

## THE DIAGNOSTIC VALUE OF *p16/Ki67* DUAL STAINING IN HPV-POSITIVE WOMEN: HOW EFFECTIVE IS IT FOR SCREENING CIN2+ LESIONS A 5-YEAR PERIOD?

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**Introduction:** Accurate detection of high-grade squamous intraepithelial lesions (HSIL), particularly CIN2+ and CIN3+, in HPV-positive women is essential for cervical cancer prevention. Dual immunostaining with *p16/Ki67* has been proposed as an objective triage strategy to improve diagnostic performance. **Objectives:** To assess the diagnostic accuracy of *p16/Ki67* dual staining for detecting CIN2+ and CIN3+ in HPV-positive women through a systematic review and meta-analysis. **Methods:** A systematic review and meta-analysis were conducted following PRISMA-DTA guidelines. Eight observational prospective studies, including 12,810 HPV-positive women, were analyzed. Outcomes included pooled sensitivity, specificity, positive and negative likelihood ratios (LR<sup>+</sup>/LR<sup>-</sup>), diagnostic odds ratio (DOR), and area under the SROC curve (AUC). A bivariate random-effects model was used. Meta-regression and subgroup analyses assessed sources of heterogeneity. Publication bias was examined using Deeks' test. **Results:** For CIN2+, pooled sensitivity was 0.83 (95% CI: 0.79–0.87; I<sup>2</sup> = 65.67%) and specificity was 0.60 (95% CI: 0.50–0.68; I<sup>2</sup> = 62.27%). The diagnostic odds ratio (DOR) was 7.0 (95% CI: 5–11), with AUC of 0.80 (95% CI: 0.76–0.83). For CIN3+, sensitivity was 0.87 (95% CI: 0.82–0.91; I<sup>2</sup> = 67.94%) and specificity was 0.55 (95% CI: 0.42–0.67; I<sup>2</sup> = 53.40%), DOR of 8.0, and AUC of 0.80. Meta-regression identified SurePath, ThinPrep, prospective design, and follow-up ≥5 years as modifiers of

sensitivity and specificity ( $p < 0.05$ ). Bayesian modeling estimated post-test probabilities of 41% (CIN2+) and 39% (CIN3+) after positive results. No publication bias was detected. **Conclusion:** Dual staining with *p16*/Ki67 offers acceptable diagnostic accuracy for detecting CIN2+ and CIN3+ in HPV-positive women. Standardized protocols and longer follow-up enhance its performance in clinical screening.

**Keywords:** P16/Ki67; Dual staining; Cervical intraepithelial neoplasia; HPV