

Guidelines and management of cervical screening – When to do HPV testing

DR. JOAN MURPHY
CLINICAL LEAD, ONTARIO CERVICAL SCREENING PROGRAM
ONTARIO HEALTH (CANCER CARE ONTARIO)

Cancer Care Ontario

Ontario

Learning Objectives

Following this presentation participants will

1. Have an increased understanding of the current state of cervical screening in Ontario and the transition to risk based screening & management.
2. Be more familiar with factors leading to the decision to transition to HPV testing in cervical screening and the implications for clinical management.
3. Be better prepared to advise patients about the impact of the transition from cytology to HPV testing

Cancer Care Ontario

The Ontario Cervical Screening Program (OCSP)

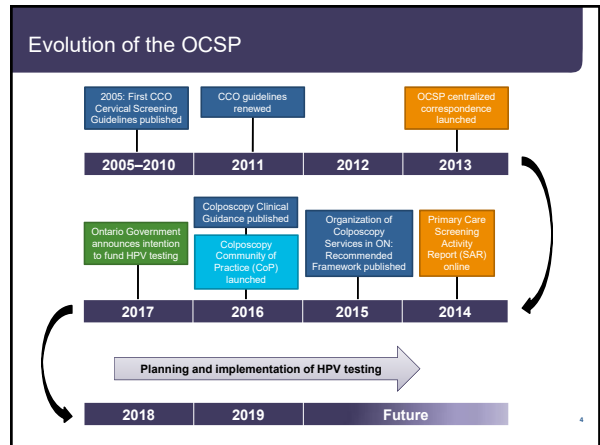
- The OCSP is a **population-based organized screening program** with the goal of **reducing cervical cancer incidence and mortality**, and in a future state, **fully integrating colposcopy into screening** to create a continuum of care.
 - Provides support to health care providers to offer the best possible cervical screening and colposcopy care to their patients.
 - Supportive of school-based HPV immunization (immunization is a mandate of Public Health Ontario)
- The OCSP is a part of Ontario Health (Cancer Care Ontario)

Elements of an Organized Screening Program*

- Defined target population
- Invitations to screen
- Timely access
- Quality oversight
- Tracking of outcomes

*International Agency for Research on Cancer, World Health Organization, IARC Handbook of Cancer Prevention: Breast Cancer Screening, Volume 13, Lyon, France, 2010.

Cancer Care Ontario



Cervical Screening in Ontario

- 1,100,000 screening tests/year
- 7% abnormal
- 86% are low grade abnormalities

Cancer Care Ontario

Transition to HPV testing

Cancer Care Ontario



Drivers for Transitioning to HPV Testing

- Decreased performance of cytology as prevalence of HPV decreases due to school-based immunization
- Better detection of pre-cancer and early cervical cancer
- Reduction of unnecessary colposcopy referrals
- Safer, earlier, more appropriate discharge from colposcopy
- Risk-based intervals after discharge from colposcopy

↓

Improving quality and effectiveness of cervical screening and colposcopy in Ontario

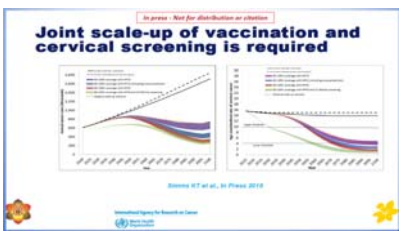
WHO: Eliminate Cervical Cancer

By 2030:

- 90% of girls immunized by age 15
- 70% of women screened at age 35 & 45
- 90% of women with cervical cancer have access to high quality treatment

WHO Elimination Goal: Modelling



Source: IIT et al., in Phase 2018

HPV Testing: An Overview

- Tests for oncogenic HPV and some sub-types (e.g. 16/18)
- HPV testing quickly and accurately determines whether a person is at risk for developing cervical cancer
 - Higher sensitivity than Pap test (98% vs. 55%)
 - High NPV (>99%)
 - Objective, reproducible
 - Determines risk status
 - Longer screening interval possible due to longer duration of protection (5 year vs. 3 year)

Definition of HPV testing in the OCSP


HPV	Refers specifically to high-risk oncogenic (i.e. cancer-causing) HPV subtypes, including HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68
HPV 16/18	High-risk oncogenic HPV subtypes 16 and/or 18
HPV-other (HPV non-16/18)	High-risk oncogenic HPV subtypes that are not 16 and/or 18
HPV-negative	No high-risk oncogenic subtype of HPV detected
HPV-positive	At least one high-risk oncogenic subtype of HPV detected
HPV testing	Molecular testing that includes clinically necessary subtyping, reflective of evidence and clinical appropriateness (e.g., extended subtyping)

Transition to HPV Testing in Ontario

- CCO and Ministry of Health are working together to transition from cytology to HPV testing within the OCSP

Work Underway

- Planning work is nearing completion
- Work to-date includes:
 - Detailed analysis of current HPV and Pap testing in Ontario
 - Defining future design of the OCSP with HPV testing
 - Understanding public and provider communication and information needs to support change to HPV testing
 - Defining IT changes required to support HPV testing
 - Drafting laboratory quality requirements for the OCSP
 - Determining approach for working with laboratories to implement HPV testing





13

OCSP Screening Recommendations Refresh

- OCSP is updating our screening recommendations based on most current evidence
- Summary tool expected in summer 2020

OCSP Screening Recommendations Summary

- Eligibility for Screening
- Age of Initiation
- Interval
- Cessation
- Special Populations





14

Special considerations & guidance

- Self-sampling
- Stand-alone cytology-screening
- Screening for people who have been vaccinated

- Self-sampling will not be included in the OCSP when HPV is launched
- Anticipate piloting this in future post HPV-launch




15

Special considerations & guidance

- Self-collected samples
- Stand-alone cytology-screening
- Screening for people who have been vaccinated

- Stand-alone cytology will not be available for use in OCSP once HPV-testing is implemented in screening




16

Special considerations & guidance

- Self-collected samples
- Stand-alone cytology-screening
- Screening for people who have been vaccinated

- Screened according to the OCSP screening recommendations, which does not differ by vaccination status



17


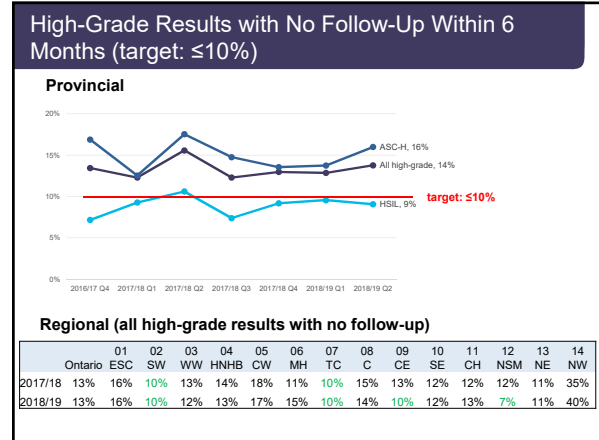
When will HPV testing be available in Ontario?

- Pap remains the recommended cervical screening test in Ontario
- We are actively working towards implementing HPV testing!

18

In the Meantime...

- Current challenges we would like to address in the program before launch include:
 - Too many people with high-grade results who are lost to follow-up
 - Lack of clarity regarding appropriate use of HPV testing in the current state
 - Sub-optimal screening participation rates


Importance of Referral of High-Grade Results

- People with **ANY** high-grade results are at a higher risk of having or developing cervical cancer and therefore require referral to colposcopy

Result	Depiction
Atypical squamous cells of undetermined significance (ASC-US)	Borderline or mild pre-cancerous abnormal cells detected (low grade)
Low-grade squamous intraepithelial lesion (LSIL)	Borderline or mild pre-cancerous abnormal cells detected (low grade)
Atypical squamous cells – cannot rule out high-grade squamous intraepithelial lesion (ASC-H)	Significant pre-cancerous abnormal cells detected (high grade)
High-grade squamous intraepithelial lesion (HSIL)	
Atypical glandular cells (AGC)	
Adenocarcinoma in situ (AIS)	Cancer cells detected
Squamous cell or glandular cell carcinoma	


In the Meantime...

- Current challenges we would like to address in the program before launch include:
 - Too many people with high-grade results who are lost to follow-up
 - **Lack of clarity regarding appropriate use of HPV testing in the current state**
 - Sub-optimal screening participation rates




Current State of HPV Testing in Ontario

- HPV testing is available in Ontario:
 - On a patient-pay basis; or
 - Provided without charge in some hospitals
- OCSP currently recommends HPV testing as an optional triage test for women ≥30 years old with cytology ASCUS
 - LSIL or ASCUS with HPV + → colposcopy
 - LSIL or ASCUS with HPV - → routine screening with cytology in 3 years



Overview of Current OCSP Screening Recommendations



Cervical Screening Guidelines Summary Tool

Ontario Cervical Screening Guidelines Summary
Revised October 2019 – based on current 2013 screening guidelines

Ontario Cervical Screening Program

Screening initiation
Screening should begin at age 21 for all women aged 21 to 69. Women aged 20 and under should not be screened. Women aged 70 and over should not be screened unless they have a history of abnormal cytology or are at high risk of cervical cancer.

Screening interval
Screening should be performed every three years for women aged 21 to 69.

Screening cessation
Screening should be stopped at age 70 for women with an adequate and negative cytology screening history in the previous 10 years.

Ontario Guidelines for Follow-Up of Abnormal Cytology

Refer directly to colposcopy for the following cytology report:

- High-grade squamous intraepithelial lesion (HSIL)
- Atypical squamous cells of undetermined significance (ASC-H)
- Atypical glandular cells (AGC)
- Squamous carcinoma, adenocarcinoma, other malignant neoplasms

Special screening circumstances

- Women who have sex with women
- Pregnant women
- Women who have undergone subtotal hysterectomy
- Transgender men who have retained their cervix
- Women who are immunocompromised

OCSP Current Recommendations: Initiation, Interval and Cessation

Screening initiation
Anyone with a cervix at **age 21**, if they are or have ever been sexually active.

Screening interval
If cytology is normal, screening with a cytology test should occur **every three years**.

Screening cessation
Cervical screening can stop at **age 70** if they have an adequate and negative cytology screening history in the previous 10 years (i.e., three or more negative cytology tests).

OCSP Current Recommendations: Special Circumstances

Special Circumstances

The following groups should be **screened according to guidelines**:

- Women who have sex with women
- Pregnant women
- Women who have undergone subtotal hysterectomy
- Transgender men who have retained their cervix

Women who are immunocompromised should receive **annual screening**

OCSP Current Recommendations: Direct Referral

Refer directly to colposcopy for the following cytology results:

- High-grade squamous intraepithelial lesion (**HSIL**)
- Atypical squamous cells – cannot rule out high-grade squamous intraepithelial lesion (**ASC-H**)
- Atypical glandular cells (**AGC**), atypical endocervical cells, atypical endometrial cells
- Squamous carcinoma, adenocarcinoma, other malignant neoplasms

Any visible cervical abnormalities or abnormal symptoms must be investigated by a specialist

Recommended Management: ASCUS

Diagnosis	Recommended Management				
ASCUS (atypical squamous cells of undetermined significance)	Women <30 years old (HPV triage not recommended)				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy		
	Women ≥30 years old				
	HPV testing for oncogenic strains	Negative	Routine screening in 3 years		
Positive		Colposcopy			
HPV status unknown					
Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years	
	≥ASCUS	Colposcopy			

Recommended Management: ASCUS

Diagnosis	Recommended Management				
ASCUS (atypical squamous cells of undetermined significance)	Women <30 years old (HPV triage not recommended)				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy		
	Women ≥30 years old				
	HPV testing for oncogenic strains	Negative	Routine screening in 3 years		
Positive		Colposcopy			
HPV status unknown					
Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years	
	≥ASCUS	Colposcopy			

Recommended Management: ASCUS in Young Women

Diagnosis	Recommended Management				
ASCUS (atypical squamous cells of undetermined significance)	Women <30 years old (HPV triage not recommended)				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy	≥ASCUS	Colposcopy
	Women ≥30 years old				
	HPV testing for oncogenic strains	Negative	Routine screening in 3 years		
		Positive	Colposcopy		
	HPV status unknown				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy	≥ASCUS	Colposcopy

Cancer Care Ontario 31

Recommended Management: ASCUS in Young Women

Diagnosis	Recommended Management				
ASCUS (atypical squamous cells of undetermined significance)	Women <30 years old (HPV triage not recommended)				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy	≥ASCUS	Colposcopy
	Women ≥30 years old				
	HPV testing for oncogenic strains	Negative	Routine screening in 3 years		
		Positive	Colposcopy		
	HPV status unknown				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy	≥ASCUS	Colposcopy

Cancer Care Ontario 32

Recommended Management: ASCUS in Young Women

Diagnosis	Recommended Management				
ASCUS (atypical squamous cells of undetermined significance)	Women <30 years old (HPV triage not recommended)				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy	≥ASCUS	Colposcopy
	Women ≥30 years old				
	HPV testing for oncogenic strains	Negative	Routine screening in 3 years		
		Positive	Colposcopy		
	HPV status unknown				
	Repeat cytology in 6 months	Normal	Repeat cytology in 6 months	Normal	Routine screening in 3 years
		≥ASCUS	Colposcopy	≥ASCUS	Colposcopy

Cancer Care Ontario 33

≥ASCUS

Result	Depiction
Atypical squamous cells of undetermined significance (ASC-US)	Borderline or mild pre-cancerous abnormal cells detected (low grade)
Low-grade squamous intraepithelial lesion (LSIL)	
Atypical squamous cells – cannot rule out high-grade squamous intraepithelial lesion (ASC-H)	Significant pre-cancerous abnormal cells detected (high grade)
High-grade squamous intraepithelial lesion (HSIL)	
Atypical glandular cells (AGC)	
Adenocarcinoma in situ (AIS)	Cancer cells detected
Squamous cell or glandular cell carcinoma	

Cancer Care Ontario 34

Abnormal Cytology Terminology

Result	Depiction
Atypical squamous cells of undetermined significance (ASC-US)	Borderline or mild pre-cancerous abnormal cells detected (low grade)
Low-grade squamous intraepithelial lesion (LSIL)	
Atypical squamous cells – cannot rule out high-grade squamous intraepithelial lesion (ASC-H)	Significant pre-cancerous abnormal cells detected (high grade)
High-grade squamous intraepithelial lesion (HSIL)	
Atypical glandular cells (AGC)	
Adenocarcinoma in situ (AIS)	Cancer cells detected
Squamous cell or glandular cell carcinoma	

Cancer Care Ontario 35

Discharge from Colposcopy

```

graph LR
    A[Target population] --> B[Screening in Primary Care]
    B --> C[Colposcopy]
    C --> D[Return to Primary Care]
    style D fill:#4a69bd,color:#fff
  
```

Cancer Care Ontario 36

Discharge from Colposcopy Letter Template

**FINAL DISCHARGE RECOMMENDATIONS
COLPOSCOPY SERVICES**

Colposcopist name: _____ Patient identifier: _____
 Contact information: _____ Date: _____

Recommendations on next screening interval

This patient is now discharged from colposcopy. She requires Pap screening by a primary care provider:

- Every three years (include cervical screening)
- Every year (cervical only)

No referral to colposcopy in the future should be guided by her screening results.

According to the Ontario Cervical Screening Program's recommendations, whether or not a woman has been tested, further colposcopic examinations are not required and she can be discharged to primary care if:

Discharge Criteria

HPV testing was done:

- Colposcopy negative AND negative cytology on 3 consecutive visits (Pap screening every 3 years by a primary care provider). These patients are at **very low risk** for high-grade dysplasia or cervical cancer.
- HPV test is negative AND normal or low-grade cytology (Pap screening every 3 years by a primary care provider). These patients are at **very low risk** for high-grade dysplasia or cervical cancer.
- Colposcopy negative AND any combination of normal or low-grade cytology on 3 consecutive visits (Pap screening every year by a primary care provider). These patients are at **slightly elevated risk** for high-grade dysplasia or cervical cancer and should be **referred annually**.
- HPV test is positive AND normal or low-grade cytology (Pap screening every year by a primary care provider). These patients are at **slightly elevated risk** for high-grade dysplasia or cervical cancer and should be **referred annually**.

For further information on screening and colposcopy recommendations for Ontario see www.ontario.ca/health/working/2016/03/01

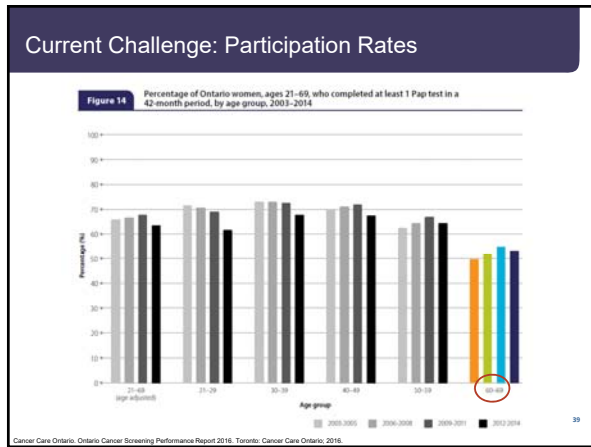
MD, Colposcopist

Screening/Surveillance in Primary Care

Screening/surveillance intervals after discharge from colposcopy

HPV status	Recommended interval
Negative	3 years
Positive	Annual
Unknown	Follow recommendations from colposcopist

Cancer Care Ontario



Cervical Screening Awareness Week

- Cervical Cancer Awareness Week campaigns:

Cancer Care Ontario

OCSP Focusing on Supporting Screening in Mature Women

- Key messaging:
 - You still need to go for cervical screening even if you:
 - Feel healthy and have no symptoms;
 - Are no longer sexually active;
 - Have only had one partner;
 - Are in a same-sex relationship;
 - Have been through menopause;
 - Have no family history of cervical cancer; or
 - Have received the HPV vaccine.

Cancer Care Ontario

Key Take-Aways

- Appropriate follow-up of high-grade results is important given the increased risk of having or developing cancer

High-grade cytology results include:

- ✓ **ASC-H:** Atypical squamous cells – cannot rule out high-grade squamous intraepithelial lesion
- ✓ **HSIL:** High-grade squamous intraepithelial lesion
- ✓ **AGC:** Atypical glandular cells
- ✓ **AIS:** Adenocarcinoma in situ

Cancer Care Ontario

Key Take-Aways Continued

- HPV testing is coming, but in the meantime the current cytology-based guidelines should be used
 - Today, HPV testing is being used on a patient-pay basis or provided without charge in some hospital labs
- Where HPV testing is available or patient's accept as a self-pay option:
 - Our guidelines recommend optional HPV triage for women ≥ 30 years old with cytology ASCUS



Key Take-Aways Continued

Encourage Screening Participation among all eligible candidates according to guidelines

- For individual benefit
- To achieve elimination goals



Questions?

