Introduction/Background WHO guidelines recommend HPV-PCR testing for primary screening. Due to low specificity (~20%) for detecting true dysplasia triage is necessary to avoid over-diagnosis and overtreatment. Because of its higher specificity (~60–80%), mRNA-based testing of cellular transformation-specific biomarkers is highly accurate in detecting clinically relevant pre-cancer. We report results of an innovative mRNA assay (QuantiGene-Molecular-Profiling-Histology, QG-MPH) on samples from real-world HIC and LMICs screening/ triage routine and its potential to detect pre-cancer compared to standard of care.

Methodology QG-MPH (ThermoFisher) and targeted sequencing (ciRNaseq, Predica) were used for multiplexed mRNA quantification of 18 HR-HPV oncogenes and cellular-biomarkers in cervical smear samples. Accuracy to identify CIN2+, CIN3+ and invasive cancer was calculated on condition-specific risk scores (ROC analysis: AUC >80% for CIN2/3 and >92% for invasive cancer). Study smear samples from screening and triage populations in HIC (n=550, n=719) and LMIC (n=893, n=110), respectively, were reanalyzed and results compared to standard of care assays. Study results were descriptively evaluated in the given context.

Results The QG-MPH assay discriminated <CIN2/CIN2+ lesions with higher accuracy than cytology or PCR. QG-MPH assay outperformed cytology (sens. >80% vs 50%; spec. 83% vs 80%) and PCR-based or co-testing strategies (sens. 83% vs 80%; spec. >80 vs 25–70%), respectively. Results are comprehensive diagnoses from the first screening smear within 48h. It reports i) 18 HR-HPV genotypes individually, ii) identifies and discriminates <CIN2 vs CIN2+ vs CIN3+ vs invasive cancer and iii) is prognostic for lesion development. Its high accuracy supports decision making on treatment strategies. Low complexity workup, robust transportable instruments and assay cost comparable to PCR-based tests allows use in LMIC.

Conclusion Molecular biomarker-based mRNA testing has the potential to solve current diagnostic problems of cervical cancer screening. Higher assay accuracy can reduce over-referral and restrict treatment to progressive lesions when indicated by biomarker expression reducing overtreatment of regressive dysplasia.

Disclosures QG-MPH patented by Charite-Universitaetsmedizin Berlin.

ciRNaseq patented by WL.