

CERVICAL CANCER SCREENING

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Box S1 PICOS components of the research question

P: Women participating in hrHPV screening for cervical cancer, with a positive hrHPV DNA test result

I: (1) Reflex cytology triage at a threshold of ASC-US+ (used as comparator for the other triage options); (2) triage with VIA; (3) triage with HPV16/18 genotyping; (4) triage with cytoimmunochemistry for protein markers p16/Ki-67 (dual staining); (5) combination of HPV16/18 genotyping and cytology at a threshold of ASC-US+; (6) combination of HPV16/18 genotyping and VIA

Note: Triage options 5 and 6 mean that women with HPV16 and/or HPV18 infection are referred for diagnostic workup, whereas women who are positive only for other hrHPV types undergo triage with cytology at a threshold of ASC-US+ (option 5) or VIA (option 6).

C: Reflex cytology triage at a threshold of ASC-US+

O: Cross-sectional and/or longitudinal accuracy to detect histologically identified disease (CIN2+, CIN3+/AIS, and invasive cervical cancer); triage test positivity rate; referral rate for colposcopy; PPV for CIN2+ and CIN3+; risk of CIN2+, CIN3+, and cancer after negative triage testing

S: Follow-up of randomized trials comparing cytology with HPV-based screening and applying different follow-up algorithms. Complete diagnostic studies (all subjects tested with triage method and verification with the reference standard of colposcopy or targeted biopsy). Incomplete diagnostic studies, where subjects who underwent multiple triage tests had verification with the reference standard (colposcopy or targeted biopsy) or where outcome assessment was assured through comprehensive screening or follow-up or cancer registries. Cohort studies applying at least two alternative triage algorithms involving verification with the reference standard if there is one or more positive triage test result

AIS, adenocarcinoma in situ; ASC-H+, atypical squamous cells, cannot exclude HSIL or worse; ASC-US+, atypical squamous cells of undetermined significance or worse; CIN2+, cervical intraepithelial neoplasia grade 2 or worse; CIN3+, cervical intraepithelial neoplasia grade 3 or worse; HPV, human papillomavirus; hrHPV, high-risk human papillomavirus; HSIL+, high-grade squamous intraepithelial lesion or worse; LSIL+, low-grade squamous intraepithelial lesion or worse; PICOS, population, intervention, comparator, outcome, and studies; PPV, positive predictive value; VIA, visual inspection with acetic acid.