely to change the conclusions about cost effectiveness. Such studies would be excluded from further consideration and there is no need to continue with the Drummond Plus table.

Studies that are directly or partially applicable will move on to step 2.

STEP 2:
The ERSC completes the Drummond Plus table for studies that passed the initial screening.

Step 2: Quality Appraisal of the Economic Studies Adapted from Drummond (Drummond Plus)			
		Study 1	Study 2
Drummond	1. Was a well-defined question posed in answerable form?		
Drummond	2. Was a comprehensive description of the competing alternatives given (i.e. can you tell who did what to whom, where, and how often)?		
Drummond	3. Was the effectiveness of the program or services established?		
Drummond	4. Were all the important and relevant costs and consequences for each alternative identified?		
Drummond	5. Were costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, and gained life years)?		
Drummond	6. Were the cost and consequences valued credibly?		
Drummond	7. Were costs and consequences adjusted for differential timing?		

[1] Appendix H: Methodology checklist: economic evaluations, National Institute for Health and Clinical Excellence (January 2009)

Drummond	8. Was an incremental analysis of costs and consequences of alternatives performed?		
Drummond	9. Was allowance made for uncertainty in the estimates of costs and consequences?		
Drummond	10. Did the presentation and discussion of study results include all issues of concern to users?		
Plus	11. Were all the relevant comparators considered?		
Plus	12. Were all the relevant outcomes considered?		
Plus	13. Does the study population consider appropriate subgroups that require special attention for the guideline (e.g. high risk population)?		
Plus	14. Were the ethical/distributional implications discussed?		
Plus	15. Is there no potential conflict of interest (includes funding considerations)?		
Plus	16. Was the generalizability of outcomes discussed?		
Plus	17. Are the outcomes and input parameters applicable to the Canadian context?		
Plus	18. Are the conclusions of the evaluation justified by the evidence presented?		

STEP 3:

Two modeling consultants (a consultant from the ERSC and an independent modeling consultant hired by the TF) complete the "characteristics of included modeling studies table" (below) and use these data and the results presented in Step 2 to evaluate the level of methodological quality for each study. Studies identified with an overall quality assessment of "very well done" and "well done" move on to Step 4 of the process. In case of conflict between the recommendations put forward by the two different consultants, the issue will be raised with the WG Chairs to come to a decision.

The overall methodological study quality of the economic evaluation is assessed in two ways:

- level of limitations (minor, potentially serious, and very serious)[2]
- overall quality of the model (very well done, well done, fair, poor)

Limitations definitions:

Minor limitations – the study meets all quality criteria, or the study fails to meet one or more quality criteria but this is unlikely to change the conclusions about cost effectiveness.

[2] Adapted from Appendix H: Methodology checklist: economic evaluations © National Institute for Health and Clinical Excellence (January 2009)

Potentially serious limitations – the study fails to meet one or more quality criteria and this could change the conclusions about cost effectiveness.

Very serious limitations – the study fails to meet one or more quality criteria and this is highly likely to change the conclusions about cost effectiveness. Such studies should usually be excluded from further consideration.

Step 3: Characteristics of included modeling studies		
	Study 1	Study 2
Author		
Year		
Country		
Screening for		
Screening mechanism		
Screening programs		
Model format		
Time horizon		
How risk of diabetes modeled		
Quality of model		
How time to detection modeled		
Other risk factors changing prior to detection		
Treatment at point of diagnosis		
Results		
Funding source		
Conclusion Step 3		
Overall assessment of the quality of the model (very well done, well done, fair, poor)		
Limitations assessment (minor, potentially serious, and very serious)		
Provide details of limitations		

STEP 4:

The modeling consultant completes the following table for those studies that perform well in steps 1-3 and chooses the ones to include into the evidence review by applying the criteria below.

Step 4: Selecting the studies that will be incorporated into the evidence			
		Study 1	Study 2
Criteria	1. Relevance of the model's focus to the key questions and contextual questions addressed by the guideline: High/Medium/Low		
	Reason – explain:		
Criteria	2. Relevance of the model's sensitivity and scenario analyses to the key questions and contextual questions addressed by the guideline: High/Medium/Low		
	Reason – explain:		
Criteria	3. Capacity to use the model for de novo analyses		

	relevant to our KQ and CQ		
	Reason – explain:		
Criteria	4. Is the model up to date? Yes/No		
Criteria	5. Other considerations? List other reasons why the selected model is the best to move forward with.		

STEP 5:
The independent modeling consultant applies GRADE to the final included study/studies. The approach to rating quality of evidence for modeling studies is as follows:

Design: "modeling", including mathematical models, decision analyses, and economic analyses.These studies always start at "very low" quality, to account for the inherent and often hidden risk of bias that accompanies the modeling process. In addition, the Task Force only considers admitting evidence from modeling studies that are determined to be "well done" or "very well done".

Limitations: used to highlight appraisal issues related to the modeling studies. The rule being that "very serious limitations" identified would negate any later increase in the evidence rating. This category should also be used to highlight limitations that emerge due to individual studies that are used in the model, where well done RCTs would be considered to have a "minor limitations" (and this would mean there could potentially be a rating up to maximum of 2 depending on results of subsequent categories), and that other designs (i.e. observational studies) or RCTs that are not well done would have very serious limitations and this would limit the rating up to a maximum of 1. Since it is not possible to go below "very low" for the quality of the evidence, no further downgrading is necessary. And given the inherent assumptions of models we suggest it is not possible to have a model with "no study limitations" so this designation would not apply.

Inconsistency: In the case of "well done" modeling studies that show inconsistent outcome results (for example, substantial variability between clinically plausible scenarios), the quality should be rated down. Note: studies cannot be pooled given the nature of these studies.

Indirectness: modeling studies are usually designed to provide a more direct estimate of benefits and harms for specific groups. But if the groups in the study are not the groups of interest for the guideline, the TF will rate down for indirectness.

Imprecision: in the case of modeling studies this is not applicable as there will be no confidence intervals for relative risks. ("NA" is inserted in the corresponding box on the evidence profile).

Other considerations: this box can be used as an opportunity to increase the rating by 1 or 2 based on the limitations and 3 additional variables:

1) Range of comparators: at least 3 comparators
2) Outcomes: at least 1 outcome from the list of important and critical outcomes
3) Validated: the standard definition used in relation to modeling studies applies and evidence of demonstration of sensitivity analysis is also considered.

Number of patients and effect: does not apply, given the nature of these studies. ("NA" is inserted in the corresponding box on the evidence profile).

A sample of the GRADE Evidence Profile and Summary of Findings Table for modeling studies using Diabetes data v.2 is showed at the end of this document.

STEP 6:
ERSC or staff or the independent modeling consultant prepares a summary of the evidence that addresses the key questions, which is included in the systematic review

GRADE Evidence Profile and Summary of Findings Table for modeling studies using Diabetes data v.2

Quality Assessment							Summary of Findings					
							No of patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations[10]	Screening	Control	Relative (95% CI)	Absolute	Quality	Importance
2[1]	modeling studies[2]	serious limitations[3]	no serious inconsistency[4]	no serious indirectness[5]	no serious imprecision[6]	Use of appropriate range of comparators.[7] Evidence of sensitivity analysis.[8] Validation of model.[9]	NA	NA	NA	NA	□□□□ Low	CRITICAL

[1]Kahn et al, 2010; Waugh et al, 2007

[2]GRADE does not currently accommodate modeling studies; however, the CTFPHC methods include an appraisal approach that suggests admitting evidence from modeling studies (decision analyses; economic analyses; simulation studies) when such studies are determined to be methodologically rigorous ("well done" or "very well done"). The CTFPHC methods specify that modeling studies should always start at "very low" quality of evidence, to account for the inherent and often hidden risk of bias that accompanies the modeling process.

[3] modeling studies as appraised using Drummond tool were determined to be "well done" with low risk of bias; additional assessment undertaken by a modeling expert identified minor methodological limitations in the Waugh study (one-off screening rather than repeated screening; appropriateness of HbA1c test) and potentially serious limitations in the Kahn study (lack of details concerning certain diabetes complications possibly alleviated by extensive model validation; limited description of screening test and how time to clinical detection is modeled undermines relevance), Kahn et al used NHANES observational data (1999-2004) which in the context of a model is suggest minor limitations and thus limits rating up to a maximum of 1.

[4] both modeling studies reported on screening for diabetes and reported on the same outcomes; lacking a statistical analysis we think it is inappropriate to put these two studies together

[5]the studies addressed the same (simulated) population, intervention, comparator and outcome of interest and both models are for populations in developed countries (US and UK)

[6]for GRADE this assessment considers samples sizes, number of events (threshold rule-of-thumb value is 300) as well as the width of the confidence intervals; in the modeling studies the simulated sample sizes were large but event numbers are not meaningful and confidence intervals were not available; we have not downgraded based on this

[7]Range of comparators was at least 3 and deemed to be appropriate

[8]the relevant patient important outcomes including myocardial infarction, stroke, angina and retinopathy were included in the modeling analysis

[9]models used (Archimedes and Markov) are validated

[10] Based on these favorable considerations we have rated up the quality by 1

Appendix XII: Data abstraction form

Study	Author(s), Date, Country
Objective	
Methods	Design: Selection: Recruitment, inclusion/exclusion Blinding: Confounders:
Participants	Sample: total N Intervention: study group n = and control group(s) n = Characteristics: Loss to follow-up: Other relevant information such as years of recruitment:
Intervention	Description of intervention and control, duration of intervention, length of follow-up
Measurement (screening) tool	
Outcomes	Related to the key questions
Comments	Study limitations identified by the study or review authors

Appendix XIII: Headings from a GRADE risk-of-bias table[2]

Author/Year	Randomization	Allocation concealment	Blinding	Loss to follow-up / ITT principle observed or per protocol analysis	Other

Note: GRADE = Grading of Recommendations Assessment, Development and Evaluation, ITT = intention-to-treat.

Appendix XIV: Example of a GRADE summary-of-findings table*

Does screening with mammography (film and digital) reduce all cause mortality?

Outcomes	Illustrative Comparative Risks* (95% CI) Assumed Risk Control	Corresponding Risk Screening with Mammography (film and digital)	Relative Effect (95% CI)	No of Participants (Studies)	Quality of the Evidence (GRADE)
All Cause Mortality for Ages 39-49 Follow-up: 10-16 years	**18,070 per 1,000,000**	**17,528 per 1,000,000** (16,443 to 18,793)	**RR 0.97** (0.91 to 1.04)	211,270 (2 studies[3])	⊕⊕⊕⊕ **high**[1,2]
All Cause Mortality for Ages 50-59	**35,040 per 1,000,000**	**37,142 per 1,000,000** (33,638 to 41,347)	**RR 1.06** (0.96 to 1.18)	39,465 (1 study)	⊕⊕⊕⊕ **high**[2,3]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] no heterogeneity exists. P-value for testing heterogeneity is 0.65 and I^2=0%.
[2] sample size is large and total number of events is greater than 300 (a threshold rule-of-thumb value)
[3] truly randomized

Note: GRADE = Grading of Recommendations Assessment, Development and Evaluation.
*Source: Fitzpatrick-Lewis D, Hodgson N, Ciliska D, et al. Breast cancer screening. Manuscript in preparation.