

HPV 16 Confers a 6.65-Fold Adjusted CIN2+ Risk at Colposcopy Independent of Cytology. Evidence from 11,307 Women with Documented HPV Status

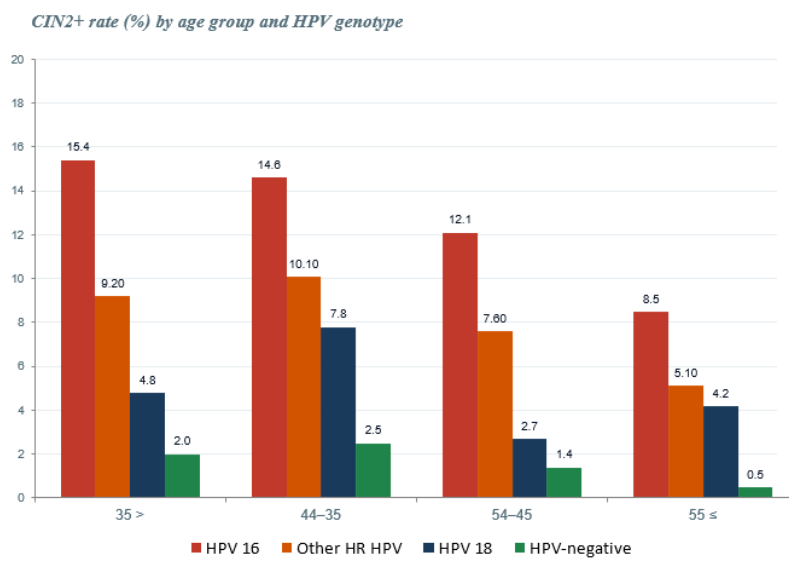
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Introduction: HPV 16 is the leading oncogenic genotype, but its independent contribution to CIN2+ risk at colposcopy beyond cytology grade has not been well quantified in large real-world cohorts. This study evaluated the adjusted association between HPV genotype and CIN2+ in women undergoing colposcopic biopsy.

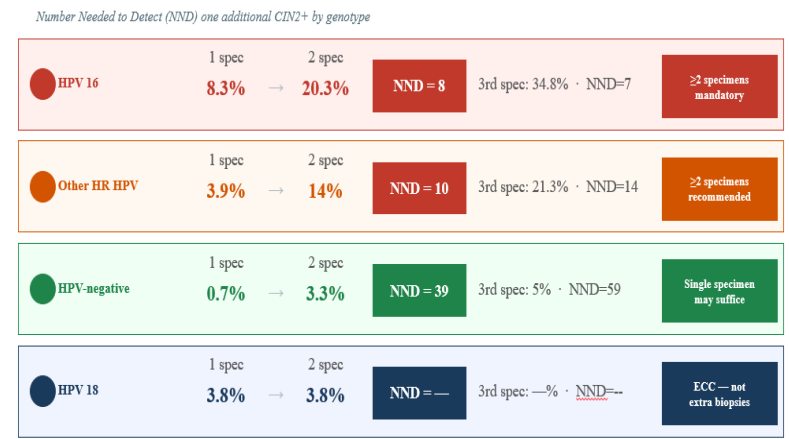
Methods: We conducted a retrospective study of 11,307 colposcopic biopsies from Assuta clinics during 2020-2026 in women with documented HPV status. HPV was classified as HPV 16, HPV 18, other high-risk HPV, or HPV-negative. Cytology was categorized as HSIL, ASCH, ASCUS, LSIL, or normal. The outcome was CIN2+ based on SNOMED histopathology. Multivariable logistic regression adjusted for cytology grade, age, clinic site, and visit type. Ethics approval: ASMC-0021-26.

Results: CIN2+ was identified in 835/11,307 women (7.4%). HPV 16 was the strongest independent predictor beyond cytology (aOR 6.65, 95% CI 4.22–10.48; $p < 0.001$), followed by HPV 18 (aOR 3.24) and other high-risk HPV (aOR 3.16). After adjustment for HPV genotype, LSIL and ASCUS were not independently associated with CIN2+. The highest CIN2+ rate was observed in women with HPV 16 plus HSIL (43.2%), and the lowest in HPV-negative women with normal cytology (1.6%). Rishon LeZion was the strongest site-level predictor (aOR 2.82).

Age Modifies Risk - Most Strongly for HPV 16



Who Benefits from a Second Specimen?



27× Range in CIN2+ Risk

Observed CIN2+ rate by HPV genotype × cytology category — all program encounters

	HPV 16	HPV 18	Other HR HPV	HPV-negative
Highest: 43.2% → HSIL	43.2%	35.0%	47.8%	28.3%
ASCH	28.1%	15.8%	18.8%	14.3%
LSIL	14.7%	3.4%	6.7%	2.1%
ASCUS	22.4%	1.0%	5.2%	2.6%
Normal	11%	9.8%	7.4%	1.6%

▲ Normal cytology + HPV 16 = 11.0% CIN2+ → above ASCCP 4% colposcopy threshold — Lowest: 1.6%

Against ASCCP 2019: Where Risk Crosses the Line

ASCCP 2019: ≥4% CIN3+ five-year risk → immediate colposcopy | This analysis uses CIN2+ endpoint (conservative reference)

↑ Above 4% threshold		↓ Below 4% threshold	
Normal + HPV 16	11.0% Biopsy warranted despite normal cytology	LSIL + HPV-negative	2.1% Minimal risk - observation appropriate
LSIL + HPV 16	14.7% Manage as ASCH - not standard LSIL	ASCUS + HPV-negative	2.6% Below threshold - surveillance, not biopsy
ASCUS + HPV 16	22.4% Highest-risk ASCUS encounter in program	ASCUS + HPV 18	1.0% ECC over biopsy - low exocervical risk
All ASCH	~19% High priority regardless of HPV genotype	LSIL + HPV 18	3.4% Borderline - ECC advisable
Normal + HPV 18	9.8% Endocervical AIS risk - ECC indicated		

Conclusions: HPV 16 independently and substantially increases CIN2+ risk beyond cytology grade. In contrast, LSIL and ASCUS are not significant after adjustment for HPV genotype. These findings support HPV genotype-based colposcopy risk

HPV 16: The Independent Driver of CIN2+ Risk at Colposcopy

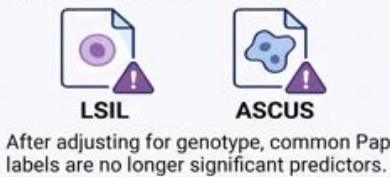
To demonstrate that HPV genotype (specifically 16 and 18) is a more powerful predictor of high-grade cervical lesions than cytology and should dictate clinical management.

6.65x Higher Risk with HPV 16
11,307 women Study at Assuta Medical Centers (2020–2026) shows HPV 16 is the strongest independent predictor of CIN2+.



The Power of Genotype Over Cytology

Cytology Alone is Deceptive.



27-Fold Risk Gradient

Cytology Result	HPV 16+ (Risk)	HPV Negative (Risk)
Normal	11.0%	1.6%
LSIL	14.7%	2.1%
HSIL	43.2%	28.3%

New Clinical Protocols

Mandatory Biopsy for HPV 16
HPV 16+ women with normal cytology/colposcopy still carry 11% risk and require biopsy.

Mandatory ECC for HPV 18
HPV 18 targets the endocervical canal; ECC is essential as exocervical biopsies often miss disease.

Sampling Intensity by Genotype
LSIL with HPV 16 should be managed as high-priority (similar to ASCH) regardless of appearance.