S Table 2. Methods of Cervical Cancer Screening

Screening Tests	Performance				Advantages	Limitations	Remarks
	Sensitivity	Specificity	PPV	NPV			
1. Cervical Cytology Cells from transformation zone of the cervix are collected for cytological examination for dysplasia, pre-cancerous or cancerous changes	**Conventional Cytology**[40] Cells collected by a spatula or endo-cervical brush, smeared onto a microscope slide and fixed with ethyl alcohol				Conventional Cytology		Cytology
	[CIN2+]* 65.9% (54.9% – 75.3%)[40]	[CIN2+] 96.3% (94.7% – 97.4%)[40]	[CIN2+] 20.4% (18.3% – 22.7%)[41]		◆ Simple ◆ Easily available ◆ Low cost	◆ Sampling error (e.g. inadequate sample and/or slide preparation) may result in 20% false negative rate.[46] ◆ Risk of misinterpretation due to presence of obscuring material such as inflammatory cells, blood and overlapped epithelial cells.[47, 48] ◆ Do not allow for additional HPV and/or biomarkers testing using the same sample	◆ Sampling by trained healthcare professionals, may induce bleeding after the procedure ◆ Cervical cytology service should be provided by an accredited laboratory with appropriate quality assurance procedures ◆ Cytology reports should be issued by a qualified anatomical pathologist or (for negative results associated with absence of clinical findings) by a qualified cytotechnologist ◆ Reporting of cervical cytology should be based on the 2014 Bethesda System for Reporting Cervical Cytology
	Liquid-based Cytology[40] Cells collected using an endo-cervical brush and placed in liquid fixative solution				Liquid-Based Cytology		
	[CIN2+] 75.5% (66.6% – 82.7%)[40]	[CIN2+] 91.9% (88.4% – 94.3%)[40]	[CIN2+] 10.1% (8.7% – 11.3%)[42]	[CIN2+] 98.8% (98.3% – 99.2%)[42]	◆ Lower rate of unsatisfactory sample[6] ◆ Allows for additional HPV and/or biomarkers testing using the same sample	◆ More costly as requires further processing using automated device ◆ Sampling error may result in inadequate sample for HPV testing requiring re-sampling	
2. HPV Testing Cells from the cervix or vagina are tested for the presence of specific DNA or RNA sequences of high-risk human papilloma virus (HPV-16, 18, 31, 33, 45, 52, and 58[43]	**Clinical Sample**[40] Cells from the cervix are collected by healthcare professional using an endo-cervical brush and placed in either in liquid fixative solution or HPV test transport medium				Clinical HPV Sample		
	[CIN2+] 97.2% (95.6% – 98.4%)[41]	[CIN2+] 88.7% (88.3% – 89.0%)[41]	[CIN2+] 15.0% (13.9% – 16.1%)[41]		◆ Superior sensitivity and slightly lower specificity than cervical cytology in detecting HPV-associated CIN grade 2 or worse (CIN2+), ◆ Earlier detection of cervical precancerous lesions than cytology.[24, 40, 49] ◆ Higher reproducibility, reduced reliance on screener competency, and greater potential for automation[6] ◆ HPV-negative status was associated with lower cumulative risk of CIN2+/CIN3+, hence interval of HPV-based screening method can be extended to 5 years[26] ◆ HPV-based testing starting at age 30 every five years offers the most favorable harm-to-benefit ratio, resulting in increased life years gained and a reduced rate of colposcopies.[50] ◆ Potentially more cost-effective	◆ More false-positive results and higher colposcopy rates necessitate triage testing necessary ◆ False-negative as there exists a variety of HPV-independent cervical neoplasm	◆ Only clinically validated HPV tests should be used ◆ Laboratory standard operating procedures and quality assurance programmes should be in place for use of any HPV testing procedures ◆ Reports should be issued by an accredited laboratory with participation in quality assurance programmes[6]
	Self-sampling HPV Test Cells from the vagina are collected by the client using a swab, and sent to the laboratory in HPV test transport medium				Self-Collected HPV Sample		
	[CIN2+] 40 – 94.6% (5.3% – 85.3%, 90.7% – 98.5%)[44, 45]	[CIN2+] 85% (75.3% – 92%, 84.4% – 86.3%)[44, 45]			◆ Convenient ◆ More comfortable (compared to speculum examination) ◆ Potential to increase cervical cancer uptake by overcoming of barriers such as embarrassment and fear of pain[51]	◆ Education required on proper self-sampling technique ◆ Likely user-dependent, accuracy varies across study[44] ◆ Local data not yet available, study on the validation of HPV self-sampling test is underway	◆ There should be validation of sampling devices for self-collected vaginal specimens, and performance and regulatory approval of HPV tests for self-collected specimen[6]

HPV = Human Papillomavirus; CIN = Cervical Intraepithelial Neoplasia

*CIN2+ refers to Cervical Intraepithelial neoplasia 2 or above and is equivalent to High-grade Squamous intraepithelial lesion (HSIL)