

Cervical Intraepithelial Neoplasia in the HPV Era: Transformation Zone, Screening, Colposcopy, and Management

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Abstract

Background: Cervical intraepithelial neoplasia (CIN) refers to a spectrum of precancerous changes involving the squamous epithelial cells of the cervix. It represents dysplastic transformation limited to the epithelial layer, without invasion beyond the basement membrane. Persistent infection with high-risk HPV types leads to the development of precancerous lesions and, if untreated, invasive cervical cancer.

Aim: To review cervical intraepithelial neoplasia, human papillomavirus, cervical cancer screening, and colposcopy.

Conclusion: Colposcopy allows magnified visual examination after acetic acid application to highlight abnormal epithelium. Directed biopsy is performed to confirm histological diagnosis and grade. Because the disease can be effectively treated and largely prevented when caught early, it is essential to detect and manage its pre-invasive stages as cervical intraepithelial neoplasia.

Keywords: Cervical Intraepithelial Neoplasia; Human Papillomavirus; Transformation Zone; Cervical Screening; Colposcopy

Introduction

Cervical cancer remains a significant global health challenge, especially in low- and middle-income countries where access to preventive healthcare is limited. It is primarily caused by persistent infection with high-risk types of human papillomavirus (HPV), particularly types 16 and 18. According to the World Health Organization, cervical cancer was responsible for approximately 660,000 new cases and 350,000 deaths worldwide in 2022, with over 90% of these deaths occurring in resource-limited settings ⁽¹⁾.

Because the disease can be effectively treated and largely prevented when caught early, it is essential to detect and manage its pre-invasive stages as cervical intraepithelial neoplasia (CIN). Cervical intraepithelial neoplasia refers to a spectrum of precancerous changes involving the squamous epithelial cells of the cervix. It represents dysplastic transformation limited to the epithelial layer, without invasion beyond the basement membrane ⁽²⁾.

The transformation zone is of great clinical significance because over 90% of precancerous cervical lesions and invasive carcinomas originate here, primarily due to the susceptibility of immature metaplastic cells to persistent high-risk HPV infection. The classification of transformation zone type is essential during colposcopic examination, as it guides sampling adequacy, diagnostic accuracy, and management of cervical lesions ⁽³⁾.

Physiological Aspect and Transformation Zone of the Cervix

The cervix is the lower, cylindrical portion of the uterus that connects the uterine cavity to the vagina, functioning as both a mechanical and immunological barrier. Its physiology is dynamic and influenced by cyclic hormonal changes, primarily estrogen and progesterone. The ectocervix is lined by stratified squamous epithelium, while the endocervical canal is covered by columnar epithelium, and the meeting point between these

two is known as the squamocolumnar junction. The squamocolumnar junction continuously shifts due to hormonal status, age, and childbirth. In addition, metaplastic transformation occurs in the transformation zone, where columnar epithelium is replaced by squamous epithelium, a normal physiological process that also represents the most common site for the development of precancerous lesions following persistent HPV infection ⁽⁴⁾⁽⁵⁾⁽⁶⁾.

The transformation zone is a dynamic area on the cervix where the columnar epithelium of the endocervix is replaced by stratified squamous epithelium through a physiological process known as squamous metaplasia. The process of transformation is influenced by hormonal fluctuations, pH changes, and inflammatory stimuli. Under estrogenic influence, the endocervical columnar epithelium proliferates and extends outward, exposing it to the acidic vaginal environment, which induces the conversion to squamous epithelium through reserve cell proliferation and differentiation. This process ensures epithelial stability but also creates a vulnerable site for oncogenic transformation when infected by HPV ⁽⁷⁾.

According to the International Federation for Cervical Pathology and Colposcopy classification, the transformation zone is categorized into three main types based on visibility and location: Type 1 is entirely ectocervical and fully visible; Type 2 has both ectocervical and endocervical components but is still fully visible; and Type 3 has an endocervical component that is not fully visible ⁽⁸⁾.

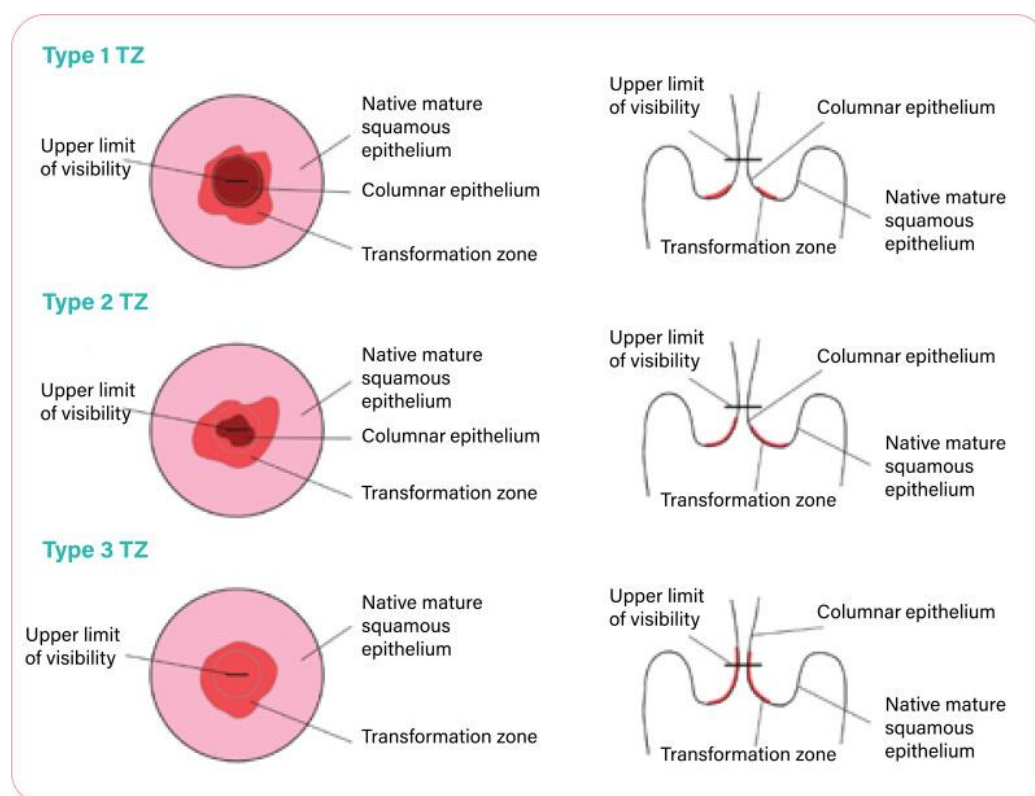


Figure 1. Types of transition zone of cervix (Bornstein et al. ⁽⁸⁾).

Cervical Intraepithelial Neoplasia

Cervical intraepithelial neoplasia refers to the premalignant transformation and abnormal proliferation of squamous epithelial cells on the cervix, confined to the epithelium without invasion of the basement membrane. It represents a spectrum of histopathological changes resulting from persistent infection with high-risk human papillomavirus types, most commonly HPV 16 and 18. CIN lesions are considered precursors to invasive cervical carcinoma, making their detection and management crucial for cervical cancer prevention ⁽⁹⁾.

The key etiologic factor in CIN is persistent infection with high-risk HPV strains. HPV infects basal epithelial cells via microabrasions, integrating viral DNA into host cells, leading to oncogene expression (E6 and E7), which disrupt tumor suppressor proteins p53 and Rb, promoting cell proliferation and dysplasia ⁽¹⁰⁾.

CIN is classified into three grades based on the proportion of the cervical epithelium affected by abnormal cells. CIN 1 involves the lower one-third of the epithelium and may regress spontaneously. CIN 2 extends to two-thirds of the epithelial thickness with a higher risk of progression, but regression is still possible. CIN 3 involves more than two-thirds up to the full thickness of the epithelium and carries the highest risk of progression to invasive carcinoma if untreated ⁽¹¹⁾⁽¹²⁾.

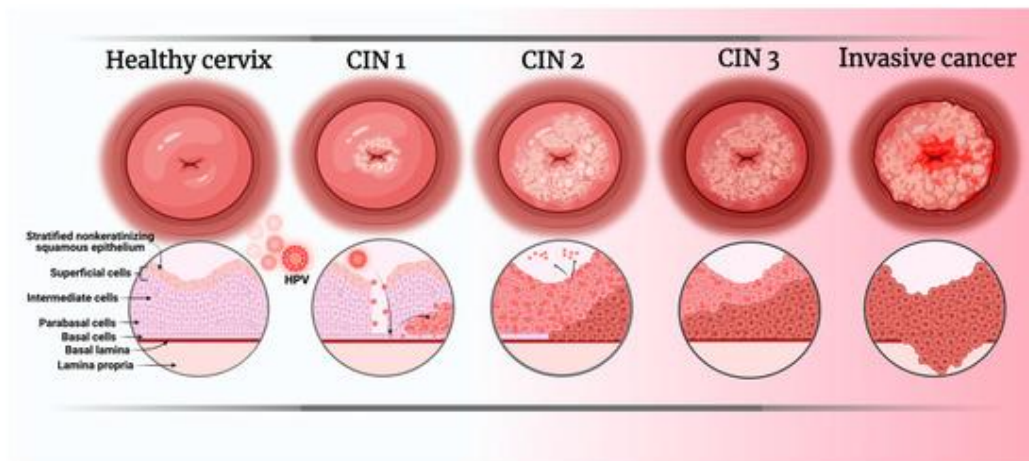


Figure 2. Cervical intraepithelial neoplasia histopathology classification ⁽¹³⁾.

The World Health Organization classification, following the Lower Anogenital Squamous Terminology guidelines, has simplified the grading of cervical precancerous lesions into a two-tiered system. Low-grade squamous intraepithelial lesion corresponds to CIN 1, usually associated with transient HPV infection and low risk of progression. High-grade squamous intraepithelial lesion encompasses CIN 2 and CIN 3 and is considered precancerous and more likely to persist or progress to invasive carcinoma ⁽¹¹⁾.

CIN is a common premalignant lesion of the cervix, with prevalence varying worldwide depending on the availability and uptake of cervical cancer screening programs. CIN prevalence peaks in young adult women, typically between ages 25 and 35, corresponding with the period of highest HPV infection prevalence ⁽¹⁴⁾. The incidence of high-grade CIN increases slightly with age but remains highest in women under 40 years. Low- and middle-income countries face a higher cervical cancer burden due to limited access to screening and treatment, resulting in underdiagnosis of CIN and higher progression rates to invasive cancer ⁽¹⁵⁾.

Smoking is associated with increased CIN prevalence and progression risk due to local immunosuppression and carcinogenic effects on cervical epithelium. Immunocompromised individuals have a higher prevalence of persistent HPV infection and CIN progression ⁽¹⁴⁾. Early onset of sexual activity, multiple sexual partners, and having a partner with multiple partners increase HPV acquisition risk and thus CIN risk. Women with multiple full-term pregnancies have an increased risk of cervical cancer, potentially due to hormonal changes, cervical trauma during childbirth, or increased duration of HPV persistence. Infections such as Chlamydia trachomatis or herpes simplex virus may cause chronic inflammation and epithelial damage, facilitating HPV integration and lesion progression ⁽¹⁶⁾.

Human Papillomavirus and Cervical Carcinogenesis

Human Papillomavirus belongs to the virus family Papillomaviridae and is the primary cause of cervical cancer worldwide. Persistent infection with high-risk HPV types leads to the development of precancerous lesions and, if untreated, invasive cervical cancer ⁽¹⁾.

More than 200 HPV types have been identified, but high-risk types—especially HPV 16 and HPV 18—are responsible for approximately 70% of cervical cancers globally. Other high-risk types include HPV 31, 33, 45, 52, and 58. ⁽³²⁾

HPV infects the basal epithelial cells of the cervix, particularly at the transformation zone. The virus integrates its DNA into host cells, leading to expression of viral oncoproteins E6 and E7. E6 protein promotes degradation of the tumor suppressor protein p53, preventing apoptosis and enabling genetic mutations. E7 protein binds to the retinoblastoma protein, disrupting cell cycle regulation and promoting uncontrolled cell proliferation. These changes result in dysplasia, which can progress from cervical intraepithelial neoplasia to invasive carcinoma over several years.⁽³²⁾

Prevention and Vaccination of HPV

Using condoms reduces the risk of HPV transmission but does not eliminate it entirely, as HPV can infect areas not covered by condoms⁽¹⁷⁾. Limiting the number of sexual partners decreases the likelihood of exposure to HPV⁽¹⁾.

Human Papillomavirus vaccines protect against infection by certain types of HPV, which are linked to cervical cancer, other anogenital cancers, and some head and neck cancers⁽¹⁾⁽¹⁷⁾. The bivalent vaccine protects against HPV types 16 and 18. The quadrivalent vaccine protects against HPV types 6, 11, 16, and 18⁽¹⁸⁾. The nonavalent vaccine protects against nine HPV types: 6, 11, 16, 18, 31, 33, 45, 52, and 58⁽¹⁹⁾.

Vaccination is most effective when administered before the onset of sexual activity, typically between ages 9 and 14. Catch-up vaccination is recommended up to age 26⁽¹⁾. Recent evidence supports the efficacy of a single-dose vaccine schedule, which can improve global vaccine coverage and accessibility, especially in low-resource settings⁽²⁰⁾⁽²¹⁾.

	Cervarix	Gardasil	Gardasil 9
Gender	Females Only	Females and Males in the US Females only in the UK	Females and Males in the US
Age	9-25	9-26	Females 9-26 and Males 9-21
Recommended Age at Vaccination	11-12 in the US 12-13 in the UK	11-12 in the US 12-13 in the UK	11-12 in the US
HPV Strains the Vaccine Covers	HPV-16 and HPV-18	HPV-6, 11, 16 and 18	HPV-6, 11, 16, 18, 31, 33, 45, 52, and 58
Protects Against	Cervical Cancer	Anal, Cervical, Vulvar and Vaginal Cancer; Anogenital Warts; Vaginal, Vulvar, Cervical and Anal Intraepithelial Neoplasia	Anal, Cervical, Vulvar and Vaginal Cancer; Anogenital Warts; Vaginal, Vulvar, Cervical and Anal Intraepithelial Neoplasia
Dosage	3 over 6 month period	3 over 6 month period	3 over 6 month period

Figure 3. characteristics of vaccines against Human Papilloma virus⁽²²⁾.

Countries with widespread HPV vaccination have seen dramatic reductions in HPV infection rates, genital warts, and cervical precancerous lesions⁽²³⁾. The WHO Cervical Cancer Elimination Strategy was launched in 2020 as a global initiative to eliminate cervical cancer as a public health problem. The 90-70-90 targets include 90% of girls fully vaccinated with HPV vaccine by age 15, 70% of women screened with a high-performance test by ages 35 and 45, and 90% of women identified with cervical disease receiving appropriate treatment⁽¹¹⁾.

Screening and Diagnosis of CIN

Screening tests include Pap smear cytology, which detects abnormal squamous cells indicative of CIN, and HPV DNA testing, which identifies high-risk HPV types to improve risk stratification ⁽¹⁴⁾. Colposcopy allows magnified visual examination after acetic acid application to highlight abnormal epithelium. Directed biopsy is performed to confirm histological diagnosis and grade ⁽¹⁵⁾.

Multiple testing methods are introduced to assess HPV DNA. The Hybrid Capture 2 test detects 13 high-risk HPV types but does not specify genotypes. PCR-based tests amplify and identify specific HPV genotypes. mRNA-based tests detect E6/E7 oncogene expression indicating active infection. Next-generation sequencing tests provide detailed genotype profiling. Rapid point-of-care tests are suitable for low-resource settings. These methods enhance screening accuracy, enable early detection, and guide risk-based management ⁽²⁴⁾.

Visual inspection with acetic acid is commonly used in low-resource settings due to its cost-effectiveness and immediate results, although it has lower specificity compared with HPV DNA testing ⁽²⁵⁾.

Colposcopy

A colposcope is a specialized optical instrument used to magnify and illuminate the cervix, vagina, and vulva for the evaluation of precancerous lesions and other abnormalities. Modern colposcopes have evolved to incorporate high-resolution digital imaging, documentation systems, and artificial intelligence-based decision support, enhancing diagnostic accuracy and enabling more consistent interpretation. These technological advancements have also facilitated the use of colposcope imaging in low-resource settings through portable and mobile colposcopes, increasing access to cervical cancer screening and triage. Recent studies emphasize the integration of digital colposcopy with automated visual evaluation systems to improve the objectivity of cervical cancer screening ⁽²⁶⁾.

Colposcopes are generally categorized into optical and digital colposcopes, with further divisions based on design and function. Binocular colposcopes provide stereoscopic visualization. Digital colposcopes allow real-time imaging, documentation, and remote consultation. Portable and handheld colposcopes are compact devices designed for low-resource or outreach settings. AI-integrated colposcopes combine digital imaging with artificial intelligence to provide automated visual evaluation, reduce interobserver variability, and support cervical cancer prevention programs ⁽²⁷⁾.

Colposcopy is primarily indicated for the evaluation of women with abnormal cervical cancer screening results. It serves as a diagnostic follow-up to cytology, HPV testing, or visual inspection with acetic acid. Key indications include abnormal Pap smear, positive high-risk HPV test, suspicious cervical lesions, follow-up of previously treated cervical lesions, inconclusive or inadequate cytology, and evaluation of women at high risk. Recent guidelines emphasize colposcopy's role in risk-based management, recommending its use based on a combination of cytology, HPV genotype, and patient history ⁽²⁸⁾.

Colposcopy is a stepwise clinical procedure used to examine the cervix, vagina, and vulva under magnification for early signs of neoplasia. The patient is placed in the lithotomy position and a vaginal speculum is inserted to visualize the cervix. The cervix is initially examined under low magnification. Acetic acid is applied to the cervix, making areas of dysplasia appear white. The cervix is examined under varying magnification to assess lesion margins and vascular patterns. Lugol's iodine may be applied, and targeted biopsies are taken from the most suspicious areas. Findings are recorded and the patient is counseled on the results and follow-up plan ⁽²⁹⁾.

The diagnostic assessment during colposcopy is based on visual patterns of the cervical epithelium following the application of acetic acid and/or Lugol's iodine. Minor abnormal changes include thin acetowhite epithelium, irregular borders, fine mosaic, and fine punctation. Major abnormal changes include dense acetowhite epithelium, sharp lesion borders, coarse mosaic or coarse punctation, inner border sign, or ridge sign. Suspicious features for invasion include atypical vessels, irregular surface contour, friable tissue, and bleeding on contact. The accuracy of colposcopic diagnosis depends on the colposcopist's experience and adherence to standardized criteria. The use of AI-assisted digital colposcopy is emerging as a promising tool to improve consistency in lesion grading and reduce interobserver variability ⁽³⁰⁾.

2011 IFCCPC colposcopic terminology of the cervix ¹			
General assessment		- Adequate/inadequate for the reason ... (i.e.: cervix obscured by inflammation, bleeding, scar) - Squamo-columnar Junction visibility: completely visible, partially visible, not visible - Transformation zone types 1,2,3	
Normal colposcopic findings		Original squamous epithelium: - Mature - Atrophic Columnar epithelium - Ectopy Metaplastic squamous epithelium - Nabothian cysts - Crypt (gland) openings Deciduous in pregnancy	
Abnormal colposcopic findings	General principles	Location of the lesion: Inside or outside the T-zone, Location of the lesion by clock position Size of the lesion: Number of cervical quadrants the lesion covers, Size of the lesion in percentage of cervix,	
	Grade 1 (Minor)	Thin aceto-white epithelium Irregular, geographic border	Fine mosaic, Fine punctation
	Grade 2 (Major)	Dense aceto-white epithelium, Rapid appearance of acetowhitening, Cuffed crypt (gland) openings	Coarse mosaic, Coarse punctuation, Sharp border, Inner border sign, Ridge sign
	Non specific	Leukoplakia (keratosis, hyperkeratosis), Erosion Lugol's staining (Schiller's test): stained/non-stained	
Suspicious for invasion		Atypical vessels Additional signs: Fragile vessels, Irregular surface, Exophytic lesion, Necrosis, Ulceration (necrotic), tumor/gross neoplasm	
Miscellaneous finding		Congenital transformation zone, Condyloma, Polyp (Ectocervical/ endocervical) Inflammation,	Stenosis, Congenital anomaly, Post treatment consequence, Endometriosis

Figure 4. 2011 IFCCPC colposcopic terminology of cervix (Bornstein et al. ⁽⁸⁾).

To assess the severity of cervical lesions and guide decisions about treatment, the Swede Score is used especially in the context of cervical cancer screening and management of abnormal Pap smears. The Swede Score assigns points from 0 to 2 across five variables based on colposcopic findings ⁽³¹⁾.

Table 1. Swede Score variables used during colposcopy

Variable	Score 0	Score 1	Score 2
Acetowhitening	Transparent	Intermediate	Dense white
Margins and surface	Diffuse, indistinct margins	Regular/irregular with sharp margins	Rolled, peeling edges; coarse surface

Vessels	Fine, regular, reticular vessels	Absent or atypical but not coarse	Coarse punctation or mosaic pattern
Lesion size	<5 mm	5–15 mm	>15 mm or occupying ≥ 3 quadrants
Iodine staining	Normal (brown uptake)	Partial iodine uptake	No iodine uptake (yellow areas)

Management of CIN

CIN 1 represents transient HPV infection in most cases and often regresses spontaneously within 12–24 months. Observation and follow-up are preferred, especially in young or reproductive-age women. Repeat cytology and/or HPV testing at 12 months is recommended. If results remain abnormal, treatment may be considered. Ablative methods include cryotherapy, thermal ablation, or laser ablation when the entire transformation zone is visible and invasion is excluded. Excisional methods include loop electrosurgical excision procedure or cold-knife conization when the transformation zone is not fully visualized or endocervical involvement is suspected ⁽¹⁰⁾.

CIN 2 has a higher risk of progression but still has potential for regression, especially in young women. Management is tailored to patient age and future fertility desire. Observation with colposcopy and cytology may be used in younger women or those desiring fertility, while excisional treatment is preferred in women older than 25 years or those who have completed fertility. Loop electrosurgical excision is most commonly used due to low morbidity and good tissue yield. Cold-knife conization is reserved for endocervical involvement or suspicion of glandular lesions ⁽¹⁵⁾.

CIN 3 has a high risk of progression to invasive carcinoma if untreated. Excisional therapy is mandatory. Preferred options include loop electrosurgical excision procedure and cold-knife conization for lesions extending into the canal or when margin status is critical. Cytology and HPV testing are performed during follow-up ⁽¹⁵⁾.

Conclusion

Cervical intraepithelial neoplasia represents a spectrum of precancerous changes involving the squamous epithelial cells of the cervix, and persistent infection with high-risk HPV strains is the key etiologic factor. Screening tests include Pap smear cytology and HPV DNA testing, while colposcopy allows magnified visual examination and directed biopsy for histological diagnosis and grading. Because the disease can be effectively treated and largely prevented when caught early, it is essential to detect and manage its pre-invasive stages.

References

1. World Health Organization. (2023). Cervical cancer fact sheet. World Health Organization.
2. Arbyn, M., Snijders, P. J., Meijer, C. J., Berkhof, J., Cuschieri, K., Kocjan, B. J., & Poljak, M. (2020). 2020 list of human papillomavirus assays suitable for primary cervical cancer screening: A systematic review. *Clinical Microbiology and Infection*, 26(7), 892–900.
3. Dreyer, G., van der Merwe, F. H., & Becker, P. (2024). Re-evaluating transformation zone types and colposcopic outcomes in women screened with HPV testing: A prospective analysis. *International Journal of Gynecological Pathology*, 43(1), 10–19.
4. Rees, M., Pizzo, A., & Crosbie, E. J. (2021). The cervix and its transformation zone: An overview of structure, function, and significance in cervical pathology. *Obstetrics, Gynaecology & Reproductive Medicine*, 31(8), 243–250. <https://doi.org/10.1016/j.ogrm.2021.05.002>
5. Timmons, B., & Akins, M. L. (2023). The extracellular matrix of the human cervix and its dynamic role during pregnancy and labor. *Frontiers in Reproductive Health*, 5, 1132109. <https://doi.org/10.3389/frph.2023.1132109>

6. Yang, H., Sun, J., & Chen, X. (2024). Hormonal regulation and epithelial remodeling of the cervix across the menstrual cycle. *Journal of Reproductive Biology*, 72(2), 145–157. <https://doi.org/10.1016/j.repbio.2024.02.006>
7. Ghosh, I., Banerjee, D., & Singh, M. (2023). Morphological and hormonal influences on cervical transformation zone and its relevance to carcinogenesis. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 286, 45–52. <https://doi.org/10.1016/j.ejogrb.2023.02.015>
8. Bornstein, J., Bentley, J., Bösze, P., Girardi, F., Haefner, H., Menton, M., Perrotta, M., Prendiville, W., & Sideri, M. (2012). 2011 terminology of the International Federation for Cervical Pathology and Colposcopy. *Obstetrics and Gynecology*, 120(1), 166–172. <https://doi.org/10.1097/AOG.0b013e318254f90c>
9. Crosbie, E. J., Einstein, M. H., Franceschi, S., & Kitchener, H. C. (2023). Human papillomavirus and cervical cancer: From pathogenesis to prevention. *International Journal of Gynecology & Obstetrics*, 162(2), 245–255. <https://doi.org/10.1002/ijgo.14610>
10. Dillon, S. M., Brüssow, H., & Arbyn, M. (2022). Accuracy and effectiveness of HPV mRNA testing in cervical cancer screening: A systematic review and meta-analysis. *The Lancet Oncology*, 23(7), 950–960.
11. World Health Organization. (2020). WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention (2nd ed.). World Health Organization.
12. Egemen, D., Cheung, L. C., Kinney, W. K., & Castle, P. E. (2023). Risk estimates supporting the 2019 ASCCP risk-based management consensus guidelines for abnormal cervical screening tests. *Journal of Lower Genital Tract Disease*, 27(1), 1–10. <https://doi.org/10.1097/LGT.0000000000000721>
13. Chen, Y., Wang, X., & Li, J. (2023). Prevalence and genotype distribution of high-risk human papillomavirus among women in Xianning, China: a retrospective analysis from 2020 to 2022. *Virology Journal*, 21, Article 13.
14. Wentzensen, N., Schiffman, M., & Kinney, W. (2019). Accuracy of cervical cancer screening methods: A look at HPV primary screening versus cytology. *Journal of the National Cancer Institute*, 111(1), 72–80.
15. Massad, L. S., Einstein, M. H., Huh, W. K., et al. (2023). Colposcopy standards: Guidelines for endocervical curettage at colposcopy. *Journal of Lower Genital Tract Disease*, 27(1), e1–e10.
16. He, Y., Xia, L., & Wang, W. (2022). Cervical cancer screening and prevention: Review and perspectives. *Cancer Biology & Medicine*, 19(4), 383–397.
17. Centers for Disease Control and Prevention. (2023, April 4). Human papillomavirus (HPV) infection: STI treatment guidelines. U.S. Department of Health & Human Services.
18. Garland, S. M., Hernandez-Avila, M., Wheeler, C. M., Perez, G., Harper, D. M., Leodolter, S., ... Muñoz, N. (2007). Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *New England Journal of Medicine*, 356(19), 1928–1943.
19. Joura, E. A., Giuliano, A. R., Iversen, O. E., Bouchard, C., Mao, C., Mehlsen, J., ... Luxembourg, A. (2015). A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *New England Journal of Medicine*, 372(8), 711–723.
20. DoRIS Study Team. (2022). Immunogenicity and safety of one-dose human papillomavirus vaccine compared with two or three doses in Tanzanian girls (DoRIS): An open-label, randomised, non-inferiority trial. *The Lancet Global Health*, 10(10), e1473–e1484.
21. Prem, K., Choi, Y. H., Bénard, É., Burger, E. A., Hadley, L., & Laprise, J. F., ... et al. (2023). Global impact and cost-effectiveness of one-dose versus two-dose human papillomavirus vaccination schedules: A comparative modelling analysis. *BMC Medicine*, 21, Article 313.
22. World Health Organization. (2022). Human papillomavirus (HPV) vaccines: WHO position paper. *Weekly Epidemiological Record*, 97(31), 349–376.

23. Brisson, M., Kim, J. J., Canfell, K., Drolet, M., & the WHO Cervical Cancer Elimination Modelling Consortium. (2020). Impact of HPV vaccination and cervical screening on cervical cancer elimination: A comparative modelling analysis in 78 low-income and lower-middle-income countries. *Lancet*, 395(10224), 575–590.
24. Clifford, G. M., Tenet, V., & Franceschi, S. (2024). The evolving role of HPV DNA and mRNA testing in cervical cancer prevention. *Nature Reviews Clinical Oncology*, 21(2), 85–100.
25. Mohamed, A. A., Hemida, A. S., El-Khouly, N. I., & El-Kelani, O. A. (2022). Comparison of visual inspection with acetic acid and Pap smear for cervical cancer screening. *Menoufia Medical Journal*, 35(1), Article 38.
26. Hu, L., Mwanahamuntu, M. H., Sahasrabudhe, V. V., Barrett, C., Horning, M. P., Shah, I., ... Parham, G. P. (2023). Validation of automated visual evaluation (AVE) on smartphone images for cervical cancer screening in a prospective study in Zambia. *medRxiv*. Advance online publication.
27. Mwamba, M. H., Hu, L., & Sahasrabudhe, V. V. (2023). Integration of digital colposcopy with automated visual evaluation to improve cervical cancer screening in low-resource settings. *Infectious Agents and Cancer*, 18, Article 29.
28. Perkins, R. B., Guido, R. S., Castle, P. E., Chelmow, D., Einstein, M. H., Garcia, F., Huh, W. K., Kim, J. J., Moscicki, A.-B., Nayar, R., Sawaya, G. F., Wentzensen, N., & Schiffman, M. (2023). 2019 ASCCP risk-based management consensus guidelines for colposcopy and cervical cancer screening—updates through 2023. *Journal of Lower Genital Tract Disease*, 28(1), e3–e6.
29. López-Rodríguez, R., Pérez-Ortiz, M., & García-García, F. (2023). Digital colposcopy image analysis techniques requirements and their role in clinical diagnosis: A systematic review. *Journal of Medical Systems*, 47, Article 42.
30. Wu, A., Xue, P., Abulizi, G., Tuerxun, D., Rezhake, R., & Qiao, Y. (2023). Artificial intelligence in colposcopic examination: A promising tool to assist junior colposcopists. *Frontiers in Medicine*, 10, Article 1060451.
31. Knudsen, A. K. S., Randrup, T. H., Kesmodel, U. S., Booth, B., Gustafson, L., Tropé, A., Strander, B., Nieminen, P., & Hammer, A. (2024). Assessment of a colposcopic scoring system (Swedescore) to reduce the number of cervical biopsies: A protocol for a clinical multicentre non-randomised intervention study in Denmark. *BMJ Open*, 14(12), e085382.