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# Performance of short-term repeat HPV testing, HPV viral load and HPV16/18 genotyping for triage of HPV positive women in Latin America

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**Background.** A single HPV test is highly sensitive for precancerous cervical lesions but has limited specificity leading to unnecessary referral. We aimed to evaluate the performance of short-term repeat HPV testing, semi-quantitative HPV viral load, and HPV16/18 genotyping for triage of HPV positive women in the ESTAMPA study. **Methods.** ESTAMPA is a multicentric study across Latin America in which women aged 30-64 years are screened with HPV testing (HC2 or Cobas) and Pap, and referred to colposcopy if positive for either test. We evaluated the performance of short-term repeat HPV test done at colposcopy ~2 months after enrolment, viral load reflected by HC2 relative light units (RLU), and HPV16/18 genotyping by Cobas for the detection of cervical intraepithelial neoplasia grade 3 or more severe (CIN3+) in screened HPV positive women. Results were adjusted by age, study centre, and time to repeat HPV testing using random intercepts from linear mixed models. **Results.** 3,122 and 1,434 participants testing positive for HC2 and Cobas, respectively, were included in the analyses, of which 283 and 201 had CIN3+. The adjusted risk of CIN3+ in HPV positives was 8.8% (95%CI 6.7-10.8) for HC2 and 11.5% (95%CI 5.2-17.9) for Cobas. Positive predictive values (PPVs) of repeat HPV testing were 13.6% (95%CI 11.0-16.1) for HC2 and 16.4% (95%CI 11.1-21.8) for Cobas, with sensitivities greater than 80% (83.4% [95%CI 76.1-90.8] and 90.2% [95%CI 82.6-97.7], respectively), and referral rates around 60% (56.7% [95%CI 52.6-60.7] and 67.6% [95%CI 62.3-72.8], respectively). The performance of HC2 RLU≥10 (moderate/high viral load) was similar to repeat HC2 (PPV: 13.1% [95%CI 10.4-15.8], sensitivity: 83.3% [95%CI 76.2-90.4], and referral rate: 57.6% [95%CI 54.2-60.9]); while HC2 RLU≥100 (high viral load) had a higher PPV (20.0% [95%CI 17.3-22.7]) and lower referral rate (28.8% [95%CI 24.5-33]) but sensitivity was limited (59.3% [95%CI 52.5-66.1]). The sensitivity of combined approaches with repeat HPV testing in women with RLU<10 (93.3% [95%CI 90.4-96.2]) or RLU<100 (87.7% [95%CI 83.7-91.6]) was higher than strategies separately, although at the expense of a greater referral rate (72.1% [95%CI 69.7-74.4], and 62.5% [95%CI 59.7-65.3], respectively). The performance of HPV16/18 genotyping was similar to having a high viral load (PPV: 24.1% [95%CI 13.2-34.9], sensitivity: 59.4% [95%CI 41.8-77], and referral rate: 28.1% [95%CI 20.8-35.4]). The sensitivity of HPV16/18 genotyping with repeat HPV test for non-16/18 positives was similar to repeat HPV testing alone (91.7% [95%CI 85.2-98.2]) but the referral rate was higher (73.9% [95%CI 69.5-78.4]). **Conclusions.** Short-term repeat HPV testing alone or in combination with HPV testing intrinsic characteristics seems to be useful for triage of HPV positive women. This triage approach may have the potential to better guide clinical management of HPV positives in the short-term with the advantage of not requiring additional tests such as cytology or visual techniques which is appealing, even more in the context of self-sampling.

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