

Supplementary material

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Supplement to: SF Ngu, ANY Cheung, KK Jong, et al. 2024 Hong Kong College of Obstetricians and Gynaecologists Guidelines for cervical cancer prevention and screening. Hong Kong Med J 2024 Dec;30(6):488-97 | Epub 3 Dec 2024. <https://doi.org/10.12809/hkmj2411547>.

Supplementary Table 1. Management of cytology results of normal and squamous lesions

Cervical cytology result	Suggested actions
NILM (normal cytology) [Fig 1]	<p>Cytology alone: repeat cytology every 3 years (after two initial annual screenings)</p> <p>Co-testing:</p> <p>If hrHPV-negative, repeat co-testing every 5 years</p> <ul style="list-style-type: none"> - If hrHPV-negative but with history of hrHPV positivity or abnormal cytology in the last screening, repeat screening (co-testing or cytology) in 3 years - If hrHPV-positive, choose from three options: <ul style="list-style-type: none"> o Repeat cytology every 6 months, three times o Repeat co-testing in 12 months o Conduct HPV16/18 genotyping <ul style="list-style-type: none"> ▪ If HPV 16/18-positive, refer for colposcopy ▪ If HPV 16/18-negative, repeat co-testing or cytology in 1 year, then in 3 years, then resume routine screening
Normal, transformation zone absent	<p>If age <30 y: manage as normal smears</p> <p>If age ≥30 y: perform HPV testing (preferred) or manage as normal smears</p>
ASCUS (Fig 3)	<p>Cytology alone: repeat cytology at 6 and 12 months</p> <p>HPV triage or co-testing:</p> <ul style="list-style-type: none"> - If hrHPV-positive, refer for colposcopy - If hrHPV-negative, repeat screening (co-testing or cytology) in 3 years
LSIL (Fig 4)	<p>Cytology alone: refer for colposcopy</p> <p>Co-testing:</p> <ul style="list-style-type: none"> - If hrHPV-positive, refer for colposcopy - If hrHPV-negative, repeat co-testing or cytology in 12 months <ul style="list-style-type: none"> o If any result is abnormal, refer for colposcopy o If result is normal, repeat co-testing or cytology in 3 years, then resume routine screening
ASC-H (including cases with coexisting LSIL) [online supplementary Fig 3]	<p>Refer for colposcopy</p> <ul style="list-style-type: none"> - Perform endocervical sampling if colposcopy results are unsatisfactory - If no pathology is identified, a review of materials is recommended <p>If no change in diagnosis, repeat cytology every 6 months or HPV test/co-testing annually</p> <ul style="list-style-type: none"> o If cytology result is normal for two consecutive 6-month intervals, resume routine screening o If two consecutive annual HPV test/co-testing results are normal, repeat HPV test/co-testing in 3 years, then resume routine screening

- Repeat colposcopy if abnormal cytology results persist or hrHPV positivity is observed
- Diagnostic excisional procedure is recommended if ASC-H persists for 2 years

HSIL	Refer for colposcopy <ul style="list-style-type: none"> - If there is no significant pathology to explain the source of abnormal cells, a review of materials is recommended. If no change in diagnosis, a diagnostic excisional procedure is recommended
Squamous cell carcinoma	Biopsy if visible growth is present; otherwise, arrange early referral for colposcopy and biopsy

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

Supplementary Table 2. Management of cytology results of glandular lesions*

Cervical cytology result	Suggested actions
AGC-NOS (or atypical endocervical cells), AGC-FN and AIS	Refer for colposcopy, endometrial sampling, and endocervical sampling For AGC-FN and AIS: If no significant pathology can explain the source of abnormal cells, a diagnostic excisional procedure is recommended. Cold-knife conisation is preferred
Atypical endometrial cells	Perform endometrial and endocervical sampling If no endometrial pathology is identified, refer for colposcopy
Adenocarcinoma	Biopsy if visible growth is present; otherwise, arrange early referral for colposcopy, endometrial sampling, and endocervical sampling
Endometrial cells (in a woman aged ≥ 45 y)	Postmenopausal women: endometrial assessment is recommended Asymptomatic premenopausal women: no further investigation is required Offer endometrial assessment to those at increased risk of endometrial pathology, such as women with abnormal vaginal bleeding or obesity (body mass index ≥ 25 kg/m ²)

Abbreviations: AGC-FN = atypical glandular cells (favour neoplasia); AGC-NOS = atypical glandular cells (not otherwise specified); AIS = adenocarcinoma in situ

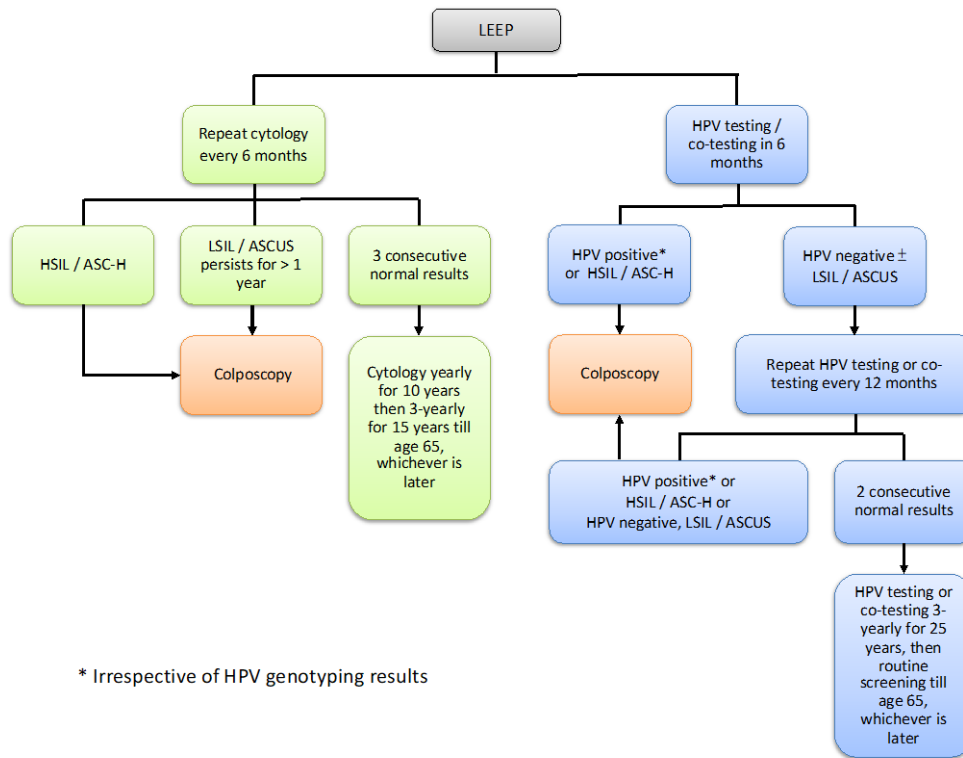
* Also refer to online supplementary Figure 2

Supplementary Table 3. Management of cytology results of others

Cervical cytology result	Suggested actions
Unsatisfactory	Cytology alone: repeat cytology in 2 to 4 months. If two consecutive cytology results are unsatisfactory, refer for colposcopy Co-testing: <ul style="list-style-type: none">- If HPV16/18-positive, refer for colposcopy- If other high-risk/untyped HPV-positive, repeat cytology in 2 to 4 months or refer for colposcopy- If HPV-negative, repeat cytology in 2 to 4 months. If two consecutive cytology results are unsatisfactory, refer for colposcopy
Other malignant neoplasms	Biopsy if visible growth is present; otherwise, arrange early referral for colposcopy and biopsy

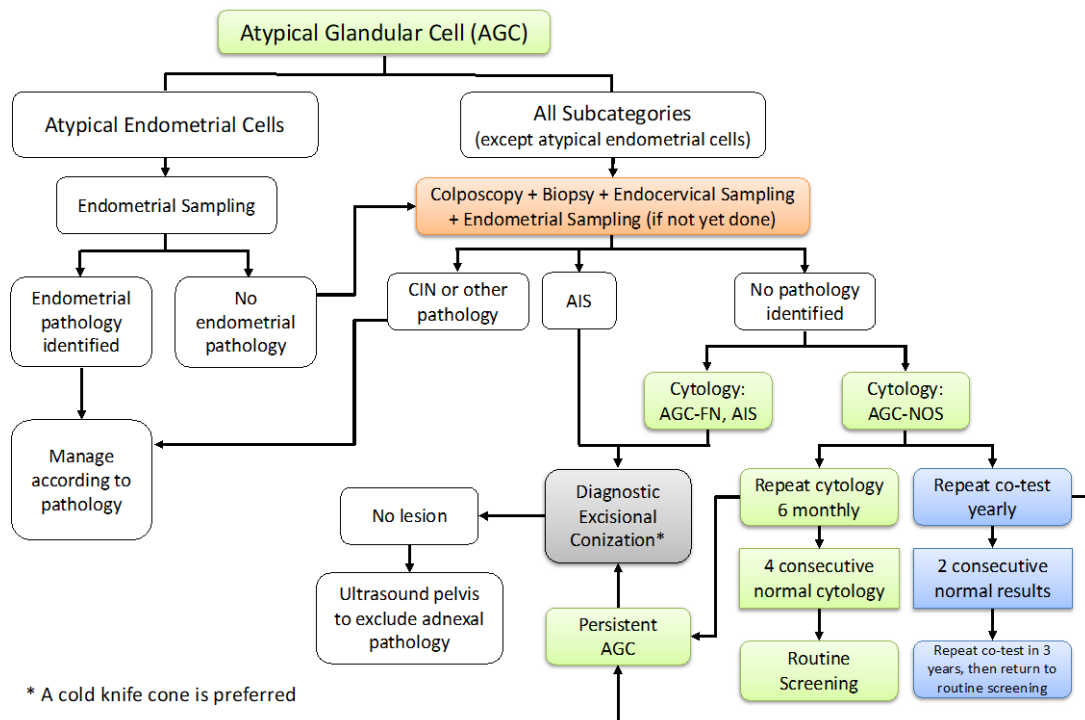
Abbreviation: HPV = human papillomavirus

Supplementary Figure 1. Management after loop electrosurgical excision procedure



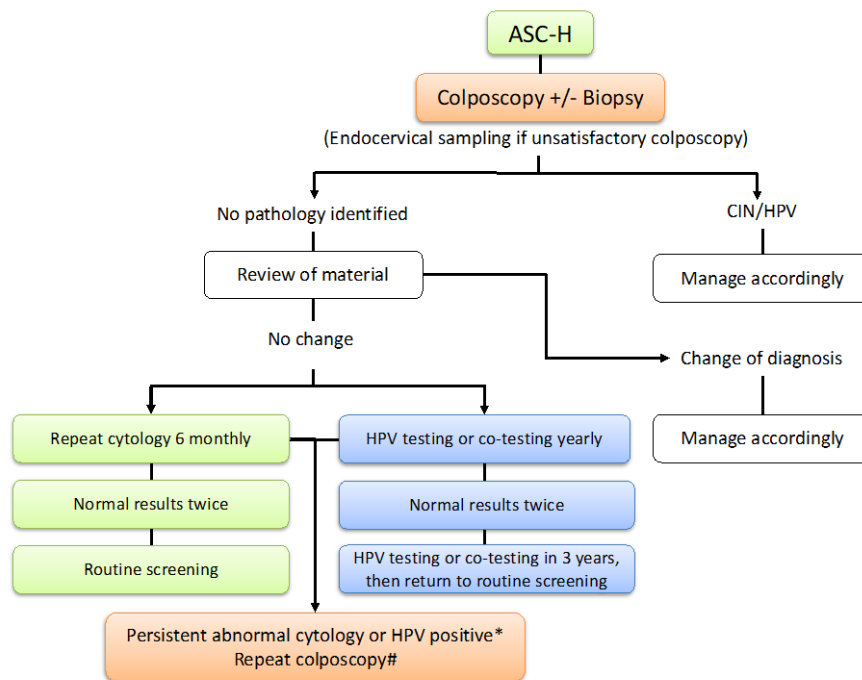
Abbreviations: ASC-H = atypical squamous cells cannot rule out high-grade squamous lesion; ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus; HSIL = high-grade squamous intraepithelial lesion; LEEP = loop electrosurgical excision procedure; LSIL = low-grade squamous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

Supplementary Figure 2. Management of cytology showing atypical glandular cells



Abbreviations: AGC = atypical glandular cell; AGC-FN = atypical glandular cells (favour neoplasia); AGC-NOS = atypical glandular cells (not otherwise specified); AIS = adenocarcinoma in situ; CIN = cervical intraepithelial neoplasia

Supplementary Figure 3. Management of cytology showing atypical squamous cells cannot rule out high-grade squamous lesion



* Irrespective of HPV genotyping results

Diagnostic excisional procedure if ASC-H persists at 2 years

Abbreviations: ASC-H = atypical squamous cells cannot rule out high-grade squamous lesion; CIN = cervical intraepithelial neoplasia; HPV = human papillomavirus