2024 Hong Kong College of Obstetricians and Gynaecologists Guidelines for cervical cancer prevention and screening

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ABSTRACT

Primary prevention of cervical cancer is best achieved by vaccinating girls with a prophylactic human papillomavirus (HPV) vaccine. Despite the high efficacy of such vaccines, cervical cancer screening remains necessary because current vaccines do not offer full protection. Secondary prevention via cervical screening should target all women from age 25 years or at the onset of sexual activity, whichever occurs later, until age 64 years. Screening is recommended at 3-year intervals after two consecutive normal annual cytology results, or at 5-year intervals using HPV-based testing (either HPV co-test with cytology or HPV stand-alone). Women who have undergone hysterectomy with cervix removal for benign disease and have no prior history of cervical dysplasia can discontinue screening. Women with HPV-positive, cytology-negative co-test results should either undergo repeat co-testing in 12 months or immediate HPV16/18 genotyping. Immediate referral of women with positive stand-alone HPV test results for colposcopy without further triage is not recommended. A second triage test using cytology, genotyping for HPV16/18, or p16/Ki-67 dual-stain should be conducted to accurately identify women at high risk for high-grade lesions who thus require colposcopy referral. Women with HPV-positive, cytology-positive co-test results, or high-grade abnormal cytology results should be referred for colposcopy. Treatment with a loop electrosurgical excision procedure is recommended for women with high-grade squamous intraepithelial lesions (HSILs). After HSIL treatment, long-term follow-up with HPV-based testing over 25 years is preferred. When cytology results show atypical glandular cells, colposcopy and sampling of the endocervix and endometrium are recommended.

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Introduction

To achieve the goal of the World Health Organization (WHO) of eliminating cervical cancer by 2030,[1] strategies should include human papillomavirus (HPV) vaccination for girls, high-performance screening of eligible women, and treatment of pre-invasive disease. The Guidelines for cervical cancer prevention and screening was last updated in 2016.[2] Since then, there have been several important new developments. Thus, the authors were invited to form a working group to revise the Guidelines. This article summarises the guidelines (January 2024 revised version) available on the Hong Kong College of Obstetricians and Gynaecologists website.[3]

Primary prevention: prophylactic vaccine

Primary prevention of cervical cancer is best achieved by vaccinating girls with a prophylactic HPV vaccine before they become sexually active. All HPV vaccines contain virus-like particles (VLPs) for protection against high-risk HPV (hrHPV) types 16 and 18, which cause approximately 70% of cervical cancer worldwide.[4] The nonavalent vaccine contains

additional VLPs for protection against hrHPV types 31, 33, 45, 52, and 58. These seven HPV types cause approximately 90% of squamous cell carcinomas.[5] The quadrivalent and nonavalent vaccines also contain VLPs to protect against HPV types 6 and 11, which are associated with anogenital warts. Human papillomavirus vaccines are highly immunogenic, generating stronger antibody responses than those produced via natural infection. Real-world data have demonstrated the vaccines' effectiveness in reducing HPV infections, anogenital warts, and cervical intraepithelial neoplasia (CIN) grade 2 or worse (CIN2+) among hrHPV-naive women.[6,7] Despite the high efficacy of HPV vaccines, cervical cancer screening remains necessary because current vaccines do not offer full protection.

All HPV vaccines are indicated for use in girls and women aged ≥9 years; they demonstrate high efficacy and excellent safety profiles. Human papillomavirus vaccines were initially licensed with a three-dose vaccination schedule. The WHO recommends primarily targeting girls aged 9 to 14 years with two-dose schedule administered at least 6 months apart, ideally within a 12-month period, through national immunisation programmes.[8] The nonavalent HPV vaccine has been incorporated into the Hong Kong Childhood Immunisation Programme, with a two-dose schedule and a coverage rate exceeding 80%.[9] Current HPV vaccines do not influence viral clearance in women with preexisting infection.[10] Meta-analyses have suggested that adjuvant HPV vaccination might reduce the risk of subsequent disease after an excisional procedure for CIN, irrespective of causal HPV type.[11,12] However, higher-quality studies are needed to confirm this suggestion.

2024年香港婦產科學院關於子宮頸癌預防和篩查的指引

吳麻慧、張雅賢、莊國坤、羅欣珮、李縈、李灝思、李偉漢、馬懷思、王靜妍、黃穎卓、陳嘉倫

為女童接種預防性人類乳頭瘤病毒（HPV）疫苗可以最好地實現子宮頸癌的初級預防。儘管此類疫苗功效很高，但由於目前的疫苗無法提供全面保護，子宮頸癌篩查仍屬必要。子宮頸癌的二級預防通過子宮頸篩查實現，應針對所有25歲或性生活開始後（以較晚者為準）的女性，直到64歲。我們建議在連續兩個年度細胞學結果均為正常後每3年進行一次篩查，或每5年通過基於HPV檢測（HPV與細胞學聯合檢測或HPV獨立檢測）進行篩查。因良性疾病接受子宮切除術並已切除子宮頸且沒有子宮頸上皮內瘤病變史的婦女可以停止篩查。HPV與細胞學聯合檢測結果為HPV陽性而細胞學陰性的婦女應在12個月後重複聯合測試或立即進行HPV16/18基因分型測試。對於HPV獨立檢測結果為陽性的婦女，未進行任何進一步分流測試前，不建議直接轉介陰道鏡檢查，而應使用細胞學、HPV16/18基因分型測試或p16/Ki-67雙染色進行分流測試，以準確識別患有高級別病變的高風險女性，從而轉介陰道鏡檢查。聯合測試結果為HPV陽性及細胞學陽性，或細胞學結果為高級別異常的婦女應被轉介陰道鏡檢查。對於高級別鱗狀上皮病變的婦女，建議進行電圈切除手術治療。治療後，推薦使用基於HPV的檢測進行25年以上的長期隨訪。當細胞學結果顯示非典型腺細胞時，建議進行陰道鏡檢查及子宮頸內膜和子宮內膜活檢。

Secondary prevention: screening

Target population

The target population encompasses all women aged ≥25 years, or those beginning sexual activity (whichever is later), and continues until age 64 years (Table). Considering the low incidence of cervical carcinoma among women aged <25 years in Hong Kong,[13] along with the relatively high rates of spontaneous regression for HPV infection and cytological abnormalities in this age-group, screening before age 25 years is less cost-effective and could result in unnecessary interventions. Nevertheless, women aged <25 years with a high-risk profile may be screened after assessment by doctor. The Table shows the recommended intervals for routine screening.

Screening methods

Cervical cytology

Cervical cytology may be used as a screening test (either alone or as part of a co-test) or triage test (for hrHPV-positive cases in stand-alone HPV screening).[14]

Human papillomavirus testing

Human papillomavirus testing can be used as a screening test (either as part of a co-test or stand-alone in primary HPV screening) [Figs 1 and 2, respectively], a triage test (in cytology-based screening for cases reported as atypical squamous cells of undetermined significance [ASCUS]) [Fig 3], or a test of cure (after treatment for HPV-associated lesions) [online supplementary Fig 1].

The main advantage of HPV testing is its high sensitivity in detecting HPV-associated malignancies and precursor lesions. Various studies have shown that HPV-based screening exhibits greater sensitivity than cytology in detecting high-grade squamous intraepithelial lesions (HSILs) and more severe lesions.[14,15] Considering the lower specificity of a positive HPV test result, a triage test is generally necessary. Similar to other laboratory tests, HPV testing has limitations and may yield false negative results due to various biological and technical factors.[16] Importantly, a negative HPV test result does not definitively exclude cervical pathology because multiple HPV-independent cervical neoplasms exist and false negatives are possible.

TABLE. Routine screening recommendations

Age/Condition	Screening recommendation
25-29 y	Cytology annually for two consecutive years, then every 3 years HPV-based test (HPV stand-alone or HPV co-test with cytology) can be considered for women who received the HPV vaccine
30-64 y	Cytology annually for two consecutive years, then every 3 years OR Co-test (HPV + cytology) every 5 years OR HPV stand-alone every 5 years
≥65 y with previous negative screening results	Can discontinue screening if routine screening results have been negative over the last 10 years
≥65 y, no prior cervical cancer screening, and sexually active	Offer routine screening
Previous LSIL (histological findings)	Continue follow-up in accordance with guidelines Exit screening at age ≥65 years if all routine screening results have been negative for the last 10 years
Previous HSIL (histological findings)	Continue follow-up in accordance with guidelines Exit screening at age ≥65 years if all routine screening results have been negative for the last 25 years
History of hysterectomy with cervix removal for benign disease, no prior cervical dysplasia	Can discontinue screening
Chronically immunosuppressed	Screen regardless of age if sexually active

Abbreviations: HPV = human papillomavirus; HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion

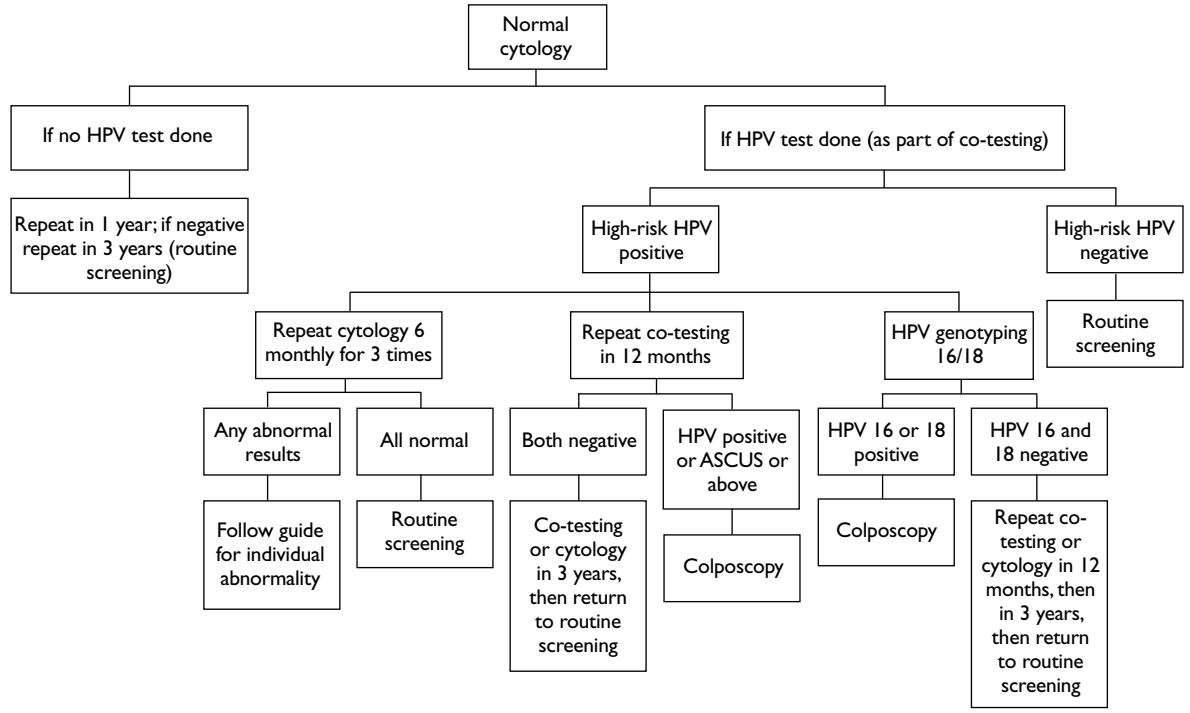

FIG 1. Management of normal cytology with or without human papillomavirus test
Abbreviations: ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus

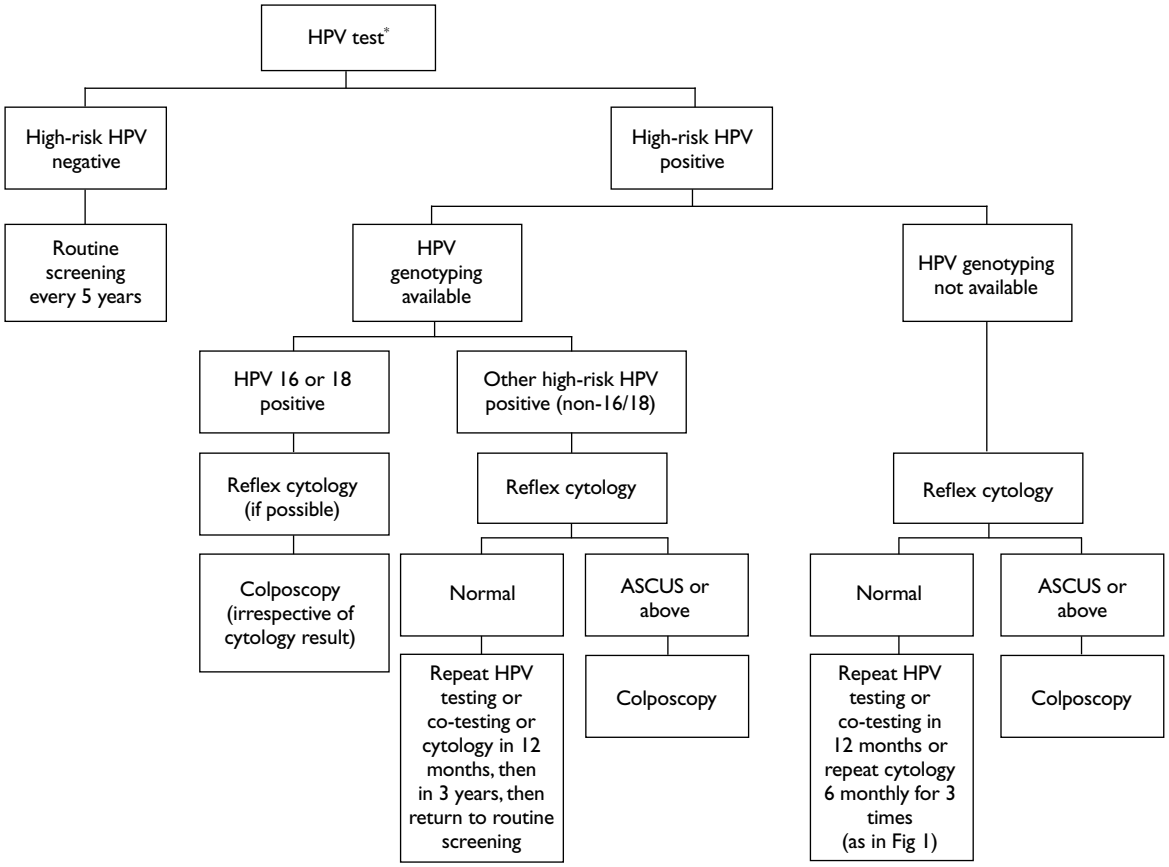

FIG 2. Management options for human papillomavirus as a stand-alone test
Abbreviations: ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus
* Only applies to specific tests approved for primary screening

Human papillomavirus testing should exclusively target hrHPV types.[17] There is a wide range of commercially available HPV testing devices with diverse technologies and detection targets.[18,19] Although no local regulatory body governs which HPV testing devices are suitable for screening or non-screening purposes, regulatory approval statuses in other countries can be considered when selecting an HPV test.

The use of self-collected specimens for HPV testing (also known as self-sampling) is emerging as an alternative strategy to increase cervical screening coverage and compliance. The WHO has suggested using self-collected vaginal samples for screening[20]; some countries (such as Australia[21] and Malaysia[22]) now offer this option. Specific considerations for self-collected samples include the validation of sampling devices for self-collected vaginal specimens as well as the performance and regulatory approval of HPV tests for these specimens.[23] Other self-collected specimens (eg, urine and menstrual blood) have

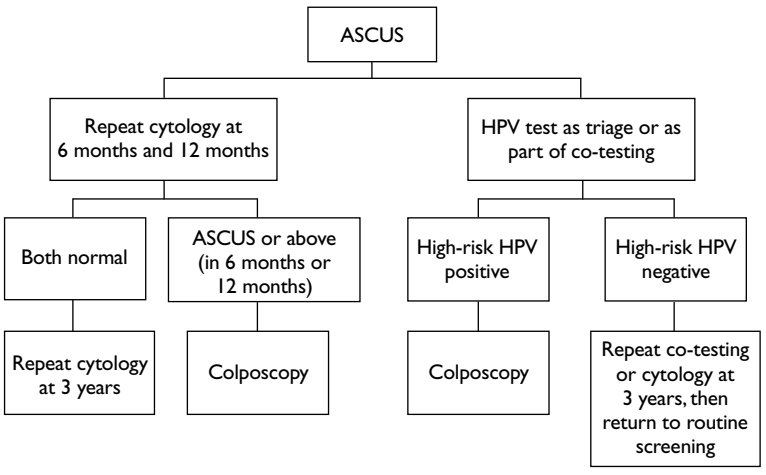

FIG 3. Management of atypical squamous cells of undetermined significance smear (with or without human papillomavirus triage or co-testing)
Abbreviations: ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus

been explored for HPV testing. Currently, the use of these additional specimens is not recognised or recommended as a standard primary screening method, although this perspective may change when data from more definitive studies become available.

Biomarkers

Several cellular and molecular biomarkers have been evaluated for potential applications in cervical screening; some have been shown to improve the identification and triage of women with positive screening tests.[24] Currently, most biomarkers have not been specifically approved for clinical use in primary screening. The p16/Ki-67 dual-stain is an immunocytochemistry-based technique that detects cells co-expressing p16 and Ki-67 on a cytology slide. The presence of both markers is relatively specific to HPV-associated dysplastic lesions. The p16/Ki-67 dual-stain was recently approved by the United States Food and Drug Administration for the triage of patients with hrHPV positivity.[25]

Use of human papillomavirus testing in screening

Testing for the triage of atypical squamous cells of undetermined significance smears

Reflex HPV testing as a triage option for patients with ASCUS constitutes an alternative to repeat cytology at 6 months when making decisions regarding colposcopy referral,[26] except among women aged <20 years (Fig 3).

Testing as primary screening

The implementation of HPV testing as a screening strategy may enhance disease detection and extend the screening interval. However, this increased sensitivity must be balanced with the potential risks of unnecessary testing and treatment. Considering the high prevalence of HPV in young women and the median age of cervical cancer patients in Hong Kong, primary HPV screening is not recommended for women aged <30 years. Among women who previously underwent HPV vaccination, primary HPV screening can be considered before the age of 30 years. In a population with high vaccine uptake among women aged 25 to 33 years, primary HPV screening was associated with significantly increased detection of CIN2+ relative to cytology; there was no significant difference in the colposcopy referral rate.[27]

Testing as a co-test with cytology

In many studies, the addition of HPV testing to cytology resulted in greater CIN3 detection sensitivity during the first round of screening, along with a decrease in CIN3 or cancer detection during subsequent rounds of screening.[14,28,29] Women with negative co-test results have low risks of concurrent CIN3+[30] and cervical cancer.[31] Immediate colposcopy is not recommended for women with HPV positivity and negative cytology results. Instead, either repeat co-testing in 12 months or immediate HPV16/18 genotyping is acceptable (Fig 1).

Testing as a stand-alone test

Although HPV and cytology co-testing improves detection sensitivity for high-grade lesions, this approach requires each woman to undergo two tests; thus, it carries substantial resource and cost implications. Stand-alone HPV testing can be considered for cervical screening (Fig 2). In several studies in a systemic review,[32] primary HPV screening significantly increased CIN3+ detection during the initial round of screening compared with cytology. A negative HPV test result has high negative predictive value. However, immediate colposcopy referral is not recommended for HPV-positive women without further triage tests. A second triage test should be conducted to accurately identify women at high risk for CIN2+ lesions who thus require colposcopy referral. Various triage strategies can be considered. Reflex cytology is recommended for all women with positive stand-alone HPV test results to guide colposcopy referral and subsequent management. Alternatively, HPV16/18-positive women should be referred for colposcopy, regardless of cytology results. Another triage method for HPV-positive women (particularly those with non–16/18 hrHPV types) involves the p16/Ki-67 dual-stain. Dual-stain cytology has significantly higher detection sensitivity for CIN3+ relative to cytology, with comparable specificity. After referring all HPV16/18-positive women for colposcopy, the use of dual-stain cytology as a triage test for women with other hrHPV positivity resulted in higher CIN3+ sensitivity relative to cytology-based triage, with a similar number of colposcopies.[33]

Management of normal and abnormal smears

Figures 1, 3 and 4 summarise the management of normal and low-grade abnormal cytology. Patients with high-grade abnormal cytology should be referred for colposcopy. Suggested actions for other cervical cytology results of normal and squamous lesions, glandular lesions, and others are shown in online supplementary Tables 1, 2, and 3, respectively.

Colposcopy and treatment for cervical intraepithelial neoplasia

The colposcopist examines the transformation zone, defines the extent of the lesion, and biopsies the most abnormal area for tissue diagnosis. Histological confirmation of the colposcopic diagnosis is recommended before treatment. In

patients with a colposcopic diagnosis of high-grade lesion, a 'see and treat' approach (ie, loop excision without biopsy) is adopted by some colposcopists. Immediate treatment is an option for women aged ≥25 years with HSIL cytology who have rarely or never undergone screening, especially if they exhibit HPV16 positivity.[34] Although this approach decreases the need for additional visits, it risks over-treatment of patients with low-grade lesions.

Most low-grade lesions spontaneously regress within 2 years; thus, immediate treatment may be unnecessary.[35,36] Approximately 15% of patients show progression to high-grade lesions and eventually require treatment. If a low-grade lesion is confirmed by colposcopy and biopsy, follow-up with HPV testing or co-testing at 12 months is recommended, irrespective of the patient's age (Fig 5). Because a negative cytology result is not associated with lower subsequent risk of CIN3 relative to a negative HPV test result,[37] HPV testing is preferred for follow-up after colposcopy. Cytology remains acceptable if HPV testing is unavailable.

For non-pregnant women with CIN3, treatment is recommended. For non-pregnant women with CIN2, treatment is also recommended; however, if the squamocolumnar junction is fully visualised, observation can be considered for women with concerns regarding the effect of treatment on future pregnancies. Treatment should be performed if CIN2 persists for >24 months. The preferred treatment method is loop electrosurgical excision procedure (LEEP). Hysterectomy is not recommended unless there are concomitant gynaecological issues that justify the procedure; it should not be performed solely for cytological abnormalities without proper colposcopy examination and biopsy.

For women with high-grade abnormal cytology but only low-grade lesions on colposcopy-directed biopsy, a review of materials is recommended. If the low-grade lesions are confirmed, HPV testing or co-testing should be conducted at 12 and 24 months. For women with HSIL cytology whose biopsy results indicate histological low-grade squamous intraepithelial lesion (LSIL) or not worse than LSIL, an immediate diagnostic excisional procedure is acceptable. An alternative option is observation with HPV testing or co-testing and colposcopy at 1 year. This approach requires the squamocolumnar junction and upper limit of any lesion to be fully visualised at the initial colposcopic examination; if collected, endocervical samples must show less than CIN2. A diagnostic excisional procedure is recommended for women with cytologic HSIL at either the 1- or 2-year visit, as well as women with persistent ASC cannot rule out high-grade squamous lesion at the 2-year visit.

For patients with LSIL involving >2 quadrants of the cervix and patients with LSIL who are unable or unwilling to attend follow-up visits, treatment should be considered. Treatment is also acceptable if the lesion persists for >2 years. If the final histology analysis after treatment confirms low-grade lesions, the patient should be monitored in a manner similar to other patients with low-grade lesions on cervical biopsies. Positive treatment margins for CIN2/3 are associated with a higher recurrence rate, but this association is insufficient to justify routine repeat excision.[38]

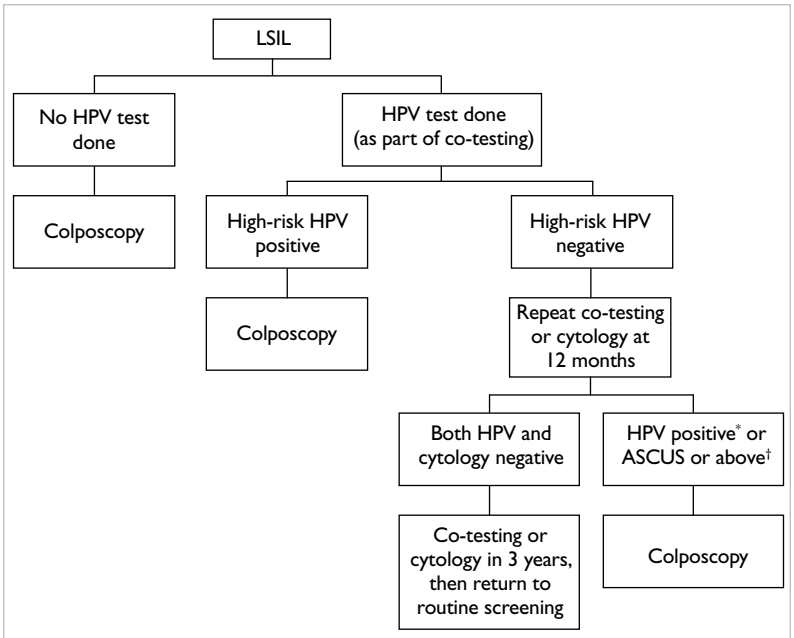

FIG 4. Management of low-grade squamous intraepithelial lesion smears
Abbreviations: ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus; LSIL = low-grade squamous intraepithelial lesion
* Irrespective of cytology results
† Irrespective of HPV results

Human papillomavirus testing or co-testing is preferred over cytology for follow-up after histological HSIL treatment because it provides the most accurate prediction of treatment outcomes.[15] Human papillomavirus testing or co-testing should be performed at 6 months, then annually until two consecutive normal results are obtained. Cytology only is less preferred for surveillance after histological HSIL treatment but remains acceptable if HPV testing is unavailable (online supplementary Fig 1).

Among patients who underwent hysterectomy for CIN with clear margins, HPV testing or co-testing with a vaginal smear should be performed annually for two consecutive years. If both results are normal, further vaginal smears are unnecessary. If HPV testing is unavailable, vaginal smear cytology should be performed at 6, 12, and 24 months. No further vaginal smears are needed after three consecutive

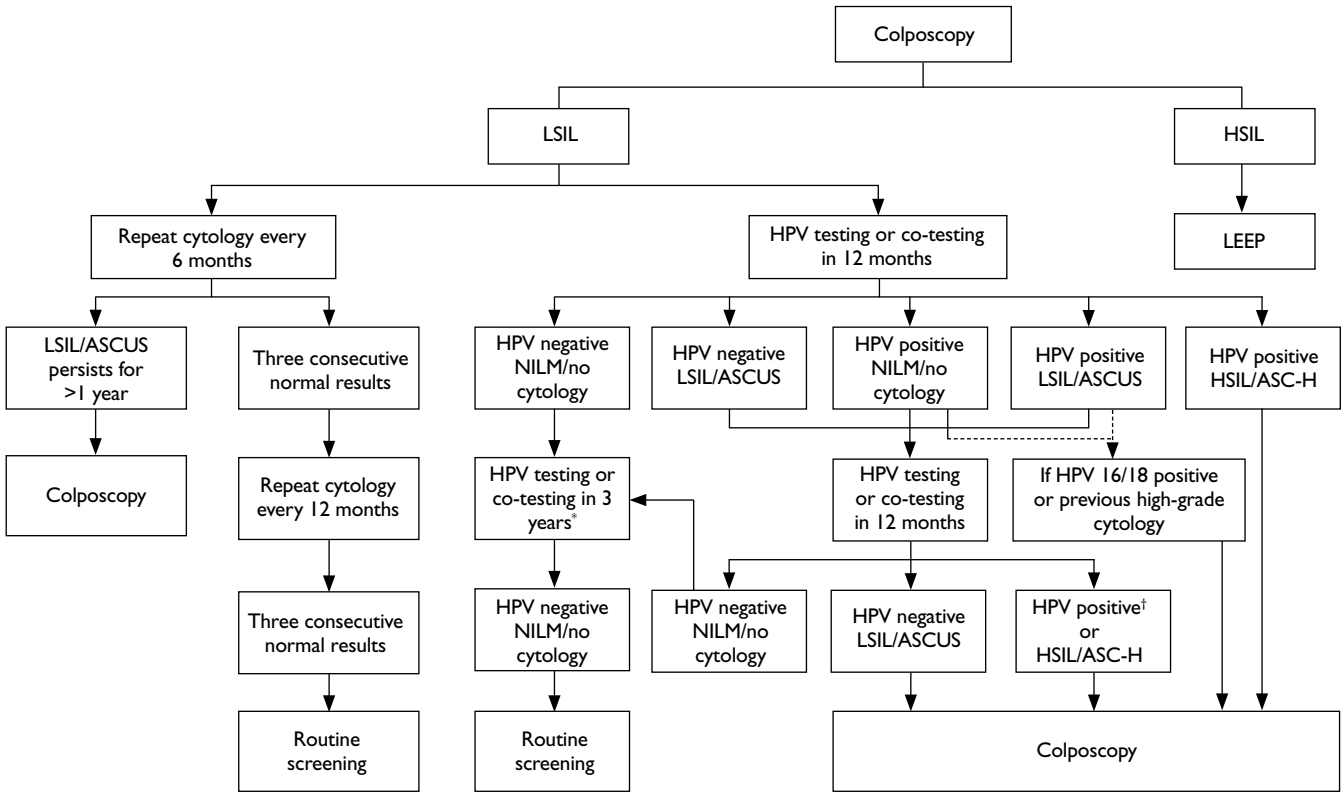

FIG 5. Management after colposcopy

Abbreviations: ASC-H = atypical squamous cells cannot rule out high-grade squamous lesion; ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus; HSIL = high-grade squamous intraepithelial lesion; LEEP = loop electrosurgical excision procedure; LSIL = low-grade squamous intraepithelial lesion; NILM = negative for intraepithelial lesion or malignancy

* For women who had low-grade cytology leading to colposcopy

† Irrespective of cytology results

normal cytology results. If excision was incomplete, margin clearance is uncertain on hysterectomy, or the patient exhibited vaginal intraepithelial neoplasia, HPV testing or co-testing with a vaginal smear should be performed at 12 and 24 months. If both results are negative, HPV testing or co-testing with a vaginal smear should be continued every 3 years for 25 years or until age 65 years, whichever is later. If HPV testing is unavailable, vaginal smear cytology should be performed at 6 and 12 months, then annually for 10 years, then every 3 years for 15 years or until age 65 years, whichever is later.

Management of glandular lesions

For cytology results indicating adenocarcinoma in situ (AIS) and all subcategories of atypical glandular cells—except those specified as 'atypical endometrial cells'—colposcopy, endometrial sampling, and endocervical sampling are recommended, regardless of HPV test results (online supplementary Table 2 and online supplementary Fig 2). Reflex HPV testing is not recommended. For atypical glandular cells (favour neoplasia) and AIS, if no significant pathology can explain the source of abnormal cells, a diagnostic excisional procedure (preferably cold-knife conisation) is recommended.

Management of adenocarcinoma in situ

A diagnostic excisional procedure is recommended for all patients with a diagnosis of AIS on cervical biopsy or cytology to rule out invasive adenocarcinoma, even if a definitive hysterectomy is planned. Excisional procedures should aim to provide an intact specimen to facilitate accurate interpretation of margin status. The excision specimen length should be at least 10 mm, where feasible. Endocervical sampling above the excision site to assess residual disease is recommended. A 'top hat' endocervical excision to increase specimen length is not recommended.

In cases of concomitant AIS and CIN, management should follow recommendations for AIS. Hysterectomy is the preferred option for all patients with histologically confirmed AIS. For

women with confirmed AIS and negative margins on the excision specimen, simple hysterectomy is preferred. For women with confirmed AIS and a positive margin on the excision specimen, re-excision to achieve a negative margin is preferred to rule out malignancy, even if a hysterectomy is planned. If a positive margin is present on the re-excision specimen, or further excisional procedures are not feasible, a simple or modified radical hysterectomy is acceptable. Fertility-sparing management is not recommended for these patients. However, fertility-sparing treatment with an excisional procedure alone may be considered for women with negative margins on the excisional specimen who are willing to adhere to surveillance recommendations.

Management for special categories

Young women, including adolescents

Considering the low prevalence of high-grade cytological abnormalities and rarity of cervical cancer in adolescents aged <21 years,[39] cervical screening is not recommended in this age-group. Unnecessary screening could lead to avoidable procedures and over-treatment.[40] Most cytological abnormalities in adolescents are minor and exhibit spontaneous clearance within 2 years; thus, immediate colposcopy is discouraged. For ASCUS or LSIL, cervical cytology should be repeated annually; routine screening can be resumed after two consecutive negative cytology results. Colposcopy should be performed if high-grade abnormal cytology is evident or abnormal cytology persists for 2 years.

If CIN3 is confirmed on biopsy, LEEP is indicated. If CIN2 is confirmed on biopsy, observation via cytology and colposcopy every 6 months is suggested due to the high regression rate in this age-group.[41] However, treatment is recommended if CIN2 persists for 2 years. If no high-grade lesion is detected on satisfactory colposcopic examination, cytology should be repeated every 6 months. If HSIL persists at 1 year, colposcopy should be repeated; if HSIL persists at 2 years, LEEP should be considered.[29] If colposcopy for HSIL yields unsatisfactory results, cytology and colposcopy should be repeated at 6 months. If HSIL persists and colposcopy results remain unsatisfactory at 1 year, LEEP should be offered.

Pregnant women

The goal of colposcopy in pregnant women is exclusion of invasive cancer. Cancer risk is relatively low among pregnant women with ASCUS or LSIL; thus, deferred colposcopy is acceptable (until at least 6 weeks after delivery). Pregnant women with high-grade abnormal cytology or HPV16/18 positivity should undergo colposcopic examination. Endocervical curettage is contraindicated, but repeat colposcopy early in the third trimester may be considered. Pregnancy does not appear to alter the risk or rate of progression from cervical precancer to cancer. The only indication for immediate treatment is invasive cancer; otherwise, treatment for high-grade disease can be postponed until the postpartum period. A colposcopy-guided biopsy or diagnostic excisional procedure is indicated only if malignancy is suspected.

Chronically immunocompromised women

Women with chronic immunosuppression have a higher risk of persistent HPV infection, increasing the likelihood of progression to CIN and cervical cancer. They should be informed of the increased risk associated with HPV infection and encouraged to undergo regular screening. Given the limited literature regarding cervical screening for immunocompromised women without human immunodeficiency virus (HIV), screening and management guidelines generally follow recommendations for women with HIV.[42] Cervical cancer rates among women with HIV are elevated across all age-groups from 25 to 54 years; zero cases were reported among women aged <25 years.[43] Although there is limited and inconsistent evidence concerning the benefit of cervical screening for younger age-groups, it may be helpful to screen women aged 21 to 24 years; this would provide an early detection window prior to age 25 years, when the cervical cancer risk in women with HIV exceeds that of the general population.[43] Recent data suggest that screening intervals may be extended for these women.[44] A 3-year interval can be considered after two consecutive normal annual cytology results[45] or a negative HPV-based screening test result. Subsequent management for any abnormal screening results and treatment of high-grade cytological abnormalities should follow guidelines for non-immunocompromised individuals. Low-grade lesions should be regularly monitored for progression because they respond poorly to treatment.

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Analysis or interpretation of data: All authors.
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Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practising in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognised clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the needs of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty in which further research may be indicated.

Declaration

The content of this guideline has been published in the Hong Kong College of Obstetricians and Gynaecologists Guidelines Number 4, revised January 2024,[3] which is a revised version of the 2016 Hong Kong College of Obstetricians and Gynaecologists Guidelines for Cervical Cancer Prevention and Screening.[2]

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Supplementary material

The supplementary material was provided by the authors and some information may not have been peer reviewed. Accepted supplementary material will be published as submitted by the authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (https://doi.org/10.12809/hkmj2411547).

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