Appendix 2 (as supplied by the authors): Detailed Methods

Task Force Methods

For every topic selected by the Task Force, a topic working group is formed. This working group consists of three or more Task Force members who volunteer to join the working group (one of whom is selected as chair), a scientific research manager from the Public Health Agency of Canada and members from the Evidence Review and Synthesis Centre, as well as from partner organizations, if any such organizations are involved for the particular topic.

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 Task Force as a whole and partner organizations (if applicable) review and approve these documents. The chair or co-chair of the working group then sends the analytical framework and key questions to the Evidence Review and Synthesis Centre and they begin the review.

The Evidence Review and Synthesis Centre and its clinical experts develop a protocol based on information received from the working group. 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 Task Force for approval and comment. The protocol is then peer reviewed by 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 Task Force.

The Evidence Review and Synthesis Centre conducts a systematic review of the available evidence according to the final, approved protocol. The quality of evidence and strength of recommendations is determined using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Please see the http://www.canadiantaskforce.ca/docs/grade_ENG.pdf) for the GRADE Companion Document to Task Force Guidelines.

The draft systematic review is peer reviewed and comments are incorporated. The systematic review is finalized once the members of the working group and the Task Force have reviewed and approved the revisions. Subsequently, 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 Task Force.

During a meeting of the Task Force, the Evidence Review and Synthesis Centre presents the findings of the systematic review, and the working group presents the draft recommendations. Members of the Task

Appendix to: Canadian Task Force on Preventive Health Care. Recommendations on screening for cervical cancer. *CMAJ* 2013. DOI:10.1503/cmaj121505.

Force discuss the systematic review and recommendations and may propose changes to the wording of the recommendations. The Task Force votes on the draft recommendations. The timeline from approval of the protocol to presentation of the draft recommendations to the Task Force is usually 9 to 15 months.

Following the discussion and voting during a meeting of the Task Force, the chair of the topic working group revises the recommendations and shares the revised version with all members for the Task Force for approval. The approved statement of recommendations is then sent to external peer reviewers for comment. Comments provided by peer reviewers are shared with the topic working group who decide whether any changes are required. If substantial revisions are required or if the recommendations are controversial, the entire Task Force may be asked to review and discuss the comments. If no substantial revisions are required, the Task Force 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 Task Force for approval. The Canadian Task Force Procedures Manual provides more details on Task Force methods[1].

Cervical Cancer Systematic Review

An original search was conducted for this review. Medline, EMBASE, and Cochrane Central were searched from 1995 to June 2011 in three separate search strategies which focused on Key Question 1 (effectiveness of screening), Key Question 2 (harms of screening), and the contextual questions (including harms of treatment, subgroups, resource implications, patient values and preferences) . A fourth search was conducted to find relevant Canadian statistics in the grey literature.

The primary indicator of screening effectiveness is its ability to reduce the risk of dying from the disease of interest – cervical cancer. Therefore for this purpose, high-grade cervical abnormalities (i.e. cervical intraepithelial neoplasia (CIN) 2 and CIN 3 including carcinoma in situ [CIS]) were not considered to be clinically relevant outcomes, since the majority of these lesions will not progress to invasive cervical cancer or lead to death from cervical cancer. In two retrospective cohort studies examining untreated CIN3 diagnosed between 1960 and 1980, progression to invasive cancer occurred in 4% of Canadian women at 10 years[2], and 30% of New Zealand women over 30 years[3]. A Danish study estimated that 6 women with CIN are treated for every cervical cancer prevented. Based on this estimate, only 16% (1/6) of CIN, most of which was CIN 2 or 3, will ultimately progress to cervical cancer[4].

Systematic reviews, randomized controlled trials (RCTs), and observational studies with a comparison group were eligible to address the effectiveness of screening for cervical cancer (Key Question 1). Studies of any design were eligible to address the harms of screening (Key Question 2) and the contextual questions (Appendix 1). Epidemiologic data were consulted to provide information for estimating the potential benefits and harms of screening.

Eligible studies included women aged 15 to 70 years who were or had been sexually active. A review of the selected studies revealed that some also included women over the age of 70. Further scrutiny of the initial search results (prior to age selection) confirmed that there were no other studies in the literature of

women aged 70 and older that had been excluded. Thus, the included literature likely represents all relevant available evidence on women over the age of 70 as well.

Cervical cancer screening methods that were considered included conventional and liquid-based Pap tests, and HPV DNA tests. Evidence regarding the effectiveness of screening included systematic reviews, randomized controlled trials, and observational studies with comparison groups. For harms and contextual questions, any study design was considered. Harms of screening included over diagnosis, false-positives, colposcopy rates, anxiety and depression, and sexual dysfunction.

Identified titles and abstracts were reviewed by two members of the synthesis team. Any article marked for inclusion by either team member went on to a full text rating. Full text inclusion, quality assessment, and data extraction was conducted by two people and all disagreements were resolved through discussion. The inclusion results were reviewed by a third person. Data were extracted from the selected studies using a standard format. The exception to this process were studies related to the contextual questions, for which title and abstract screening and data extraction was done by one person. Further details on the methods used for the cervical cancer evidence review and synthesis can be found in the systematic review, which is published on the CTFPHC website (www.canadiantaskforce.ca).

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