Self-sampling (PaVDaG) study from Scotland

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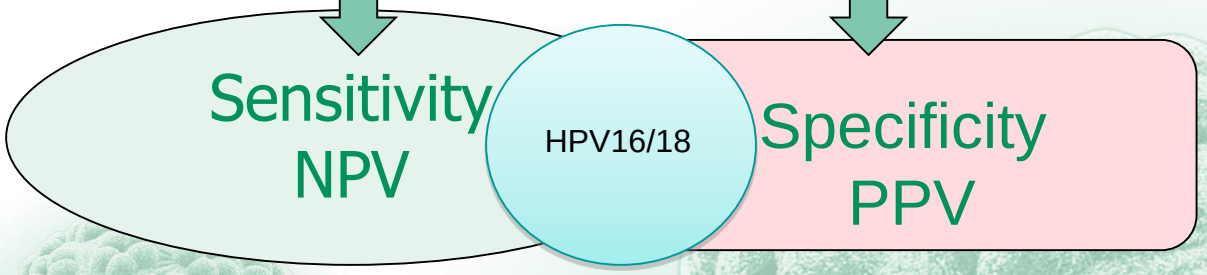
CERVICAL CANCER=

HPV + BAD LUCK



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Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis

M Arbyn, F Verdoodt, PJF Snijders, V Verhoef, E Suonio, L Dillner, S Minozzi, C Bellisario, R Banzi, FH Zhao, P Hillemanns, A Anttila

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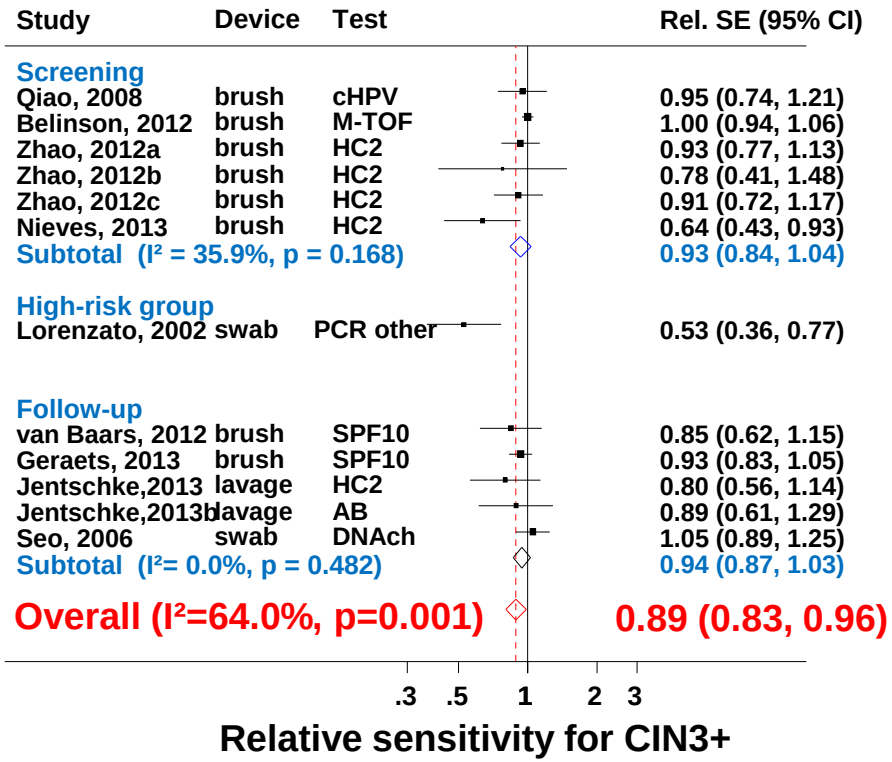
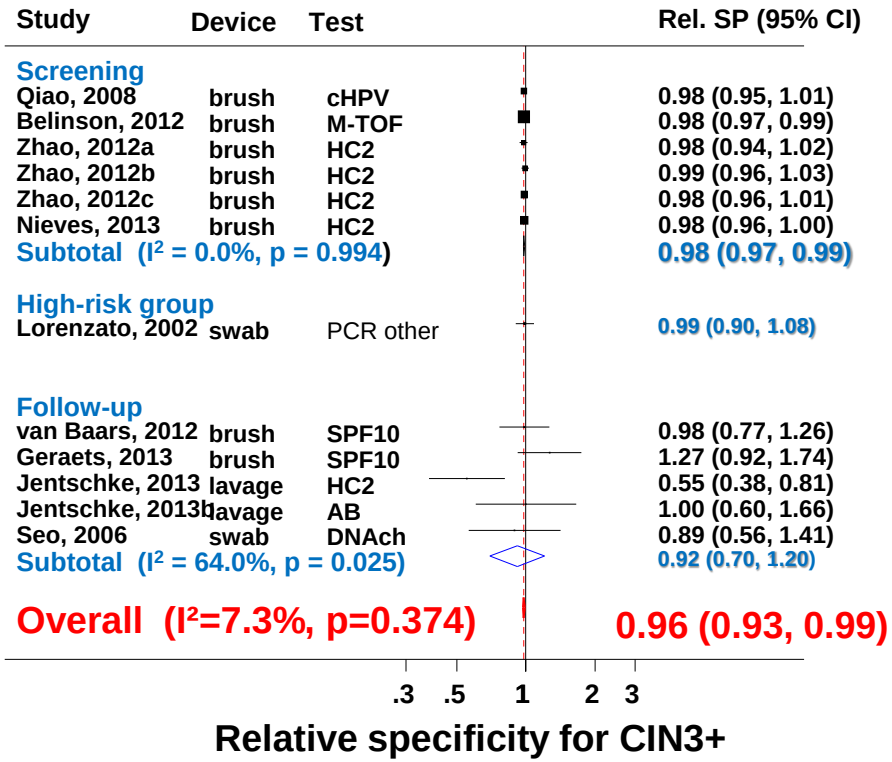
Strong test effects

- Signal amplification tests less sensitive and specific on self- compared to clinician-samples
- Validated PCR assays: similar sensitivity and specificity on self- as on clinician samples

Relative accuracy hrHPV on self-vs clininican sample: all studies, outcome CIN3+





PaVDaG (PapillomaVirus Dumfries and Galloway) Study

AIM

- To analytically optimise HPV detection of self-collected vagina and urine samples using PCR HPV test.

- To clinically validate PCR HPV detection using self-collected vagina and urine samples.

Validation guidelines for candidate HPV assays; *Meijer et al., 2009*

1. The candidate test should have a relative sensitivity for CIN2+ not less than 90%.

2. The candidate test should have a relative specificity for CIN2+ not less than 98%.

3. The intra- and inter-laboratory reproducibility should be determined by evaluation of at least 500 samples, 30% of which tested HPV positive.

PAVDAG (PapillomaVirus Dumfries and Galloway) Study

Open Access Research

BMJ Open

Clinical validation of hrHPV testing on vaginal and urine self-samples in primary cervical screening (cross-sectional results from the Papillomavirus Dumfries and Galloway – PaVDaG study)

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NHS Dumfries & Galloway

5332 women (20-60yrs)
April 2013-March 2015

- LBC
  - Managed as per national guidelines
- Cervical HPV
  - LBC-/HPV+
    - Repeat HPV testing after 4-6 months
      - LBC HPV
        - HPV16/18+
          - Colposcopy
      - Self-collected Vaginal HPV
      - Urine HPV
- Self-collected Vaginal HPV
- Urine HPV

611 LBC samples had CINtec *plus* testing

Sampling

Sample collection

1. The random void urine samples were collected and transported in the universal containers.

2. Self-collected vaginal samples were obtained using cobas PCR female swab sample packet

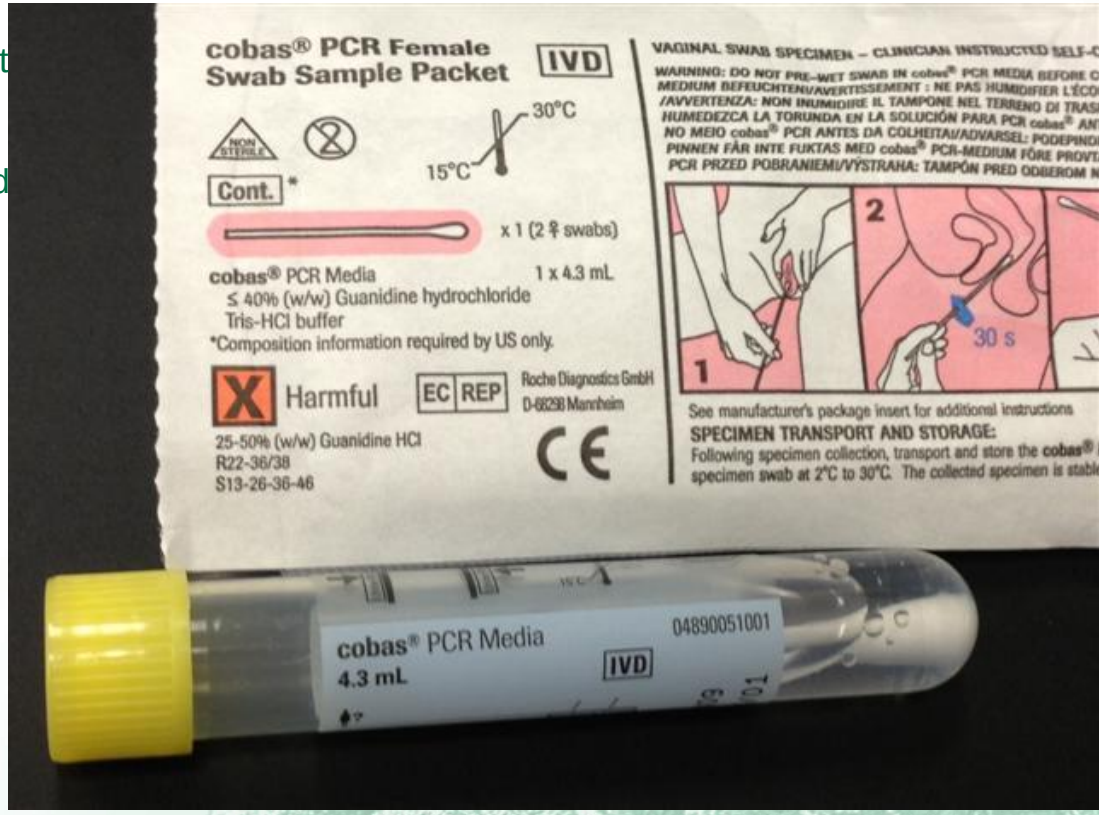
3. Cervical LBC samples were clinician-collected using Rovers® Cervex-Brush

   in 20ml of *ThinPrep* solution

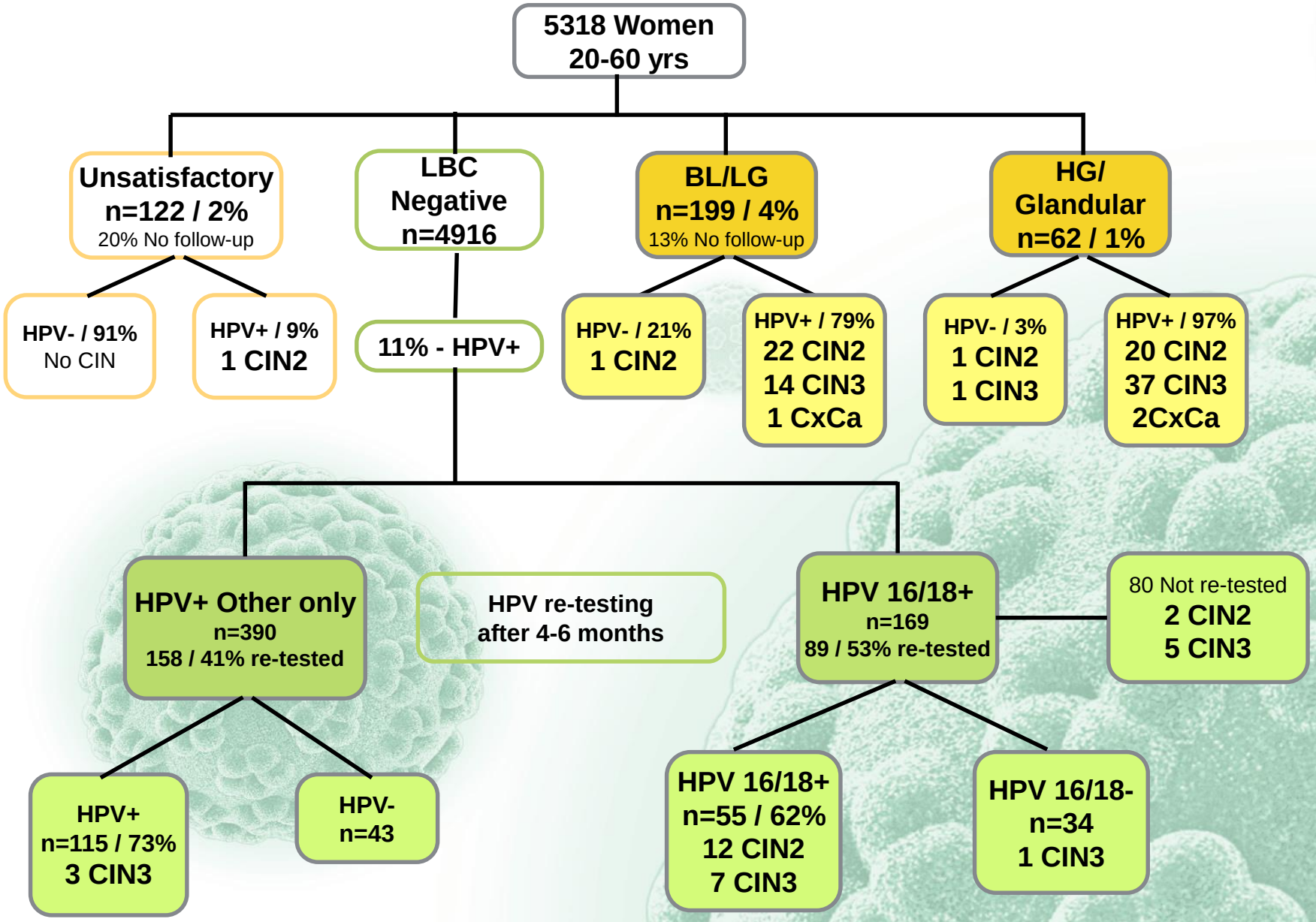
Sample processing

- Six ml of urine was mixed with 3 ml of Roche PCR media
- Three ml of LBC sample was aliquot into a separate tube for HPV testing.
- All three samples were tested using the cobas 4800 DNA HPV test with the program currently used for HPV detection in LBC samples.

Cobas PCR female swab sample packet



PAVDAG flow chart of cytology outcome, cervical HPV results and detection of CIN2+



Prevalence of cytological abnormalities, unsatisfactory smears and high-grade cervical intraepithelial neoplasia/cancer by age groups.

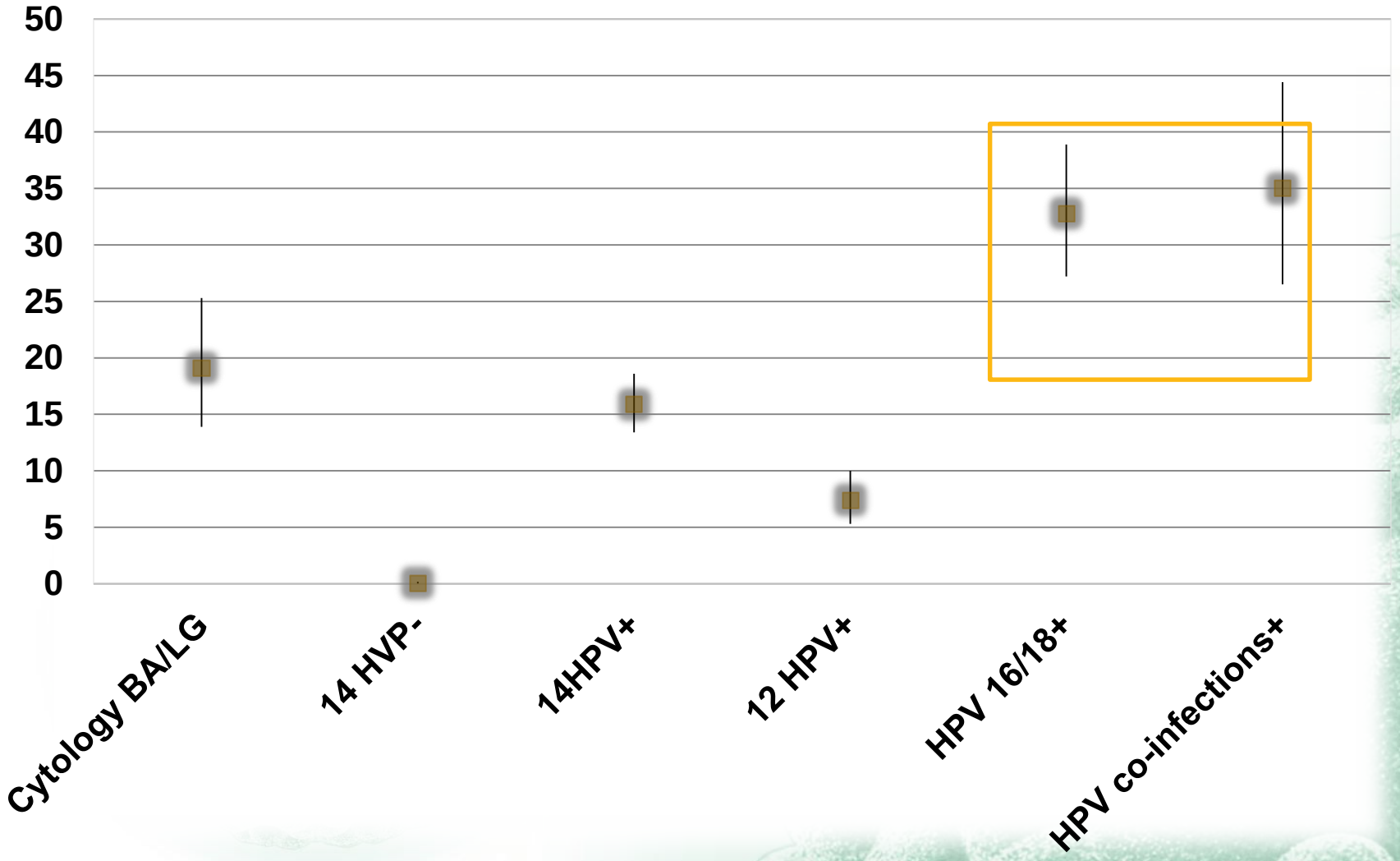
Age Total number	20-24 629	25-29 486	30-34 513	35-39 577	40-44 691	45-49 853	50-54 831	55-59 593	60+ 145	Total 5318
Cytology n/%										
BA/LG	77/12	30/6	25/5	16/3	18/3	21/2	6/0.7	6/1	0	**199/4**
HG	10/2	17/3.4	12/2	9/2	5/0.7	4/0.4	1/0.1	3/0.5	1/0.6	**63/1**
Unsatisfactory	3/0.4	9/2	8/2	7/1	14/2	17/2	25/3	30/5	10/7	**123/2**
Histology n/%										
Cancer	0	0	2	0	1	0	0	0	0	**3/0.05**
CIN3	14	20	9	8	5	7	1	2	1	**68/1**
CIN2	14	19	9	8	6	4	0	0	0	**59/1**
CIN2+	28/4	39/8	20/4	16/3	12/2	11/1	1	2	1	**130/2**

	Vaccinated N=354 (66%)	Non-vaccinated N=179
Abnormal cytology	**44/12**	**23/13**
Cervical HPV+	**127/36**	**81/45**
Vaginal/urine HPV+	**29**	**7**
Total HPV+	**156/44**	**88/49**
Cervical HPV16/18+	**10/3**	**29/16**
Vaginal/urine HPV+	**1**	**2**
Total HPV+	**11/3**	**31/17**
CIN2	**1**	**4**
CIN3	**1**	**7**

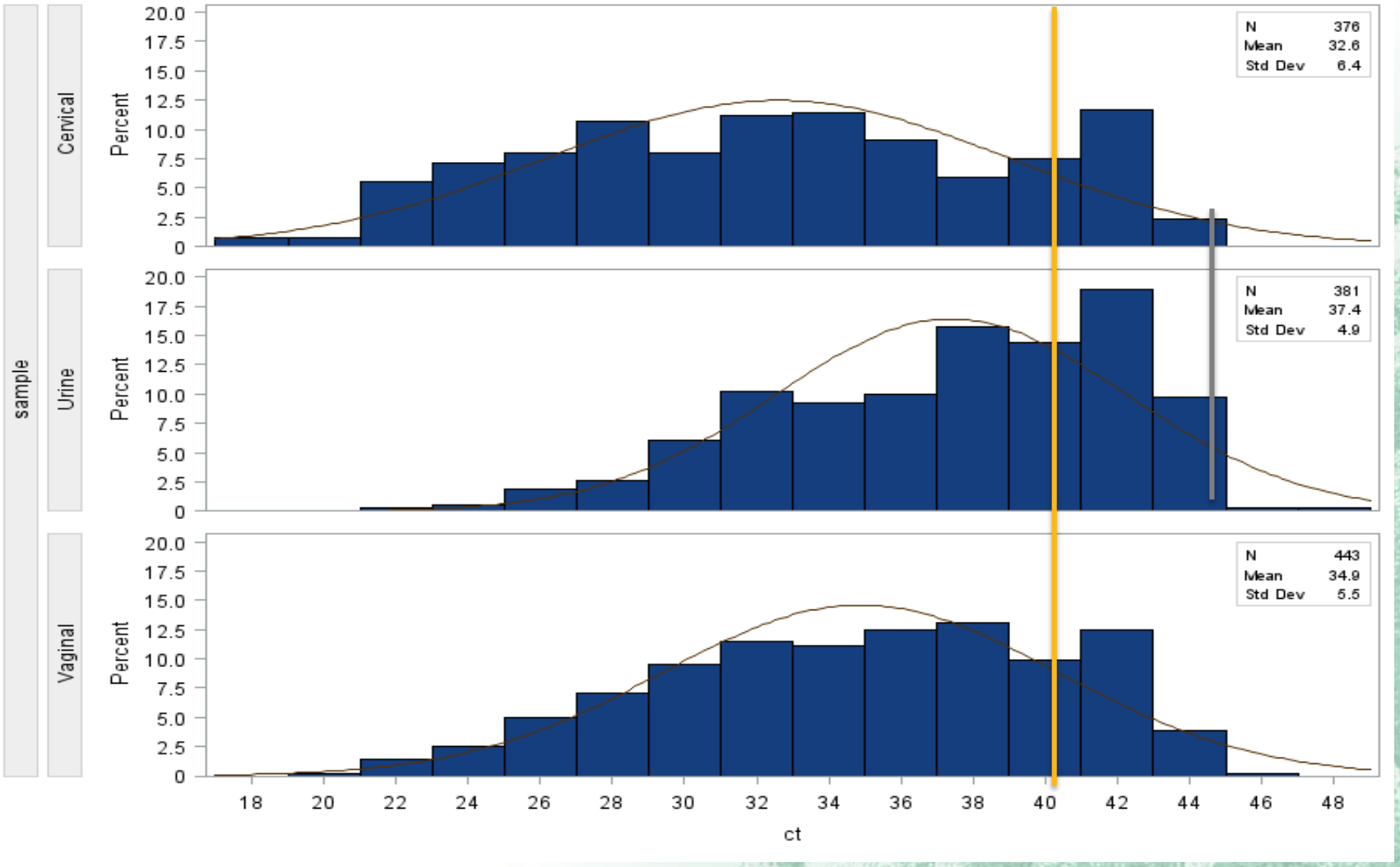
The cobas 4800 HPV detection in all three samples presented in %.
Furthermore distribution of HPV detection in women with normal cytology (Cyto-/HPV+)

Age Total number	20-24 629	≥20 yrs 5318	≥25 yrs 4689	≥30 yrs 4203
HPV+				
Cervical %	41	15	11	9
Vaginal %	43	17	13	11
Urine %	33	12	9	7
HPV- 16/18				
Cervical %	10	5	4	3
Vaginal %	10	6	5	4
Urine %	5	3	3	2
Cyto-/HPV+				
Cervical %	28	11	8	6
Vaginal %	29	12	10	8
Urine %	22	8	7	5
Cyto-/HPV 16/18+				
Cervical %	6	3	3	2
Vaginal %	5	4	4	3
Urine %	2	2	2	1
Cyto-/HPV Others +				
Cervical %	23	7	5	4
Vaginal %	24	8	6	5
Urine %	18	6	5	4

The risk of CIN2+ at baseline stratified by BA/LG cytology and HPV status in PAVDAG population



The distribution of ct values observed in PCR HPV DNA amplification using cobas 4800 assay in three samples.



Absolute sensitivity and specificity of cobas 4800 HPV testing on cervical, vaginal and urine samples and LBC to detect CIN2+ or CIN3+.

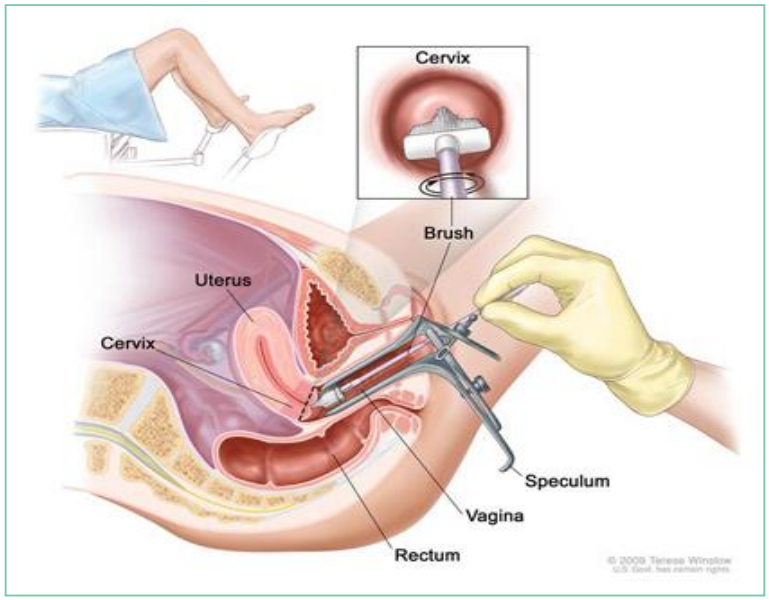
Test	Outcome	Sensitivity	(95% CI)	Specificity	(95% CI)
Cervical HPV	CIN2+	97.7%	95.0 - 100.0	87.3%	86.4 - 88.2
Vaginal HPV		**94.6%**	90.7 - 98.5	**85.4%**	84.4 - 86.3
Urine HPV		63.1%	54.6 - 71.7	89.8%	89.0 - 90.7
Cervical LBC		75.4%	68.0 - 82.8	96.9%	96.4 - 97.3
Cervical HPV	CIN3+	98.6%	95.9 - 100.0	86.4%	85.5 - 87.3
Vaginal HPV		**95.8%**	91.1 - 100.0	**84.8%**	83.8 - 85.8
Urine HPV		50.7%	39.1 - 62.3	89.7%	88.8 - 90.5
Cervical LBC		76.1%	66.1 - 86.0	96.1%	95.5 - 96.6

Relative sensitivity and specificity of cobas 4800 HPV; 95% confidence interval.

Comparison	Outcome	Relative Sensitivity (95% CI) ≥20 yrs	Relative Specificity (95% CI) ≥20 yrs	Relative Sensitivity (95% CI) ≥25 yrs	Relative Specificity (95% CI) ≥25 yrs
Vaginal vs. Cervical HPV	CIN2+	**0.97 (0.94-1.00)**	**0.98 (0.97-0.99)**	**0.96 (0.94-1.00)**	**0.98 (0.97-0.99)**
Urine vs. Cervical HPV		0.67 (0.59-0.76)	1.05 (1.04-1.06)	0.66 (0.59-0.76)	1.02 (0.99-1.04)
Cytology vs. Cervical HPV		0.78 (0.71-0.87)	1.11 (1.09-1.12)	0.79 (0.71-0.87)	1.08 (1.06-1.11)
Vaginal vs. Cervical HPV	CIN3+	**0.97 (0.93-1.01)**	**0.98 (0.97-0.99)**	**0.96 (0.93-1.01)**	**0.98 (0.97-0.99)**
Urine vs. Cervical HPV		0.53 (0.42-0.67)	1.03 (1.01-1.04)	0.56 (0.42-0.67)	1.02 (1.01-1.04)
Cytology vs. Cervical HPV		0.77 (0.68-0.88)	1.11 (1.09-1.14)	0.79 (0.68-0.91)	1.08 (1.06-1.11)

Conclusion:

Our data shows that the Cobas 4800 HPV test done on self-collected vaginal sample using vaginal swab self-collection kit (*as per* C/G testing, Roche) fulfils the criteria of international guidelines of HPV testing requirements for cervical screening.



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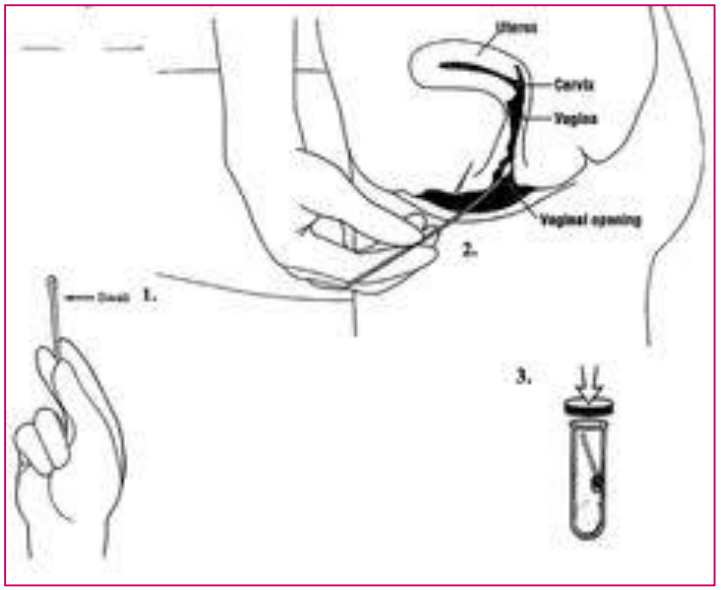
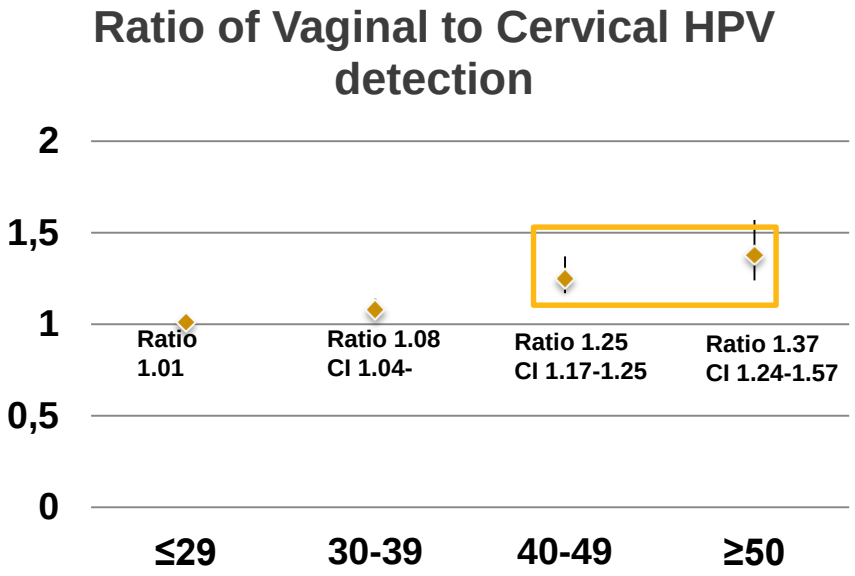
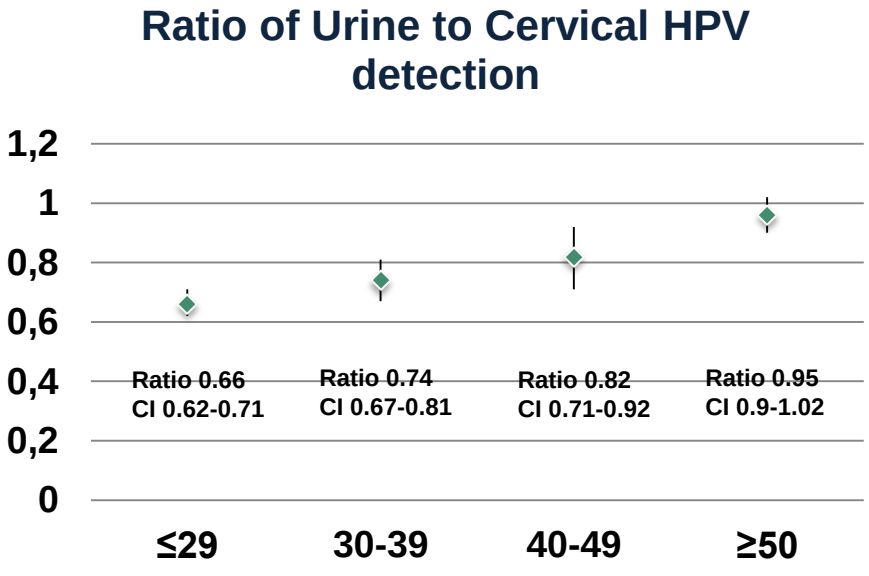


Age specific distribution of cobas 4800 HPV detection.

Age Total number	20-24 629	25-29 486	30-34 513	35-39 577	40-44 691	45-49 853	50-54 831	55-59 593	60+ 145	Total 5318
HPV+										
Cervical %	41	33	20	11	8	8	4	6	4	15
Vaginal %	43	33	20	14	12	9	6	7	8	17
Urine %	33	23	14	10	8	6	4	5	6	12

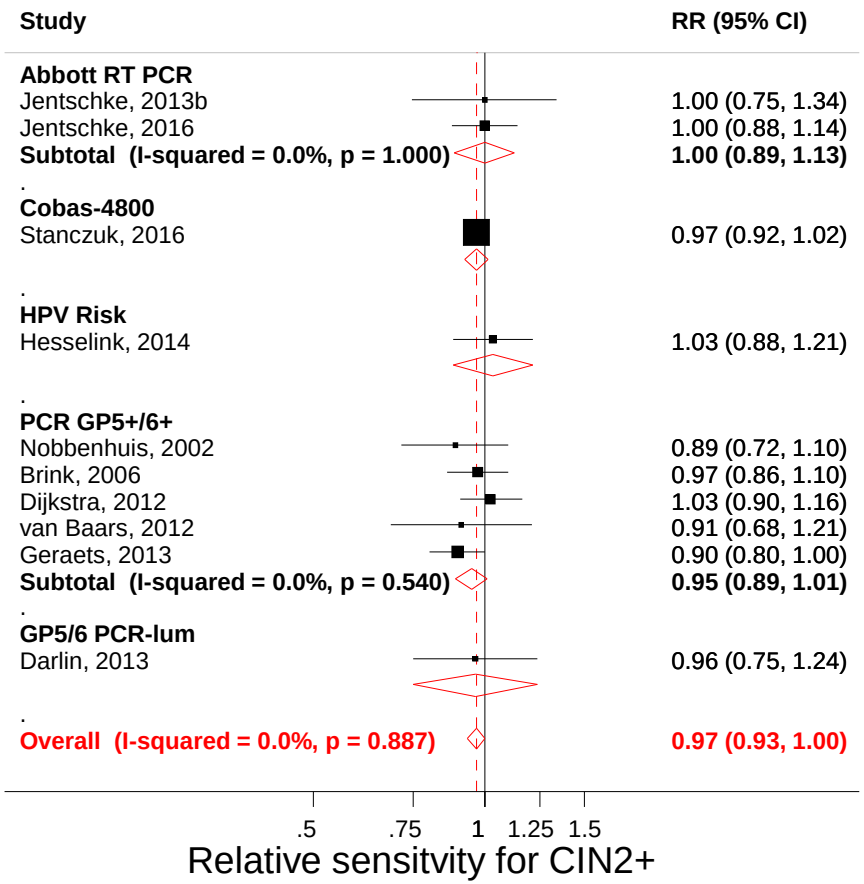


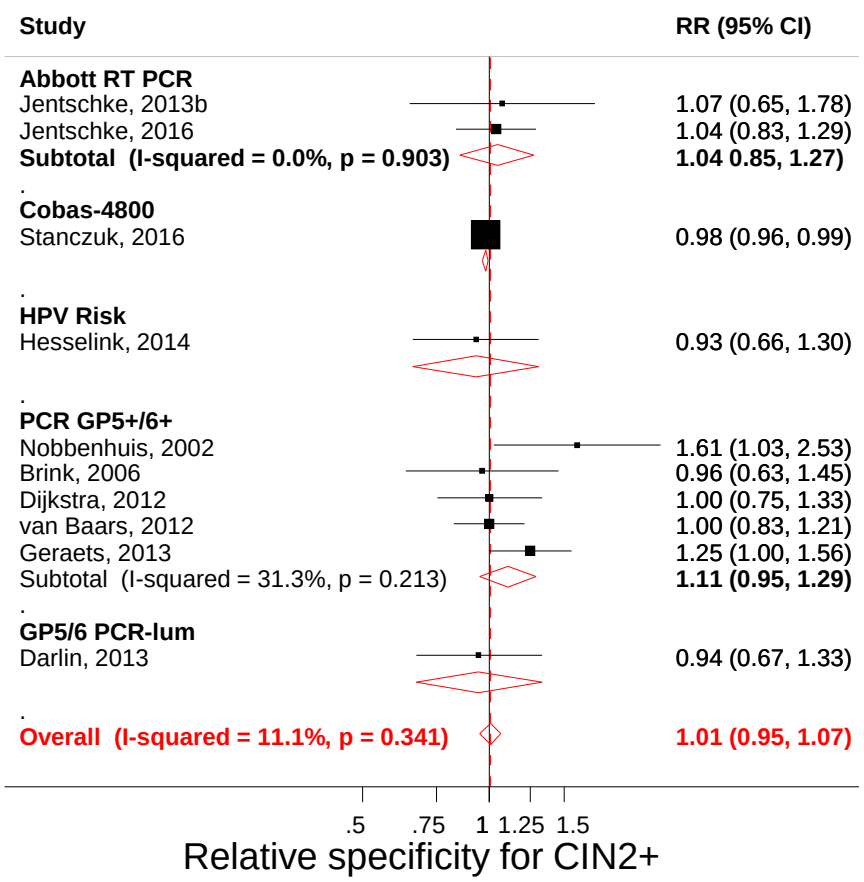


Age Total number	20-24 629	25-29 486	30-34 513	35-39 577	40-44 691	45-49 853	50-54 831	55-59 593	60+ 145	Total 5318
Unsatisfactory	3/0.4	9/2	8/2	7/1	14/2	17/2	25/3	30/5	10/7	**123/2**

Relative sensitivity and specificity for CIN2+ hrHPV DNA testing of self- vs clinician-collected *Validated PCRs* (Update May 2016)

Update: signal amplification vs validated PCR





Arbyn & Castle, CEBP 2015

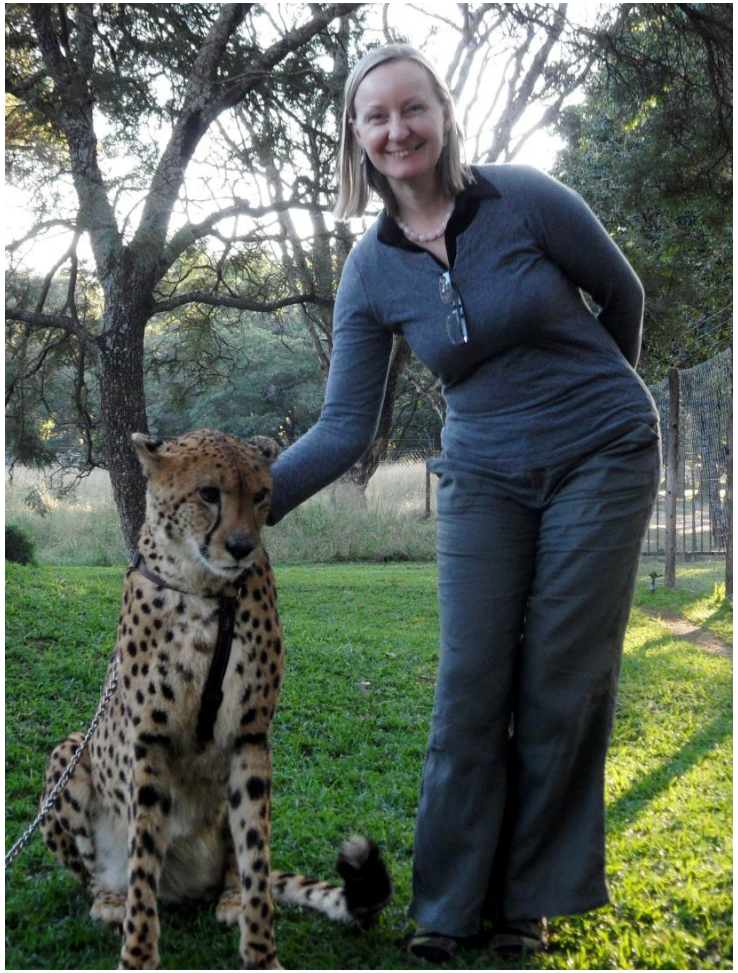
Accuracy of multiple triage test to detect CIN2+ among HrHPV+ women identified by vaginal self-sampling.

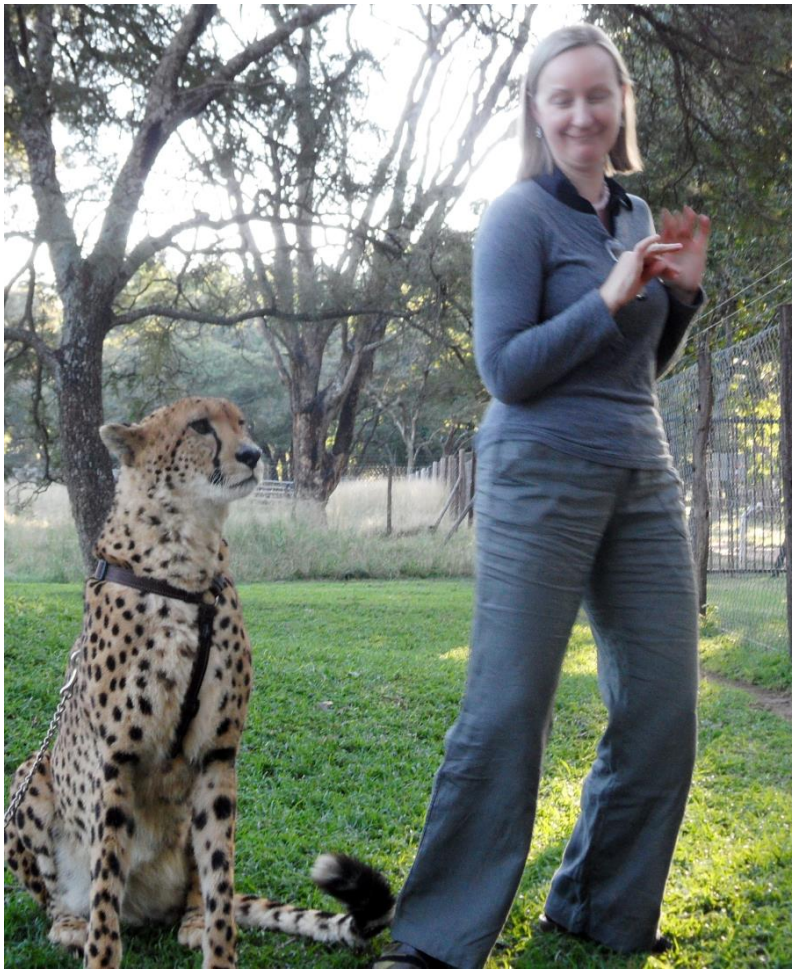
Triage	Sensitivity (95% CI)	Specificity (95% CI)	PPV	cNPV *(Complement of NPV=1-NPV)*	No of colps	RV (NNR)
CINtec PLUS	86 (76-95)	77 (71-82)	0.437	0.025	282	2.3
HPV-16/18	61 (47-74)	80 (75-84)	0.328	0.075	261	3.1
LBC (ASC-US+)	74 (60-84)	91 (87-94)	0.569	0.046	181	1.8

Triage	Sensitivity (95% CI)	Specificity (95% CI)	PPV	cNPV *(Complement of NPV=1-NPV)*	No of Colposcopy	RV (NNR)
Cytology CINtec PLUS	93 (83-98)	78 (73-82)	0.408	**0.015**	321	2.4
HPV-16/18 CINtec PLUS	95 (85-99)	56 (50-62)	0.277	**0.015**	482	3.6
HPV-16/18 Cytology	95 (85-99)	64 (58-70)	0.299	**0.014**	446	3.3
HPV-16/18 Cytology CINtec PLUS	**98 (90-100)**	**57 (51-62)**	**0.270**	**0.005**	**512**	**3.7**

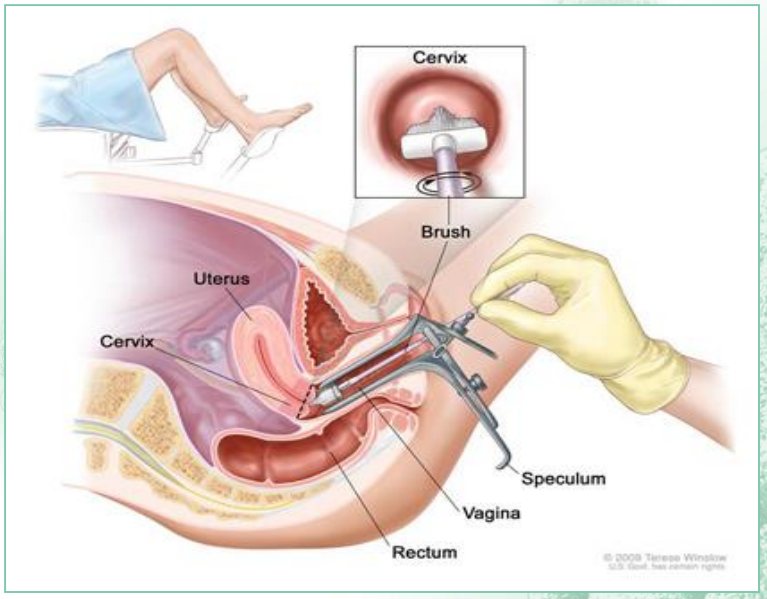
Stanczuk et al, 2018

Not a trivial experience





Should a primary sampling method be cervical or vaginal self-sample?



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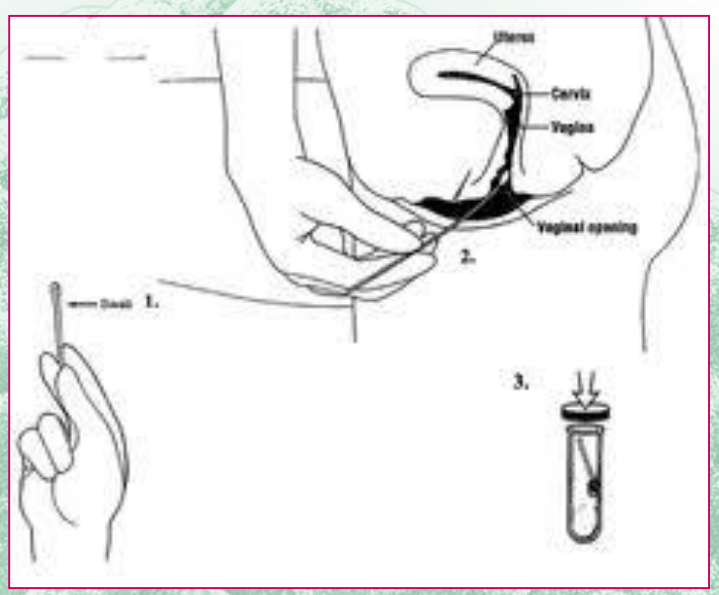

Is it ethical not to offer the two options?


Thank you