S Table 3. Screening Strategies for Cervical Cancer Screening

Ctrotonica	Performance				Considerations
Strategies	Sensitivity	Specificity	PPV	NPV	Considerations
1. Cytology+ HPV testing Co-test on the same LBC sample	[CIN2+] 63.4% (56.7- 70.1) <sup>52</sup>	[CIN2+] 95.1% (94.8-95.3) <sup>52</sup>	[CIN2+] 17.8% (15.8-19.8) <sup>52</sup>	[CIN2+] 99.4% (99.2-99.5) <sup>52</sup>	<ul> <li>HPV-based co-test leads to 40% lower risk of invasive cervical carcinoma when compared with cytology alone.<sup>28</sup></li> <li>Co-testing led to earlier detection of clinically significant pre-invasive lesions.<sup>53</sup></li> <li>Women who are cotest negative have a lower 5-year risk of CIN3+ (0.12%) compared to following a negative cytology alone (ranged from 0.33-0.52%).<sup>54</sup></li> </ul>
2. Cytology+ Reflex HPV testing if ASCUS cytology is found	[CIN2+] 40.6% (36.1- 45.1) <sup>52</sup>	[CIN2+] 97.3% (97.1- 97.5) <sup>52</sup>	[CIN2+] 24.8% (22.3- 27.4) <sup>52</sup>	[CIN2+] 98.7% (98.5- 98.9) <sup>52</sup>	<ul> <li>Among women with ASCUS cytology, 50% are high risk HPV carriers<sup>55</sup>, who are more likely to have high-grade lesions (CIN2/3).<sup>56</sup></li> <li>No role for LSIL or above due to high prevalence of high-risk HPV.<sup>57</sup></li> </ul>
3. Primary HPV testing+ Reflex genotyping+ cytology if high risk HPV is positive	[CIN2+] 64.8% (58.4- 71.1) <sup>52</sup>	[CIN2+] 95.2% (95- 95.5) <sup>52</sup>	[CIN2+] 18.5% (16.4- 20.6) <sup>52</sup>	[CIN2+] 99.4% (99.2- 99.5) <sup>52</sup>	The lower specificity of a positive HPV test necessitates a triage test by cytology or genotyping to determine referral for colposcopy.6 HPV stand-alone test led to a significantly increased colposcopy rate: from 2.3% to 13.1% with HPV testing versus 1.9% to 4.7% with cytology in < 30-35 years; from 0.9% to 5.8% with HPV testing versus 1.0% to 2.5% with cytology in > 30-35 years.6  mous Cells of Undetermined

HPV = Human Papillomavirus; CIN = Cervical Intraepithelial Neoplasia; ASCUS = Atypical Squamous Cells of Undetermined Significance; LBC = Liquid Based Cytology; PPV = Positive Predictive Value; NPV = Negative Predictive Value