

Bern, 3 June 2019

Invitation for conducting a scoping report on cervical cancer screening

1. Introduction

The aim of the Cancer Screening Committee is to develop recommendations in the field of cancer screening for the Swiss context. The Cancer Screening Committee is a project of the National Strategy against Cancer. The committee develops recommendations for or against cancer screening modalities in four phases: Topic Identification and Selection, Scoping report, Assessment report, Appraisal (for more information).

One of the chosen topics is cervical cancer screening which has been recommended for decades in Europe, North America and Canada. Cytology is the foundation for long-standing cervical cancer screening recommendations in many countries. In recent years testing for high risk human papilloma virus (hrHPV) has been developed and has been proposed by some organisations as an alternative to cytological screening or even as primary screening test for defined patient groups^{1,2}.

The US preventive services task force and other organisations have recently reviewed the evidence of quantifying the benefits and harms of cervical cancer screening^{1,3-7}. The optimal way for cervical cancer screening might depend on the age of the screened women (<30 years, 30-35 years, >35 years), the findings of previous screening rounds and the vaccination status.

2. Question of the scoping report

What is the relative performance of different cervical cancer screening strategies – which may contain cytology-based and/or HPV-testing based components in different combinations and algorithms?

3. PICO outline:

Population	<ul style="list-style-type: none"> • Adult asymptomatic women
Intervention	<ul style="list-style-type: none"> • HPV testing • Cytology-based testing • A combination of HPV and cytology-based testing
Comparator	<ul style="list-style-type: none"> • Cytology-based testing or usual care
Reference	<ul style="list-style-type: none"> • Gold-standard (colposcopy; with biopsy when needed)

Outcomes	<ol style="list-style-type: none"> 1. Cervical cancer mortality 2. Cervical cancer incidence 3. Cervical intraepithelial neoplasia grade 2 (CIN2) or worse (CIN2+) (surrogate marker for cervical cancer) 4. Interval cancer incidence 5. Costs of screening 6. Overall strategy costs (including costs of cancer screening) 7. Quality-adjusted life years per strategy 8. Incremental cost-effectiveness ratio (cost per QALY gained) 9. Budget impact 10. Overdiagnosis 11. Referral for colposcopy 12. Anxiety/worry associated with taking the test 13. Unnecessary treatments 14. Harms associated with taking the HPV test
Setting	<p>Outpatient screening (within a program OR opportunistic screening)</p> <p>Industrialized countries (results from low-resource countries may not be applicable to the Swiss context)</p>
Study design	<p>For the clinical effectiveness: RCTs randomizing women to HPV- or cytological screening or both</p> <p>Non-randomized intervention studies evaluating HPV test and cytological screening concomitantly</p> <p>For the health economic evaluation: de-novo modelling, literature review or a combination of these two approaches.</p>

Ad population:

The women have to be close to or within the recommended age range for cervical screening (21-70 years) according to the guidelines of the Swiss Society for Gynecology and Obstetrics (SGGG). Other organizations such as the USPTF or NHS recommend slightly different screening age range (USPTF: 21-65 years; NHS: 25-64 years).

The screened women should not have any cytological abnormalities or being followed up for earlier cytological abnormalities.

Subgroup analysis: HPV-vaccinated versus -unvaccinated women

Ad intervention:

Only HPV tests that are currently approved by health authorities (national and international), are validated and fulfil the Meijer criteria⁸ should be included in the assessment

These tests could be for example:

- PCR
- HC2
- Aptima
- Or other techniques identified during the literature search

Results of effectiveness should be described according to the category of tests used.

Screening intervals: results should be categorized according to screening intervals.
The thresholds for the different HPV screening tests should be defined.

Ad control:

The threshold for an abnormal PAP smear should be defined.

4. Content of the scoping report

a.) For the assessment of the **clinical effectiveness** of cervical cancer screening:

- To describe the rationale for the evaluation of the effectiveness of cervical cancer screening
- To define the main question(s) for the systematic review and make a first prioritization of the outcomes
- To describe the outlines of the systematic review of the literature (including first explorative results of the search): aims of the literature search, outline of the literature search (such as study design, databases or period of search that will be considered or the tool that will be used for evaluating the quality of the studies)
- To describe subgroups that should be analyzed separately in the systematic review (e.g. HPV-vaccinated versus non-vaccinated women)
- To describe possible sensitivity analyses (e.g. different HPV screening tests)

b.) For the **health economic assessment** of cervical cancer screening:

- To describe the rationale for the economic evaluation of the cervical cancer screening
- To define the main question(s) for the health economic assessment
- To describe the outlines of the systematic review of the literature (including first explorative results of the search): aims of the literature search, outline of the literature search (such as study design, databases or period of search that will be considered or the tool that will be used for evaluating the quality of the studies)
- To define the cost-effectiveness and budget impact models that will be used for the assessment
- To describe subgroups that should be analyzed separately in the systematic review (e.g. HPV-vaccinated versus non-vaccinated women)
- To describe possible sensitivity analyses (e.g. different HPV screening tests)

c.) For the assessment of **patients' values and perspectives, ethical and legal issues**

- To describe how patients' values and perspectives are planned to be evaluated
- To describe how potential ethical and legal issues are going to be identified

The scoping report will serve as study protocol for the full assessment report.

Examples of external scoping reports can be found [here](#) (scoping reports from the Swiss Medical Board).

5. Contracting authority, Duration, Expenditure

The Swiss Cancer League is the contracting authority and is responsible for the implementation of the project 2.3 Cancer Screening Committee from the National Strategy against Cancer.

This invitation for conducting the scoping report for cervical cancer screening is addressed to potential mandate holders. The mandate is initially limited to the scoping report. If the Cancer Screening Committee decides after the scoping report to continue with the topic, an assessment will be commissioned. Ideally the assessment report will be conducted by the same team as for the scoping report.

Payments will be issued 50% upfront and 50% upon completion. A budget according to the following schema is recommended.

Output	Time expenditure in hours	Amount in CHF
1.		
2.		
Sub-total excl. additional charges and VAT		
3. Additional charges (expenses, mailings, etc.)		
Sub-total excl. VAT		
4. VAT		
Total		

Only the offers, which arrive by the deadline and are structured according to the following points will be considered:

1. Letter of intent
2. Expertise and proof of activities for example experience in conducting HTA, systematic reviews (including meta-analysis)
3. Relevant reference projects
4. Work and time schedule
5. Budget

Attachment: Information on the planned project staff members.

6. Offer submission

The offer is to be sent on or before 10 July 2019 to the office of the Cancer Screening Committee: office@cancerscreeningcommittee.ch

Any questions regarding this invitation procedure need to be addressed via email to the office of the Cancer Screening Committee (see above). Answers will be provided for all invited potential mandate holders.

Schedule for the offer and mandate

Offer	
Invitation	3 June 2019
Deadline for submitting questions	18 June 2019
Answers to all invited potential mandate holders	25 June 2019
Deadline for submitting the offer	10 July 2019
Order confirmation and conclusion of contract	31 July 2019
Mandate scoping report	
Draft report	31 August 2019
Meeting Cancer Screening Committee	5 September 2019
Stakeholder Meeting	26 September 2019
Final version	13 October 2019

The draft report will be followed by a meeting with stakeholders to hear and gather their comments. The mandate holder should be present at this meeting.

7. Award criteria and evaluation

For the selection of the offer, the following award criteria will be considered:

Award criterion	Question for the rating	Weighted score
Letter of intent	Is the motivation comprehensible and convincing?	10% 0-10 points
Expertise	Does the provider have the necessary expertise?	20% 0-20 points
Reference projects	Do the reference projects or does a reference project indicate that the supplier is able to perform the task in the required quality?	30% 0-30 points
Work and time schedule	Is the work and time schedule realistic and comprehensible? Is the staff secured?	10% 0-10 points
Costs	Are the cost estimate and pricing comprehensible? What are the costs compared to other providers?	30% 0-30 points

The award criteria are evaluated as follows:

The requirements are ...	Evaluation
... fully met and demonstrated by evidence comprehensible	100 points
... partially fulfilled or only partly and incompletely explained	50 points
... not met or evidence missing	0 points

References:

1. Melnikow J, Henderson JT, Burda BU, Senger CA, Durbin S, Weyrich MS. Screening for Cervical Cancer With High-Risk Human Papillomavirus Testing. *JAMA*. 2018;320(7):687. doi:10.1001/jama.2018.10400
2. Rebolj M, Rimmer J, Denton K, et al. Primary cervical screening with high risk human papillomavirus testing: observational study. *BMJ*. 2019;364:l240. doi:10.1136/BMJ.L240
3. Koliopoulos G, Nyaga VN, Santesso N, et al. Cytology versus HPV testing for cervical cancer screening in the general population. *Cochrane Database Syst Rev*. 2017;(8). doi:10.1002/14651858.CD008587.pub2
4. CADTH. *HPV Testing for Primary Cervical Cancer Screening: A Health Technology Assessment*. Ottawa; 2019.
5. Arbyn M, Haelens A, Desomer A, Verdoodt F, Thiry N, Francart J, Hanquet G RJ. *Cervical Cancer Screening Program and Human Papillomavirus (HPV) Testing, Part II: Update on HPV Primary Screening. Health Technology Assessment (HTA)*. Brussels; 2015.
6. Curry SJ, Krist AH, Owens DK, et al. Screening for Cervical Cancer. *JAMA*. 2018;320(7):674. doi:10.1001/jama.2018.10897
7. Health Information and Quality Authority. *Health Technology Assessment of Human Papillomavirus Testing as the Primary Screening Method for Prevention of Cervical Cancer*. Ireland; 2017.
8. Meijer CJLM, Berkhof J, Castle PE, et al. Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women 30 years and older. *Int J cancer*. 2009;124(3):516-520. doi:10.1002/ijc.24010