



Cancer Care Ontario

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Clinical Guidance: Recommended Best Practices for Delivery of Colposcopy Services in Ontario

Cancer Care Ontario
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Abbreviations and Acronyms

5-FU	5-Fluorouracil
AC	adenocarcinoma
AGC-N	atypical glandular cells, favor neoplastic
AGC-NOS	atypical glandular cells, not otherwise specified
AIDS	acquired immune deficiency syndrome
AIS	adenocarcinoma in situ
ASCCP	American Society for Colposcopy and Cervical Pathology
ASC-H	atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion
ASCUS	atypical squamous cells of undetermined significance
CEAG	Clinical Expert Advisory Group
CI	confidence interval
CIN	cervical intraepithelial neoplasia
CIN 2/+	cervical intraepithelial neoplasia 2 or greater
Colposcopy Clinical Guidance document	<i>Clinical Guidance: Recommended Best Practices for Delivery of Colposcopy Services in Ontario</i>
colpo	colposcopy
cyto	cytology
DEP	diagnostic excisional procedure (both diagnostic and therapeutic tool)
ECC	endocervical curettage
histo	histology
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSIL	high-grade squamous intraepithelial lesion
HR	hazard ratio
LEEP/LLETZ	loop electrosurgical excision procedure/large loop excision of the transformation zone
LSIL	low-grade squamous intraepithelial lesion
NHS	National Health Services
OCSP	Ontario Cervical Screening Program
PAIN	perianal intraepithelial neoplasia
PEBC	Program in Evidence-Based Care
Recommended Framework document	<i>Organization of Colposcopy Services in Ontario: Recommended Framework</i>
SCJ	squamocolumnar junction
VAIN	vaginal intraepithelial neoplasia
VIN	vulvar intraepithelial neoplasia

Executive Summary

Colposcopy is an essential tool for the diagnosis and management of women with pre-invasive lower genital tract disease, usually detected through cervical screening. To date, Ontario's colposcopy services have not, at a system level, been organized, and practices have been left to the clinical decision-making of individual colposcopists and supported by resources in hospital-based clinics or elsewhere.

Clinical Guidance: Recommended Best Practices for Delivery of Colposcopy Services in Ontario (the Colposcopy Clinical Guidance document) provides evidence-informed best practice guidance for high-quality colposcopy care for eligible women with an abnormal cervical screening test. This document and its companion document, the *Organization of Colposcopy Services in Ontario: Recommended Framework* (the Recommended Framework document), support ongoing efforts to organize quality colposcopy services in Ontario, ultimately providing care that is coordinated and integrated, so a patient can receive care that is uniform and evidence-based from appropriately trained healthcare providers who maintain colposcopy-related expertise and knowledge.

The Colposcopy Clinical Guidance document is informed by best available evidence gathered from literature reviews and jurisdictional scans of existing international and Canadian guidelines, as well as expert advice and consensus from a multidisciplinary Colposcopy Expert Advisory Group. The best practices for colposcopy included in the Colposcopy Clinical Guidance document were developed by examining and evaluating the extent to which evidence was present in peer-reviewed literature and existing guidelines, the strength of the available evidence and its clinical relevance. Clinical consensus and expert opinion were used in areas where evidence was limited.

The purpose of this document is to provide evidence-informed clinical best practices for healthcare providers involved in the provision of colposcopy services in Ontario. The goal of this Colposcopy Clinical Guidance document is to optimize the quality of colposcopy services for eligible women with an abnormal cervical screening test by:

- Defining appropriate clinical criteria for entry into the colposcopy system, subsequent investigations and interventions, follow-up practices, exit criteria and seamless reintegration strategies back into surveillance or screening in a primary care setting to reduce harms and over-treatment;
- Supporting equitable access to appropriate and consistently high-quality care in colposcopy through data collection that allows for monitoring of quality indicators; and
- Creating a framework to guide the organization of colposcopy services and their integration with cervical screening to ultimately enable system-wide performance management and improvements.

The evidence-informed best practices described in this document are meant to provide guidance for colposcopy care, but should be applied with the unique needs of each patient and



specific resource considerations in mind. Clinical judgement must be employed in individual circumstances. Given the variability of access to HPV testing, best practice pathways for colposcopy care both with and without HPV testing have been provided. These best practices will be updated with feedback from the intended audience, as new evidence emerges, and when programmatic performance evaluation strategy and new programmatic changes are implemented.

Implementation of the Colposcopy Clinical Guidance document will play a key role in the evolution and ongoing evaluation of an organized colposcopy program and its integration into cervical screening to create a cohesive patient-centered continuum of care in Ontario.

1. Introduction

Vision

Cancer Care Ontario is responsible for continuous improvement of cancer services in Ontario. Our vision is a fully organized and integrated system that will minimize the burden of cervical cancer in Ontario by providing a continuum of care that includes best practices in screening and early detection, diagnosis and appropriate treatment of pre-invasive cervical disease, and seamless reintegration back to primary care. We are committed to working with our partners to ensure evidence-informed, consistent, equitable, effective and measurable high-quality care for all Ontarians.

Building on the established Ontario Cervical Screening Program (OCSP), Cancer Care Ontario plans to launch an organized colposcopy program to manage services for screen-detected pre-invasive cervical/vaginal disease, including diagnosis, treatment, and appropriate discharge and return to primary care. The Colposcopy Clinical Guidance document summarizes and recommends clinical best practices for diagnosis, treatment and discharge based on current evidence and expert opinion. Implementation of these best practices will help ensure consistent, evidence-informed care for pre-invasive cervical disease across Ontario.

Purpose and Goal

Publication of the Colposcopy Clinical Guidance document and subsequent implementation efforts will aim to promote adoption of evidence-informed clinical best practices and adherence to recommended organizational best practices among clinicians and administrators.

The goal is to optimize the quality of colposcopy services for eligible women with an abnormal cervical screening test by:

- Defining appropriate clinical criteria for entry into the colposcopy system, subsequent investigations and interventions, follow-up practices, exit criteria and seamless reintegration strategies back into surveillance or screening in a primary care setting to reduce harms and over-treatment;
- Supporting equitable access to appropriate and consistently high-quality care in colposcopy through data collection that allows for monitoring of quality indicators; and
- Creating a framework to guide the organization of colposcopy services and their integration with cervical screening to ultimately enable system-wide performance management and improvements.

Target Audience

The Colposcopy Clinical Guidance document is developed for healthcare providers trained in colposcopic assessment of the lower genital tract, commonly referred to as colposcopists. Specifically, the intended audience includes Ontario colposcopists who perform colposcopic assessments in an ambulatory setting, such as hospital clinics or private offices, and those who perform colposcopically directed treatments.

These recommendations are also meant to offer guidance to the entire team of healthcare providers involved in colposcopy services, including primary care providers and specialist physicians, nurses, pathologists, administrators and other care decision-makers.

Background

Cancer of the cervix is highly preventable with HPV immunization¹ and regular screening², appropriate and timely follow-up of abnormal results. Yet, every year in Ontario, approximately 640 women are diagnosed with cervical cancer and about 150 women die of this disease³. A publically funded school-based HPV vaccine program is available for boys and girls beginning in Grade 7. To date, uptake in the school-based program has reached 80 per cent in the 2012/2013 school year^a. Despite improved coverage against oncogenic HPV strains provided by the recently approved nonavalent vaccine and increasing uptake of the quadrivalent vaccine in Ontario's school-based program, immunization alone does not offer complete protection against cervical cancer at a population level. Cervical screening and appropriate follow-up of screen-detected abnormalities are, and will remain, important and effective elements of cervical cancer prevention.

Regular cervical screening can detect abnormal cell changes in the cervix that can be treated before they develop into cancer. The OCSP is an organized, population-based provincial screening program whose aim is to reduce cervical cancer incidence and mortality^b. In 2016, it was reported that 2.8 million women between the ages of 21 and 69 were screened for cervical cancer once over a three-year period⁴. Women whose screening test (currently cervical cytology) is abnormal usually require further investigation. Colposcopy is the essential tool for the diagnosis and management of women with pre-invasive lower genital tract disease, ideally detected through cervical screening.

Although colposcopy services are available throughout Ontario, in the absence of organization it is not possible to ensure the accessibility, efficiency, appropriateness or quality of these services. A number of opportunities for improvement have been observed across the province, including the need to address issues such as high practice variation, unnecessary use of colposcopy, scarce access to HPV testing for risk stratification, and the lack of standardized exit criteria from colposcopy, which results in many women receiving prolonged colposcopy care and subsequent unnecessary interventions. Due to the absence of organization, there currently

^a Based on a survey of public health units, estimated HPV immunization coverage was 80% (in the 2012/2013 school year), with large variation by health unit. For more information about HPV school-based vaccination program, visit the Ministry of Health and Long Term Care website: health.gov.on.ca/en/ms/hpv/.

^b For more information on the OCSP, visit cancercare.on.ca/pcs/screening/cervscreening/OCSP/



is no established mechanism for information management, performance monitoring or quality improvement of colposcopy services.

Moreover, there is a need to integrate specialist care in colposcopy with primary care to connect screening, colposcopy and surveillance services, and ensure smooth and safe transitions among these care settings. Developing an organized colposcopy program that can become fully integrated with cervical screening will create a cohesive continuum of care and support efforts to prevent cervical cancer in Ontario.

1.2 Guidance Development Process

The Clinical Expert Advisory Group (CEAG) was instrumental in the development of this document. The CEAG was convened to provide expert advice on how to improve the colposcopy system for Ontarians and to define clinical best practices for colposcopy services in Ontario. This group consists of representatives from across the province in multiple disciplines (all with some involvement in providing colposcopy services), including obstetrician/gynecologists, gynecologic oncologists, pathologists, family physicians, nurse educators and administrative personnel.

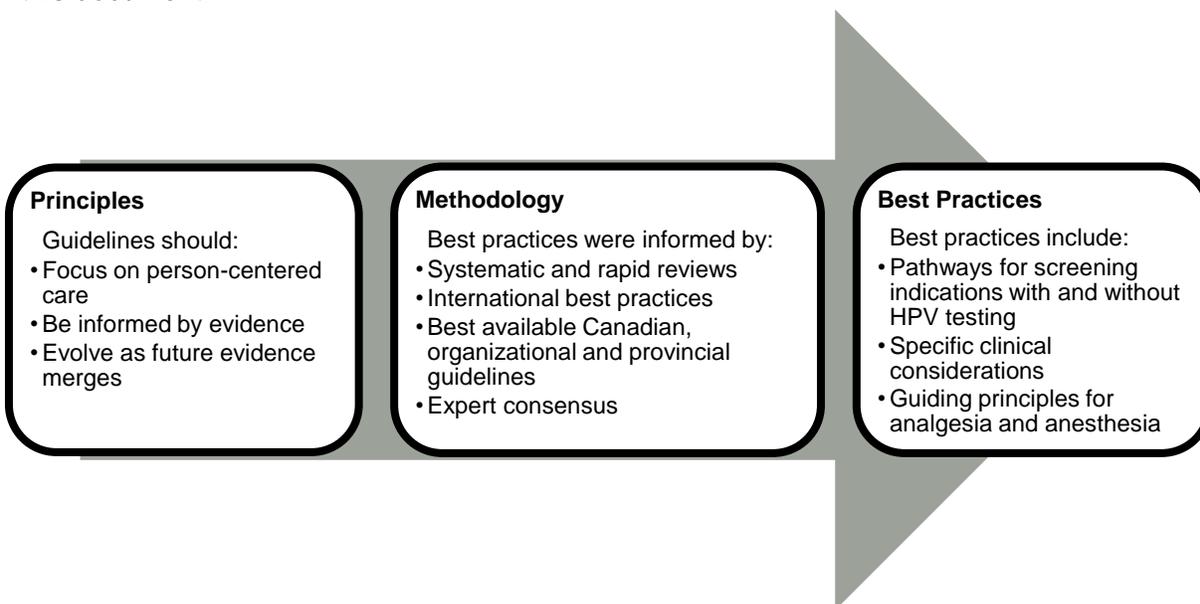
With a focus on person-centred care and informed by evidence, the CEAG developed best practice pathways and advice for special clinical considerations for colposcopy, which are detailed in this document. The CEAG will continue to provide guidance around key clinical engagement strategies and further development related to colposcopy.

For a complete list of CEAG members, refer to Appendix A.

Best Practice Development Methodology

This section describes the approach used by the CEAG to develop best practices for colposcopy, including the principles and methodology guiding best practice development.

The resulting best practices are summarized below and described in greater detail in Section 2 of this document.



Methodology

Evidence used to support CEAG best practice development was sought from a variety of sources, including peer-reviewed literature and existing guidelines. Where evidence was limited,

clinical consensus and expert opinion were used. Clinical best practice development was specifically informed by:

- Rapid reviews and a systematic review providing a summary of the current knowledge of the efficacy of cytology, HPV testing and co-testing in:
 - Post-treatment management of women treated in colposcopy (refer to Appendix B1 for an evidence summary^{5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24});
 - Conservative management, where clinically appropriate, of women who desire fertility and/or do not require treatment in colposcopy (refer to Appendices B1 and B2 for evidence summaries^{5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24});
 - Management of women post-treatment for AIS (refer to Appendix B3 for an evidence summary^{25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44}); and
 - Management of younger women (≤ 24 years of age) in colposcopy (refer to Appendix B4 for an evidence summary^{45,46,47,48,49,50,51,52}).
- A scan of available international best practices and guidelines for cervical screening and colposcopy programs. In particular, the following guidelines informed these colposcopy best practices:
 - The United Kingdom National Health Services (NHS), Cervical Cancer Screening Program^{53,54};
 - American Society for Colposcopy and Cervical Pathology (ASCCP), 2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors⁵⁵;
 - New Zealand Cervical Screening Guidelines^{56,57};
 - Irish Guidelines for Quality Assurance in Cervical Screening⁵⁸;
 - European Guidelines for Quality Assurance in Cervical Cancer Screening⁵⁹; and
 - Australian National Health and Medical Research Council, Guidelines for the Management of Asymptomatic Women with Screen Detected Abnormalities⁶⁰;
 - International Federation for Cervical Pathology and Colposcopy (IFCPC), 2011 Colposcopic Terminology of the International Federation for Cervical Pathology and Colposcopy⁶¹.
- A scan of all available Canadian, organizational and provincial guidelines for colposcopy:
 - Alberta Guidelines and Screening for Cervical Cancer⁶²;
 - BC Cancer Agency: Screening for Cancer of the Cervix⁶³;
 - New Brunswick Cervical Cancer Prevention and Screening Clinical Practice Guidelines⁶⁴; and
 - Society of Canadian Colposcopists/Society of Obstetricians and Gynaecologists of Canada Joint Clinical Practice Guidelines⁶⁵.
- A scan of available best practices and clinical considerations for vaginal, vulvar and perianal abnormalities, including squamous lesions. The following recommendations and consensus statements informed the colposcopy best practices for women with these abnormalities:

- College of American Pathologists and the American Society for Colposcopy and Cervical Pathology: Lower Anogenital Squamous Terminology for HPV-Associated Lesions—Summary of Consensus Recommendations⁶⁶;
 - Canadian Partnership Against Cancer. Reporting on Histopathology Specimens from the Cervix and Vagina—Consensus Statements. Pan-Canadian Cervical Screening Initiative⁶⁷;
 - American College of Obstetricians and Gynecologists and American Society for Colposcopy and Cervical Pathology: Committee Opinion—Management of Vulvar Intraepithelial Neoplasia⁶⁸; and
 - Royal College of Obstetricians and Gynecologists: Lower Genital Tract Neoplasia – Study Group Statement⁶⁹;
 - The International Society for the Study of Vulvovaginal Disease (ISSVD) Terminology of Vulvar Squamous Intraepithelial Lesions⁷⁰.
- Expert consultation with the CEAG and with other expert clinical representatives from centrally organized colposcopy systems in Ontario, Alberta and British Columbia.

Terminology

For documenting cervical colposcopic findings, the best practices in the Colposcopy Clinical Guidance document have adopted the 2011 Colposcopic Terminology of the International Federation for Cervical Pathology and Colposcopy recommendations.⁶¹

For histology, the best practices in the Colposcopy Clinical Guidance document have adopted the Canadian Partnership Against Cancer’s Pan-Canadian Cervical Screening Initiative’s recommended reporting of histopathology⁶⁷ and the International Society for the Study of Vulvovaginal Disease’s accepted terminology⁷⁰.

For cytology, Bethesda terminology⁷¹ is used throughout as follows:

- High-grade squamous intraepithelial lesion (HSIL) and atypical squamous cells, cannot rule out HSIL (ASC-H);
- Adenocarcinoma in situ (AIS);
- Atypical glandular cells (AGC); and
- Atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesion (LSIL).

For a glossary of terms refer to Appendix C.

1.3 Clinical Guidance Overview

The Colposcopy Clinical Guidance document summarizes clinical best practices for the management of screen-detected cervical abnormalities in colposcopy and is organized into specific clinical pathways, which include the following components:

- Referral criteria and investigation strategies;
- Indications for treatment and preferred therapies;
- Follow-up algorithms for treated and untreated women;
- Exit criteria and protocol for ongoing screening following discharge from the colposcopy system; and
- Relevant clinical considerations and guiding principles for specific elements of colposcopy.

The development of the clinical best practices described in this section was informed by systematic reviews, rapid reviews, primary literature, jurisdictional guideline reviews, expert opinion and clinical consensus.

The clinical best practices that were developed for Ontario are as follows:

- **Clinical pathways with HPV testing for screening indications:** The CEAG defined clinical pathways considered current best practice for the management of women ≥ 21 years of age who are referred for colposcopy after abnormal cervical screening (Section 2.1).
- **Clinical pathways without HPV testing for screening indications:** The CEAG defined clinical pathways considered best practice, in the absence of HPV testing, for the management of women ≥ 21 years of age who are referred for colposcopy after abnormal cervical screening (Section 2.2).
- **Clinical considerations:** The CEAG defined clinical considerations for the following:
 - Screening indications in special populations (Section 2.3):
 - Pregnant women;
 - Women with physical limitations; and
 - Lesbian, bisexual and queer women, and transgender men.
 - Indications not arising from an abnormal screening test relating to other potentially neoplastic abnormalities of the lower genital tract, including the vagina, vulva and perianal region (Section 2.4).
 - Screening and non-screening indications for immune-compromised women where colposcopy is needed to rule in or out lower genital tract neoplasia (Section 2.5).
- **Guiding principles for analgesia and anesthesia:** The CEAG defined best practice in analgesia/anesthesia for colposcopy-related interventions of the cervix, vagina and vulva (Section 2.6).



The Colposcopy Clinical Guidance document also contains organizational best practices, including standards relating to patient experience, clinical facilities, equipment, clinical resources, and training and competency for all participants involved in care. Created by the Program in Evidence-Based Care, a partner of Cancer Care Ontario, broad themes from the Recommended Framework document (2015) and specific recommendations (e.g., as they related to transitioning care from colposcopy back to primary care) have been included within the Colposcopy Clinical Guidance document (Section 3).

Clinical and organizational best practices will be updated as new evidence emerges and programmatic performance evaluation is conducted.

2. Clinical Best Practices

2.1 Clinical Pathways (with HPV Testing) in Colposcopy Indicated by Screening Abnormalities

High Risk HPV Testing

There is a well-established causal link between persistent infections with oncogenic strains of HPV and lower genital tract cancers, most notably cancer of the cervix.⁷² There are 12 to 15 types of high risk HPV infections associated with the development of cervical cancer.⁷³ Infection with HPV 6, 11 and other non-oncogenic types carries with it essentially no risk of cervical cancer; however, infections with non-oncogenic HPV may result in an abnormal Pap test.⁷⁴ Testing for non-oncogenic HPV is not commercially available nor clinically relevant in cervical cancer prevention. In this document, “HPV testing” refers only to testing for high risk (oncogenic) HPV.

Integrating HPV testing into the colposcopy clinical pathways, particularly given its high negative predictive value, allows for risk stratification, so that women at average (or lower) risk can resume routine screening. It also allows those at elevated risk (with or without treatment) due to persistent HPV infection to be identified, so they can be advised to undergo closer surveillance.⁷⁵ Appropriate risk stratification will reduce unnecessary follow-up colposcopy visits for HPV-negative women who are at little or no risk and reduce patient anxiety, wait times and unnecessary interventions.

While ongoing clinical trials^{c,d} will further define the role of HPV testing in the colposcopy setting, using HPV as an exit test and risk stratification tool for women with low-grade abnormalities is becoming the standard of care internationally⁵³⁻⁶⁰. As a result, the best practice pathways presented in Section 2.1 include the use of HPV testing within colposcopy to enable risk stratification and discharge of women from colposcopy to appropriate screening intervals based on their risk status.

Best Practice Pathways

The following section presents five pathways that define best practices for the management of women ≥ 21 years of age referred for colposcopy after abnormal cervical screening. The five pathways are as follows:

- Workup and treatment: SIL referral in women ≥ 25 (Figure 2);

^c Colposcopy Versus HPV Testing to Identify Persistent Cervical Precancers (CoHIPP). Estimated study completion date: December 2015. Study results not yet posted as of April 2016.

^d Balancing benefits and harms of cervical cancer prevention, Mayrand et al. Estimated completion date: Spring 2016.

- Conservative SIL management of women ≥ 25 in whom child bearing is of concern (Figure 3);
- Post-treatment SIL management regardless of age (Figure 4);
- Management of younger women ages 21 to 24 (Figure 5); and
- Workup, treatment and management of AGC/AIS referral regardless of age (Figure 6).

Tables preceding the clinical pathways provide more detailed information on them. **The key points and clinical pathways outline typical scenarios, but do not account for every possible situation. Therefore, clinical judgement in individual circumstances must be employed.**

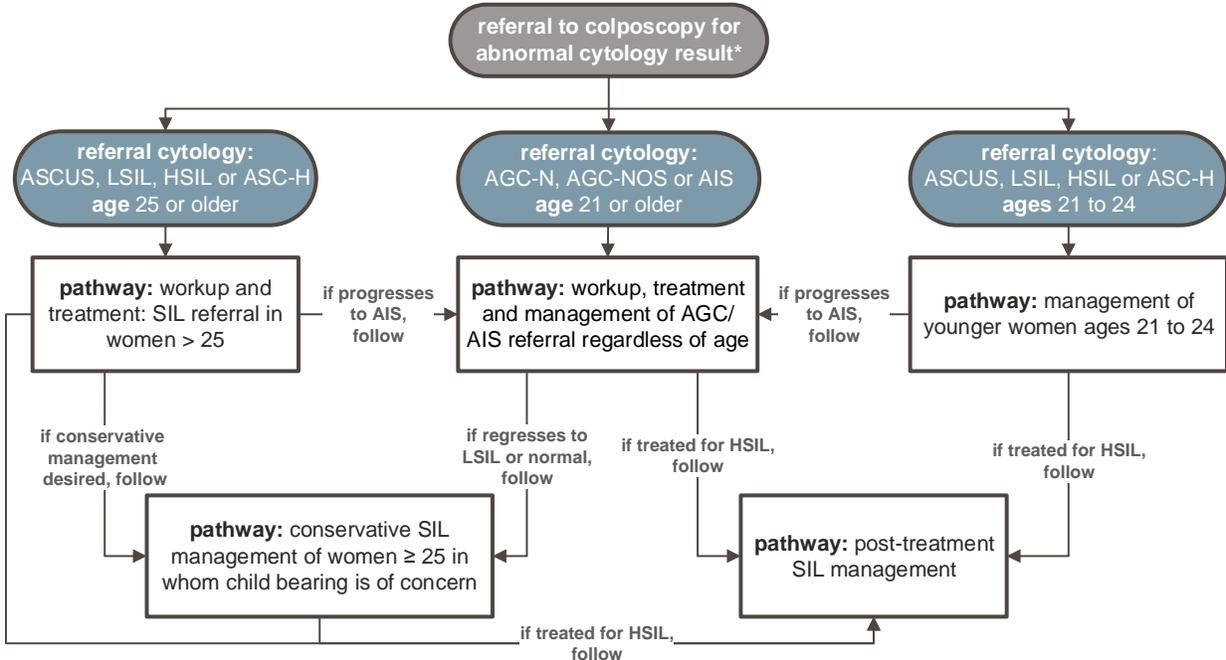
The tables summarizing clinical pathways are divided into two sections:

- Entry criteria: the cytological result, treatment circumstance or age that would lead to entry into the pathway; and
- Diagnostic, therapy and post-treatment follow-up: the processes and procedures used to manage confirmed histological abnormalities, as well as safely exit women from the colposcopy system.

Clinical Flow Across Pathways

Because women may pass through multiple pathways depending on individual circumstance, Figure 1 shows the clinical flow across the five pathways to provide fullsome guidance on the management of women with abnormal cytology.

Figure 1: Clinical flow across best practice clinical pathways for screening indications



*If findings are suggestive of cancer at any point, exit to the Regional Cancer Program.

Key Considerations for All Clinical Pathways

Table 1 below provides key considerations for all clinical pathways included in this document.

Table 1: Best practice key considerations for **all** clinical pathways

<p>Diagnosis, Therapy and Post-Treatment Follow-Up Key Considerations (All Pathways)</p>	<ul style="list-style-type: none"> • The referral cervical cytology report should be available to the colposcopist before colposcopic assessment. • Cervical cytology may be repeated at the initial colposcopy if indicated^e, as long as it has been three months since the last cytology test. • Cervical colposcopic findings must be documented⁶¹, including at minimum: <ul style="list-style-type: none"> ○ Satisfactory/adequate, vs. unsatisfactory/inadequate; ○ Location of lesion(s); and ○ Colposcopic impression. • Random biopsies may be used at the discretion of the colposcopist. If a biopsy is performed, the management decision must be informed by the histologic diagnosis.
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^e Such indications include prolonged time interval from referral specimen, specimen availability for clinical correlation and/or quality assurance purposes.

	<ul style="list-style-type: none">• For lactating women, colposcopists should consider deferring colposcopy until the hypo-estrogenic state has resolved.• All women undergoing ablative therapy must have an established histologic diagnosis.• Regardless of age, women whose future child bearing status is of concern should be counselled on the risks and merits of conservative management if chosen/appropriate.• To make an adequate histologic diagnosis, a DEP must be considered when:<ul style="list-style-type: none">○ A lesion extends into the canal beyond vision of the colposcopist;○ The squamocolumnar junction is not completely visible; or○ There is discordance among cytology, histology and/or colposcopic impression.• If a directed biopsy is inadequate for histological interpretation, the biopsy should be repeated.• Prior to treatment, a woman's written consent is required.• Where possible, conservative management is preferred, especially in women who wish to retain fertility options.• Excisional procedures allow for further pathology evaluation and assessment of margins. If neither is required, ablation is acceptable.• Pathology reviews:<ul style="list-style-type: none">○ A pathology review is advised to resolve significant discordance (among cytology, histology and colposcopic impression) in cases where it affects management decisions. Pathology reviews should be documented in the patient chart and should report on the specific discordant elements.○ Because there is no formal recognition of a sub-speciality in gynecologic pathology, these pathology reviews should be conducted by a gynecologic pathologist practicing at a designated gynecologic oncology centre.
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Best Practice Pathway for Workup and Treatment: SIL Referral in Women ≥ 25

Figure 2 demonstrates the best practice management of women entering the colposcopy system with a cytological abnormality of ASCUS, LSIL, HSIL or ASC-H and who are age 25 or older. Table 2, which precedes the pathway, provides clarity on key practice points.

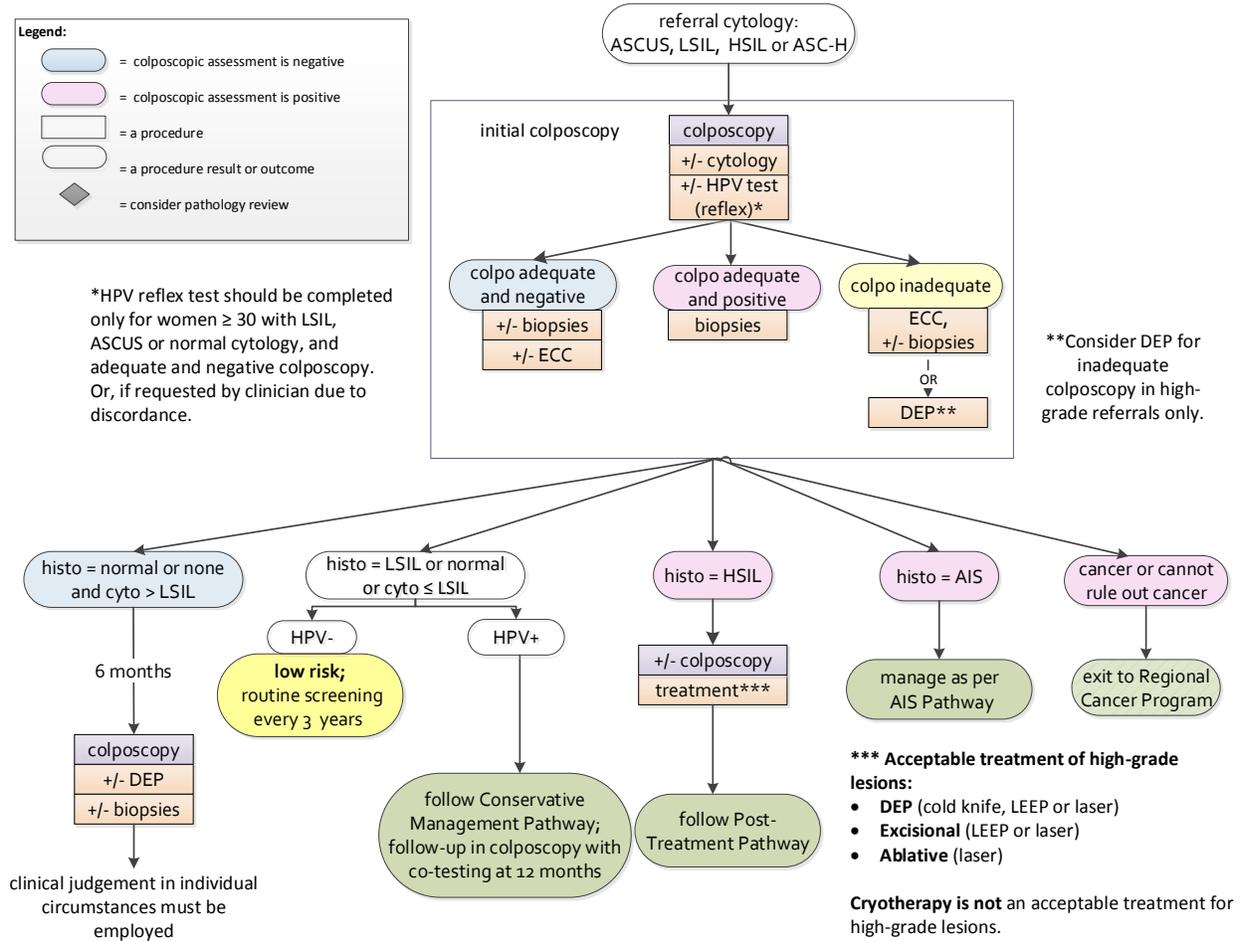
Table 2: Key practice points for workup and treatment: SIL referral in women ≥ 25 entering colposcopy for an abnormal screening test

Entry Criteria	<ul style="list-style-type: none"> • Women age 25 and older who have an abnormal squamous result on screening Pap (ASCUS, LSIL, HSIL or ASC-H).
Diagnosis, Therapy and Post-Treatment Follow-Up: Key Considerations	<ul style="list-style-type: none"> • An initial colposcopy should be performed for all women, with the option of repeat cytology (refer to Table 1 for indications for repeat cytology). <ul style="list-style-type: none"> ○ Optional HPV reflex test should be completed only for women age 30 and older whose cytology is LSIL, ASCUS, or normal with adequate and negative colposcopy. If requested by a clinician due to discordance, a reflex HPV^f test should also be conducted. ○ Due to high prevalence, an HPV reflex test is generally not recommended in women ages 25 to 29, but it may be used based on individual clinical judgement. Otherwise, women ages 25 to 29 women should be managed as per the non-HPV pathway for workup and treatment for SIL referral (Figure 7). • If there is no or normal histology, and cytology is HSIL or ASC-H after the initial colposcopy, a woman should have a follow-up colposcopy with optional DEP and/or biopsies within six months of the initial colposcopy. Thereafter, clinical judgement in individual circumstances must be employed. • If the histology is LSIL or normal, or if the cytology is LSIL, ASCUS or normal after the initial colposcopy and the HPV result is negative, a woman should be discharged to routine, triennial screening. • Conservative management is favoured for women with LSIL or normal histology, or LSIL, ASCUS or normal cytology whose HPV result is positive. <ul style="list-style-type: none"> ○ Follow the pathway for conservative SIL management (Figure 3). • If the histology is HSIL at the initial colposcopy, a woman should be treated. Acceptable forms of treatment for HSIL include DEP (cold knife, LEEP or laser), excisions (LEEP or laser) or ablations

^f HPV reflex testing enables women who are HPV-negative (i.e., the majority of women) to be discharged from colposcopy to routine screening.

	<p>(laser). Cryotherapy is not an acceptable treatment for high-grade lesions.</p> <ul style="list-style-type: none"> ○ For treated women, the post-treatment pathway should be followed (Figure 4). • If the histology is AIS at the initial colposcopy, a woman should be managed as per cases with histologically confirmed AIS in the AGC/AIS pathway (Figure 6). • If the histology is suggestive of cancer or cancer cannot be ruled out, a woman should be referred to the Regional Cancer Program.
<p>Additional Information on SIL Referral</p>	<ul style="list-style-type: none"> • Consider DEP for inadequate colposcopy in high-grade referrals only. • Upon discharge, if screening cytology is persistently abnormal, a woman should be re-referred to colposcopy according to the Ontario Cervical Screening Program screening guideline recommendations.

Figure 2: Recommended clinical pathway for workup and treatment: SIL referral in women $\geq 25^g$



^g See page 29 for the best practice pathway without HPV testing in workup and treatment: SIL referral in women ≥ 25 .

Best Practice Pathway for Conservative SIL Management of Women ≥ 25 in Whom Child Bearing is of Concern

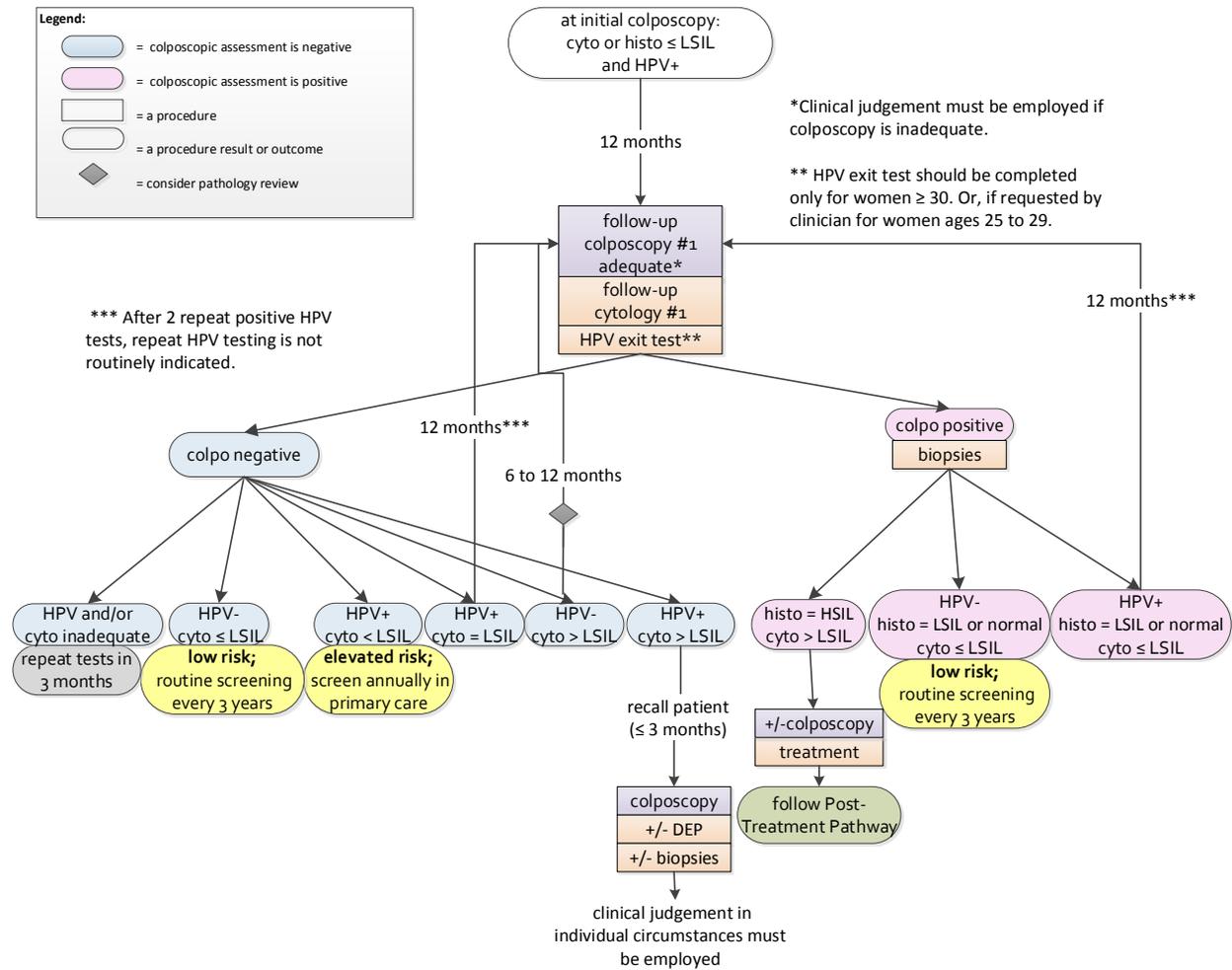
Figure 3 demonstrates the best practice conservative management of women with low-grade abnormalities who are age 25 or older in whom child bearing is of concern. Table 3, which precedes the pathway, provides clarity on key practice points.

Table 3: Key practice points for the conservative SIL management of women ≥ 25 in whom child bearing is of concern

Entry Criteria	<ul style="list-style-type: none"> • Women age 25 or older who may be contemplating pregnancy in the future; have LSIL, ASCUS or normal cytology or LSIL, or normal histology; are HPV-positive (if known) after the initial colposcopy; and were not treated.
Diagnosis, Therapy and Post-Treatment Follow-Up Key Considerations	<ul style="list-style-type: none"> • A woman should have a follow-up colposcopy with cytology and an HPV exit test 12 months after the initial colposcopy. <ul style="list-style-type: none"> ○ An HPV exit test should be completed only for women age 30 and older. ○ Due to high prevalence, an HPV exit test is generally not recommended in women ages 25 to 29, but it may be used based on individual clinical judgement. Otherwise, women ages 25 to 29 women should be managed as per the non-HPV pathway for conservative SIL management (Figure 8); ○ Clinical judgement must be employed if follow-up colposcopy is inadequate. • If the colposcopy is adequate and negative at the first follow-up visit and: <ul style="list-style-type: none"> ○ The cytology and/or HPV are inadequate, the test(s) should be repeated in three months; ○ The cytology is LSIL, ASCUS or normal, and the HPV result is negative, a woman should return to routine, triennial screening; ○ The cytology is ASCUS or normal and the HPV result is positive, a woman should be discharged to annual screening in a primary care setting; ○ The cytology is LSIL and the HPV result is positive, a woman should return for colposcopy and cytology in 12 months; ○ The cytology is HSIL or ASC-H and the HPV result is negative, a pathology review should be considered. If the pathology review is unable to resolve the discordance, a woman should return for colposcopy, cytology and an HPV exit test in six to 12 months; or ○ The cytology is HSIL or ASC-H and the HPV result is positive, a woman should be seen within three months for a follow-up colposcopy with optional DEP and/or biopsies. Thereafter,

	<p>clinical judgement in individual circumstances must be employed.</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and positive at the first follow-up visit and: <ul style="list-style-type: none"> ○ The histology is HSIL and cytology is HSIL or ASC-H, a woman should be treated. After treatment, follow the post-treatment pathway (Figure 4); ○ The histology is LSIL or normal, cytology is LSIL, ASCUS or normal and the HPV result is negative, a woman should return to routine, triennial screening; or ○ The histology is LSIL or normal, cytology is LSIL, ASCUS or normal, and the HPV result is positive, a woman should return for colposcopy and cytology in 12 months.
<p>Additional Information on Conservative Management</p>	<ul style="list-style-type: none"> • Conservative management is favoured in this population. • Treatment of persistent LSIL is acceptable in women for whom: <ul style="list-style-type: none"> ○ LSIL or high risk HPV infection persists for two years or more; or ○ Child bearing is complete. • Acceptable treatment of low-grade lesions include: <ul style="list-style-type: none"> ○ Excisional (LEEP); and ○ Ablative (laser). • Due to higher failure rates, cryotherapy is only acceptable when other options do not exist. • HPV testing is not routinely indicated after two repeat positive HPV tests. • Upon discharge, if screening cytology is persistently abnormal, a woman should be re-referred to colposcopy according to the Ontario Cervical Screening Program screening guideline recommendations.

Figure 3: Recommended clinical pathway for conservative SIL management of women ≥ 25 in whom child bearing is of concern^h



^h See page 31 for the best practice pathway without HPV testing in conservative SIL management of women ≥ 25 in whom child bearing is of concern.

Best Practice Pathway for Post-Treatment SIL Management Regardless of Age

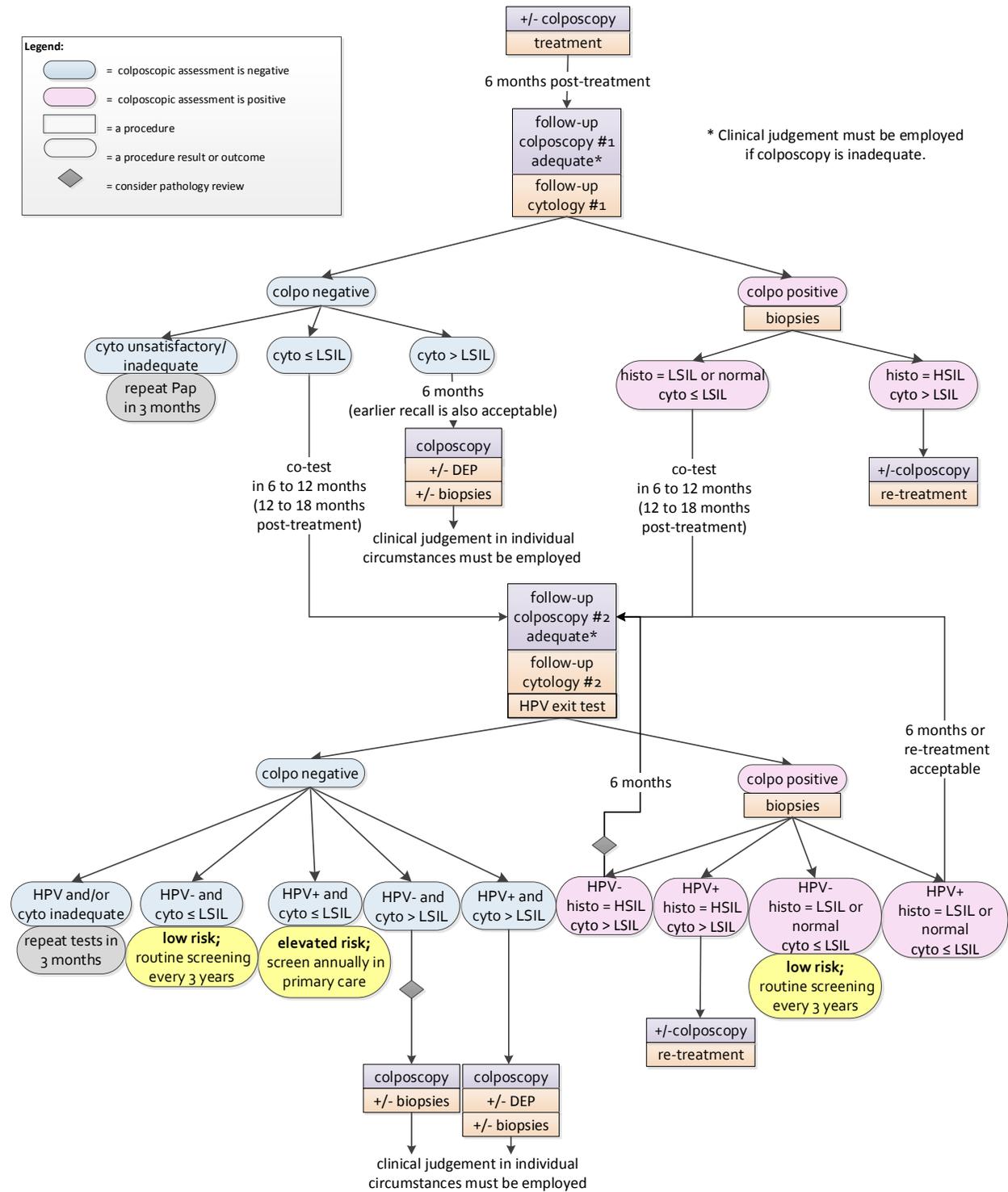
Figure 4 demonstrates the best practice management of women treated for cervical dysplasia regardless of age. Table 4, which precedes the pathway, provides clarity on key practice points.

Table 4: Key practice points for the management of women post-treatment of cervical dysplasia regardless of age

Entry Criteria	<ul style="list-style-type: none"> • Women who have been treated for cervical dysplasia, regardless of age.
Diagnosis, Therapy and Post-Treatment Follow-Up Key Considerations	<ul style="list-style-type: none"> • Women should have follow-up colposcopy and cytology six months post-treatment for cervical dysplasia. <ul style="list-style-type: none"> ○ Clinical judgement must be employed if follow-up colposcopy is inadequate. <p>Post-treatment follow-up visit #1:</p> <ul style="list-style-type: none"> • If colposcopy is adequate and negative at the first post-treatment follow-up visit and: <ul style="list-style-type: none"> ○ The cytology is unsatisfactory/inadequate, a Pap test should be repeated in three months; ○ The cytology is LSIL, ASCUS or normal, a woman should return for co-testing (cytology and HPV test) and colposcopy at 12 to 18 months post-treatment; or ○ The cytology is HSIL or ASC-H, a woman should be seen within six months for a follow-up colposcopy with optional DEP and/or biopsies. Earlier recall is also acceptable. Thereafter, clinical judgement in individual circumstances must be employed. • If colposcopy is adequate and positive at the first post-treatment follow-up visit and: <ul style="list-style-type: none"> ○ The histology is LSIL or normal, and cytology is LSIL, ASCUS or normal, a woman should return for co-testing (cytology and HPV test) and colposcopy at 12 to 18 months post-treatment; or ○ The histology is HSIL and cytology is HSIL or ASC-H, a woman should return for re-treatment. <p>Post-treatment follow-up visit #2:</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and negative at the second visit 12 to 18 months post-treatment and: <ul style="list-style-type: none"> ○ The HPV and/or cytology result are inadequate, a woman should have the test(s) repeated in three months; ○ The HPV result is negative and cytology is LSIL, ASCUS or normal, a woman should return to routine, triennial screening;

	<ul style="list-style-type: none"> ○ The HPV result is positive and cytology is LSIL, ASCUS or normal, a woman should be discharged to annual screening in a primary care setting; ○ The HPV result is negative and cytology is HSIL or ASC-H, a pathology review should be considered. If the pathology review does not resolve the discordance, a woman should be seen for a colposcopy with optional biopsy. Thereafter, clinical judgement in individual circumstances must be employed; or ○ The HPV result is positive and cytology is HSIL or ASC-H, a woman should be seen for a colposcopy with optional DEP and/or biopsies. Thereafter, clinical judgement in individual circumstances must be employed. ● If colposcopy is adequate and positive at the second visit 12 to 18 months post-treatment and: <ul style="list-style-type: none"> ○ The HPV result is negative, histology is HSIL and cytology is HSIL or ASC-H, a pathology review should be considered. If the pathology review does not resolve the discordance, repeat the co-test and colposcopy in six months; ○ The HPV result is positive, histology is HSIL and cytology is HSIL or ASC-H, a woman should return for re-treatment; ○ The HPV result is negative, histology is LSIL or normal and cytology is LSIL, ASCUS or normal, a woman should return to routine, triennial screening; or ○ The HPV result is positive, histology is LSIL or normal, and cytology is LSIL, ASCUS or normal, a repeat co-test and colposcopy in six months should be considered; re-treatment is also acceptable.
<p>Additional Information on Post-Treatment Management</p>	<ul style="list-style-type: none"> ● Women who do not meet discharge criteria may continue to be managed in colposcopy. Clinical judgement must be employed in individual circumstances. ● Upon discharge, if screening cytology is persistently abnormal, a woman should be re-referred to colposcopy according to the Ontario Cervical Screening Program screening guideline recommendations.

Figure 4: Recommended clinical pathway for post-treatment SIL management regardless of ageⁱ



ⁱ See page 34 for the best practice pathway without HPV testing in post-treatment SIL management regardless of age.

Best Practice Pathway for Management of Younger Women Ages 21 to 24

Figure 5 demonstrates the best practice management of younger women ages 21 to 24. Table 5, which precedes the pathway, provides clarity on key practice points.

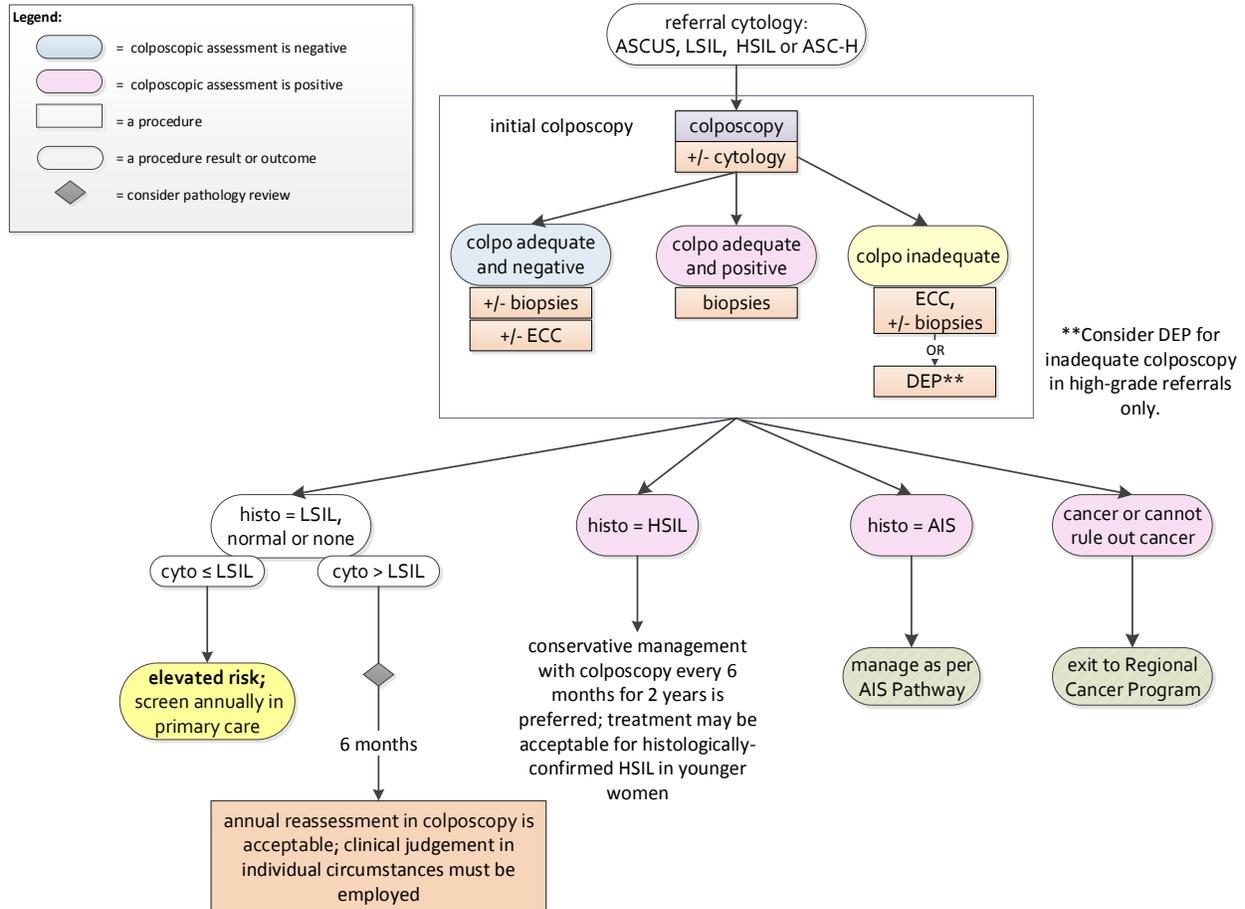
Table 5: Key practice points for the management of younger women entering the colposcopy system with an abnormal screening test

Entry Criteria	<p>Women ages 21 to 24 with an abnormal screening cytology result (ASCUS, LSIL, HSIL or ASC-H).</p> <p>Note: Women under age 21 should not participate in cervical screening, as per Ontario Cervical Screening Program guideline recommendations. However, if a woman has an abnormal screening result and has been referred for colposcopy, please follow this pathway. HPV testing is not to be used in this population.</p>
Diagnosis, Therapy and Post-Treatment Follow-Up Key Considerations	<ul style="list-style-type: none"> • An initial colposcopy should be performed for all women, with the option of repeat cytology (refer to Table 1 for indications for repeat cytology). • If there is LSIL, normal or no histology, and cytology is LSIL, ASCUS or normal, younger women should be discharged to annual screening in a primary care setting. • If there is LSIL, normal or no histology, and cytology is HSIL or ASC-H, a pathology review should be considered. If the pathology review does not resolve the discordance, younger women should be seen in colposcopy in six months. Thereafter, annual re-assessment in colposcopy is acceptable and clinical judgement in individual circumstances must be employed. • If the histology is HSIL, younger women should be managed as per the conservative management pathway (Figure 2), preferably with colposcopy every six months for a duration of two years. Treatment may be acceptable for histologically confirmed HSIL. See factors contributing to treatment under “Additional Information on Younger Women” below. • If the histology is AIS, younger women should be managed as per cases with histologically confirmed AIS in the AGC/AIS pathway (Figure 6). • If the histology is suggestive of cancer or cancer cannot be ruled out, younger women should be referred to the Regional Cancer Program.
Additional Information on Younger Women	<ul style="list-style-type: none"> • Upon discharge, if screening cytology is persistently abnormal, a woman should be re-referred to colposcopy, according to the Ontario Cervical Screening Guidelines screening guideline recommendations.

	<ul style="list-style-type: none">• If any of cytology, histology or colposcopy is suspicious for malignancy, a DEP is required. Consider DEP for inadequate colposcopy in high-grade referrals only.• Evidence-informed clinical judgment with adequate counselling and consideration of patient preference should be employed in the management of high-grade lesions in younger women.• Factors contributing to the treatment of histologically confirmed HSIL include:<ul style="list-style-type: none">○ Severity of visual findings;○ Patient fertility concerns;○ Patient willingness and likely compliance to follow-up as advised; and○ Ability of the practice to ensure adherence to ongoing follow-up recommendations.
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Figure 5: Recommended clinical pathway for Management of Younger Women Ages 21 to 24*

*Women under age 21 should not participate in cervical screening, as per the Ontario Cancer Screening Program guideline recommendations. If a woman has an abnormal screening result and has been referred for colposcopy, please follow this pathway.



Best Practice Pathway for Workup, Treatment and Management of AGC/AIS Referral Regardless of Age

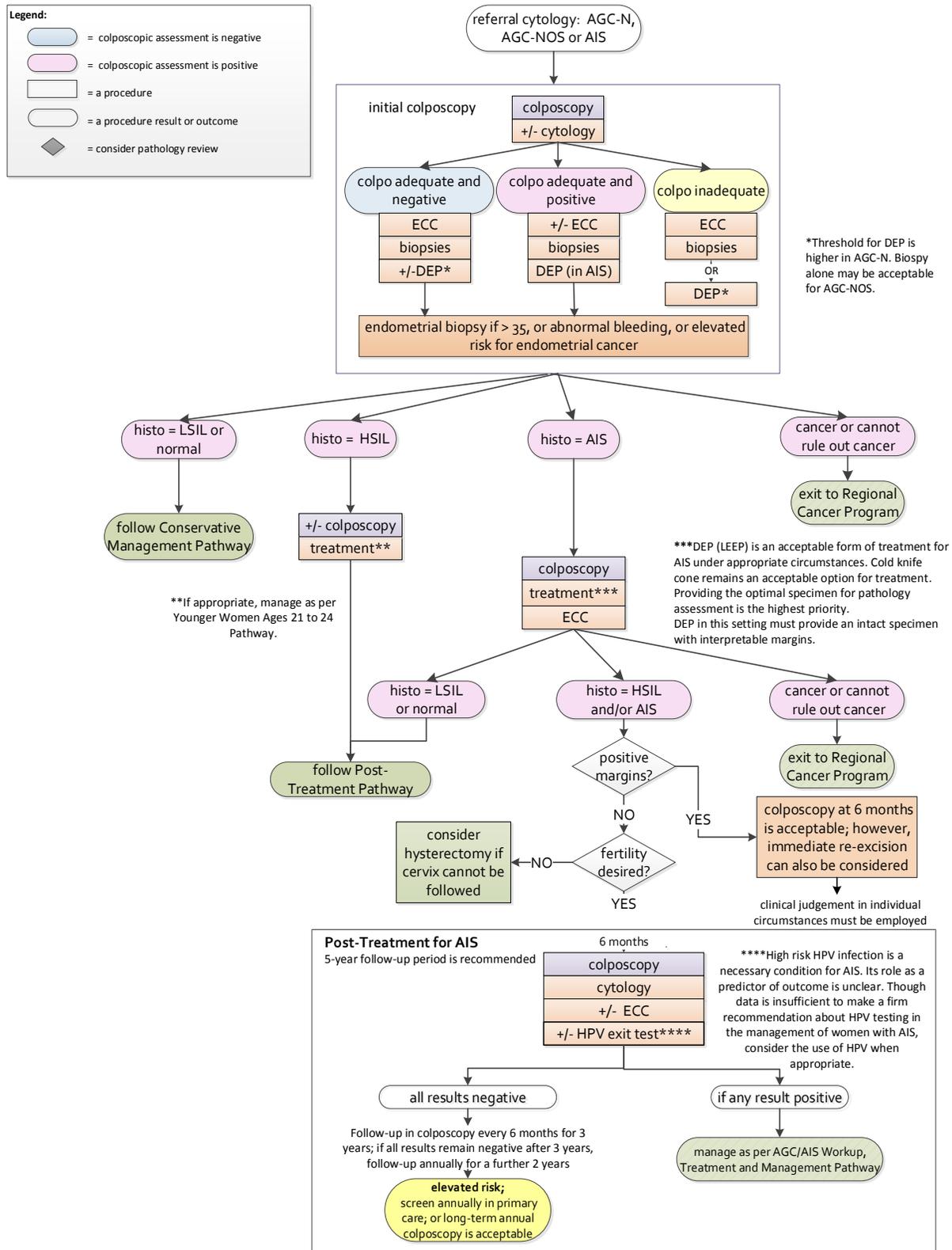
Figure 6 demonstrates the best practice workup, treatment and management of women referred with cytological results of AGC or AIS. Table 6, which precedes the pathway, provides clarity on key practice points.

Table 6: Key practice points for the workup, treatment and management of AGC/AIS referral regardless of age

Entry Criteria	<ul style="list-style-type: none"> • Women with cytology results of AGC-N, AGC-NOS or AIS, regardless of age.
Diagnosis, Therapy and Post-Treatment Follow-Up Key Considerations	<ul style="list-style-type: none"> • All women entering the pathway should have a colposcopy with the option of repeat cytology (refer to Table 1 for indications for repeat cytology). <ul style="list-style-type: none"> ○ If the colposcopy is adequate and negative, an ECC and biopsies are recommended, with the option of an accompanying DEP. The threshold for DEP is higher in AGC-N and a biopsy alone may be acceptable for AGC-NOS. ○ If the colposcopy is adequate and positive, biopsies are recommended with DEP (in AIS), with the option of an ECC. ○ If the colposcopy is inadequate, an ECC and biopsies or a DEP are recommended. The threshold for DEP is higher in AGC-N and a biopsy alone may be acceptable for AGC-NOS. ○ In the case of adequate colposcopy, an endometrial biopsy is recommended if a woman is older than age 35, if there is abnormal bleeding, or if a woman is at elevated risk for endometrial cancer. • If the histology is LSIL or normal, the conservative management pathway should be followed (Figure 3). • If the histology is HSIL, a woman should be treated. If appropriate, manage women with HSIL as per the younger women ages 21 to 24 pathway (Figure 5). <ul style="list-style-type: none"> ○ After treatment, follow the post-treatment pathway (Figure 4). • If the histology is AIS, a woman should have a colposcopy, treatment and ECC. <ul style="list-style-type: none"> ○ If the histology is LSIL or normal after treatment, the post-treatment pathway should be followed (Figure 4). ○ If the histology is HSIL and/or AIS after treatment with positive margins, a woman should be re-examined in colposcopy in six months. However, immediate re-excision can be considered. Thereafter, clinical judgement in individual circumstances should be employed.

	<ul style="list-style-type: none"> ○ If the histology is HSIL and/or AIS after treatment with negative margins and fertility is not of concern, a hysterectomy should be considered if the cervix cannot be followed. ○ If the histology is HSIL or AIS after treatment with negative margins and fertility is of concern, a woman should be seen in six months for a colposcopy with cytology, and there is an option for an accompanying ECC and/or HPV exit test. <ul style="list-style-type: none"> ▪ If any result is positive at the post-treatment colposcopy, returning to the beginning of the AGC/AIS workup, treatment and management pathway (Figure 6) should be considered. ▪ If colposcopy, cytology, optional ECC and optional HPV are negative at the post-treatment colposcopy, a woman should continue to be followed up in colposcopy every six months for three years. If all results continue to be negative, a woman should be followed-up in colposcopy annually for a further two years. After a total of five years of follow-up in colposcopy with negative results, a woman should be discharged to annual screening in a primary care setting or continue with long-term annual colposcopy. ● If the histology is suggestive of cancer or cancer cannot be ruled out, a woman should be referred to the Regional Cancer Program.
<p>Additional Information on AGC/AIS</p>	<ul style="list-style-type: none"> ● An acceptable treatment for histologically confirmed AIS is DEP (LEEP), under appropriate circumstances. Cold knife cone remains an acceptable option for treatment. Providing the optimal specimen for pathology assessment is the highest priority. ● DEP in this setting must provide an intact specimen with interpretable margins. ● High risk HPV infection is a necessary condition for AIS. Its role as a predictor of outcome post-treatment for AIS is unclear. Although data are insufficient to make a firm recommendation about the role of HPV testing in the management of women with AIS, consider the use of HPV, when appropriate.

Figure 6: Recommended clinical pathway for workup, treatment and management of AGC/AIS referral regardless of age



2.2 Clinical Pathways (without HPV testing) in Colposcopy Indicated by Screening Abnormalities

Best Practice Pathways

The following section presents three clinical pathways that define best practices in the absence of HPV testing for the management of women ≥ 21 years of age referred for colposcopy after abnormal cervical screening. The three pathways are as follows:

- Pathway without HPV testing for workup and treatment: SIL referral in women ≥ 25 (Figure 7);
- Pathway without HPV testing for conservative SIL management of women ≥ 25 in whom child bearing is of concern (Figure 8); and
- Pathway without HPV testing for post-treatment SIL management regardless of age (Figure 9).

Given the limited role of HPV testing in clinical decision-making for the pathways addressing management of younger women ages 21 to 24, and the workup, treatment and management of AGC/AIS referral regardless of age, clinical pathways without HPV testing are not provided for managing these groups of women.

Tables preceding the clinical pathways provide more detailed information on them. **The key points and clinical pathways outline typical scenarios but do not take into account every possible situation. Therefore, clinical judgement in individual circumstances must be employed.**

The tables summarizing clinical pathways are divided into two sections:

- Entry criteria: the cytological result, treatment circumstance or age that would lead to entry into the pathway.
- Diagnostic, therapy and post-treatment follow-up: the processes and procedures used to manage confirmed histological abnormalities, as well as safely exit women from the colposcopy system.

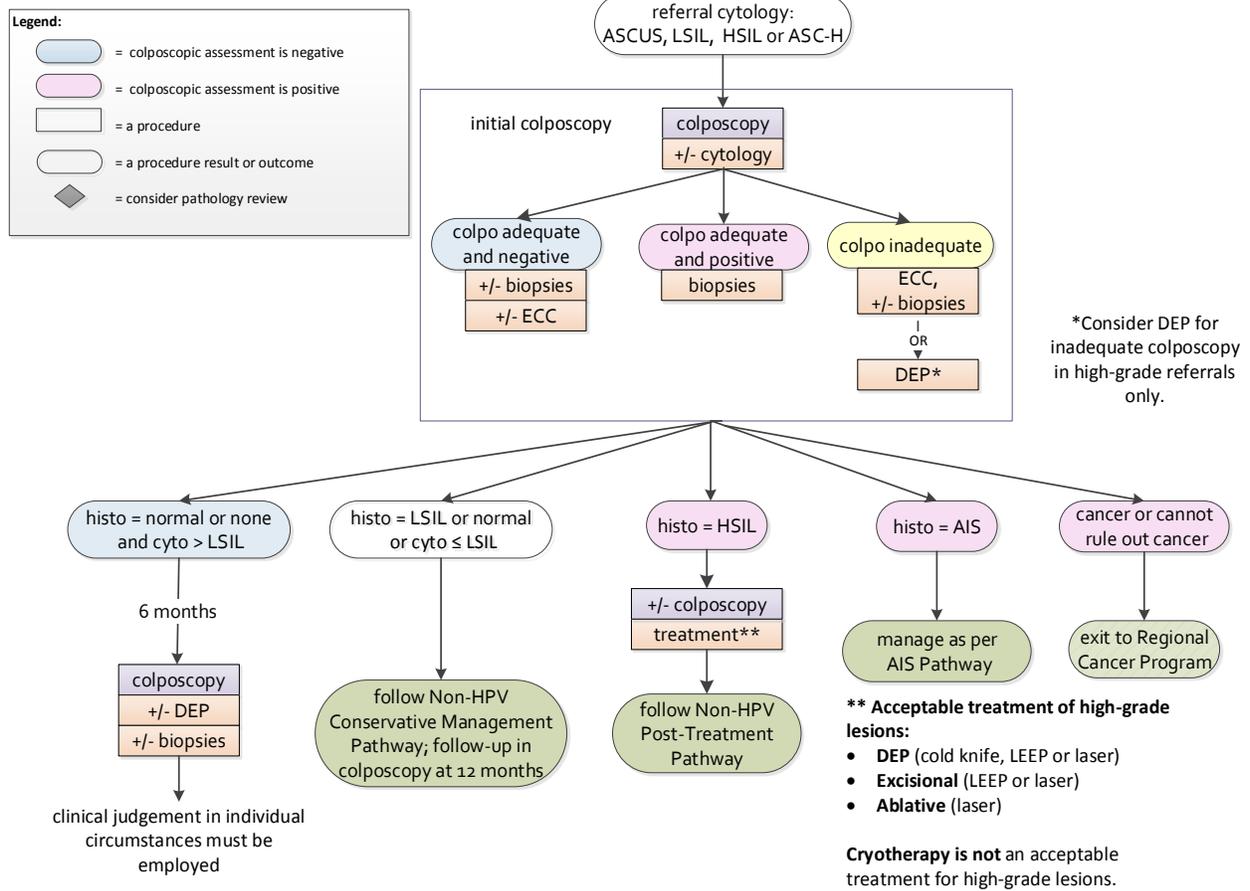
Pathway without HPV Testing for Workup and Treatment: SIL Referral in Women ≥ 25

Figure 7 demonstrates the non-HPV management of women entering the colposcopy system with a cytological abnormality of ASCUS, LSIL, HSIL or ASC-H who are age 25 or older. Table 7, which precedes the pathway, provides clarity on key practice points.

Table 7: Key practice points for the non-HPV pathway for workup and treatment: SIL referral in women ≥ 25 entering colposcopy for an abnormal screening test

Entry Criteria	<ul style="list-style-type: none"> • Women age 25 and older who have an abnormal screening Pap result (ASCUS, LSIL, HSIL or ASC-H).
Diagnosis, Therapy and Post-Treatment Follow-Up: Key Considerations	<ul style="list-style-type: none"> • An initial colposcopy should be performed for all women, with the option of repeat cytology (refer to Table 1 for indications for repeat cytology). • If there is normal or no histology, and cytology is HSIL or ASC-H after the initial colposcopy, a woman should have a follow-up colposcopy with optional DEP and/or biopsies within six months of the initial colposcopy. Thereafter, clinical judgement in individual circumstances must be employed. • Conservative management is favoured if the histology is LSIL or normal, or cytology is LSIL, ASCUS or normal. <ul style="list-style-type: none"> ○ Follow the pathway for non-HPV conservative SIL management of women ≥ 25 in whom child bearing is of concern (Figure 8). • If the histology is HSIL at the initial colposcopy, a woman should be treated. Acceptable forms of treatment for HSIL include DEP (cold knife, LEEP or laser), excisions (LEEP or laser) or ablations (laser). Cryotherapy is not an acceptable treatment for high-grade lesions. <ul style="list-style-type: none"> ○ For treated women, follow the non-HPV post-treatment pathway (Figure 9). • If the histology is AIS at the initial colposcopy, a woman should be managed as per cases with histologically confirmed AIS in the AGC/AIS pathway (Figure 6). • If the histology is suggestive of cancer or cancer cannot be ruled out, a woman should be referred to the Regional Cancer Program.
Additional Information on SIL Referral	<ul style="list-style-type: none"> • Consider DEP for inadequate colposcopy in high-grade referrals only.

Figure 7: Recommended non-HPV clinical pathway for workup and treatment: SIL referral in women $\geq 25^j$



^j See page 13 for the best practice pathway with HPV testing in workup and treatment: SIL referral in women ≥ 25 .

Pathway without HPV Testing for Conservative SIL Management of Women ≥ 25 in Whom Child Bearing is of Concern

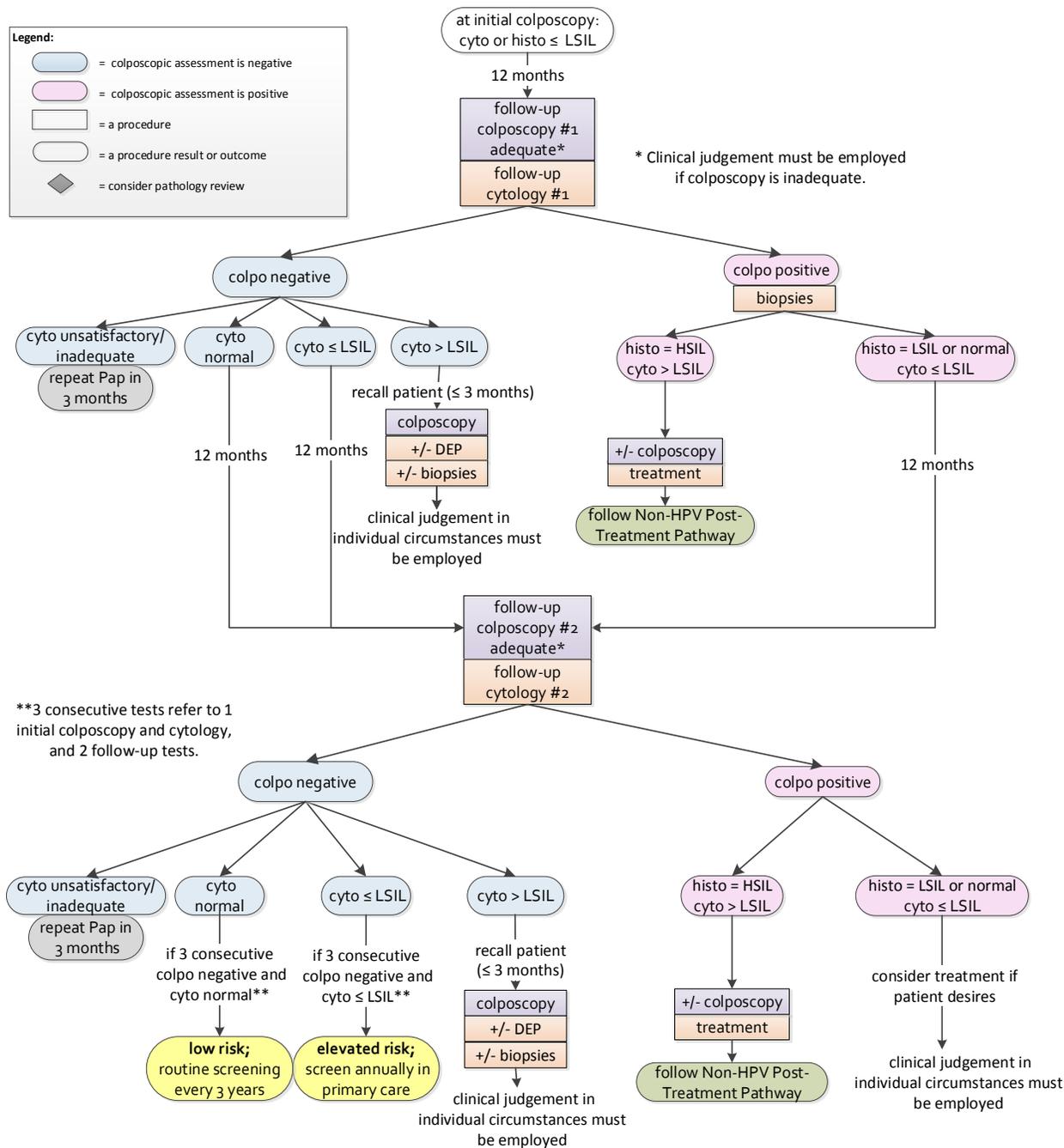
Figure 8 demonstrates the non-HPV conservative management of women with low-grade abnormalities who are age 25 or older in whom child bearing is of concern. Table 8, which precedes the pathway, provides clarity on key practice points.

Table 8: Key practice points for the non-HPV pathway for conservative SIL management of women ≥ 25 in whom child bearing is of concern

Entry Criteria	<ul style="list-style-type: none"> • Women who are 25 years or over, have cytology or histology less than or equal to LSIL after the initial colposcopy and were not treated.
Diagnosis, Therapy and Post-Treatment Follow-Up Key Considerations	<ul style="list-style-type: none"> • If the cytology is LSIL, ASCUS or normal, or the histology is LSIL or normal at the initial colposcopy, a woman should have follow-up colposcopy and cytology 12 months after the initial colposcopy. <ul style="list-style-type: none"> ○ Clinical judgement must be employed if follow-up colposcopy is inadequate. <p>Follow-up visit #1:</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and negative at the first follow-up visit and: <ul style="list-style-type: none"> ○ The cytology is unsatisfactory/inadequate, a Pap test should be repeated in three months; ○ The cytology is LSIL, ASCUS or normal, a woman should return for colposcopy and cytology in 12 months; or ○ The cytology is HSIL or ASC-H, a woman should be seen within three months for a follow-up colposcopy, with optional DEP and/or biopsies. Thereafter, clinical judgement in individual circumstances must be employed. • If the colposcopy is adequate and positive at the first follow-up visit and: <ul style="list-style-type: none"> ○ The histology is HSIL and cytology is HSIL or ASC-H, a woman should be treated. After treatment, follow the non-HPV post-treatment pathway (Figure 9); or ○ The histology is LSIL or normal, and cytology is LSIL, ASCUS or normal, a woman should return for colposcopy and cytology in 12 months. <p>Follow-up visit #2:</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and negative at the second follow-up visit and: <ul style="list-style-type: none"> ○ The cytology is unsatisfactory/inadequate, a Pap test should be repeated in three months;

	<ul style="list-style-type: none"> ○ The cytology is normal, a woman should return to routine, triennial screening if she has three consecutive negative colposcopies and normal cytology during the initial and two follow-up visits; ○ The cytology is LSIL or ASCUS, a woman should be discharged to annual screening in a primary care setting if she has three consecutive negative colposcopy and LSIL, ASCUS or normal cytology during the initial and two follow-up visits; or ○ The cytology is HSIL or ASC-H, a woman should be seen within three months for a follow-up colposcopy, with optional DEP and/or biopsies. Thereafter, clinical judgement in individual circumstances must be employed. ● If the colposcopy is positive at the second follow-up visit and: <ul style="list-style-type: none"> ○ The histology is HSIL and cytology is HSIL or ASC-H, a woman should be treated. After treatment, follow the non-HPV post-treatment pathway (Figure 9); or ○ The histology is LSIL or normal and cytology is LSIL, ASCUS or normal, consider treatment if a woman desires it. Thereafter, clinical judgement in individual circumstances must be employed.
<p>Additional Information on Conservative Management</p>	<ul style="list-style-type: none"> ● Conservative management is favoured in this population. ● Women who do not meet discharge criteria may continue to be managed in colposcopy. Clinical judgement must be employed in individual circumstances. ● Treatment of persistent LSIL is acceptable in women for whom: <ul style="list-style-type: none"> ○ LSIL persists for two years or more; or ○ Child bearing is not a concern. ● Acceptable treatment for low-grade lesions include: <ul style="list-style-type: none"> ○ Excisional (LEEP); or ○ Ablative (laser). ● Due to higher failure rates, cryotherapy is only acceptable when other options do not exist. ● Upon discharge, if screening cytology is persistently abnormal, a woman should be re-referred to colposcopy according to the Ontario Cervical Screening Program screening guideline recommendations.

Figure 8: Recommended non-HPV clinical pathway for the conservative SIL management of women ≥ 25 in whom child bearing is of concern^k



^k See page 16 for the best practice pathway with HPV testing in conservative SIL management of women ≥ 25 in whom child bearing is of concern.

Pathway without HPV Testing for Post-Treatment SIL Management Regardless of Age

Figure 9 demonstrates the non-HPV management of women treated for cervical dysplasia regardless of age. Table 9, which precedes the pathway, provides clarity on key practice points.

Table 9: Key practice points for the non-HPV pathway for management of women post-treatment of cervical dysplasia regardless of age

Entry Criteria	<ul style="list-style-type: none"> • Women who have been treated for cervical dysplasia, regardless of age.
Diagnosis, Therapy and Post-Treatment Follow-Up Key Considerations	<ul style="list-style-type: none"> • Women should have a follow-up colposcopy and cytology six months post-treatment for cervical dysplasia. <ul style="list-style-type: none"> ○ Clinical judgement must be employed if follow-up colposcopy is inadequate. <p>Post-treatment follow-up visit #1:</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and negative at the first post-treatment follow-up visit and: <ul style="list-style-type: none"> ○ The cytology is unsatisfactory/inadequate, a Pap test should be repeated in three months; ○ The cytology is LSIL, ASCUS or normal, a woman should return for follow-up colposcopy at 12 to 18 months post-treatment; or ○ The cytology is HSIL or ASC-H, a woman should be seen within three months for a follow-up colposcopy, with optional DEP and/or biopsies. Thereafter, clinical judgement in individual circumstances must be employed. • If the colposcopy is adequate and positive at the first post-treatment follow-up visit and: <ul style="list-style-type: none"> ○ The histology is LSIL or normal, and cytology is LSIL, ASCUS or normal, a woman should return for follow-up colposcopy at 12 to 18 months post-treatment; or ○ The histology is HSIL and cytology is HSIL or ASC-H, a woman should return for re-treatment. <p>Post-treatment follow-up visit #2:</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and negative at the second visit 12 to 18 months post-treatment and: <ul style="list-style-type: none"> ○ The cytology is unsatisfactory/inadequate, a Pap test should be repeated in three months; ○ The cytology is LSIL, ASCUS or normal, a woman should return for follow-up colposcopy up to 24 months post-treatment; or ○ The cytology is HSIL or ASC-H, a woman should be seen within three months for a follow-up colposcopy, with optional DEP

	<p>and/or biopsies. Thereafter, clinical judgement in individual circumstances must be employed.</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and positive at the second visit 12 to 18 months post-treatment and: <ul style="list-style-type: none"> ○ The histology is LSIL or normal, and cytology is LSIL, ASCUS or normal, follow-up in colposcopy in six months should be considered; re-treatment is also acceptable, keeping in mind a woman's child-bearing status; or ○ The histology is HSIL and cytology is HSIL or ASC-H, a woman should return for re-treatment. <p>Post-treatment follow-up visit #3:</p> <ul style="list-style-type: none"> • If the colposcopy is adequate and negative at the third visit up to 24 months post-treatment and: <ul style="list-style-type: none"> ○ The cytology is unsatisfactory/inadequate, a Pap test should be repeated in three months; ○ The cytology is normal, a woman should return to routine, triennial screening, given three consecutive negative colposcopy and normal cytology during follow-up visits; ○ The cytology is LSIL or ASCUS, a woman should be discharged to annual screening in a primary care setting, given three consecutive negative colposcopy and LSIL, ASCUS or normal cytology during follow-up visits; or ○ The cytology is HSIL or ASC-H, a woman should be seen within three months for a follow-up colposcopy, with optional DEP and/or biopsies. Thereafter, clinical judgement in individual circumstances must be employed. • If the colposcopy is adequate and positive at the third visit up to 24 months post-treatment and: <ul style="list-style-type: none"> ○ The histology is LSIL or normal, and cytology is LSIL, ASCUS or normal, re-treatment should be considered, keeping in mind a woman's child-bearing status. Thereafter, clinical judgement in individual circumstances must be employed; or ○ The histology is HSIL and cytology is HSIL or ASC-H, a woman should return for re-treatment.
<p>Additional Information on Post-Treatment Management</p>	<ul style="list-style-type: none"> • Women who do not meet discharge criteria may continue to be managed in colposcopy. Clinical judgement must be employed in individual circumstances. • Upon discharge, if screening cytology is persistently abnormal, a woman should be re-referred to colposcopy according to the Ontario Cervical Screening Program screening guideline recommendations.

2.3 Clinical Considerations in Colposcopy Indicated by Screening Abnormalities in Special Populations

The following section presents key clinical considerations for guiding best practice management of women in special populations referred for colposcopy after abnormal cervical screening. Considerations are grouped as follows:

- Managing cervical abnormalities during pregnancy;
- Clinical considerations for women with physical limitations; and
- Clinical considerations for transgender men, and lesbian, bisexual and queer women.

Best Practice Considerations for Colposcopy During Pregnancy

Best practice clinical considerations for women entering colposcopy during pregnancy are as follows:

- Pregnant women with any high-grade lesions should be seen by a colposcopist who is experienced with colposcopy and management of lower genital tract abnormalities during pregnancy.
- The aim of colposcopy during pregnancy is to exclude invasive disease and, when possible, to defer biopsy or treatment until the pregnancy has concluded.
- Biopsy is recommended if carcinoma cannot otherwise be ruled out.
- ECC should not be performed during pregnancy.
- DEP is recommended only if invasion is suspected.
- In the absence of any finding suspicious for invasive disease, follow-up with colposcopy and cytology no more frequently than every 12 weeks is recommended.
- Definitive re-evaluation should normally take place no sooner than eight to 12 weeks postpartum.
- Women with apparent low-grade lesions during pregnancy should have repeat assessment with colposcopy and cytology testing at 12 weeks postpartum.

Clinical Considerations for Colposcopy for Women with Physical Limitations

Clinical considerations for the management of women with physical limitations in colposcopy are as follows:

- All women should have equal access to colposcopic care, regardless of physical limitations.
- Hospitals equipped to provide specialized care should be identified in each Local Health Integration Network.

Clinical Considerations for Colposcopy for Transgender Men, and Lesbian, Bisexual and Queer Women

Clinical considerations for the management of transgender men, and lesbian, bisexual and queer women in colposcopy are as follows:

- All people with a cervix at birth should all follow the same clinical pathways, regardless of sexual orientation or gender identity.

2.4 Clinical Considerations in Colposcopy for Indications not Arising from an Abnormal Screening Test

The following section presents key clinical considerations for guiding best practice management of women referred for colposcopy for indications not arising from an abnormal screening test. They are grouped as follows:

- Diagnostic considerations for all lower genital tract abnormalities;
- Clinical considerations for vulvar abnormalities (Table 11);
- Clinical considerations for vaginal abnormalities (Table 12); and
- Clinical considerations for abnormalities of the perianal area (Table 13).

The key clinical considerations are divided into two sections:

- Diagnostic: key practice points for the initial workup required to determine the presence or absence of pre-invasive or invasive disease; and
- Therapy and post-treatment follow-up: key practice points for the management of confirmed histological abnormalities and follow-up.

Diagnostic Considerations for All Lower Genital Tract Abnormalities

Best practice considerations for diagnosis of all lower genital tract abnormalities are as follows:

- Asymptomatic clinical lesions detected visually or palpably by a woman or a clinician on routine examination may require colposcopic assessment for diagnosis.
- Symptoms associated with vulvar and vaginal lesions include vulvar pruritus (itching), vaginal discharge, localized pain, post-coital bleeding, other abnormal bleeding, ulceration or palpable mass. If appropriate physical examination of symptomatic women by a gynecologist or family doctor can't explain the symptoms or rule out the presence of pre-malignant lesions, colposcopy may be considered.
- Women who have had abnormal cytology results and an adequate and normal colposcopy of the cervix should have a colposcopic examination of the vulva, vagina and perianal area.
- Biopsies are required for an accurate diagnosis of lesions suspicious for pre-cancer or cancer.
- Presumed genital warts should be biopsied in women in whom clinical findings become atypical.
- Lesions with atypical response to anti-viral therapies should be considered neoplastic until proven otherwise.
- Women with HPV-related lesions at any site in the lower genital tract are at increased risk of similar lesions in all lower genital tract sites and the entire lower genital tract should be examined.

- Women should be counselled around modifiable risk factors for cancers of the lower genital tract, including smoking cessation and the importance of adherence to screening and/or follow-up recommendations. The benefit of HPV vaccination in these women is unclear, but may be considered.

Clinical Considerations for Vulvar Abnormalities in Colposcopy

Table 11 below provides best practice clinical considerations for vulvar abnormalities.

Table 11: Clinical considerations for vulvar abnormalities in colposcopy

<p>Diagnostic Key Points, Vulvar Abnormalities</p>	<ul style="list-style-type: none"> • In women with palpable and/or visible lesions, biopsies from the most suspicious area, preferably including adjacent normal tissue, should be done for definitive diagnosis. • In women with no distinct tumour boundaries, the use of topically applied acetic acid may help to localize suspicious areas. • Though regression is reported, vulvar neoplasia should be considered a pre-malignant condition.⁶⁸
<p>Therapy and Post-Treatment Follow-Up, Vulvar Abnormalities</p>	<ul style="list-style-type: none"> • Consider referral to a cancer centre prior to removal of the entire lesion if cancer is suspected. • Treatment is recommended for women with biopsy-proven HSIL (VIN) and differentiated-type VIN.^{68,70} • Wide local excision may be required for diagnosis if a definitive diagnosis cannot be made with representative biopsies. • In the absence of visual or histological findings suspicious for invasive disease, VIN can be treated with excision or laser ablation.⁶⁸ • The use of immunomodulators and other topical agents, such as imiquimod, appear to be effective in the treatment of VIN and should be considered, when appropriate.⁶⁸ • Although post-operative clinical assessment occurs at the discretion of the colposcopist, a woman should have colposcopic follow-up at six and 12 months post-treatment for vulvar neoplasia. • Women with vulvar neoplasia should be considered at high risk of recurrent disease and/or vulvar cancer throughout their lifetime.⁶⁸ • Given the uncertain malignant potential and relatively slow rate of progression, women with a complete response to therapy and no new lesions at follow-up visits should be monitored approximately annually thereafter.⁶⁸ • Although there is little evidence to support guidelines, it is recommended that annual monitoring be done in a colposcopy clinic by a colposcopist experienced in the management of female lower genital tract abnormalities.

Clinical Considerations for Vaginal Abnormalities in Colposcopy

Table 12 below provides best practice clinical considerations for vaginal abnormalities.

Table 12: Clinical considerations for vaginal abnormalities in colposcopy

<p>Diagnostic Key Points, Vaginal Abnormalities</p>	<ul style="list-style-type: none"> • Due to its length, surface area and rugae, colposcopy of the vagina may be complex and time consuming. • Following colposcopic examination with acetic acid, consideration should be given to the application of Lugol's iodine (unless contraindicated) with repeat colposcopy.
<p>Therapy and Post-Treatment Follow-Up, Vaginal Abnormalities Surveillance</p>	<ul style="list-style-type: none"> • As per all lower genital tract intraepithelial lesions, definitive diagnosis excluding malignancy must be confirmed before clinical decisions are made. • Treatment for vaginal lesions should be individualized according to a woman's characteristics, disease distribution and previous therapeutic procedures. • Surgical treatments (both excisional and ablative) include laser and partial or total vaginectomy. <ul style="list-style-type: none"> ○ CO₂ laser vaporization is preferred. ○ Local excisional treatment may be appropriate if the lesion is extensive or invasive disease cannot be ruled out. • Laser surgery should only be performed when the entire lesion is visible. • Topical 5-FU is not a preferred modality in the management of HSIL (VAIN).⁶⁹⁹ • Evidence supporting the use of immunomodulators and other topical agents, such as imiquimod, is emerging, but not conclusive. Use of these agents may be a consideration for the treatment of VAIN when appropriate.⁷⁶ • Radiotherapy is not a preferred modality in the management of HSIL (VAIN). • Although post-operative clinical follow-up is at the discretion of the colposcopist, women should have colposcopic follow-up at six and 12 months post-treatment for vaginal neoplasia. • Women with vaginal neoplasia should be considered at high risk of recurrent disease or vaginal cancer throughout their lifetime. • Given the uncertain malignant potential and relatively slow rate of progression, women with a complete response to therapy and no new lesions at six- and 12-month follow-up visits should be monitored approximately annually thereafter.

	<ul style="list-style-type: none"> Although little evidence is available to inform guidelines, monitoring should include annual vaginal cytology with re-referral to colposcopy for abnormal results. Duration is at the discretion of the colposcopist, but should likely be prolonged.
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Clinical Considerations for Abnormalities of the Perianal Area in Colposcopy

Table 13 below provides best practice clinical considerations for abnormalities of the perianal area.

Table 13: Clinical considerations for abnormalities of the perianal area in colposcopy

Diagnostic Key Points, Abnormalities of the Perianal Area	<ul style="list-style-type: none"> Any changes present in the perianal area may indicate the presence of similar lesions in the anal canal; women with these changes should have a rectal exam and be considered for anoscopy in select settings with the appropriate equipment. Clinical considerations for perianal intraepithelial lesions are similar to lesions on the vulva.
Therapy and Post-Treatment Follow-Up, Abnormalities of the Perianal Area Surveillance	<ul style="list-style-type: none"> Consider referral to cancer centre prior to removal of the entire lesion if cancer is suspected. Treatment is recommended for all women with biopsy-proven HSIL (PAIN). Wide local excision may be required if a definitive diagnosis cannot be made with representative biopsies. In the absence of findings suggestive of invasive disease, HSIL (PAIN) can be treated with excision or laser ablation. Although post-operative clinical follow-up is at the discretion of the colposcopist, women should have colposcopic follow-up at six and 12 months post-treatment for perianal neoplasia. Women with neoplasia of the perianal area should be considered at high risk of recurrent disease or cancer throughout their lifetime. Given the uncertain malignant potential and relatively slow rate of progression, women with a complete response to therapy and no new lesions at follow-up visits should be monitored approximately annually thereafter. Although there is little evidence to support guidelines, it is recommended that annual monitoring be done in a colposcopy clinic by a colposcopist experienced with the management of female lower genital tract abnormalities.

The Role of Anoscopy within the Colposcopy System

There is unanimous recognition of anoscopy as an emerging area of interest in colposcopy due to the shared pathogenesis (HPV) across lower genital tract lesions.



As of 2016, there is insufficient evidence to inform policy recommendations for routine referral for anoscopy.

Until more robust recommendations are developed:

- At minimum, a digital rectal exam is recommended for women at high risk.
- Anoscopy may be a consideration for women with perianal abnormalities.

2.5 Clinical Considerations in Colposcopy for Immune-Compromised Women

Defining Immune Compromise

Evidence for defining women living with immune compromise is relatively clear with regard to HIV/AIDS; however, it is less definitive for other conditions. For the purpose of these best practices, immune compromised is defined as:

- Women with HIV/AIDS;
- Women who are actively receiving treatment for a chronic autoimmune disease, such as systemic lupus erythematosus; and
- Women who are actively receiving treatment to support an organ transplant.

Further evidence to support immune compromise as a result of the episodic use of drugs, such as steroids or chemotherapy, is not available. In these cases, clinical judgment is required; however, it is not recommended that women who take drugs episodically routinely be considered immune compromised.

Clinical Considerations in Colposcopy for Screening Indications in Immune-Compromised Women

The evidence suggests the following implications of immune status on cervical abnormalities:

- Higher rates of persistent HPV infection;
- Lower rates of HPV regression;
- Higher rates of progression to a cancer precursor than HIV-negative women;
- Higher rates of recurrence of CIN/SIL following treatment than HIV-negative women; and/or
- Increased risk for CIN/SIL for women with systemic lupus erythematosus.

Table 14: Clinical considerations for management of immune-compromised women in colposcopy for screening indications

Clinical Considerations
<ul style="list-style-type: none">• Clinical judgment is required for the management of immune-compromised women in colposcopy.• Clinical management decisions should involve input from clinicians who are familiar with the management of immune-compromised women.• When considering treatment methods, clinical considerations should be the same for HIV-positive and negative women.

- HIV-positive women with LSIL, and possibly those who are immune compromised for other reasons, should be more carefully monitored for disease progression than immune-competent women with LSIL.
- Immune-compromised women should have more rigorous surveillance after treatment for CIN/SIL than women with a competent immune system.

Clinical Considerations in Colposcopy for Non-Screening Indications in Immune-Compromised Women

The evidence suggests the following implications of immune status on lower-genital tract abnormalities.

- The immune system plays an important role in clearance and persistence of HPV and the development of lower genital tract neoplasia.
- Lower genital tract neoplasia is common in women who are HIV-positive.
- Women using immune suppressants to prevent rejection after transplant or to treat a chronic autoimmune disease are at increased risk of developing lower genital tract neoplasia.

Table 15: Clinical considerations for management of immune-compromised women in colposcopy for non-screening indications

Clinical Considerations
<ul style="list-style-type: none"> • Clinical judgment should guide the management of immune-compromised women in colposcopy. • When considering treatment methods, clinical considerations should be the same for HIV-positive and negative women. • Clinical management decisions should include input from clinicians familiar with the management of immune-compromised women. • As part of routine surveillance, immune-compromised women should have a thorough inspection of the entire lower genital tract.

2.6 Principles Guiding the Best Practice Use of Analgesia/Anesthesia in Colposcopy

Analgesia is required for laser, LEEP and other lower genital tract treatments.

Tables 16 to 20 below provide guidance regarding best practices in analgesia/sedation for colposcopy-related interventions under usual circumstances. Clinical judgement regarding individual circumstances should always be employed.

Table 16: Best practices in analgesia/sedation for colposcopy-related interventions of the cervix

Modality	Biopsy	Laser	LEEP	Cold Knife
Topical	No	No	No	No
Injection	No	Yes	Yes	Yes
Regional/General	No	No	No	Yes

Table 17: Best practices in analgesia/sedation for colposcopy-related interventions of the vagina

Modality	Biopsy	Laser
Topical	No	No
Injection	Optional	Yes
Regional/General	No	Optional

Table 18: Best practices in analgesia/sedation for colposcopy-related interventions of the vulva

Modality	Biopsy	Laser
Topical	Yes	Yes
Injection	Yes	Yes
Regional/General	No	Optional

Table 19: Best practices in analgesia/sedation for colposcopy-related interventions of the perianal region

Modality	Biopsy	Laser
Topical	Yes	Yes
Injection	Yes	Yes
Regional/General	No	Optional

Table 20: Best practices in analgesia/sedation for all colposcopy-related interventions

Type of Anesthesia	Pharmacotherapies	Administered by	Where
Topical	<ul style="list-style-type: none"> EMLA Xylocaine 	Colposcopist	Ambulatory care
Local	<ul style="list-style-type: none"> Lidocaine or equivalent sedatives 	Colposcopist	Ambulatory care
Vasoconstrictor	<ul style="list-style-type: none"> Vasopressin (best) Epinephrine 	Colposcopist	Ambulatory care
Regional: With or Without Conscious Sedation	<ul style="list-style-type: none"> Lidocaine or equivalent sedatives 	Colposcopist	Ambulatory care
Moderate Sedation*	<ul style="list-style-type: none"> Midazolam Fentanyl Propofol or equivalent sedatives 	Anesthetist Anesthetist assistant.	Ambulatory care* Operating room
Regional or General Anesthesia	<ul style="list-style-type: none"> N/A—determined by anesthetist 	Anesthetist	Operating room

*In select settings with the appropriate equipment.

Factors Contributing to Regional or General Anesthesia

Table 21: Patient or clinical circumstances that may increase the appropriateness of spinal, epidural or general anesthesia in lower genital tract procedures arising from colposcopy

Procedures	<ul style="list-style-type: none"> Cold knife cone, extensive excision or vaporization of any single site or of multiple sites.
Patient Conditions	<ul style="list-style-type: none"> Inability to cooperate and/or previous experience indicating need. Multiple procedures being carried out during single episode of care.
Clinical Circumstances	<ul style="list-style-type: none"> Extent of treatment required. Potential invasion (if general anesthesia is required in order to obtain optimal specimen). Location of abnormality. Access/exposure is difficult (e.g., vaginal stenosis).

3. Organizational Best Practices

Organizational best practice guidelines focus on the environment and infrastructure in which colposcopy services are delivered, as well as training requirements for clinical care providers. The Recommended Framework⁷⁷ was developed by the Program in Evidence-Based Care (PEBC) and Cancer Care Ontario. It is another important initiative that will contribute to the organization of colposcopy and ultimately achieving a fully organized system that is integrated with the Ontario Cervical Screening Program.

Broad themes expanded on in the Recommended Framework document include:

- Colposcopy training, qualification and maintenance of competence:
 - Accessibility to training programs;
 - Quality of training programs;
 - Requirements to qualify as a colposcopist; and
 - Maintenance of competence.
- Practice setting requirements:
 - Group practice: hospital-based clinics and outpatient clinics located outside of hospitals; and
 - Individual office-based practice.
- Operational practices:
 - Referral criteria;
 - Wait times; and
 - Strategies to reduce drop-out rates.
- Quality indicators and outcomes:
 - Quality assurance; and
 - Performance indicators.

The Recommended Framework document can be accessed at cancercare.on.ca/common/pages/UserFile.aspx?fileId=328164.

3.1 Best Practice Recommendations for Discharge to Primary Care

Building on the Recommended Framework document, additional recommendations are provided in this section for guiding process improvement initiatives targeting a woman's transition from specialist care to primary care. Until a fully organized and integrated system is achieved, these best practice recommendations will help ensure the provision of a seamless transfer of relevant clinical information and patient care to primary care providers by colposcopists.

Best practice recommendations for women discharged from colposcopy to primary care for screening are as follows:

- Colposcopists should have a relationship with all referral sources, including primary care and regional public health cervical screening services (adapted from the Recommended Framework document).
- Before discharge, colposcopists should follow best practice pathways, as described in Sections 2.1 and 2.2, to determine risk status and appropriate screening interval in primary care for each woman, whether she is treated or untreated.
- Colposcopists should ensure that reports on colposcopy procedures are completed in reporting formats specifically designed for colposcopy and include information on the screening result that triggered referral, colposcopic findings, treatment and outcomes (if applicable), risk status at discharge and recommendations for risk-appropriate follow-up care (adapted from the Recommended Framework document).
- At discharge, colposcopists are responsible for the seamless transition of patient care to the primary care provider responsible for continued screening. This transition includes a summary of colposcopy care, including diagnosis, procedures and follow-up recommendations.
- If a woman's primary care provider is not the source of referral to colposcopy, the primary care provider should be included in colposcopy-related correspondence (unless expressly prohibited by the patient) in addition to the referring clinician. If the colposcopist records a referral to other services in the report (e.g., gynecologic oncology), a mechanism should be in place to ensure that the referral occurs (adapted from the Recommended Framework document).

Appendix A: Clinical Expert Advisory Group Membership

Name	Position	Organization
Dr. Joan Murphy	Clinical Lead, Ontario Cervical Screening Program	CCO
	Gynecologic Oncologist	Trillium Health Partners
	Professor, Department of Obstetrics and Gynecology	University of Toronto
Dr. Rachel Kupets	Lead Scientist, Ontario Cervical Screening Program	CCO
	Gynecologic Oncologist	Sunnybrook Health Sciences Centre
	Assistant Professor, Department of Obstetrics and Gynecology	University of Toronto
Dr. Laurie Elit	Past Lead Scientist, Ontario Cervical Screening Program	CCO
	Gynecologic Oncologist	Hamilton Health Science Centre
	Professor, Department of Obstetrics and Gynecology	McMaster University
Dr. Myriam Amimi	Obstetrician Gynecologist	Sault Area Hospital
Dr. Peter Bryson	Gynecologic Oncologist	Kingston General Hospital
Catriona Buick	Oncology Nurse (Colposcopy)	Women's College Hospital
	PhD Candidate	University of Toronto
Dr. Dustin Costescu	Assistant Professor, Department of Obstetrics and Gynecology	McMaster University
	Regional Cervical Screening/Colposcopy Lead	Hamilton Niagara Haldimand Brant Regional Cancer Program
Dr. Nicholas Escott	Colposcopist and Pathologist	Thunder Bay Regional Health Sciences Centre
Dr. Julie-Ann Francis	Gynecologic Oncologist	Kingston General Hospital
	Regional Cervical Screening/Colposcopy Lead	South East Regional Cancer Program
Dr. Paul Gurland	Obstetrician Gynecologist	Trillium Health Partners
	Regional Cervical Screening/Colposcopy Lead	Mississauga Halton/Central West Regional Cancer Program
Dr. Douglas Hepburn	Obstetrician Gynecologist	Durham Fertility Clinic
Dr. Naana Jumah	Obstetrician Gynecologist	Thunder Bay Regional Health Sciences Centre
	Regional Cervical Screening/Colposcopy Lead	North West Regional Cancer Program
Mike Kadour, PhD	Director, Pathology and Laboratory Medicine	London Health Sciences Centre and St. Joseph's Health Care London
Dr. Erica Mantay	Obstetrician Gynecologist	Southlake Regional Health Centre
	Regional Cervical Screening/Colposcopy Lead	Central Regional Cancer Program

Dr. Susan McFaul	Obstetrician Gynecologist	The Ottawa Hospital
	Assistant Professor, Department of Obstetrics and Gynecology	University of Ottawa
	Regional Cervical Screening/ Colposcopy Lead	Champlain Regional Cancer Program
Chantal Menard	Clinical Manager, Ambulatory Care, Obstetrics and Gynecology	The Ottawa Hospital
Victoria Noguera	Clinical Director, Perioperative Services and Gynecology	Women's College Hospital
Dr. Anna Plotkin	Pathologist	Trillium Health Partners
	Assistant Professor, Department of Laboratory Medicine	University of Toronto
Dr. Lea Rossiter	Family Physician	Spadina Health Centre
	Physician, Colposcopy Clinic	Bay Centre for Birth Control, Women's College Hospital
Dr. Michael Shier	Professor, Department of Obstetrics and Gynecology	University of Toronto
	Medical Director, Colposcopy Unit	Sunnybrook Health Sciences Centre
	Regional Cervical Screening/ Colposcopy Lead	Toronto Central Regional Cancer Program
Jill Tettmann	Chief Executive Officer	North Simcoe Muskoka Local Health Integration Network

Appendix B: Evidentiary Support

Appendix B1. Evidence Summary for Systematic Review: Colposcopy Exit Strategies and Follow-Up for Treated and Untreated Women

Research Questions	<ol style="list-style-type: none"> 1) How do we assess risk status at a point in colposcopy care when women can be discharged? 2) What are the risk-informed follow-up strategies and criteria for discharge? 3) Are these women eligible to return to routine screening?
REVIEW TYPE AND PURPOSE	<ul style="list-style-type: none"> • A systematic review of peer-reviewed clinical practice guidelines, literature reviews and original research published from January 2000 to August 2015 was conducted. • The purpose was to inform criteria for discharge from colposcopy to primary care and post-discharge follow-up in a primary care setting for multiple clinical pathways. • Evidence was available only for discharge from colposcopy to primary care and for the following two patient groups: (1) women treated in colposcopy for a histology of CIN 2, CIN 3 or AIS and (2) women untreated in colposcopy for normal colposcopy or for a histology of CIN 1 or less upon referral. • Twenty articles meeting inclusion criteria were reviewed and are summarized in this appendix⁵⁻²⁴ • This review informs the discharge from colposcopy for relevant patient groups in the following pathways: <ul style="list-style-type: none"> ○ Post-treatment SIL management regardless of age; and ○ Conservative SIL management of women ≥ 25 in whom child bearing is of concern.
DEFINITIONS AND ASSUMPTIONS	<ul style="list-style-type: none"> • Assume that women can be returned to population screening at three-year recall if their risk of cervical pre-cancer at follow-up in colposcopy is less than or equal to that of those in the general population who are cytology-negative and undergoing population screening. • The population risk threshold for return to three-year population screening was defined as three-year risk of CIN 2/+ at or below 1.7%, which is estimated to be the three-year risk of CIN 2/+ among the general U.S. population undergoing population screening.⁵
SUMMARY OF EVIDENCE	<p>Women treated in colposcopy for CIN 2, CIN 3 or AIS can return to population screening at a three-year recall after negative testing. However, the optimal timing and number of tests for discharge after treatment and the optimal setting for follow-up is unclear.</p> <ul style="list-style-type: none"> • Reported post-treatment risk of recurrent CIN 2/+ was elevated above population risk for a minimum of three years after treatment (risk ranged from 4% within 1.5 years to 13% within three years of treatment)⁶⁻¹⁰, but was at or below population risk after one or two

	<p>negative high risk HPV cytology co-tests (risks ranged from 1.2% within three years to 3% within five years after one negative co-test and 0.7% within three years to 1% within five years after two negative co-tests).^{7,11} In the absence of HPV testing, three negative cytologies have been shown to provide a five-year post-treatment risk similar to one negative co-test.^{7,11}</p> <ul style="list-style-type: none"> • Studies comparing the performance of a single co-test to a single and repeat cytology, reported that co-testing at six to 12 months outperformed a single or repeat cytology, having a higher sensitivity and a higher or similar negative predictive value than both.⁶ No studies reported performance metrics for two co-tests. • Studies recommended follow-up for a duration of two years post-treatment.^{7,11} Four studies reporting time to recurrence of CIN 2/+ found that most cases of CIN 2/+ developed within two years of treatment,¹¹⁻¹⁴ with recurrence peaking at 12 months post-treatment.^{11,15} However, studies did not agree on the number or interval of co-tests required for discharge. For example, Katki et al. (2013) from Kaiser Permanente in California recommend a return to population screening at a three-year interval after two negative co-tests at six to 12 and 18 to 24 months post-treatment,⁷ while Kocken et al. (2011) from the Netherlands, recommend a return to population screening at a five-year interval after two negative co-tests at six and 24 months post-treatment or after three negative cytology within two years of treatment.¹¹ • The optimal setting for follow-up and the role of colposcopy testing in follow-up is generally not reported. <p>Women untreated in colposcopy for normal colposcopy or a histology of CIN 1, and referred for a cytology of LSIL or less, can return to population screening at a three-year recall. However, at this time the evidence is insufficient to support return to population screening for untreated women referred for a cytology of AGC, ASC-H, HSIL or greater disease.</p> <ul style="list-style-type: none"> • Reported post-colposcopy risk of CIN 2/+ was elevated above population risk for a minimum of three years after initial colposcopy (risk ranged from 4% within 1.5 years to 21% within three years of initial colposcopy).¹⁶⁻²¹ After one negative high risk HPV cytology co-test, risk was at or below population risk for referral cytology LSIL, HSIL or ASC-H, but was elevated for referral cytology AGC (risk was 1.4% within three years for referral cytology ASC-H or HSIL+ and 0.7% within three years for referral cytology HPV-positive, ASCUS or LSIL).²⁰ In the absence of HPV testing, data were insufficient to indicate how many negative cytology are required to reach a three-year risk below population risk. • Evidence was insufficient to recommend co-test at follow-up over other tests, such as high risk HPV or cytology testing alone. One study reported a sensitivity of co-testing at 12 months follow-up similar to that for three cytology tests within two years of follow-up.¹⁶
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	<p>However, the negative predictive value of co-testing was generally not reported.</p> <ul style="list-style-type: none">• Evidence was insufficient to inform the optimal duration and setting of follow-up. Reported findings were generally not stratified by referral cytology. However, studies that comprised mostly LSIL cytology referrals reported a high rate of CIN 1 disease regression within 1.5 years of follow-up for this population.^{16,17} One study reported that most cases of CIN 2/+ disease were detected within three years of follow-up.¹⁹• Finally, evidence was also insufficient to inform the optimal timing and number of tests for discharge after initial colposcopy. However, both Katki et al. (2013) from Kaiser Permanente in California and Kelly et al. (2012) from the National Health Service in England recommend discharge for untreated women referred for low-grade cytology. Katki et al. (2013) recommend a return to population screening at a three-year interval after a single negative co-tests for women referred for LSIL or high risk HPV-positive ASCUS.²⁰ While Kelly et al. (2012) recommend a return to routine screening for HPV-positive low-grade cytology with negative colposcopy.²¹ Katki et al. (2013) did not recommend return for untreated women referred for AGC, ASC-H, HSIL or greater disease.²⁰
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Appendix B2. Evidence Summary for Rapid Review: Colposcopy Discharge with HPV for Women with Persistent and Untreated CIN 1

<p>Research Questions</p>	<p>What are the colposcopy discharge strategies with high risk HPV testing for women who are referred for persistent low-grade cytology and untreated for confirmed CIN 1?</p> <ul style="list-style-type: none"> a) What is their risk and timing of progression to high-grade disease or cancer from colposcopy diagnosis, stratified by HPV status? b) What proportion of women are high risk HPV-positive at diagnosis? c) What is the sensitivity and negative predictive value of the high risk HPV test at diagnosis and follow-up? d) What proportion of women would be referred back to colposcopy at diagnosis and follow-up?
<p>REVIEW TYPE AND PURPOSE</p>	<ul style="list-style-type: none"> • A structured, but limited, rapid review of peer-reviewed systematic reviews and original research published from January 2000 to June 2015 was conducted. • Four articles meeting inclusion criteria were reviewed and are summarized in this appendix¹⁶⁻¹⁹. • This review informs the discharge from colposcopy for relevant patient groups in the conservative SIL management of women ≥ 25 in whom child bearing is of concern pathway.
<p>DEFINITIONS AND ASSUMPTIONS</p>	<ul style="list-style-type: none"> • Progressive disease was defined as a histologic diagnosis of cervical intraepithelial neoplasia grade 2 or greater disease, including CIN 2, CIN 3, AIS, adenocarcinoma or squamous cell carcinoma. • This review included women who were referred to colposcopy for ASCUS or LSIL cytology, untreated in colposcopy for confirmed CIN 1 disease, and followed up using high risk HPV testing alone or in combination with cytology (co-testing). However, the persistence of low-grade cytology at referral was either mixed² or unclear¹⁷⁻¹⁹ among the populations studied. • Women were excluded from analysis if they were treated; diagnosed with CIN 2, CIN 3 or AIS at initial colposcopy; pregnant; HIV-positive; exposed to diethylstilbestrol in utero; or given prophylactic HPV vaccination. No restrictions were placed on age.
<p>SUMMARY OF EVIDENCE</p>	<p>Risk and Timing of Progression to CIN 2/+</p> <ul style="list-style-type: none"> • Women untreated for confirmed CIN 1 had low rates of progression to CIN 2/+. ¹⁶⁻¹⁹ Reported risk for progression ranged from < 5% of women developing CIN 2/+ within 1.5 years of CIN 1 diagnosis to 12% developing CIN 2/+ within three years of diagnosis. ¹⁶⁻¹⁹ Progression stabilized within two years, with a median time to progression of 25 months (interquartile range = 19 to 34 months).¹⁹ Less than 1% of women were reported to have progressed to cancer within two to three years of diagnosis. ¹⁶⁻¹⁹

- Moreover, studies reported that women untreated for confirmed CIN 1 had high rates of CIN 1 disease persistence or recurrence¹⁷ and high rates of CIN 1 disease regression to normal or negative colposcopy^{16, 19} upon follow-up.
- Women positive for high risk HPV types were at higher risk of progression to CIN 2 or 3.^{16,17,19} One study reporting progression risk by HPV status, found that women HPV-positive at or around the time of colposcopy diagnosis were 2.1 times more likely to progress to CIN 2 or 3 within three years than women HPV-negative at colposcopy diagnosis (relative risk = 2.1%).¹⁹

Proportion High Risk HPV-Positive at Initial Colposcopy Diagnosis

- The proportion of women HPV-positive at or around the time of colposcopy diagnosis ranged from 47% to 80% across four studies providing comment.¹⁶⁻¹⁹

High Risk HPV Test Performance for Detection of CIN 2 and 3 at Diagnosis and Follow-Up

- No studies commented on the performance of HPV testing at the time of initial colposcopy.
- Studies comparing the performance of HPV testing at six and 12 months follow-up report an improved negative predictive value of the test at 12 months compared to six months (84% vs. 69%)¹⁷ and an improved or similar sensitivity (92% versus 91%).^{17,18} One study reported that the addition of cytology co-testing at an ASCUS threshold at diagnosis resulted in a non-significant improvement in high risk HPV test sensitivity at 12 months follow-up (95% vs. 92%).¹⁸

Proportion Referred Back to Colposcopy at Diagnosis and Follow-Up

- One study found that HPV testing post-diagnosis at 12 months follow-up referred significantly fewer women back to colposcopy than testing at six months (55% vs. 62%), regardless of whether cytology co-testing was performed.¹⁸
- In the event HPV testing is not available, a strategy of three repeat cytology at six-month intervals over 18 months follow-up was found to have comparable sensitivity to HPV testing at 12 months (95% vs. 92%), but referred more women to colposcopy (70% vs. 55%) in addition to requiring more follow-up visits (three cytologies vs. one HPV testing).¹⁸

Appendix B3. Evidence Summary for Rapid Review: Colposcopy Discharge of Women Post-Treatment for AIS

<p>Research Questions</p>	<ol style="list-style-type: none"> 1) What are the colposcopy discharge strategies for a diagnosis of AIS regardless of referral cytology using high risk HPV testing, cytology/Pap test, co-testing, post-surgical margins and/or ECC as tests/procedures to inform exit? 2) How many negative tests are required for discharge and at what interval? 3) What are the most predictive factors of future residual/recurrent AIS (e.g., HPV vs. post-excision margin status)?* 4) Should these women be discharged to annual or routine screening?* <p>* Note: It was agreed to also extract information, if available, about the secondary questions from evidence identified to answer the primary question (and no further references due to time constraints).</p>
<p>REVIEW TYPE AND PURPOSE</p>	<ul style="list-style-type: none"> • A structured, but limited, rapid review of peer-reviewed systematic reviews and original research published from January 2005 to December 2015 was conducted. • Twenty articles meeting inclusion criteria were reviewed and are summarized in this appendix.²⁵⁻⁴⁴ • This review informs the discharge from colposcopy for relevant patient groups in the workup, treatment and management of AGC/AIS referral regardless of age pathway.
<p>DEFINITIONS AND ASSUMPTIONS</p>	<ul style="list-style-type: none"> • Treatment includes DEP, such as cold knife conization, LEEP/LLETZ. • The post-treatment population was defined as being treated conservatively (no hysterectomy) and having negative margins following treatment for AIS. • Colposcopy management post-treatment includes cytology, high risk HPV testing alone or in combination with cytology (co-testing) and analysis of post-surgical margins (LEEP, cold knife or ECC). • All studies selected reported on one of three outcomes at minimum, including the incidence of CIN 2/+ post-treatment of AIS, surveillance/management test (HPV test, cytology, co-testing, margins) or risk. • Pregnant women, HIV-positive women, women who have had a hysterectomy and women with positive margins on first follow-up were excluded in addition to any case studies.
<p>SUMMARY OF EVIDENCE</p>	<ul style="list-style-type: none"> • This review provided limited evidence on risk and timing of recurrent/residual disease or disease progression (n = 17), risk factors (n = 6) and recommendations for discharge strategies (n = 4). Only one study reported on test performance. <p>Risk Rates and Timing of Disease^{25-28,30-42,44}</p>

- Eleven studies report recurrent rates at or above estimated three-year CIN2/+ prevalence in the general U.S. population undergoing routine screening (Wright et al., 2012: three-year prevalence of CIN 2, CIN 3, AIS and cancer = 2.3% for women ages 25 to 34, and 1.5% for women age 35+).
- Incidence of recurrent/residual AIS ranged from 0% over a mean of 2.2 years of follow-up to 24% over a median of 3.3 years.
- Incidence of cancer progression ranged from 0% over two years of follow-up to 5% over 3.3 years.
- Study follow-up ranged from two to 15 years, while reported time to disease (recurrent AIS/cancer) ranged from 0.3 to 4.5 years.

Risk Factors^{28,29,37-40}

- Insufficient evidence to indicate high risk HPV status as a predictor of post-treatment disease (one study).
- Limited evidence indicates negative margin status as a protective factor for post-treatment disease (four studies).
- Inconsistent evidence for effectiveness of type of treatment used in achieving negative margins (one-third of studies in support of cold knife over LEEP).
- Inconsistent evidence for ECC as a predictor of post-treatment disease (half of studies report that ECC significantly predicts disease).

Test Performance²⁵:

- Co-testing showed higher predictive value and sensitivity than high risk HPV or cytology alone at 12 months.

Recommended Surveillance Timeline^{25,29,31,39}

- Consensus for Test: No consensus.
- Consensus Duration: No consensus.
- Consensus Frequency: Follow-up every six months (four studies)
- Costa et al. was the only author to provide both frequency and duration for follow-up post-treatment. In the 2007 study, they performed an analysis of test performance and recommended six-month surveillance for two years and in the 2012 study they recommended six-month co-testing for three years.

Appendix B4. Evidence Summary for Rapid review

<p>RESEARCH QUESTIONS</p>	<p>What are the special considerations, if any, for colposcopy management strategies for women under the age of 25 after a histologic diagnosis of LSIL or HSIL?</p> <ol style="list-style-type: none"> 1. For LSIL <ol style="list-style-type: none"> A) If treated, what is the risk of recurrence or progression of disease and how long is follow-up for this patient group? B) If untreated, what is the rate of persistence, progression or regression? Where, how and how long should this be patient group be surveilled? 2. For HSIL <ol style="list-style-type: none"> A) If treated, what is the risk of recurrence or progression of disease and how long is follow-up for this patient group? B) If untreated, what is the rate of persistence, progression or regression? Where, how and how long should this be patient group be surveilled?
<p>REVIEW TYPE AND PURPOSE</p>	<ul style="list-style-type: none"> • A rapid review of peer-reviewed research and clinical guidelines indexed in PubMed and published from January 2000 to December 2016 was conducted. • This review was conducted to inform the development of colposcopy management strategies for women under age 25 with a histologic diagnosis of LSIL or HSIL in Ontario (management of younger women ages 21 to 24 pathway).
<p>DEFINITIONS AND ASSUMPTIONS</p>	<ul style="list-style-type: none"> • This review included women initially referred to colposcopy for ASCUS, LSIL, HSIL or ASC-H cytological findings who had histologically-confirmed CIN 1, CIN 2 or CIN 3 at colposcopy. Women were followed up using high risk HPV testing, cytology, co-testing and/or biopsy. • Women were excluded from the analysis if they were diagnosed with AIS at initial colposcopy, had AGC on initial cytology, were pregnant or were HIV-positive at baseline analysis. • Regression for LSIL was defined as disease clearance. Regression for HSIL was defined as follow-up cytology or histology for high-grade lesions with a result of LSIL (CIN 1, HPV) or clearance (negative tests). • Recurrence was defined as follow-up cytology or histology with the same results at baseline and follow-up after treatment. • Persistence was defined as follow-up cytology or histology with the same results at baseline and follow-up after a period of observation (untreated). • Progressive disease was defined as advancing disease at follow-up on histologic diagnosis (CIN 1 to CIN2, CIN 1 to CIN 3, and CIN 2 to CIN 3).
<p>SUMMARY OF EVIDENCE</p>	<p>Seven peer-reviewed articles and one clinical guideline met inclusion criteria and were reviewed.⁴⁵⁻⁵²</p>

Risk of Disease

Comparison by histology at baseline:

- Five of seven studies reported follow-up cytology or histology for baseline histology. All five reported follow-up for baseline CIN 2 and only one reported follow-up for baseline CIN 1. Overall, regression ranged from 29% to 68% (within 0.3 to 3.9 years), recurrence or persistence ranged from 4% to 24% (within 0.3 to 10.0 years) and progression ranged from 4% to 24% (within 0.3 to 7.7 years).^{45,46,48,50,51}
 - Only one study followed women in the target age group with a baseline histologic diagnosis of CIN 1, finding that 12% progressed (to CIN 2 or CIN 3) over a mean of 4.1 years (2.0 to 7.4).⁴⁵
 - Five studies followed women with a baseline histologic diagnosis of CIN 2 or CIN 2/3. The rate of regression ranged from 29% to 68% (from 0.3 to 3.9 years), while recurrence or persistence ranged from 4% to 24% (from 0.3 to 10.0 years) and progression ranged from 4% to 24% (from 0.3 to 7.7 years). The majority (four out of five) showed a moderate to large proportion of regression and a low to moderate proportion of persistence or progression.^{45,46,48,50,51}
 - In studies with follow-up data (range: 0.3 to 10 years), only one cancer was reported following a recurrence from treatment for CIN 2/3.⁴⁹ No cancers were reported for untreated women with CIN 1 to 3 on baseline histology.

Comparison by treatment status:

- Only one study directly compared treated and untreated women in the target age group, and demonstrated that treated women had a lower risk of developing high-grade abnormalities within two years than untreated women.⁴⁵
 - Wilkinson et al. (2015) retrospectively identified three groups of women ages 16 to 24 years from colposcopy units (Year 0 to Year 2): women with conservatively managed CIN 1, women with conservatively managed CIN 2 and women with treated CIN 2.⁴⁵ In the second phase of follow-up women were observed for development of high-grade abnormalities (Year 2 to Year 5). No high-grade disease was present in any group at the beginning of Year 2. Women were followed for a mean of four years (range: 2 to 7.7 years). Those in CIN 2 conservative group were nearly three times more likely (HR = 2.97, 95% CI: 1.24 to 7.09) to develop CIN 2/+ after two years compared with those with treated CIN 2. Those with CIN 1 were 3.23 times (HR = 3.23, 95% CI: 1.66 to 6.29) more likely to develop high-grade disease than those in the CIN 2 treated group. There was no significant difference between the CIN 2 conservative and CIN 1 groups.⁴⁵

- Two studies reported follow-up for treated women (CIN 2 or CIN 3), demonstrating recurrence in 4% to 5% of women (from two to 10 years).^{45,49} Progression from CIN 2 to CIN 3 was noted in one study in 4% of the sample (mean follow-up 4.5 years, range: 2.0 to 7.7). Only one study reported progression to cancer (at six years) following two recurrences at one year after treatment (median follow-up six years, range five to 10).⁴⁹
- Five studies reported follow-up for untreated women with CIN 2 or CIN 2/3.^{45,46,48,50,51} Regression was observed in 29% to 68% of women within the target age group (follow-up range: 0.3 to 3.9 years). Persistence was observed in 17% to 24% of women over 0.3 to 7.0 years, while progression was observed in 15% to 24% over the same time period. No cancers were reported in untreated women with available follow-up data.

Comparison with reference to other age groups:

- Only two studies examined risk by age. There were no significant differences reported in risk for the target age group compared to adolescents. Additionally, those < 25 years of age may be at lower risk of CIN 2 progression compared to those age 25+.^{47,50}
 - Gargano et al. (2011) examined differences in HPV types and co-factors for development of CIN 3 by age in women referred to colposcopy. HPV-positive 22- to 24 year olds were not at increased risk of CIN 3+ compared with HPV-positive 18- to 21-year-olds. HPV-positive women > 25 years old showed risks of 2.1 times (25 to 29 years) and 2.3 times (30 to 39 years) of CIN 3+ vs. HPV-positive 18- to 21-year-olds.⁴⁷
 - Fuchs et al. (2007) examined regression rates among young women with CIN 2. Those ages 20 to 21 years old did not differ in regression rates (vs. < 16 and 17 to 19 years) (p = 0.38).⁵⁰

Time to Disease or Regression

- Evidence for time to disease or regression is limited.^{48,51}
 - Moscicki et al. (2011) demonstrated that 68% of untreated women with CIN 2 regressed to no disease within three years (55% in women HPV-positive; 78% in women HPV-negative).⁵¹
 - McAllum et al. (2011) demonstrated that 62% of untreated women with CIN 2 regressed to CIN 1/no disease/HPV after a median follow-up of eight months.⁴⁸
- A smaller proportion of women experienced progression (5% to 17%) and time to disease ranged from 2.7 to five years (two studies).^{45,51}
- It is important to note that routine screening intervals are every three years for this population.

Recommended Follow-Up/ Management Strategies

- A single clinical guideline from the American Society for Colposcopy and Cervical Pathology (ASCCP) was identified.
 - For women with CIN 1 following ASCUS or LSIL cytology, repeat cytology is recommended in 12 months, whereas a CIN 1

diagnosis following ASC-H or HSIL requires observation with colposcopy and cytology every six months for two years. For women with CIN 2 or CIN 3 on biopsy, either treatment or observation is acceptable, provided colposcopy is adequate. When CIN 2 is specified, observation every six months for one year is preferred. If high-grade cytology or colposcopy persists for one year, treatment is recommended. When CIN 3 is specified or colposcopy is inadequate, treatment is preferred.⁵²

- The authors of three studies similarly concluded that women with CIN 2 should be managed conservatively:
 - McAllum et al. (2011) recommended conservative management of CIN 2 for women under age 25.⁴⁸
 - Fuchs et al. (2007) recommended repeat colposcopy for biopsy-proven CIN 2 instead of immediate treatment for adolescents and young women.⁵⁰
 - Moscicki et al. (2010) reported that their data support ASCCP guidelines for conservative management of adolescents and young women with CIN 2.⁵¹

Obstetrical Risks

- The identified studies did not report on evidence to inform harms of surgery for the target age group.

Appendix C: Glossary of Terms

Term	Definition
Bethesda System	Standardized terminology system for reporting cytology results.
Cervical cytology	Screens exfoliated cervical cells to detect the presence or absence of abnormalities.
Cervical intraepithelial neoplasia (CIN)	Former classification of abnormal changes in the basal layers of the squamous epithelial tissues of the cervix that may be the precursor to squamous-cell carcinoma. The disorder is graded according to its pathologic progress, from CIN1 to CIN3, with CIN3 being the most severe.
Colposcope	Binocular scope providing five- to 30-fold magnification used for visual assessment of the female lower-genital tract.
Colposcopy	Examination of the cervix, vagina and, in some instances, the vulva with the colposcope after the application of a 3% to 5% acetic acid solution coupled with obtaining colposcopically directed biopsies of all lesions suspected of representing neoplasia.
Colposcopic impression	Documentation of the visual inspection of blood vessel configurations, surface contour, colour tone and lesion demarcation before and after the application of acetic acid and/or iodine. A colposcopic impression is considered “satisfactory” or “adequate” if the entire squamocolumnar junction and the margin of any visible lesion can be visualized with the colposcope. A colposcopic impression is considered “normal” if there is no visible abnormality on the cervix.
Cytopathology	A branch of pathology that studies and diagnoses diseases on the cellular level; cervical smear tests screen for abnormal cytology.
Diagnostic excisional procedure (DEP)	The process of obtaining a specimen from the transformation zone and endocervical canal for histological evaluation, and includes laser conization, cold knife conization, LEEP and loop electrosurgical conization. DEPs can act as both diagnostic and therapeutic tools.
Dysplasia	Abnormal development in the cervical epithelium.
Endocervical curettage (ECC)	Use of a spoon-shaped instrument, or curette, to scrape the mucous membrane of the endocervical canal (the passageway between cervix and uterus) to obtain a small tissue sample.
Histopathology	The microscopic study of diseased tissue.
High risk human papillomavirus (HPV) test	Tests for oncogenic HPV DNA within cervical cells.

human papillomavirus (HPV)	Family of sexually transmitted viruses common in men and women. Most HPV infections are cleared by the body naturally; however, HPV persists in some women. While there are over 100 types of HPV, approximately 12 to 15 types are oncogenic. Cervical cancer occurs only when persistent HPV infection exists.
human papillomavirus (HPV) co-test	The use of an HPV test in conjunction with cervical cytology.
human papillomavirus (HPV) exit-test	HPV test (or co-test) to ensure patients are not at increased risk of developing cancer and safe to exit the colposcopy system.
human papillomavirus (HPV) test-of-cure	HPV test (or co-test) administered following treatment for cervical abnormalities. If the HPV result is positive, or moderate or worse cervical abnormalities are detected, treatment has not cured the patient and further investigation with colposcopy and/or re-treatment is advised.
Loop electrosurgical excision procedure (LEEP) or large loop excision of the transformation zone (LLETZ)	Outpatient excisional treatment for squamous intraepithelial neoplasia.
Neoplasia	New abnormal growth of cells that may lead to a neoplasm or tumour.
Primary care provider	The healthcare provider who acts as the principal point of consultation for patients within a healthcare system and coordinates other specialist consultations, including referrals into the colposcopy system.
Primary care setting	The place where a patient receives consultation or therapy from a primary care provider. Cervical screening within a primary care setting can occur, for example, in a primary care office, a sexual health clinic, a mobile coach or a public health unit.
Rapid review	Evidence syntheses that use accelerated or streamlined methods compared with the traditional systematic review are often driven by urgency for decision-making or limited time and/or resources. In this document, rapid reviews involved searches of a single database (PubMed) for studies published in English during a time period determined to be of clinical significance for each research question. A single reviewer conducted each review and a second reviewer partially validated the articles and data abstraction processes.
Squamous cell/glandular cell carcinoma	Cancer detected in squamous or glandular cells, respectively.
Squamocolumnar junction (SCJ)	The place where the endocervix meets the ectocervix.
Transformation zone (TZ)	Area of changing cells and the most common place on the cervix for abnormalities, including pre-malignant cells, to develop.

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