

Evaluation of p16/Ki-67 Dual Stain and HPV16/18 Genotyping in HPV-Positive Women at Kaiser Northern California

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Disclosures

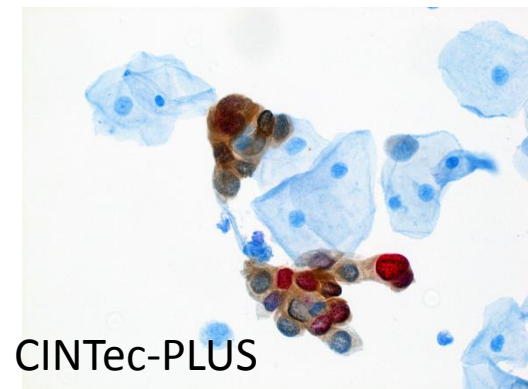
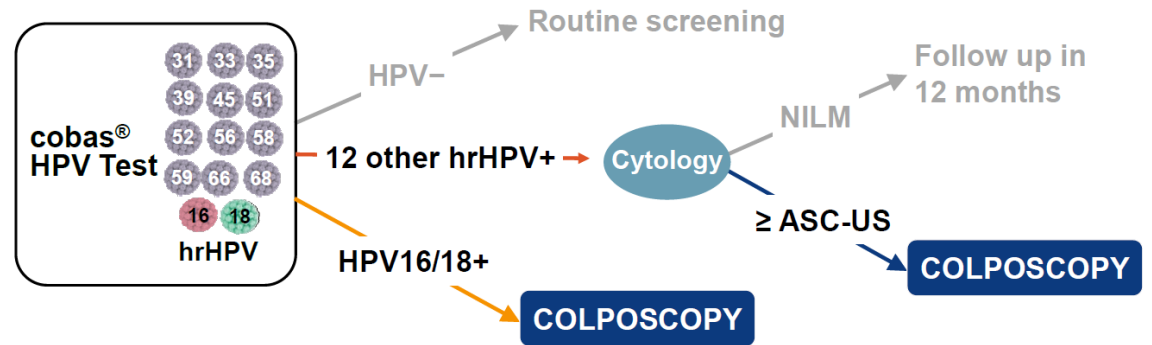
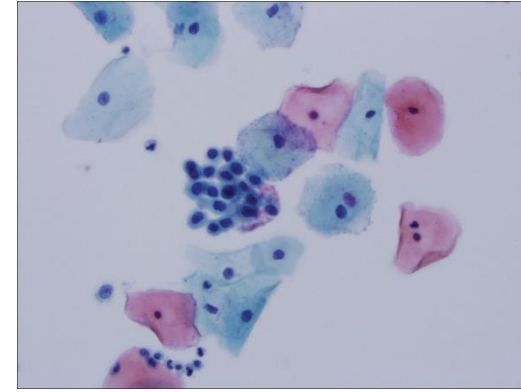
- I am evaluating new assays for cervical cancer screening that are in part donated or purchased at reduced cost from various companies, including BD, Hologic, and Roche. Otherwise, I have no conflict of interest.
- These are personal opinions and not official NCI statements

Current options for cervical cancer screening

	Cytology	HPV	Cotesting (Cytology and HPV)
Sensitivity	Lowest	Higher	Highest
Screening interval	Shortest (lowest NPV)	Longer (greater NPV)	Longest (greatest NPV)
Triage test required	For equivocal cytology results	For all positive results	For HPV-positive, cytology-negative results
Diagnostic test	Colposcopic biopsy		

Triage options

- Cytology alone
- Cytology and HPV genotyping
- p16/Ki-67 dual stain

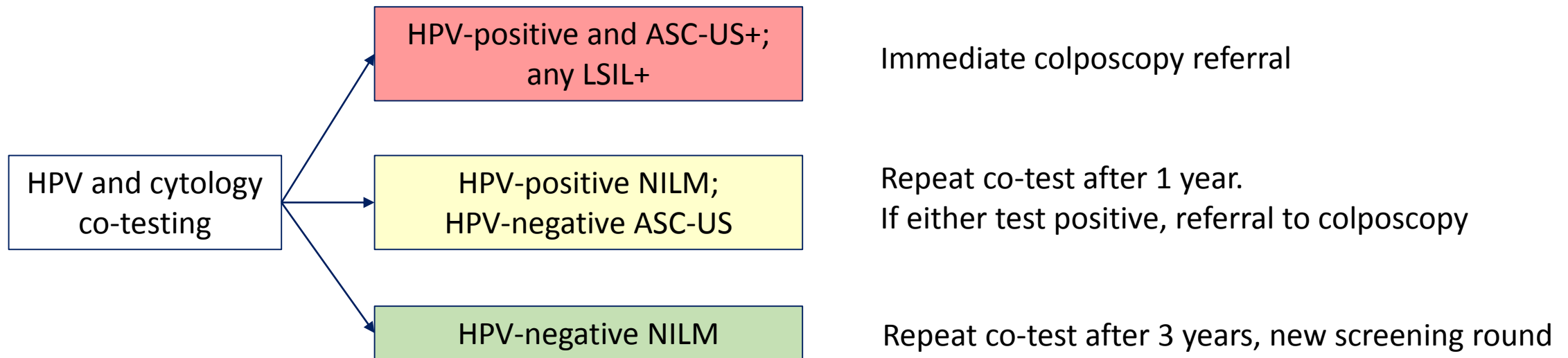


p16/Ki-67 and cobas implementation study

- Kaiser Permanente Northern California (KPNC): 1.6 Million women
- Current screening:
 - HPV (hc2)
 - Cytology (Focal Point, cytology read with knowledge of HPV status)
- Implement and run cobas and CINtec-Plus at KPNC
- Evaluate triage strategies for HPV-positive women compared to current strategies

Study design

- Over 13,000 HPV-positive women; enriched with 3,000 HPV-positive/NILM women
- Cobas testing out of residual STM specimens; CINTec-Plus out of residual Surepath specimens
- Clinical management according to KPNC clinical guidelines



Follow-up from first screening round still ongoing

Dual stain and HPV16/18 in cytology categories

Cytology Result	N	%
Negative	1236	40%
<i>HPV16/18+</i>	207	17%
<i>p16/ki-67+</i>	438	35%
ASC-US	899	29%
<i>HPV16/18+</i>	170	19%
<i>p16/ki-67+</i>	451	50%
LSIL	711	23%
<i>HPV16/18+</i>	123	17%
<i>p16/ki-67+</i>	435	61%
ASC-H	160	5%
<i>HPV16/18+</i>	60	38%
<i>p16/ki-67+</i>	142	89%
HSIL	82	3%
<i>HPV16/18+</i>	39	48%
<i>p16/ki-67+</i>	82	100%
Total	3,108	100%
<i>HPV16/18+</i>	612	20%
<i>p16/ki-67+</i>	1,565	50%

- Restricted to 3,108 women with complete results and at least 1 year of follow-up

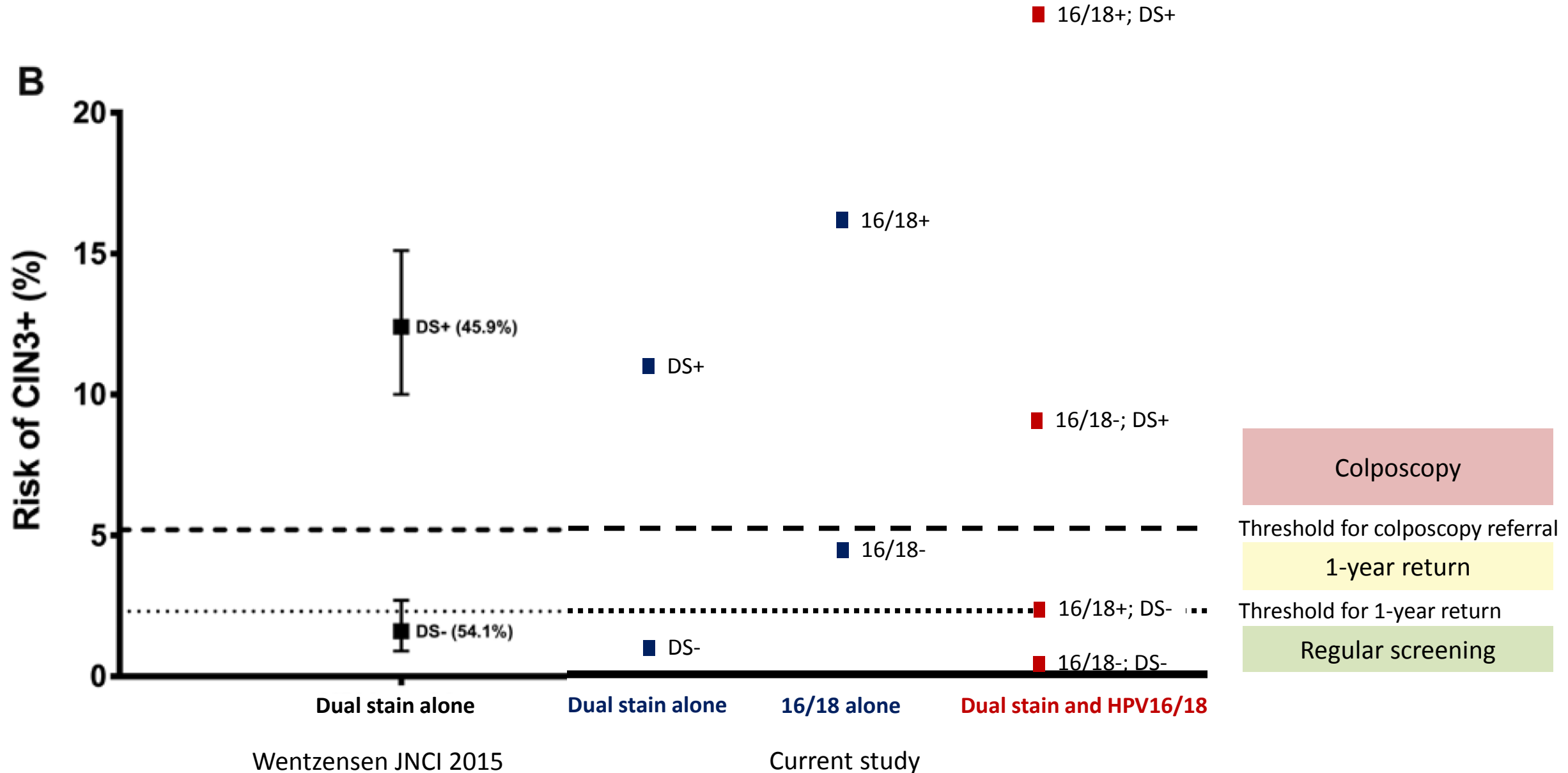
Clinical performance- interim results

	Cytology	HPV16/18	Cytology and HPV16/18	Dual stain
Threshold	ASC-US+ *	Either 16 or 18 positive	ASC-US plus or 16 or 18 positive	One dual stain positive cell

*among HPV-positive women

- Follow-up of HPV+/NILM women ongoing, ascertainment biased towards cytology

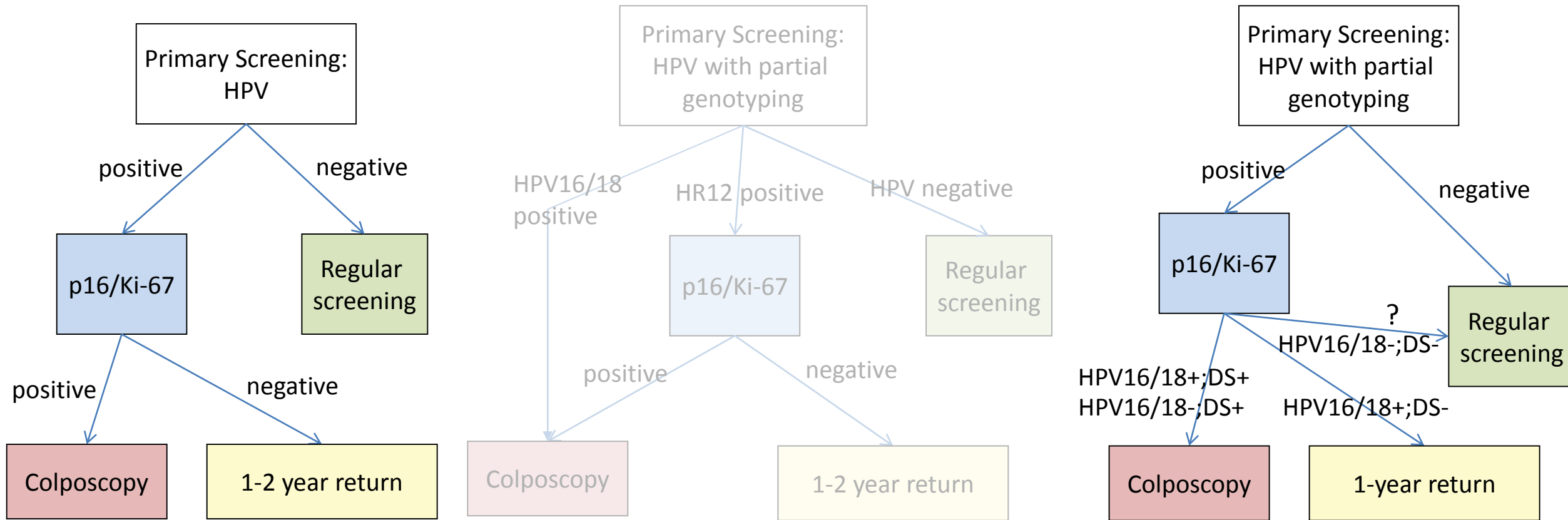
Absolute risk and clinical management



Genotyping and dual stain combinations: Colposcopy referral and risk of CIN3+

Stratum	Women in stratum	Women with CIN3+	Risk of CIN3+
HPV16/18-, DS -	1342	12	0.009
HPV16/18-, DS +	1154	83	0.072
HPV16/18+, DS -	201	5	0.025
HPV16/18+, DS +	411	95	0.231

Summary



- Performance analysis needs to consider immediate colposcopy referral and referral after 1-2 year return, screening intervals matter, automation adds options
- Analysis of triage strategies in vaccinated women: differential impact on HPV16/18 and DS

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