2026년 대한부인종양학회
제7회 동계학술대회 with Chemo-TIP Review
일자 2026년 1월 17일 (토)
장소 세종대학교 컨벤션센터

Trends and Strategic Approaches in Cervical Cancer Screening

Sung Jong Lee
Seoul St.Mary's Hospital, The Catholic University of Korea

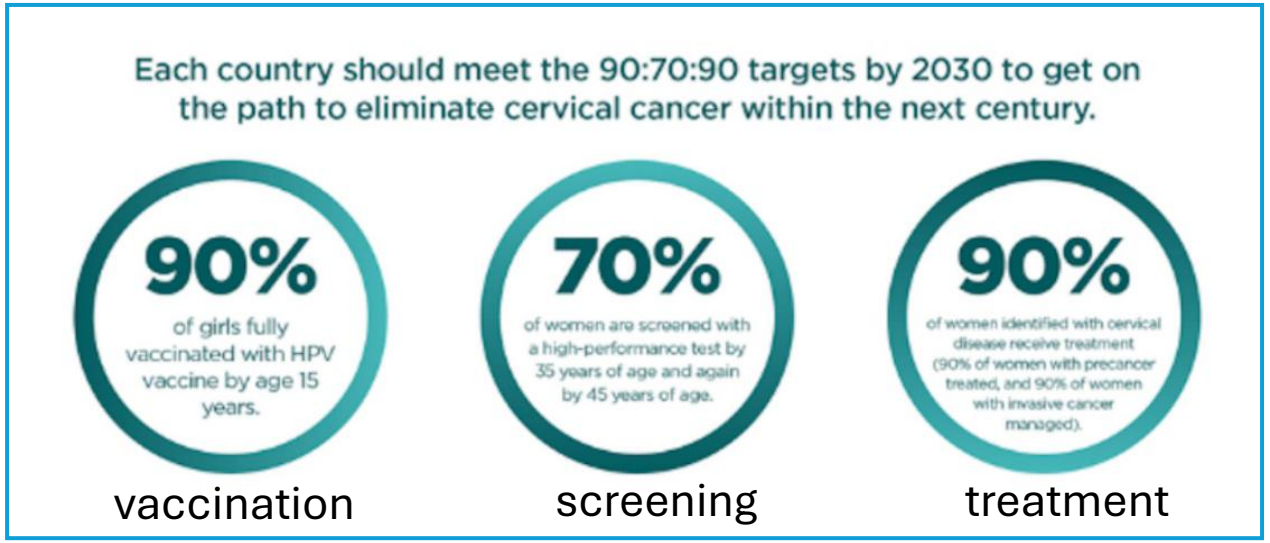
DECLARATION OF INTERESTS

Nothing to declare

WHO screening test

- A identifies potential, unrecognized diseases in asymptomatic people through rapid tests, aiming to detect early-stage issues for better treatment outcomes, not to diagnose definitively.

Cervical Cancer Elimination Initiative

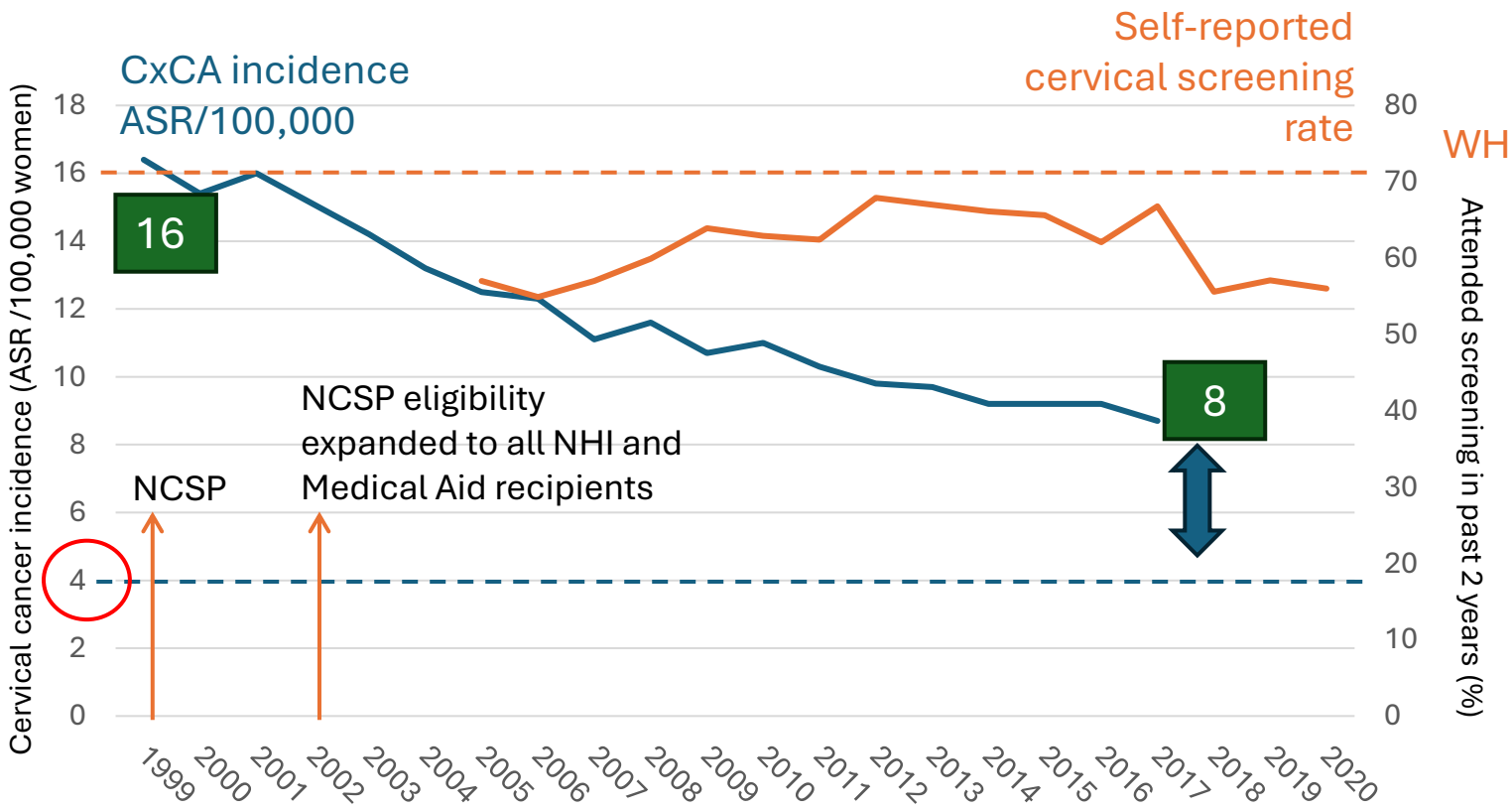


- To eliminate cervical cancer, all countries must reach and maintain an incidence rate of below 4 per 100 000 women.
- vaccination: 90% of girls fully vaccinated with the HPV vaccine by the age of 15;
- screening: 70% of women screened using a high-performance test by the age of 35, and again by the age of 45;
- treatment: 90% of women with pre-cancer treated and 90% of women with invasive cancer managed.
- Each country should meet the 90–70–90 targets by 2030 to get on the path to eliminate cervical cancer within the next century.

Overview

- Background
- Clinical validation for HPV tests
- Cytology + HPV co-testing
- Current status of HPV test

Korea's progress in Cervical Cancer Screening and Elimination

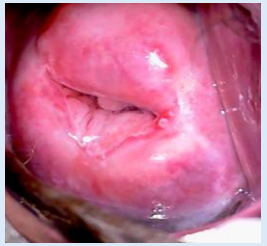
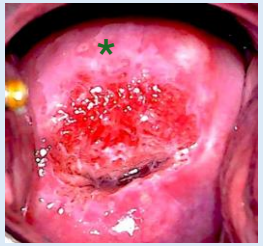
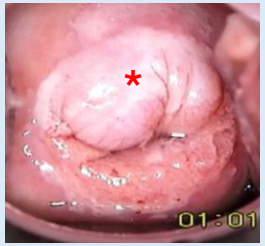
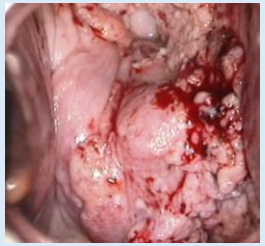
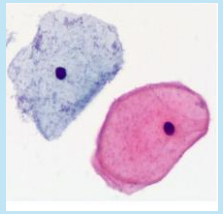
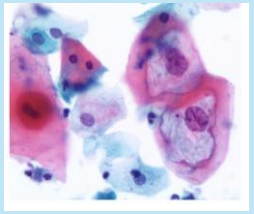
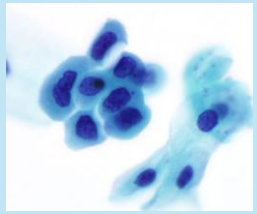
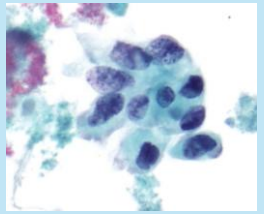


Better screening strategy is needed to achieve WHO's target screening and incidence rates

NCSP: National Cervical Screening Program

Ha et al. Obstet Gynecol Sci. 2021 Sep;64(5):444-453.
Shin et al. J Gynecol Oncol. 2022 Feb 11;33(4):e39.

Cervical screening methods

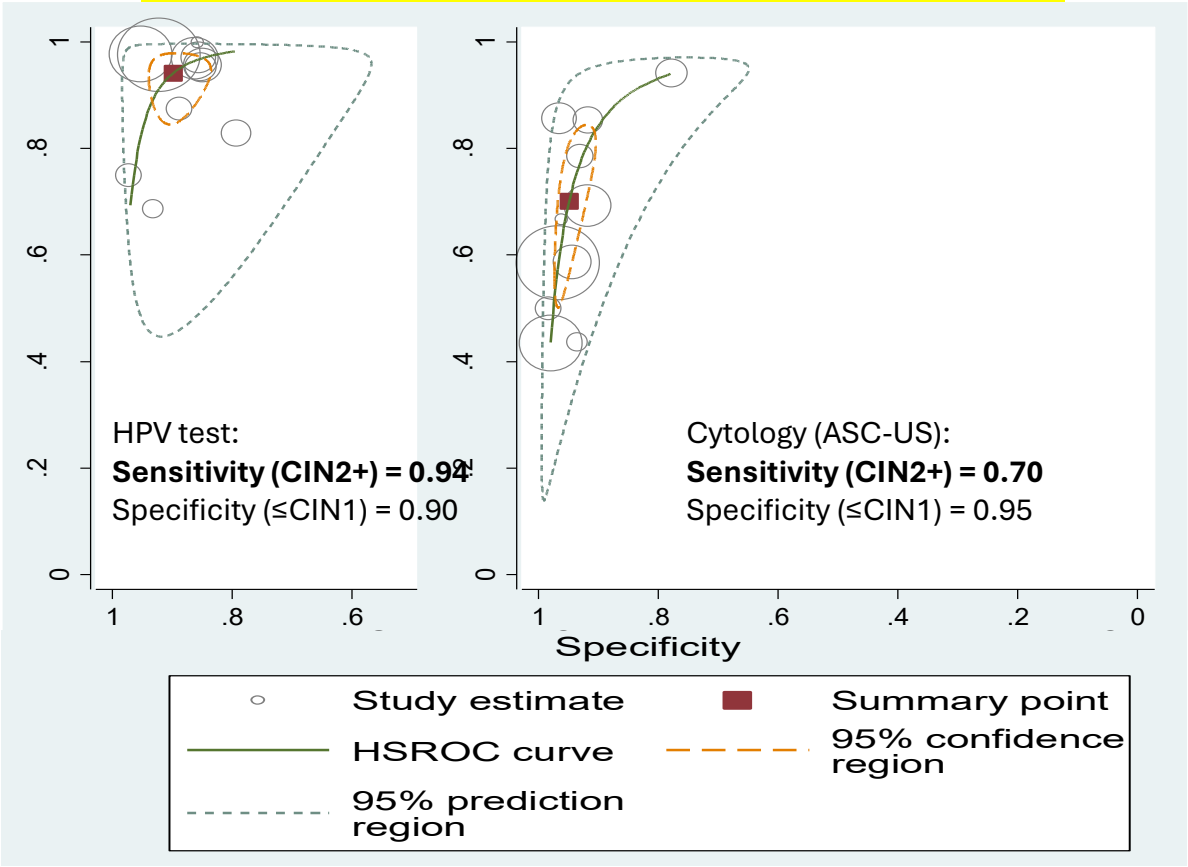
	Normal / Low-grade	High-grade / Cancer	Sensitivity for CIN2+	Specificity for ≤ CIN1
	NILM ⇄ CIN1	CIN2 ⇄ CIN3 → Cancer		
Visual Inspection with Acetic acid (VIA)	 Negative	 Negative/ Low grade	 Positive	 Suspicious for Cancer	66%	87%
Cytology (Pap smear)	 NILM	 ASC-US/LSIL	 HSIL	 SCC	76%	92%
HPV DNA test	Neg/Pos	Positive	Positive	Positive	**93%**	89%

Web Annex A, WHO cervical screening guidelines 2nd Ed (Jul 2021) https://www.who.int/publications/i/item/9789240030824
Koliopoulos et al. Cochrane Database Syst Rev. 2017 Aug 10;8(8):CD008587.

HPV-based screening significantly increases sensitivity for CIN2+

WHO Meta-analysis (11 studies, n=39,050):

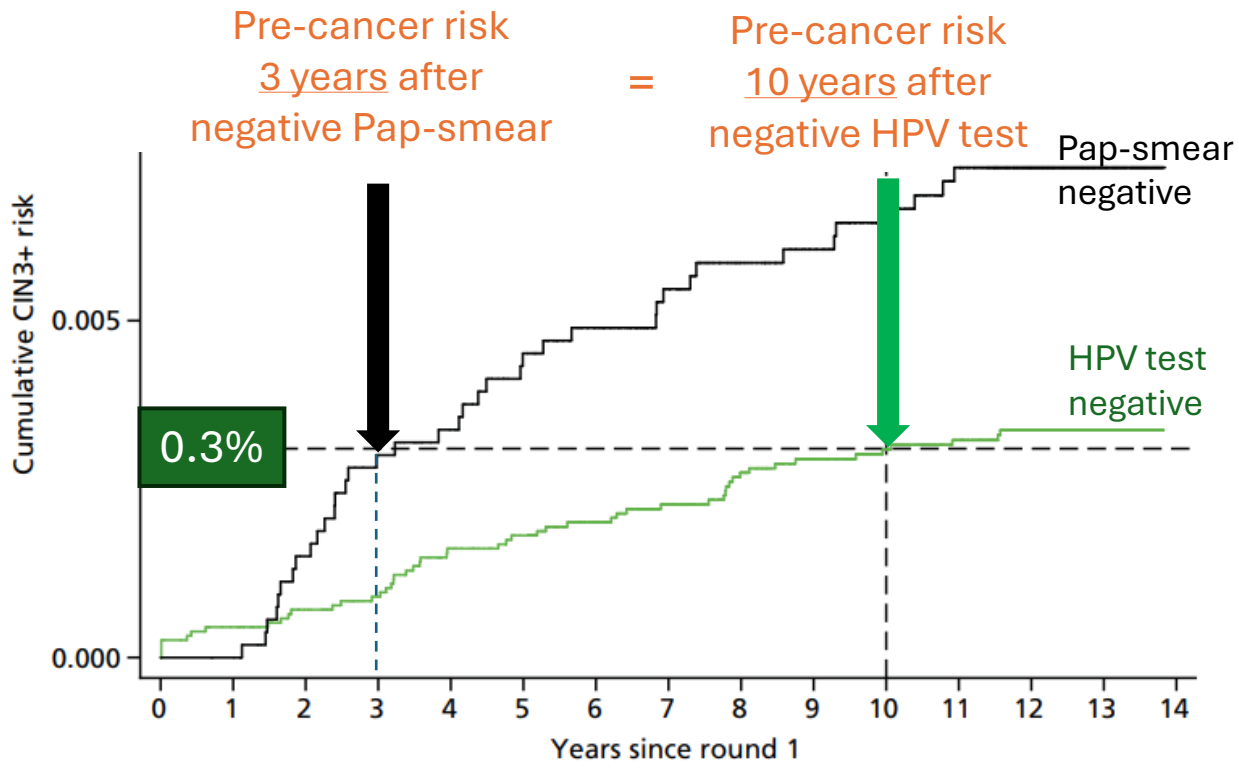
HPV tests had higher baseline sensitivity for CIN2+



Mustafa et al. Int J Gynaecol Obstet. 2016 Mar;132(3):259-65.

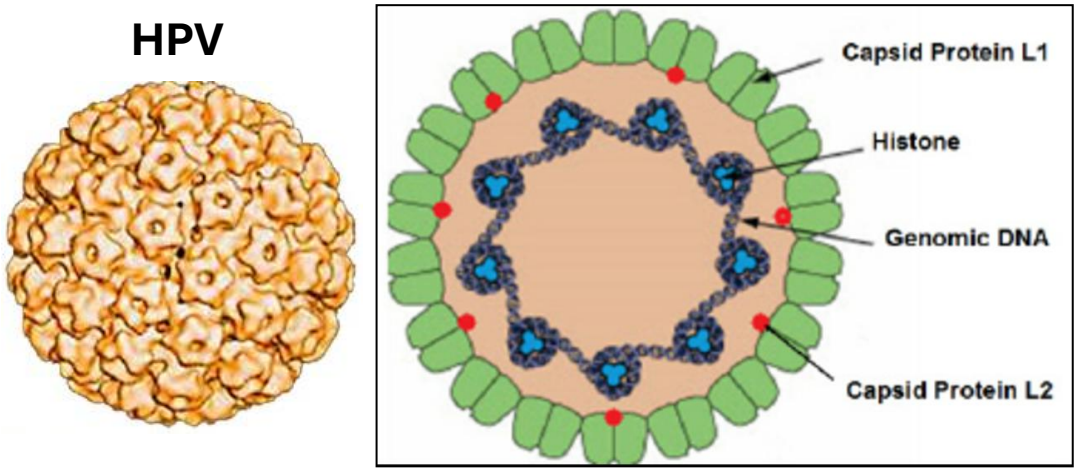
UK ARTISTIC Study (n=24,496 women, 15y follow-up)

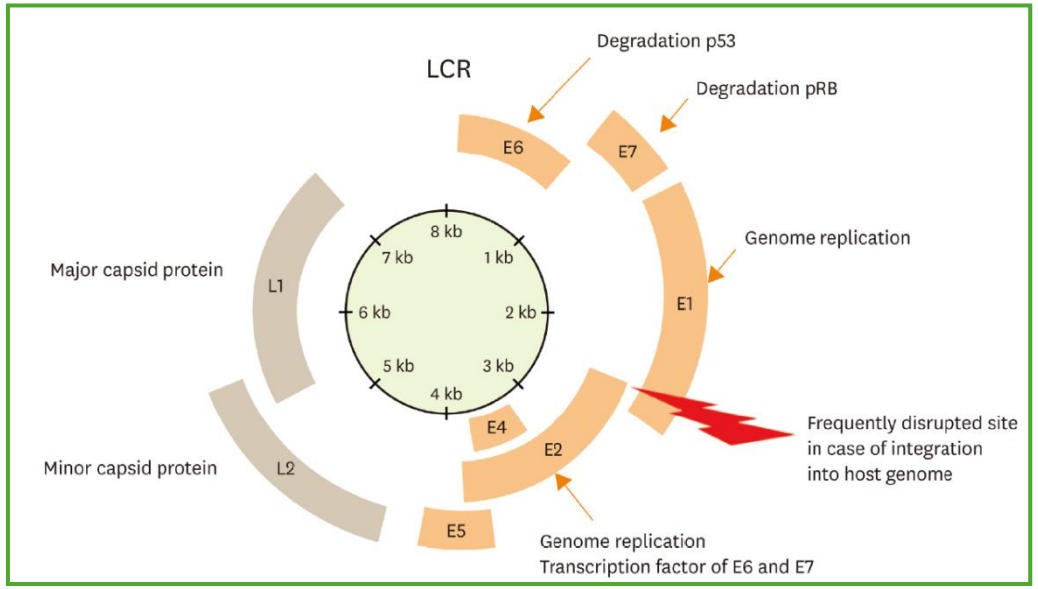
A negative HPV result had a lower risk of CIN3+ over time



Gilham et al. Health Technol Assess. 2019 Jun;23(28):1-44.

The Structure of HPV





Double stranded DNA genome

8,000 base pairs that is covered with capsid proteins

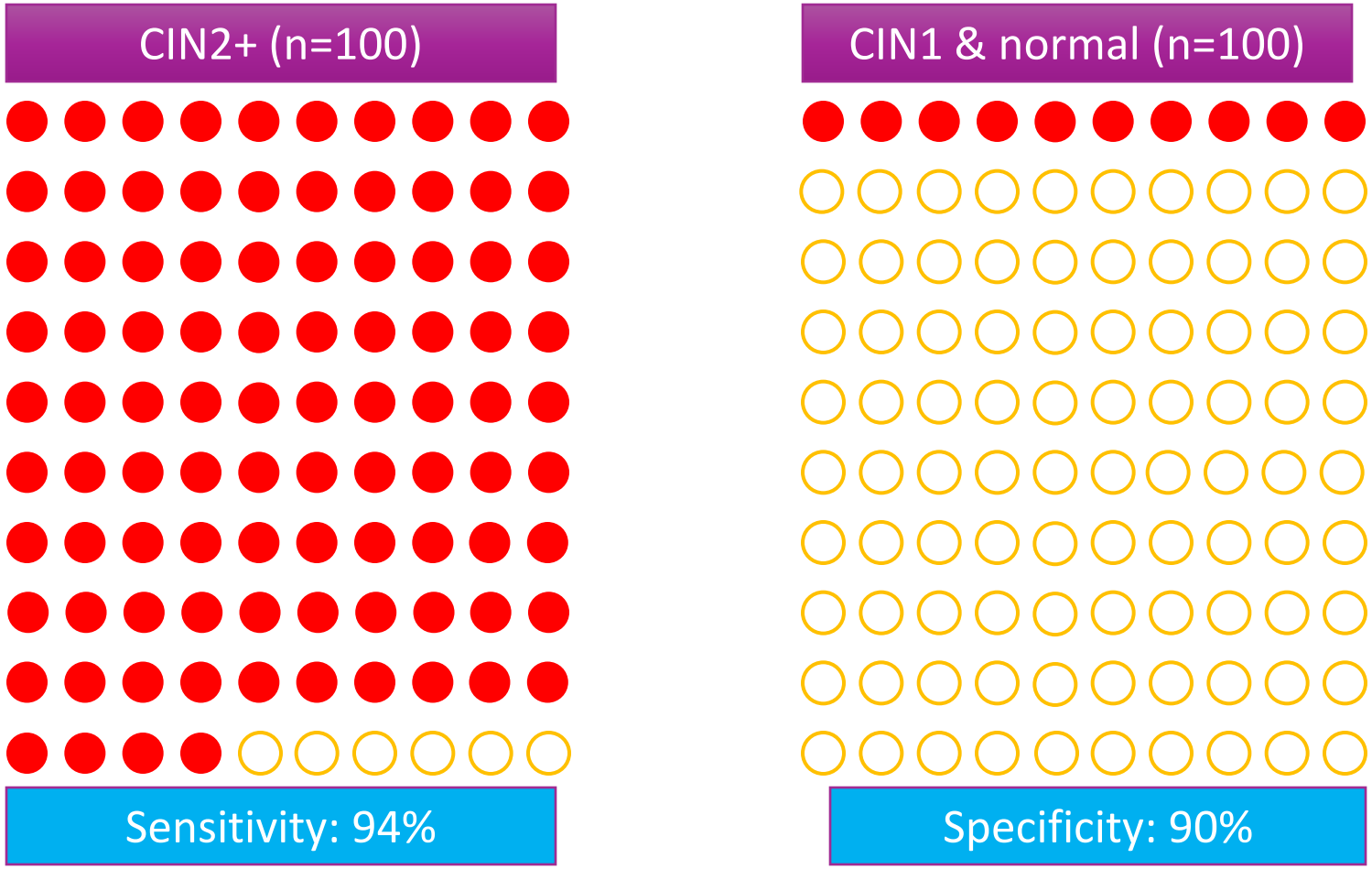
Integration process leads to deletion of many early (E1, E2, E4, and E5) and late (L1 and L2) genes.

E2 is negative regulator of HPV oncogenes E6 and E7

Absence of E2 gene after integration leads to elevated expression of E6 and E7

Lee et al, J Gynecol Oncol 2016;27(5):e51

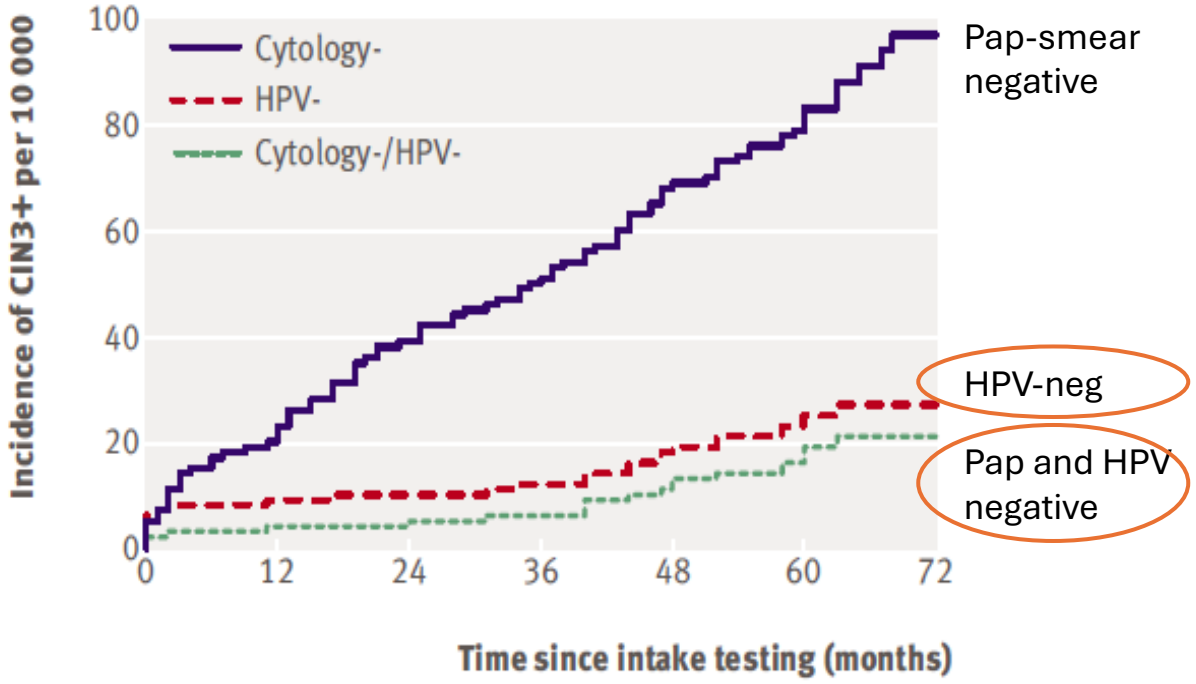
Sensitivity & Specificity



British Journal of Cancer 2011:104:863–870

Long term predictive values of cytology and human papillomavirus

7 European RCTs (n=24,295 women)
Co-testing HPV and Pap-smear



Cytology is complementary to and may cover some gaps in HPV testing

- **HR-HPV-negative cancers**
  - (~5%) HPV-independent cancer: e.g. gastric-type, endometroid, clear cell adenocarcinomas
  - (< 1-3%) Rare cancers caused by lower risk HPV not included in HR-HPV panels: e.g. HPV 73, 26, 69, 82
    - But risk of cancer is so low that testing for these types is NOT recommended
- **HR-HPV test false-negatives**
  - (~5%) L1-deleted cancers: consider an E6/E7 test
  - (?) Low HPV DNA copy number and/or loss of HPV-dependency

Dillner et al. BMJ. 2008 Oct 13:337:a1754.
Hurjui et al. Int J Mol Sci. 2025 Oct 15;26(20):10051.

Long term predictive values of cytology and human papillomavirus

7 European RCTs (n=24,295 women)
Co-testing HPV and Pap-smear

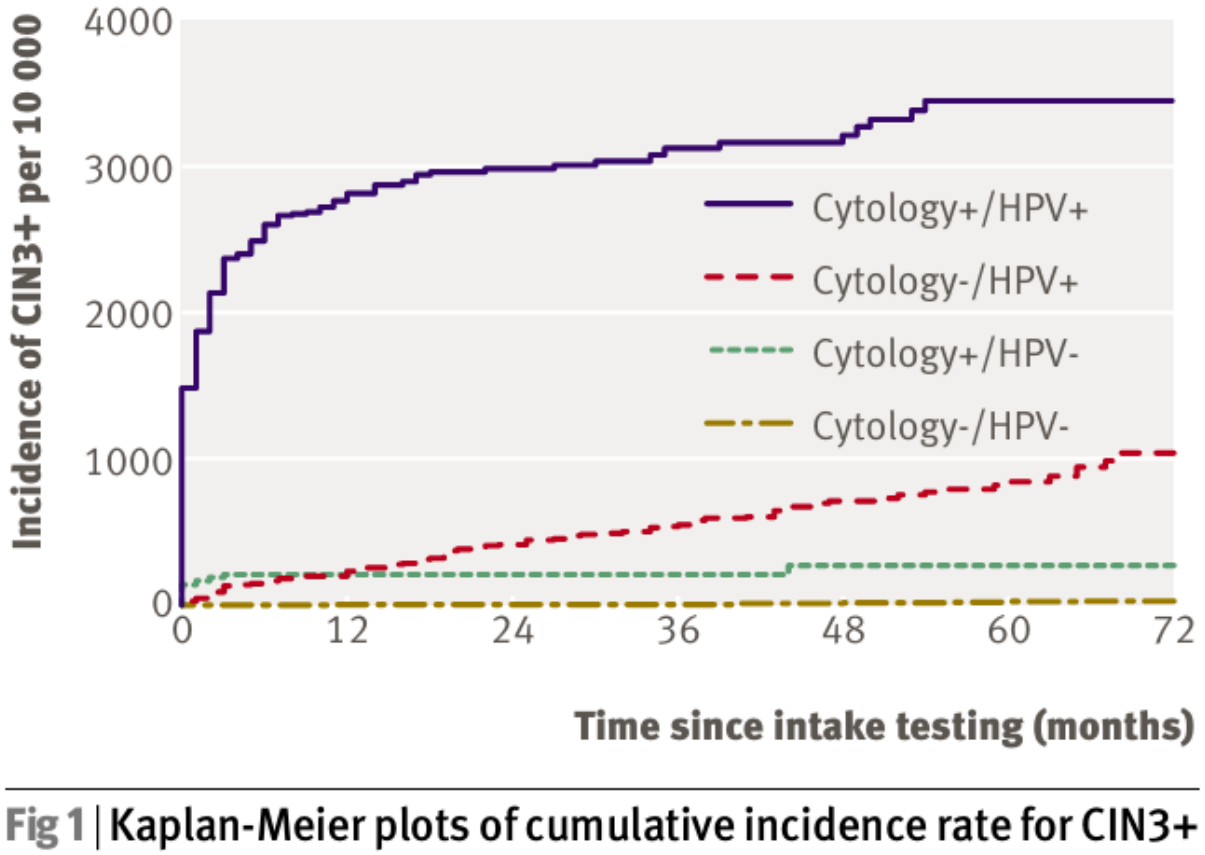


Fig 1 | Kaplan-Meier plots of cumulative incidence rate for CIN3+

Cytology- and HPV positive 10%

Cytology+ and HPV negative 2.7%

Dillner et al. BMJ. 2008 Oct 13:337:a1754.
Hurjui et al. Int J Mol Sci. 2025 Oct 15;26(20):10051.

Caution – need for clinically validated HPV tests

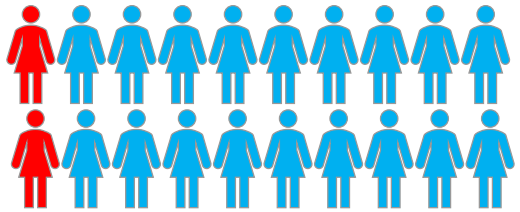
Validation of a diagnostic test/ sample brush/ sample media/ PCR machine/ etc = Proving the performance of the test/brush/media/machine

Analytical Validation of a diagnostic test = proving that it can detect the desired target to a specified sensitivity (limit of detection), in a reproducible manner (inter-day, inter-lab, inter-lot precision), without off-target effects (cross-reactivity), and without impact from common sample contaminants (interference).

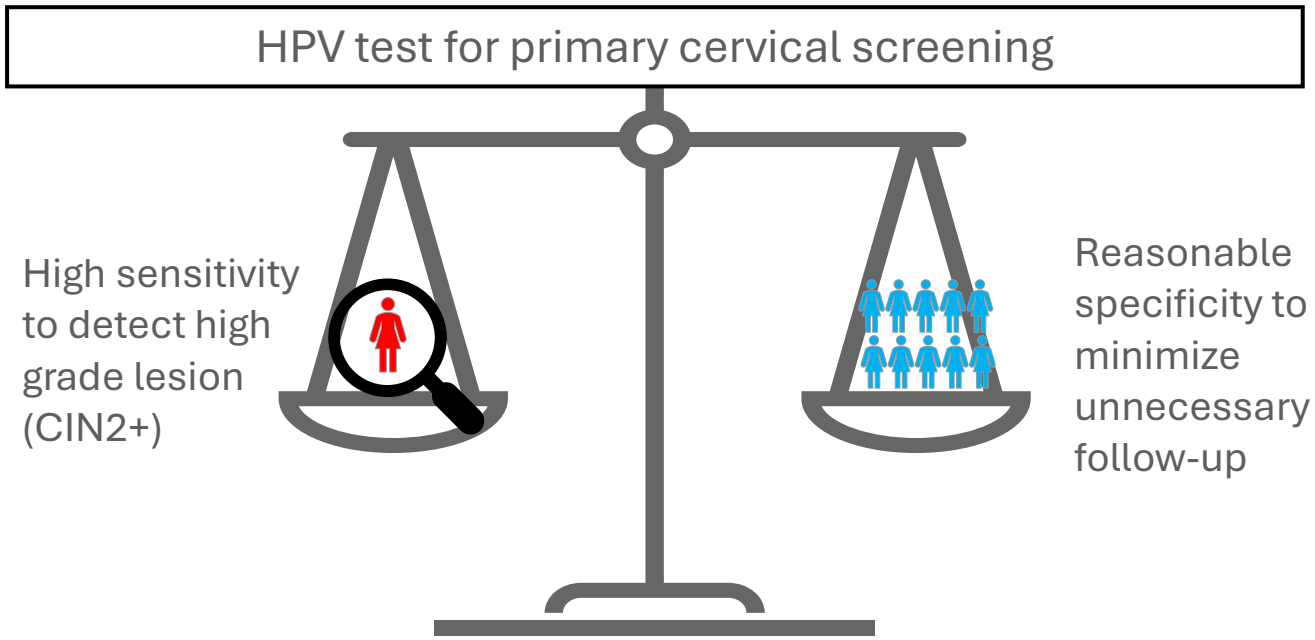
*note: validation should be performed with samples in the appropriate sample matrix (e.g. DNA or cells added to real or artificial mucus)

Clinical Validation of a diagnostic test = proving that it can correctly detect people with the disease as positive (clinical sensitivity), and correctly classify people without the disease as negative (clinical specificity), under the conditions claimed by the test manufacturer (specific patient population, specific sample types, specific testing conditions)

Meijer Criteria for HPV test validation: Sensitivity & specificity for CIN2+ Compare clinical performance to reference HPV assay (HC2 or GP5+/6+ PCR)



Usually, ≤ 10% of HPV-positive women have a high-grade lesion



Minimum criteria	Sample size
Clinical sensitivity for CIN2+: ≥90% of clinical sensitivity of Qiagen HC2 in women ≥ 30 years old	At least 60 CIN2+ cases
Clinical specificity for ≤ CIN1: ≥98% of clinical specificity of Qiagen HC2 in women ≥ 30 years old	At least 800 ≤CIN1 cases

Meijer et al. Int J Cancer. 2009 Feb 1;124(3):516-20.

20 HPV tests are Clinically Validated (publications up to Apr 2024)

	HPV test	
1	Hybrid Capture 2 HPV DNA test	**Standard comparator**
2	GP5+/6+ PCR-EIA	
3	Anyplex II HPV HR Detection	**Second generation comparator**
4	Cobas 4800 HPV test	
5	BD Onclarity HPV Assay	
6	RealTime High Risk HPV test	
7	Alinity m HR HPV Assay	≥1 validation study vs standard comparator
8	HPV-Risk Assay	
9	NeuMoDx	
10	PapilloCheck HPV Screening test	
11	Xpert HPV	
12	APTIMA HPV Assay [mRNA test]	

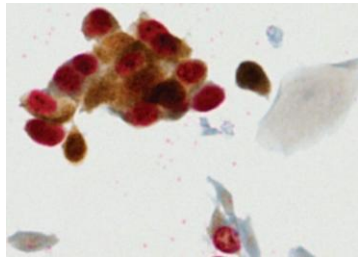
	HPV test	
13	Cobas 6800 HPV test	≥1 validation study vs 2nd Gen comparator
14	CLART HPV45	1 validation study vs standard comparator
15	OncoPredict HPV Screening	
16	REALQUALITY RQ-HPV Screen	
17	OncoPredict HPV QT	
18	RIATOL HPV genotyping qPCR	
19	Allplex II HR (“clinical cut-offs”)	
20	Vitro HPV Screening Assay	

HPV test not meeting criteria	Relative sensitivity	Relative specificity
careHPV test	0.86 (0.79 – 0.94)	1.01 (0.99 – 1.03)
INNO-LiPA	1.01 (0.97 – 1.06)	0.95 (0.93 – 0.97)

Arbyn et. al. Clin Microbiol Infect. 2021 Aug;27(8):1083-1095.; Presentation by Dr. Mario Poljak, AOGIN 2024, Seoul, July 2024;
Arbyn et al. J Med Virol. 2024 Sep;96(9):e29881

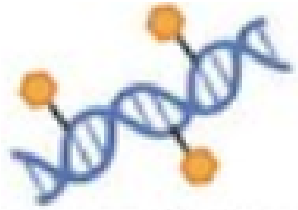
Some triage methods:

p16/Ki67 dual stain



- Combination of p16 + Ki67 in the same cell suggests a loss of cell cycle control
- Accuracy for CIN2+ / CIN3+ may be equivalent or better than cytology (published results are variable)
- Additional (high) cost

DNA methylation



- DNA hyper-methylation, especially of tumor suppressor genes, can play a role in oncogenesis
- Accuracy for CIN2+ / CIN3+ varies, and is target dependent
- Methylation of FAM19A4/miR124-2 is associated with neoplastic progression in HPV-positive cervical lesions
- Most assays are research-use only and involve many manual steps

HR-HPV genotyping

Subgroup	Carcinogenic HPV types included
Group 1a	HPV16
Group 1b	HPV18, HPV45
Group 1c	HPV31, HPV33, HPV35, HPV52 and HPV58
Group 1d	HPV39, HPV51, HPV56 and HPV59

- Oncogenic HPV are subdivided into 4 risk tiers (Grp 1 a-d)
- Baseline and long-term risk of CIN2+ / CIN3+ clearly differ by risk tier
- Exact risk level of mid-risk types may differ by ethnicity (e.g. HPV35 is higher risk in Africans)
- HPV genotype is already available with many HPV tests used in Korea

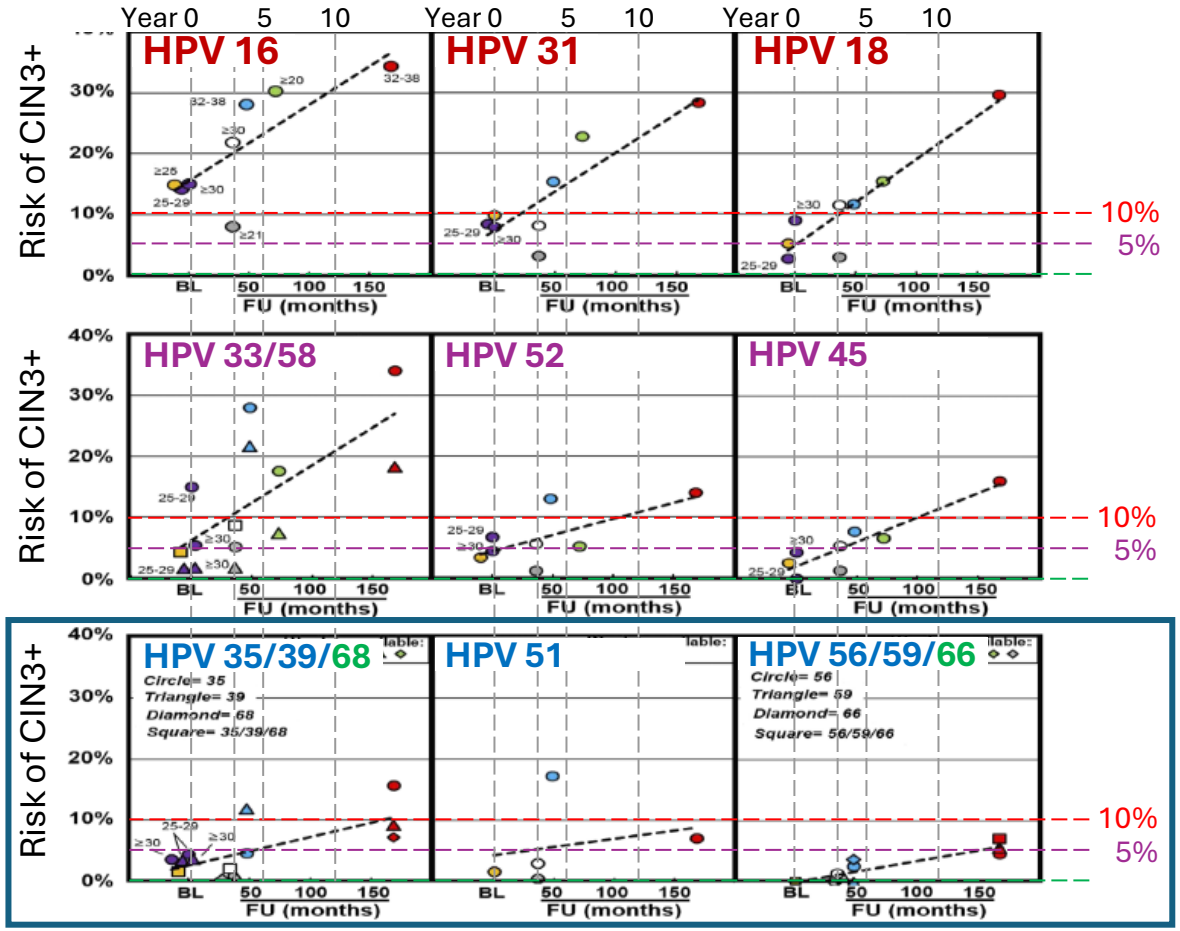
Reference

HR-HPV genotypes fall into distinct risk tiers

HPV type	% HPV type prevalence (CxCA)	% HPV type prevalence (NILM)	Odds ratio in CxCa vs normal	
HPV16	55.8	2.6	47.6	Higher oncogenic
HPV18	14.3	1	15.7	
HPV45	4.8	0.6	8.3	
HPV33	4	0.6	7.1	Mid oncogenic
HPV58	4	0.8	5.1	
HPV31	3.5	1	3.7	
HPV52	3.2	1	3.3	
HPV35	1.6	0.4	3.9	Lower oncogenic
HPV59	1.2	0.4	2.9	
HPV39	1.3	0.6	2.0	
HPV68	0.6	0.4	1.5	
HPV51	1	0.9	1.2	
HPV56	0.8	0.6	1.3	
HPV66	0.3	0.6	0.4	

IARC Handbooks of Cancer Prevention Volume 18 (2022): Cervical Cancer Screening. ISBN 978-92-832-3025-0

CIN3+ risk by HPV genotype at baseline and over 15years



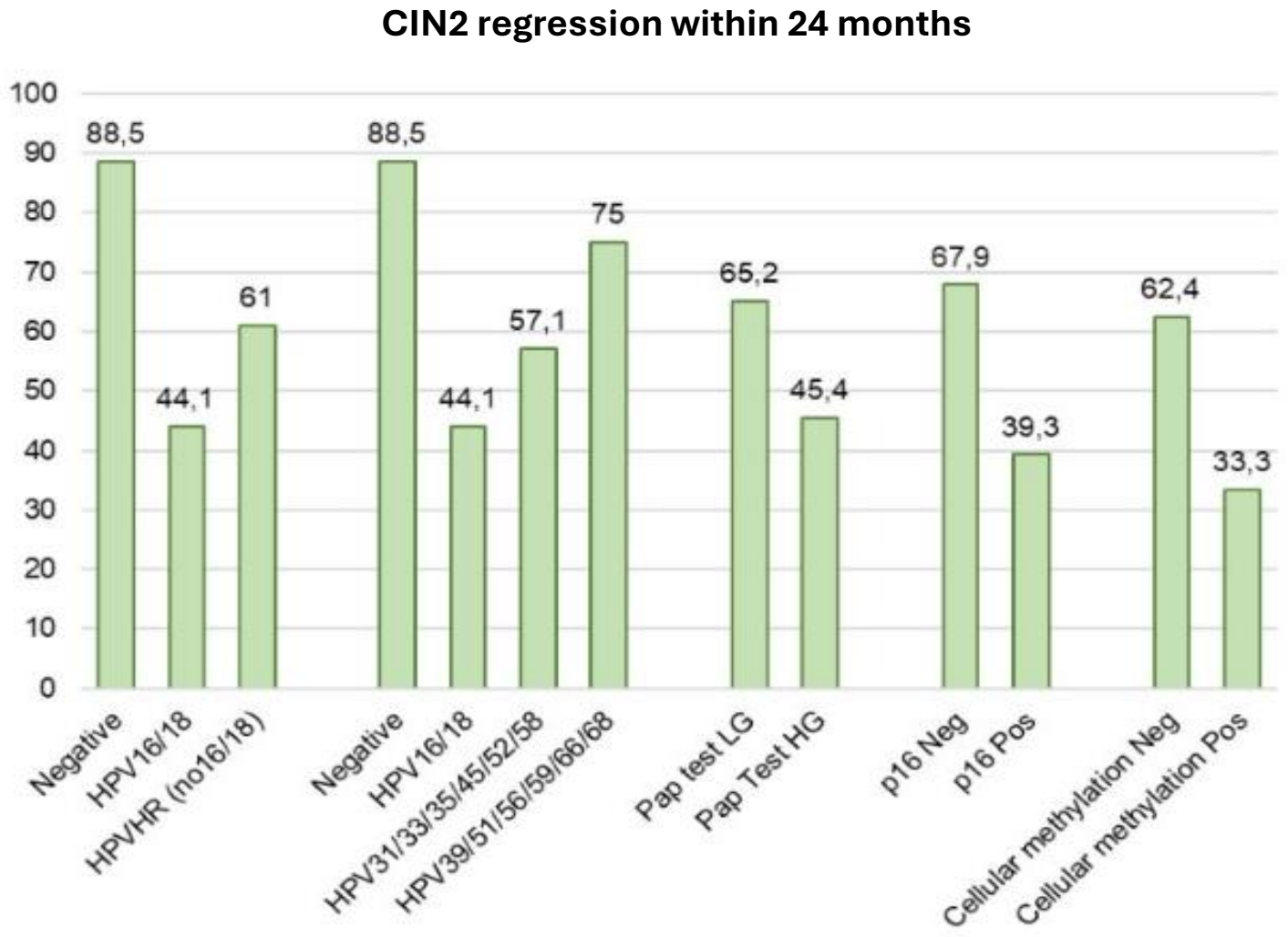
11 studies, n=240,674 subjects, in USA, Sweden, Denmark, Italy and the Netherlands
Bonde et al. J Low Genit Tract Dis. 2020 Jan;24(1):1-13.

HPV genotyping may be useful to identify young women with CIN2 who are suitable for active surveillance

- N=294 women aged 25-45 yr old
- Histologically confirmed CIN2
- LBC, HPV genotyping, p16/Ki67 dual stain and FAM194A/miR124-2 methylation performed
- Active surveillance @ 6, 12, (18), 24 month

- HPV genotyping allowed for effective risk stratification:

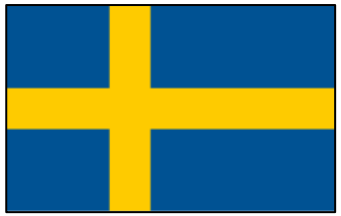
Baseline HPV type	% Regressed
16/18	44.1%
31/33/35/45/52/58	57.1%
39/51/56/59/66/68	75.0%
HR-HPV negative	88.5%



Frayle et al. Int J Cancer. 2026 Feb 1;158(3):587-596.

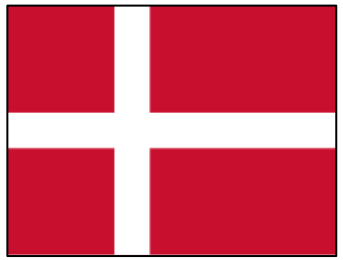
Increasing trend of genotyping – Nordics, USA, WHO

National Cervical Screening Programs



Sweden (2022)

- **3 HPV risk tiers**
- HPV+NILM: retest in 1.5, 3 or 5yr based on risk
- Colposcopy for same-genotype persistence



Denmark (2021)

- xGT piloted in Capital Region since 2021
- **2 HPV risk tiers** (“high 5” vs “lower 8” types)
- More aggressive follow-up for higher risk tier

Norway (2024)

- **3 HPV risk tiers**
- “lower 7 genotypes” retest in 1yr if ASC-US/LSIL, or in 3yr if NILM

American Society of Colposcopy & Cervical Pathology (ASCCP)

- xGT guideline issued in 2025
- **3 HPV risk tiers**
- Lowest risk tier retested in 1yr

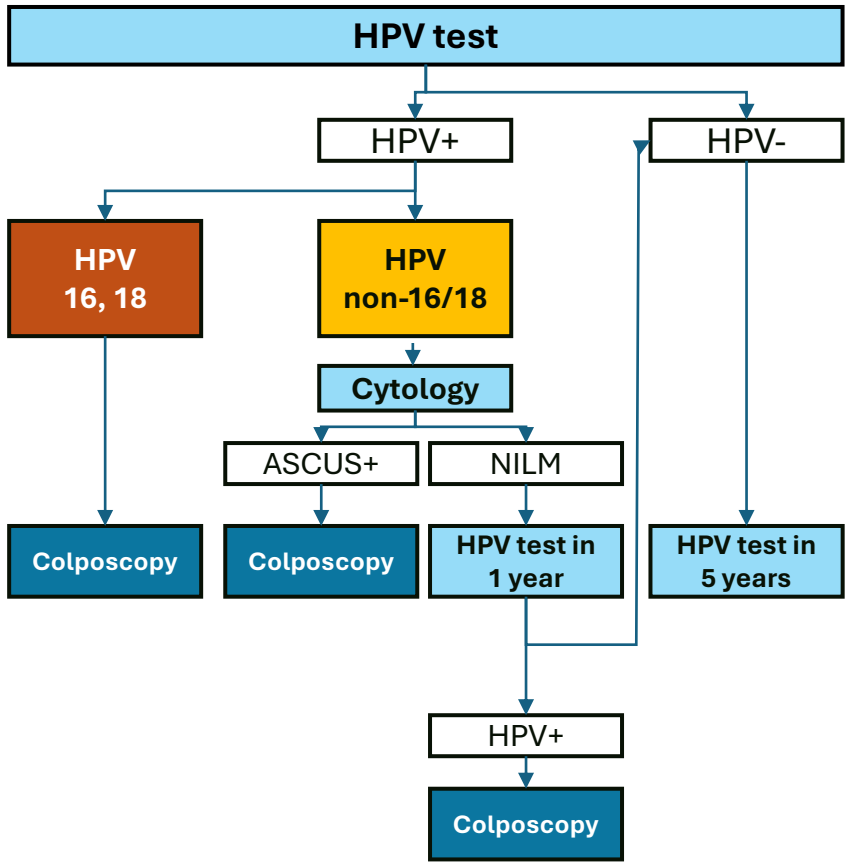
World Health Organization (WHO)

*HPV genotyping output in **4 risk tiers** is recommended*

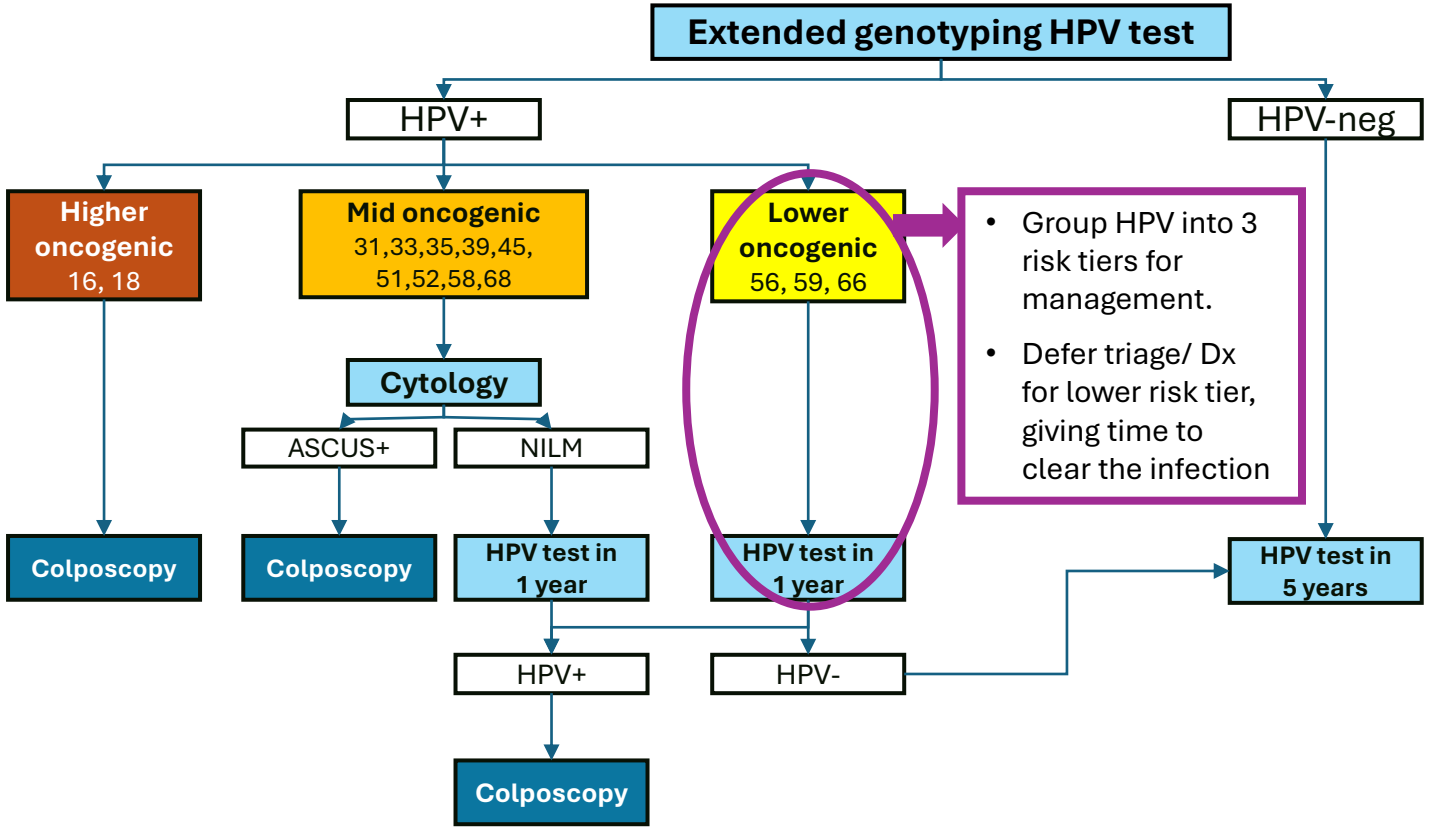
https://kunskapsbanken.cancercentrum.se/diagnoser/livmoderhalscancerprevention/vardprogram/triage-i-gck-samt-annan-handlaggning-av-avvikande-prover-vid-laboratoriet/;
Dr. Jesper Bonde, EUROGIN 2024, March 2024, Stockholm, Sweden; Courtesy of Dr. Ameli Tropè; ASCCP. J Low Genit Tract Dis. 2025 Apr 1;29(2):134-143.

How is genotyping being used to improve screening efficiency:

ASCCP Partial Genotyping algorithm



ASCCP Extended Genotyping algorithm



ASCCP 2019. J Low Genit Tract Dis. 2020 Apr;24(2):102-131;

ASCCP 2025. J Low Genit Tract Dis. 2025 Apr 1;29(2):134-143.

Summary

1. HPV testing provides superior clinical sensitivity for high grade cervical interepithelial neoplasia (CIN)

- It is globally recommended as a primary screening modality
- Clinically validated tests are strongly recommended to balance clinical sensitivity and specificity

2. Cytology as complementary to HPV testing can address some gaps in HPV tests

- HR-HPV-negative cancers (HPV-independent Ca, “borderline-oncogenic” HPV)
- HR-HPV test “false negatives” (L1 deletion, low viral copy number)

Thank you very much for kind attention

Discussion Questions

- Which countries in Asia have switched to HPV primary?
  - Singapore (2019), Malaysia (2019), Thailand (2020), Australia (2017), New Zealand (2023)

- Is there evidence that switching to HPV primary reduces rates of high grade CIN / CxCA?
  - See Wang 2024 in next slide: women randomized to screening with HPV primary had 28% lower cumulative incidence of invasive cervical cancer at 8 year follow-up.

- BD test
  - Strength: US FDA approval, quality standards, clinical validation, genotyping – sufficient for WHO risk tiers, instrument: automated dna extraction + PCR setup + PCR in 1 instrument = consistent results.

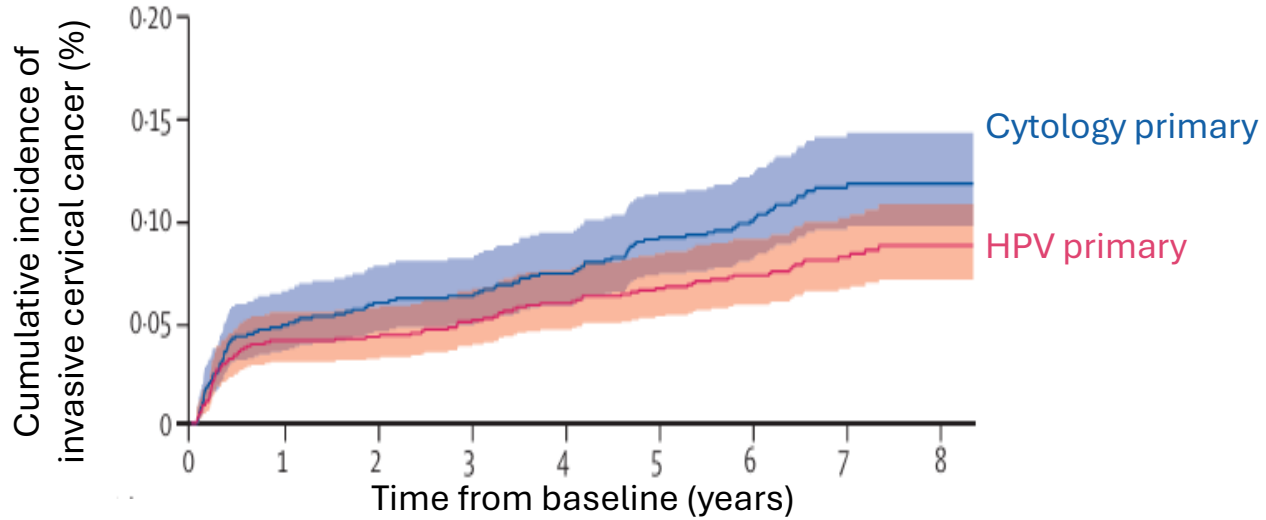
Human papillomavirus-based cervical screening and long-term cervical cancer risk: a randomised health-care policy trial in Sweden

Jiangrong Wang, K Miriam Elfström, Joakim Dillner

- Stockholm region, Sweden
- Women randomized to cervical screening by cytology primary vs HPV primary test. Women followed up by National screening and cancer registries.
- Per protocol (women who attended screening with the randomized method):
  - HPV (n=110,162); Cytology (n=90,813)
- Endpoint: invasive cervical cancer from recruitment to end of follow up (median 7.1 years)

Results:

- Cumulative incidence of cervical cancer at 8 years follow-up was 28% lower in the HPV primary group compared to the cytology primary group.
- Among patients with known histological subtype, HPV-based screening prevented 34% more squamous cell carcinoma and 27% more adenocarcinoma



	Sample size	Median follow-up	Number of invasive CxCA	Hazard ratio
All CxCA				
HPV primary	110,162	7.2 year	91	0.72 (0.54 – 0.95)
Cytology primary	90,813	7.1 year	104	1 (ref)
Squamous cell carcinoma				
HPV primary			53	0.66 (0.46 – 0.95)
Cytology primary			66	1 (ref)
Adenocarcinoma				
HPV primary			31	0.73 (0.45-1.18)
Cytology primary			35	1 (ref)

Wang et al. Lancet Public Health. 2024 Nov;9(11):e886-e895.

Issues with HPV-based primary screening

HPV-independent Cervical Cancer (CxCA)

Table 2. HPV prevalence in different histotypes of cervical cancer [9,10].

Histotypes	% HPV Positive
SCC	100
ADS	up to 86
ADC	
Usual type	80–100
Mucinous, Intestinal type	83–100
Villoglandular	100
Mucinous, signet ring cell type	100
Endometrioid	0
Gastric Type	0
Masonephric	0
Clear cell	28
Serous	30

SCC: squamous cervical cancer; ADS: adenosquamous cancers; ADC: adenocarcinoma.

HPV-independent Cx Ca:
- ~5% of all CxCA

- Gastric type is the most common HPV-independent ADC, has higher prevalence in Asia (20-25% out of all ADCs) vs Western countries (10%)
- Due to mutation of host genes and not driven by HPV infection
- Lack of precursor lesions – escapes primary and secondary prevention (very low sensitivity on Pap test, ~18%)
- More aggressive and treatments are less effective

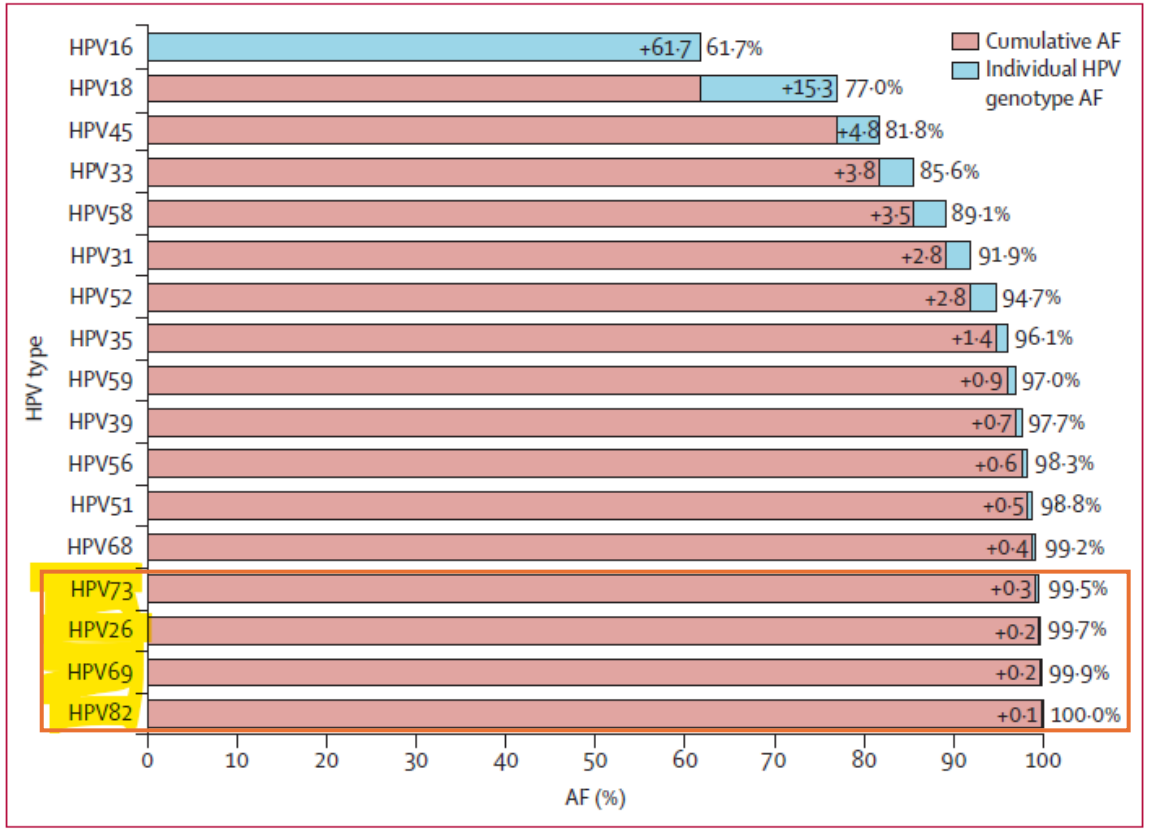
Not well detected by current screening modalities

Arezzo et al., *Diagnostics*, 2021. doi:10.3390/diagnostics11060952
Turashvili & Park, *Surg Pathol Clin*, 2019. doi:10.1016/j.path.2019.01.002
Giannella et al., *Pathogens*, 2025. doi:10.3390/pathogens14070668

Borderline oncogenic HPV and LR-HPV cancer

HPV type	DNA+(n = 9516) RC% (95% CI)
Combined nine HPV types†	89.3 (88.7 to 89.9)
HPVs 16/18	70.9 (69.9 to 71.8)
HPVs 31/33/45/52/58	18.3 (17.6 to 19.1)
Specific HPV type:	
HPV 16	60.3 (59.4 to 61.3)
HPV 18	10.5 (9.9 to 11.2)
HPV 31	3.6 (3.2 to 4.0)
HPV 33	3.7 (3.4 to 4.1)
HPV 45	6.1 (5.6 to 6.6)
HPV 52	2.7 (2.4 to 3.1)
HPV 58	2.2 (1.9 to 2.5)
HPV 6	0.1 (0.1 to 0.2)
HPV 11	0.0 (0.0 to 0.1)

de Sanjosé et al., *JNCI Cancer Spectrum*, 2018;2(4):pky045. doi:10.1093/jncics/pky045



Wei et al. *Lancet*. 2024 Aug 3;404(10451):435-444.
HPV 26, 69, 73, 82 are classified as Group 2B (”possibly carcinogenic”)

Borderline HPV: < 1% total HPV+ CxCA

Not recommended for cervical screening as their contribution to cervical cancer is very low

L1-PCR-neg, E6/E7-detected CxCA: ~5% of CxCA in Sweden

(Roberts, 2006)

- N=1848 cervical biopsies from Norwegian women
- HPV16 and HPV18 specific PCR + southern blot, separate primers for L1, E6, E7 genes

- N=597 HPV16-positive biopsies
  - N=538 (90.1%) positive for L1, E6, E7
  - N=59 (9.9%) positive for E6, E7 only (missed by L1 testing)

- N=111 HPV18-positive biopsies
  - N=90 (81.1%) positive for L1, E6, E7
  - N=21 (18.9%) positive for E6, E7 only (missed by L1 testing)

- no documented case of the loss of E6 and E7 upon HPV integration

(Mühr, 2020)

- N=2850 FFPE CxCA tumor blocks from Sweden
- HPV L1 type-specific PCR (37 genotypes)
- L1-PCR neg tested by HPV 16/18 E6/E7 PCR
- Double PCR neg tested by RNA sequencing

Results:

- N=1861 HPV 16/18 single positive CxCA
  - N=1767 (94.9%) L1 PCR positive
  - N=89 (4.8%) L1 PCR-neg, E6/E7 PCR-pos
  - N=5 (0.3%) detected by sequencing

- N=2850 total CxCA
  - N=2533 hrHPV positive (14 genotypes)
    - 2310/2850 (81%) L1 PCR positive
    - **141/2850 (4.9%) E6/E7 PCR pos or L1 deletion**
    - 82/2850 (2.9%) detected by sequencing
  - N=92 (3.2%) low-risk HPV positive
  - N=225 (7.9%) no HPV detected

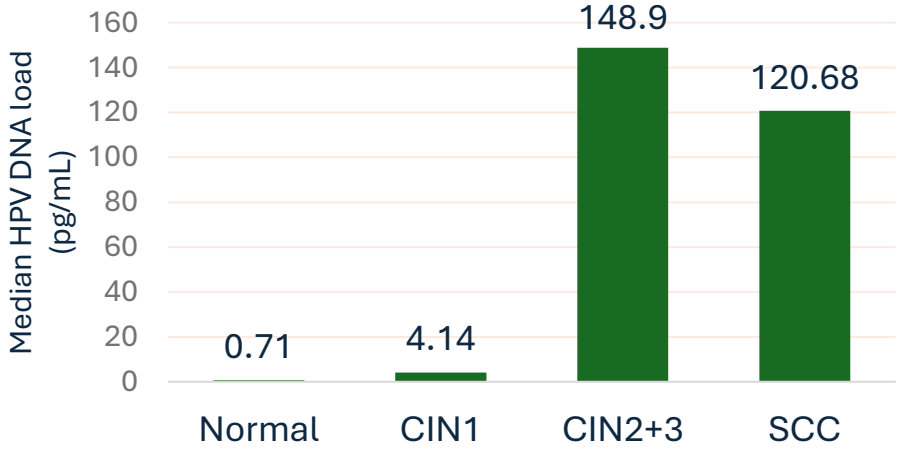
L1-PCR-neg, E6/E7-pos: ~5% of total CxCA

Roberts et al. J Clin Virol. 2006 Aug;36(4):277-82.
Mühr et al. Br J Cancer. 2020 Dec;123(12):1790-1795.

Low HPV DNA copy number and/or loss of HPV-dependency can lead to false negative HR-HPV test result

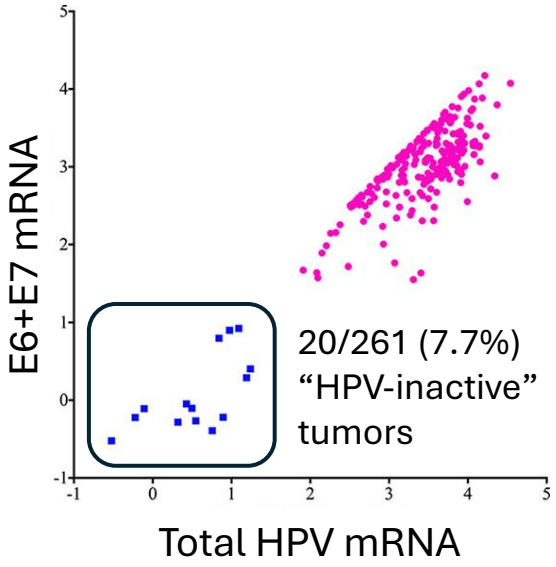
Variable viral load in high-grade CIN and SCC

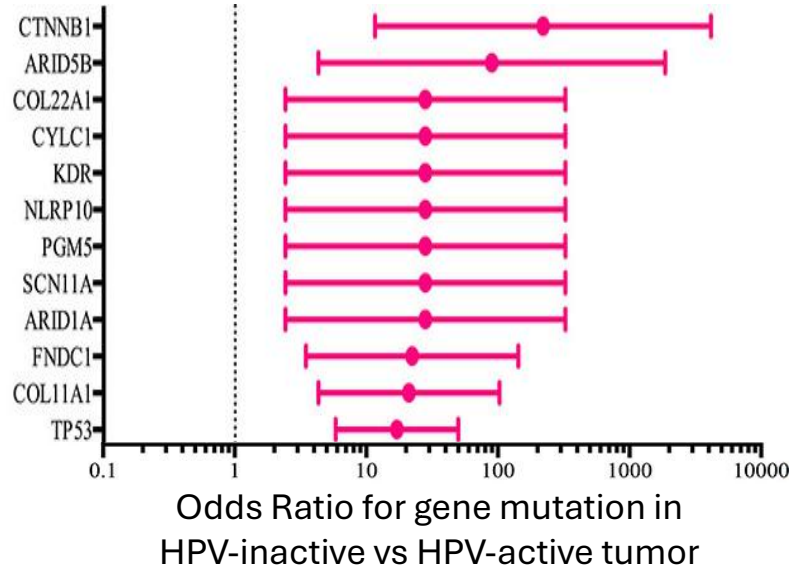
	Normal, *n* (%)	CIN, *n* (%)	SCC, *n* (%)
HPV negative	39 (56.5)	27 (13.4)	10 (4.2)
HPV positive	30 (43.5)	175 (86.6)	226 (95.8)
High viral load (≥100)	14 (20.3)	105 (52.0)	125 (53.0)
Medium viral load (≥10 to <100)	5 (7.2)	47 (23.3)	70 (29.7)
Low viral load (1 to <10)	11 (15.9)	23 (11.4)	31 (13.1)



Huang et al. Int J Gynecol Cancer. 2008 Jul-Aug;18(4):755-60.

~8% of HPV DNA-positive tumors did not have E6/E7 gene expression
(May lose HPV DNA fragments as tumor accumulates more mutations)





E6/E7 DNA is still present, but not expressed. Instead, other mutations are driving oncogenesis. → Such tumors may lose HPV genes as it further divides and mutates.

Banister et al. Oncotarget. 2017 Feb 21;8(8):13375-13386.

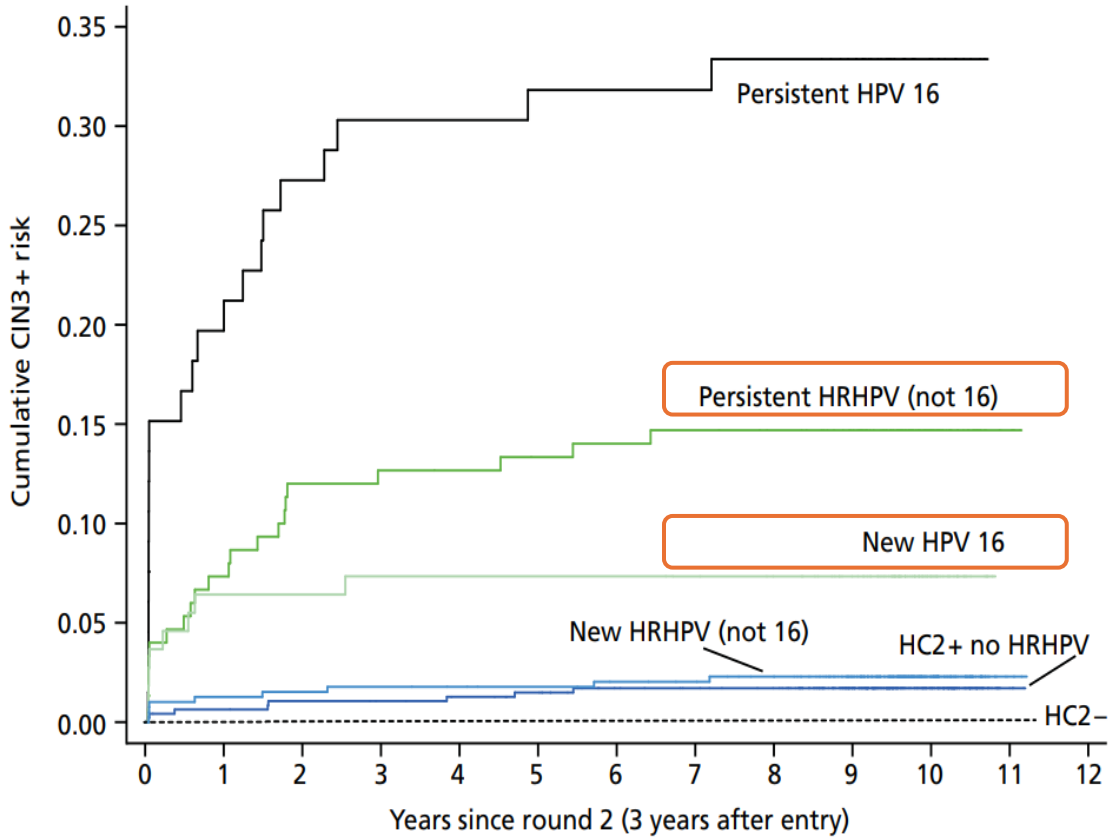
Genotype persistence vs GT switch

Persistent non-16 is higher risk than new HPV16 infection

- ARTISTIC trial, Manchester, UK. ThinPrep LBC, tested with HC2.
- HPV typing by Roche Line Blot Assay, Roche Linear Array or PapilloCheck assay
- N=331 with persistent hrHPV @ 36 months
  - N=216 (65%) same GT persistent; N=115 (35%) GT switch
- Normal screening (cytology q3/5y) and follow up via National Registry

Kitchener et al.[51] (2014) and Gilham et al.[50] (2019)	Pooled HPV persistent	Same GT persistent	Genotype switch
≥CIN 2 three-year risk[51]	12.9%	21.0%	6.2
≥CIN 3 three-year risk[51]	7.0%	13.5%	1.7%
≥CIN 3 five-year CIR; NILM[50]	7.0 (3.9–12.2)	11.3 (6.5–19.5)	0
≥CIN 3 ten-year CIR; NILM[50]	8.9 (5.4–14.5)	13.4 (8.0–22.0)	1.7 (0.2–11.3)
≥CIN 3 five-year CIR; low-grade cytology[a50]	14.5 (7.8–26.0)	23.7 (14.8–36.8)	5.1 (2.5–10.4)
≥CIN 3 ten-year CIR; low-grade cytology[50]	16.2 (9.0–28.0)	23.7 (14.8–36.8)	5.9 (3.0–11.4)

[a]Low-grade cytology = ASC-US and LSIL combined.



Gilham et al. Health Technol Assess. 2019 Jun;23(28):1-44.
Bonde et al. J Low Genit Tract Dis. 2021 Jan 1;25(1):27-37

Some Korea data

2007-2018 KNHANES: ~30% never screeners

Table 2. Compliance level with cervical cancer screening between 2007–2018

Variables	Total	Compliance level (%)		
		None	Irregular	Regular
Age at year 2007 (yr)				p<0.001
20–39	1,828	32.4	59.6	8.0
40–59	1,750	20.1	49.1	30.8
≥60	1,085	38.2	43.4	18.4
Household income/median income				p<0.001
<50% (the poorest)	1,337	33.8	48.5	17.7
50 to <100%	1,593	28.8	53.4	17.8
100 to <150%	961	23.2	55.3	21.5
150 to <200%	408	27.7	50.7	21.6
≥200% (the richest)	364	30.5	50.3	19.2
Occupational class				p<0.001
Never worked and others	2,712	30.7	50.4	18.9
Self-employed, entrepreneurs and farmers	233	23.2	52.4	24.4
Manual workers	144	33.3	54.9	11.8
Clerical, sales and service workers	538	22.5	53.0	24.5
Lower level professionals	585	27.4	54.4	18.2
Higher level professionals and managers (highest)	451	31.3	55.2	13.5
Place of residence				p<0.001
Rural area	982	33.2	52.0	14.8
Small-medium cities	1,698	27.0	50.9	22.1
Metropolitan cities	1,983	28.8	52.6	18.6
Education level				p<0.001
Elementary school graduate or less	1,387	31.9	46.7	21.3
Middle school graduate	461	22.1	46.4	31.5
High school graduate	1,484	27.1	53.8	19.1
College graduate or higher	1,331	30.8	57.0	12.2

Kim et al. J Gynecol Oncol. 2024 Mar;35(2):e18.

N=18,146 health check participants

Table 4. Prevalence of HR HPV genotypes by cervical cytology

HPV	Genotype	Normal	ASCUS	LSIL	HSIL/ASC-H	p-value
19 HR	16	214 (8.44)	13 (10.16)	9 (5.39)	16 (24.62)	<0.001
	18	109 (4.30)	4 (3.13)	10 (5.99)	2 (3.08)	<0.001
	26	8 (0.32)	0 (0)	0 (0)	0 (0)	1.000
	31	77 (3.04)	1 (0.78)	3 (1.80)	5 (7.69)	<0.001
	33	48 (1.89)	2 (1.56)	3 (1.80)	3 (4.62)	<0.001
	35	103 (4.06)	3 (2.34)	5 (2.99)	5 (7.69)	<0.001
	39	218 (8.59)	8 (6.25)	13 (7.78)	3 (4.62)	<0.001
	45	66 (2.60)	1 (0.78)	2 (1.20)	1 (1.54)	0.102
	51	152 (5.99)	9 (7.03)	14 (8.38)	3 (4.62)	<0.001
	52	295 (11.63)	20 (15.63)	10 (5.99)	9 (13.85)	<0.001
	53	377 (14.86)	15 (11.72)	22 (13.17)	2 (3.08)	<0.001
	56	147 (5.79)	6 (4.69)	20 (11.98)	0 (0.00)	<0.001
	58	282 (11.12)	21 (16.41)	29 (17.37)	8 (12.31)	<0.001
	59	54 (2.13)	4 (3.13)	2 (1.20)	3 (4.62)	0.001
	66	114 (4.49)	11 (8.59)	11 (6.59)	2 (3.08)	<0.001
	68	194 (7.65)	6 (4.69)	10 (5.99)	1 (1.54)	<0.001
	69	21 (0.83)	2 (1.56)	2 (1.20)	0 (0)	0.021
	73	15 (0.59)	0 (0)	1 (0.60)	0 (0)	0.178
	82	43 (1.69)	2 (1.56)	1 (0.60)	2 (3.08)	0.005
	Total	2,537 (100)	128 (100)	167 (100)	65 (100)	

Values are presents as number of patients (%).
ASCUS, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells-cannot exclude high-grade squamous intraepithelial neoplasia; HPV, human papillomavirus; HR, high-risk; HSIL, high-grade squamous intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial neoplasia.

Table 3. Positivity for HR H

HPV
19 HR HPV* (+)
Single
Multiple
19 HR HPV (–)

Values are presented as nu
ASC-H, atypical squamous
HPV, human papillomaviru
neoplasia.
*HR HPV includes HPV type

Ouh et al. J Gynecol Oncol. 2018 Jan;29(1):e14.

Odds ratio for histologic HSIL+ vs NILM/LSIL by HPV genotype

HPV type	OR (95% CI)	p-value
16	9.22 (5.46–15.56)	<0.001
18	3.73 (1.51–9.20)	0.004
31	6.99 (2.85–17.13)	<0.001
33	3.28 (1.54–6.96)	0.002
35	2.24 (0.94–5.33)	0.070
39	0.66 (0.28–1.58)	0.354
45	0.33 (0.04–2.64)	0.296
51	1.29 (0.68–2.43)	0.432
52	1.67 (0.85–3.25)	0.134
56	1.11 (0.57–2.16)	0.765
58	3.88 (2.12–7.10)	<0.001
59	6.59 (1.15–37.85)	0.035
66	1.03 (0.47–2.27)	0.936
68	1.29 (0.65–2.55)	0.461

Table 4. Multivariate logistic regression analyses of HR HPV types according to HSIL+ versus NILM/LSIL in the histologic results, adjusted for age. CI = confidence interval, HSIL+ = high-grade squamous intraepithelial neoplasia or worse, LSIL = low-grade squamous intraepithelial neoplasia, NILM = negative for intraepithelial lesions or malignancy, OR = odds ratio.

Vaccine subgroup	OR (95% CI)	p-value
16/18	9.46 (5.60–15.97)	0.001
31/33/45/52/58	3.93 (2.48–6.22)	<0.001
35/39/51/56/59/66/68	1.58 (1.00–2.49)	<0.001

Table 6. Multivariate logistic regression analyses of HR HPV vaccine subgroups according to HSIL+ versus NILM/LSIL in the histologic results, adjusted for age. CI = confidence interval, HR = high risk, HSIL+ = high-grade squamous intraepithelial neoplasia or worse, LSIL = low-grade squamous intraepithelial neoplasia, NILM = negative for intraepithelial lesions or malignancy, OR = odds ratio.

Park et al. Sci Rep. 2019 Aug 29;9(1):12556.

Korea HPV Cohort Study: cytological progression from ASC-US/LSIL to HSIL by HPV genotype (12m follow up)

HPV genotype	Prognosis of cytology	Single infection		Total infections	
		6 Mo	12 Mo	6 Mo	12 Mo
HPV 58	Progression	18 (37.5)	10 (30.3)	22 (29.7)	13 (26.0)
	No change	10 (20.8)	6 (18.2)	18 (24.3)	12 (24.0)
	Regression	20 (41.7)	17 (51.5)	34 (46.0)	25 (50.0)
HPV 56	Progression	1 (1.8)	1 (2.9)	1 (1.5)	2 (4.2)
	No change	11 (20.0)	2 (5.9)	22 (33.3)	7 (14.6)
	Regression	43 (78.2)	31 (91.2)	43 (65.2)	39 (81.2)
HPV 53	Progression	3 (8.6)	2 (7.7)	6 (9.2)	4 (8.5)
	No change	6 (17.1)	4 (15.4)	13 (20.0)	10 (21.3)
	Regression	26 (74.3)	20 (76.9)	46 (70.8)	33 (70.2)
HPV 52	Progression	6 (17.6)	3 (13.1)	11 (19.3)	12 (29.3)
	No change	11 (32.4)	5 (21.7)	18 (31.6)	9 (21.9)
	Regression	17 (50.0)	15 (65.2)	28 (49.1)	20 (48.8)
HPV 39	Progression	3 (11.5)	2 (11.8)	5 (11.4)	3 (10.7)
	No change	7 (26.9)	5 (29.4)	13 (29.5)	10 (35.7)
	Regression	16 (61.6)	10 (58.8)	26 (59.1)	15 (53.6)
HPV 51	Progression	2 (9.1)	1 (7.2)	5 (11.9)	5 (20.8)
	No change	5 (22.7)	3 (21.4)	14 (33.3)	5 (20.8)
	Regression	15 (68.2)	10 (71.4)	23 (54.8)	14 (58.4)
HPV 68	Progression	4 (23.5)	2 (15.4)	8 (25.0)	5 (22.7)
	No change	4 (23.5)	3 (23.1)	9 (28.1)	5 (22.7)
	Regression	9 (53.0)	8 (61.5)	15 (46.9)	12 (54.6)
HPV 66	Progression	3 (13.6)	1 (5.9)	4 (11.4)	2 (8.0)
	No change	6 (27.3)	5 (29.4)	11 (31.4)	7 (28.0)
	Regression	13 (59.1)	11 (64.7)	20 (57.2)	16 (64.0)

Values are presented as number (%). HPV, human papillomavirus.

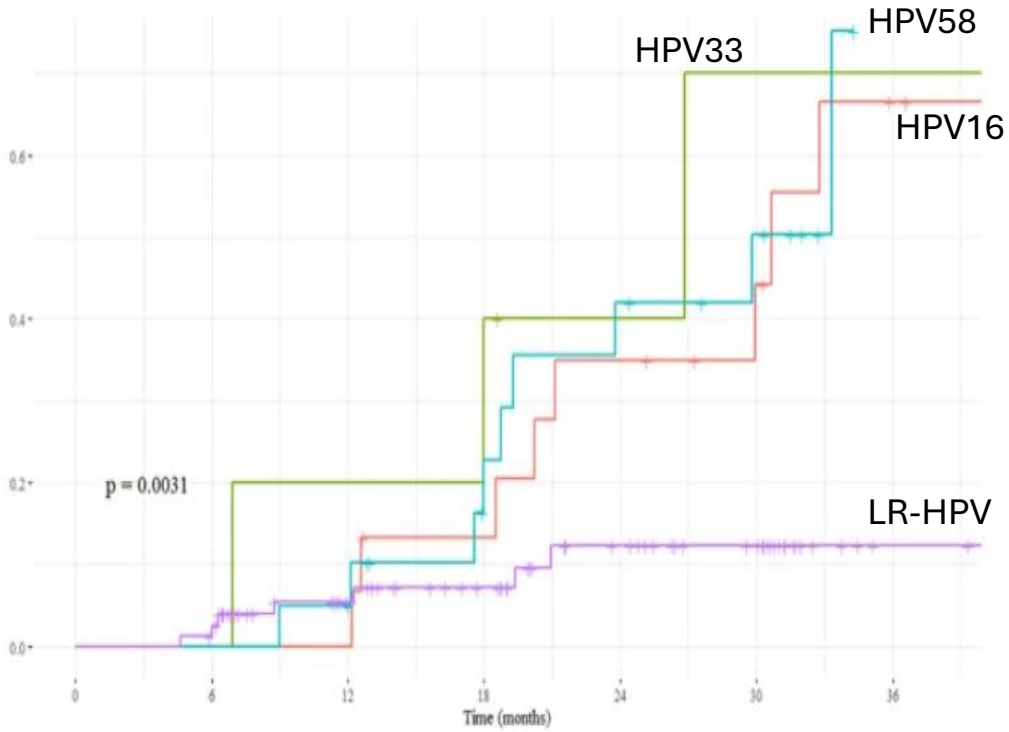
So et al. Cancer Res Treat. 2016 Oct;48(4):1313-1320.

Korea HPV Cohort Study: cytological progression from ASC-US/LSIL to HSIL by HPV genotype (36m follow up)

Table 3 Disease progression from LSIL to HSIL by HPV types

	N	Progression	Probability of progression within 36 months (95% CI)[a]	Hazard ratio (95% CI)		*P* value[c]
				Unadjusted	Adjusted[b]	
LSIL to HSIL	245	45	25.7 (18.3–32.3)			
Age						
20–29	59	10	22.5 (8.4–34.3)	Ref	Ref	
30–39	71	17	30.6 (16.3–42.5)	1.30 (0.60–2.84)	1.30 (0.58–2.90)	0.520
40–49	69	15	32.0 (15.8–45.0)	1.14 (0.51–2.53)	1.10 (0.49–2.48)	0.818
50–59	46	3	10.5 (0.0–21.2)	0.34 (0.09–1.24)	0.39 (0.11–1.48)	0.167
HPV type at baseline						
Low-risk	104	8	10.9 (2.9–18.4)	Ref	Ref	
HPV-16	49	17	45.2 (24.8–60.0)	4.69 (2.03–10.88)	4.71 (2.02–11.02)	0.001
HPV-18	22	4	20.9 (0.3–37.3)	2.34 (0.71–7.78)	2.72 (0.81–9.13)	0.105
HPV-31	12	2	16.7 (0.0–35.3)	3.08 (0.65–14.53)	2.87 (0.60–13.68)	0.186
HPV-33	14	4	68.2 (0.0–92.8)	3.96 (1.19–13.18)	4.17 (1.25–13.94)	0.021
HPV-45	9	1	11.1 (0.0–29.4)	1.59 (0.20–12.74)	2.96 (0.36–24.64)	0.316
HPV-52	34	7	22.2 (6.1–35.5)	2.64 (0.96–7.29)	3.42 (1.23–9.52)	0.019
HPV-58	51	15	43.1 (22.0–58.5)	4.17 (1.77–9.84)	4.37 (1.84–10.41)	0.001
Type-specific persistent infection	135	29	38.8 (22.4–51.7)			
Low-risk	78	7	12.4 (2.8–21.0)	Ref	Ref	
HPV-16	15	8	66.6 (20.5–85.9)	4.01 (1.45–11.10)	4.24 (1.49–12.10)	0.007
HPV-18	5	1	20.0 (0.0–48.4)	2.04 (0.25–16.62)	2.25 (0.27–18.44)	0.451
HPV-31	2	0	NA	NA	NA	NA
HPV-33	5	3	70.0 (0.0–93.7)	5.95 (1.53–23.09)	4.56 (1.165–18.04)	0.030
HPV-45	1	0	NA	NA	NA	NA
HPV-52	12	2	9.1 (0.0–24.6)	1.49 (0.31–7.18)	1.81 (0.37–8.91)	0.464
HPV-58	20	9	50.3 (17.0–70.3)	4.23 (1.58–11.37)	4.18 (1.54–11.33)	0.005

Progression from cytology LSIL to HSIL (36m FU), by HPV type-persistent infection



Seong et al. Virol J. 2021 Sep 17;18(1):188.