



# EUROGIN

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## PERFORMANCE OF A 7-TYPE HPV mRNA TEST IN TRIAGE OF HPV DNA PRIMARY SCREEN POSITIVE WOMEN COMPARED TO LIQUID-BASED CYTOLOGY

MD. PhD. Sveinung Wergeland Sørbye

Sveinung W. Sørbye, Bente M. Falang, Mona Antonsen



UNIVERSITETSSYKEHUSET NORD-NORGE  
DAVVI-NOROGGA UNIVERSITEHTABUOHCCVEIUSSU



# Disclosures

- I have nothing to declare
- This study had nonfinancial support from PreTect AS, which provided reagents for free

**HPV-based  
screening-  
a  
recommended  
public health  
policy**

- ❑ HPV-based primary screening stands as the gold standard in cervical cancer prevention strategies
- ❑ The transition to a more sensitive first-line test prompts a critical discussion on effective triage - to mitigate the risks of overdiagnosis and overtreatment of transient HPV infections
- ❑ Presently, cytology remains the predominant triage method for HPV-DNA positive women in most countries
- ❑ A range of molecular triage alternatives is under evaluation to enhance precision and efficiency

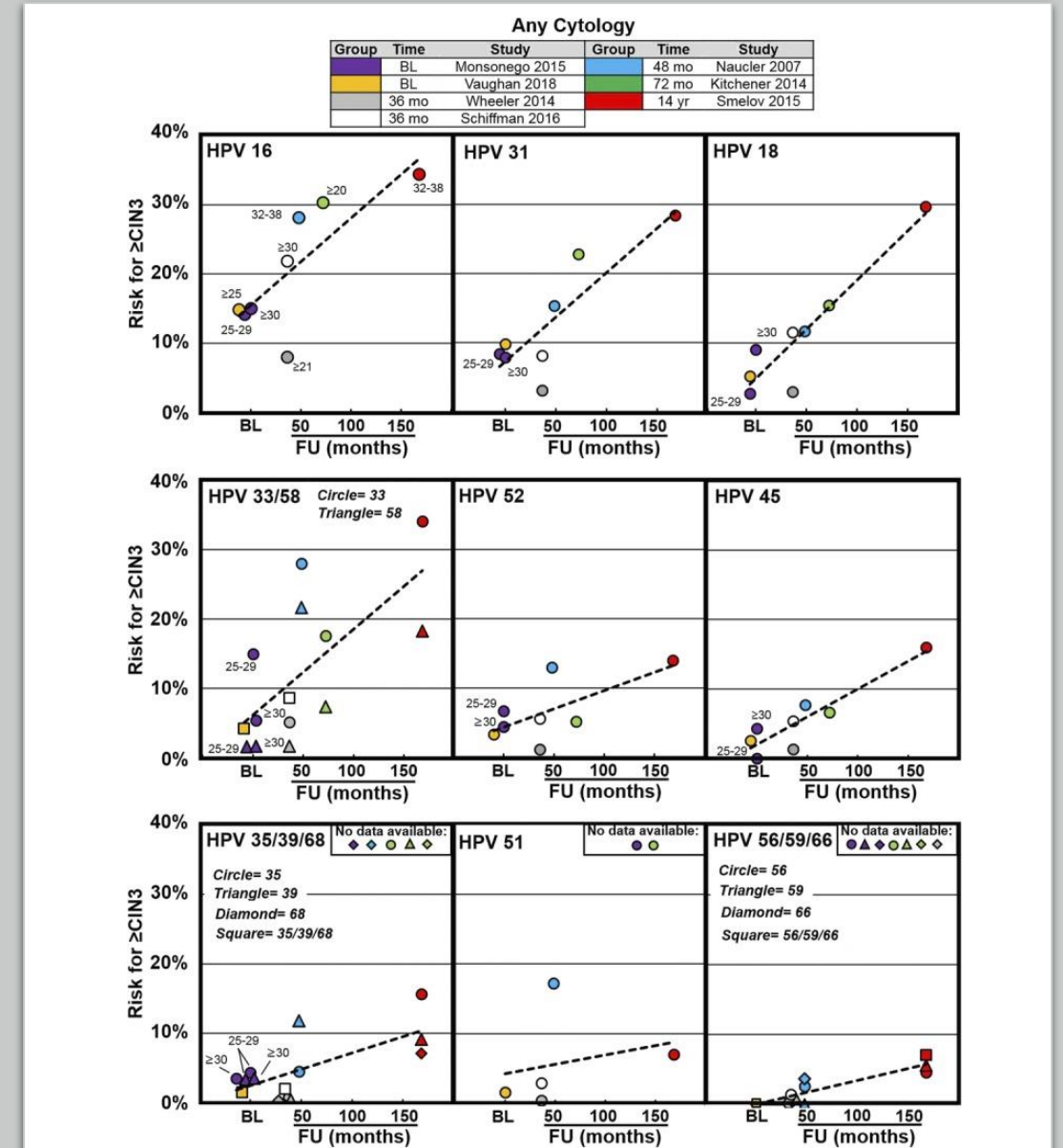
## Primary HPV-DNA Challenges

- ❑ A considerable proportion of screen positives (10-20%)
- ❑ Substantial increased number in colposcopies and biopsies strain healthcare systems and causing undue patient anxiety
- ❑ Most women with a positive HPV-DNA test do not harbor clinically significant disease
- ❑ HPV DNA tests with 14 genotypes exhibit lower specificity compared to cytology
- ❑ Effective triage and risk stratification are paramount in mitigating unnecessary colposcopies and biopsies

# HPV Genotype Specific CIN3+ Risks - regardless of Cytology

- HPV 16
- HPV 18, 31, 33, 45, 52, 58
- HPV 35, 39, 51, 56, 59, 66, 68

Risks lower than  
the colposcopy  
threshold



\*Bonde, J. et al. Clinical Utility of Human Papillomavirus Genotyping in Cervical Cancer Screening: A Systematic Review. J Low Genit Tract Dis. 2020 Jan;24(1):1-13. Fig 1.

**A risk-based  
approach:  
PreTect  
HPV-Proofer`7**

- ❑ Detects HPV mRNA E6/E7; precursors of the oncoproteins known to disturb normal cell cycle
- ❑ Genotypes the seven most prevalent HPV types responsible for approximately 90% of all cervical cancer cases
  - HPV 16, 18, 31, 33, 45, 52 and 58
- ❑ Demonstrates a low positivity rate within the general population reducing unnecessary follow-up procedures
- ❑ only one-third of HPV DNA-positive cases exhibit mRNA expression from the seven targeted types

**HPV-DNA  
primary  
screening  
  
Norway**

**Implemented in 2019:**

- Women 34-69 yrs. screened by HPV
- Women 25-33 yrs. screened by cytology

**Extended in July 2023:**

- All Women 25-69 years of age HPV tested

**Follow-up of test positives:**

- More intense follow-up of HPV16/18+
- Cytology

# Evaluation of 7-type HPV mRNA Test compared to LBC in Triage of Screen Positives

## HPV DNA Primary Screening

- ❑ Women 34-69 yrs. (2019-2022)
- ❑ HPV DNA test: Cobas 4800, Roche

## Triage of all HPV DNA positives by

- ❑ Cervical Cytology (LBC)
- ❑ HPV mRNA test (PreTect HPV-Proofer`7)

## Study endpoint:

- ❑ Histologically confirmed CIN2+
- ❑ Follow-up: October 2023

## Data Phase 1: published (2019-2021)

- ❑ J. Mol. Pathol. 2023, 4, 69-8  
<https://doi.org/10.3390/jmp4020008>

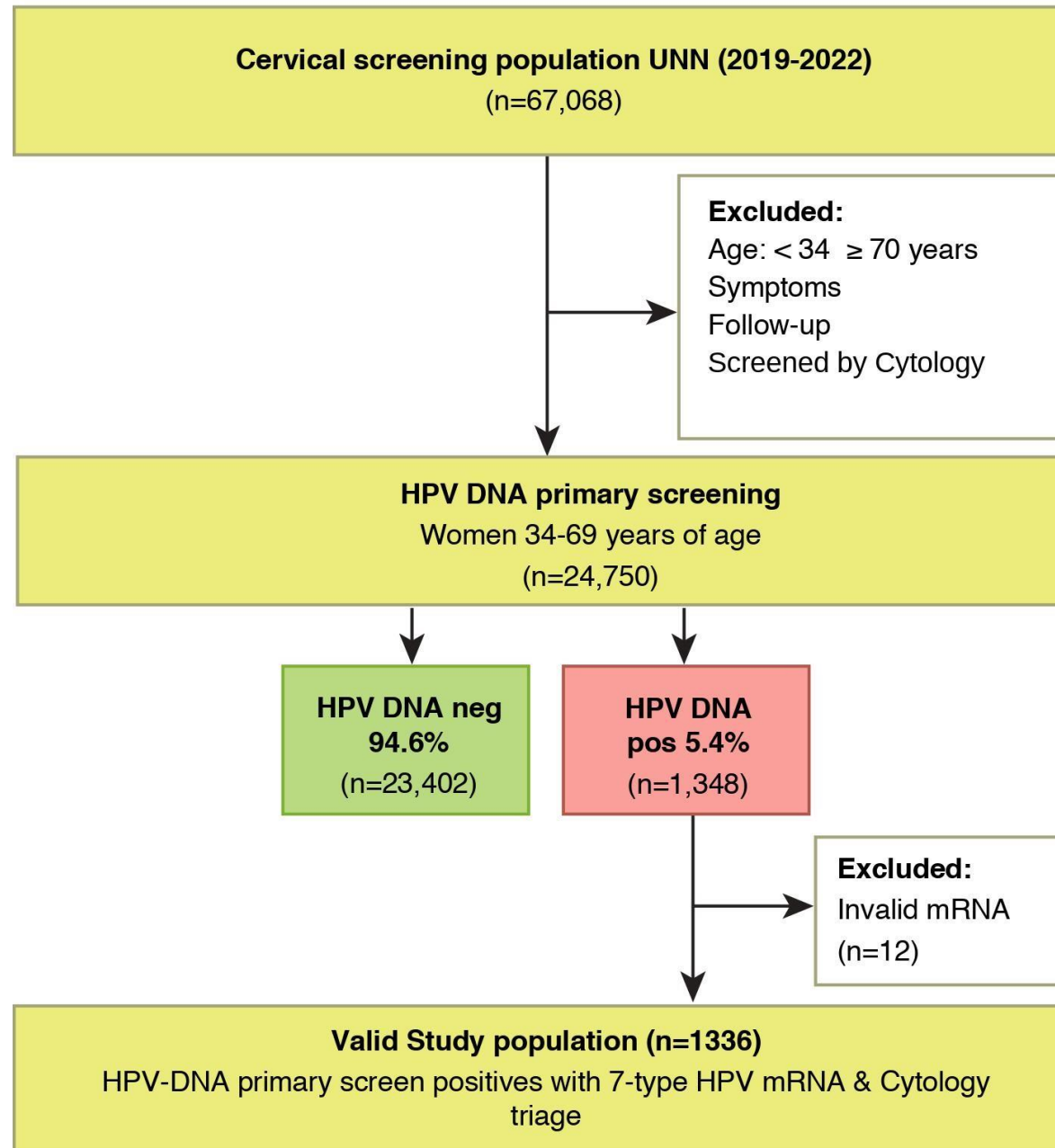




## Study Objectives

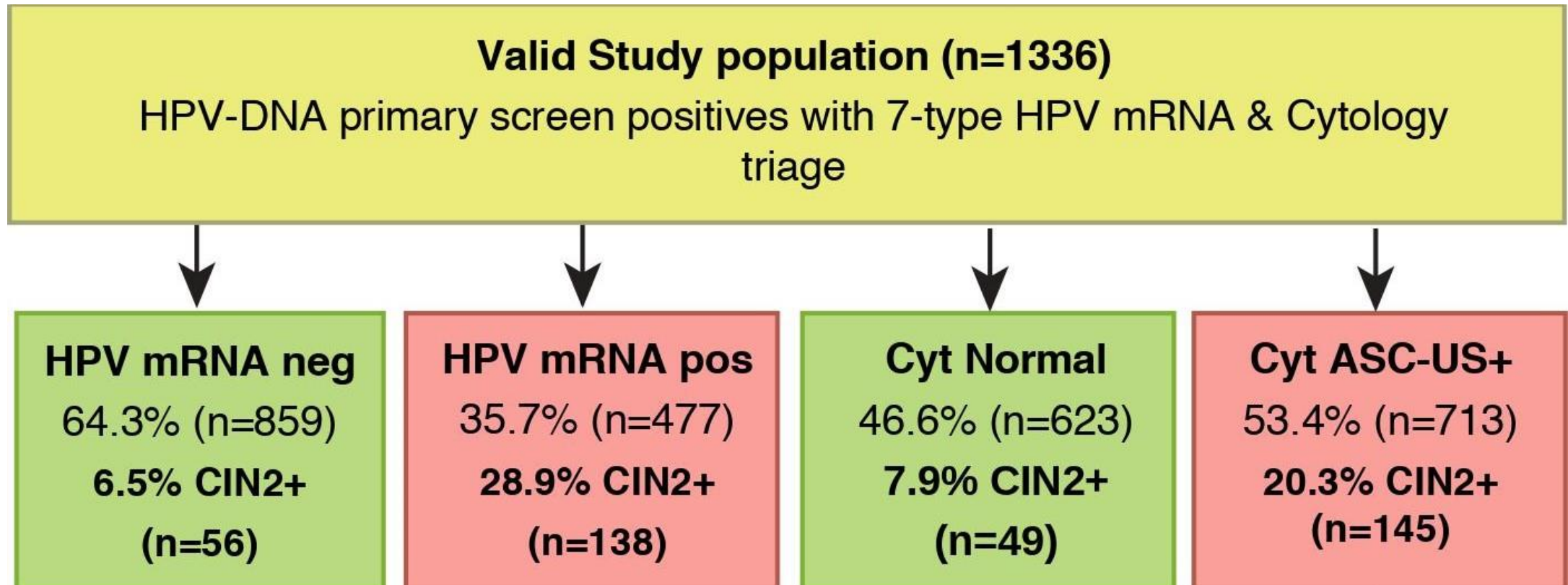
- ❑ Compare performance of 7-type HPV mRNA test to LBC in triage of HPV primary positives
  - Sensitivity, Specificity, Diagn. Accuracy, PPV, NPV
  - Cut-off ASC-US+/7-type mRNA+
- ❑ Establish the risk of CIN2+ at the point of
  - Primary screening
  - Triage
- ❑ Assess the rate of colposcopies per CIN2+
- ❑ Calculate absolute risk of CIN2+ by HPV genotypes for DNA versus mRNA detection

# Selection Study Population



# Results 1.

## Test positivity rates and CIN2+ prevalence



## Results 2.

Test performances for detection of CIN2+ in HPV DNA pos. women

Triage	TP	TN	FP	FN	SE %	SP %	AU %	PPV %	95% CI	NPV %
Cytology ASC-US+	145	574	568	49	74.7	50.3	62.5	20.3	17.5-23.5	92.1
HPV mRNA`7+	138	803	339	56	71.1	70.3	70.7	28.9	24.9-33.3	93.5

HPV mRNA`7: 16, 18, 31, 33, 45, 52, 58+

## Results 3.

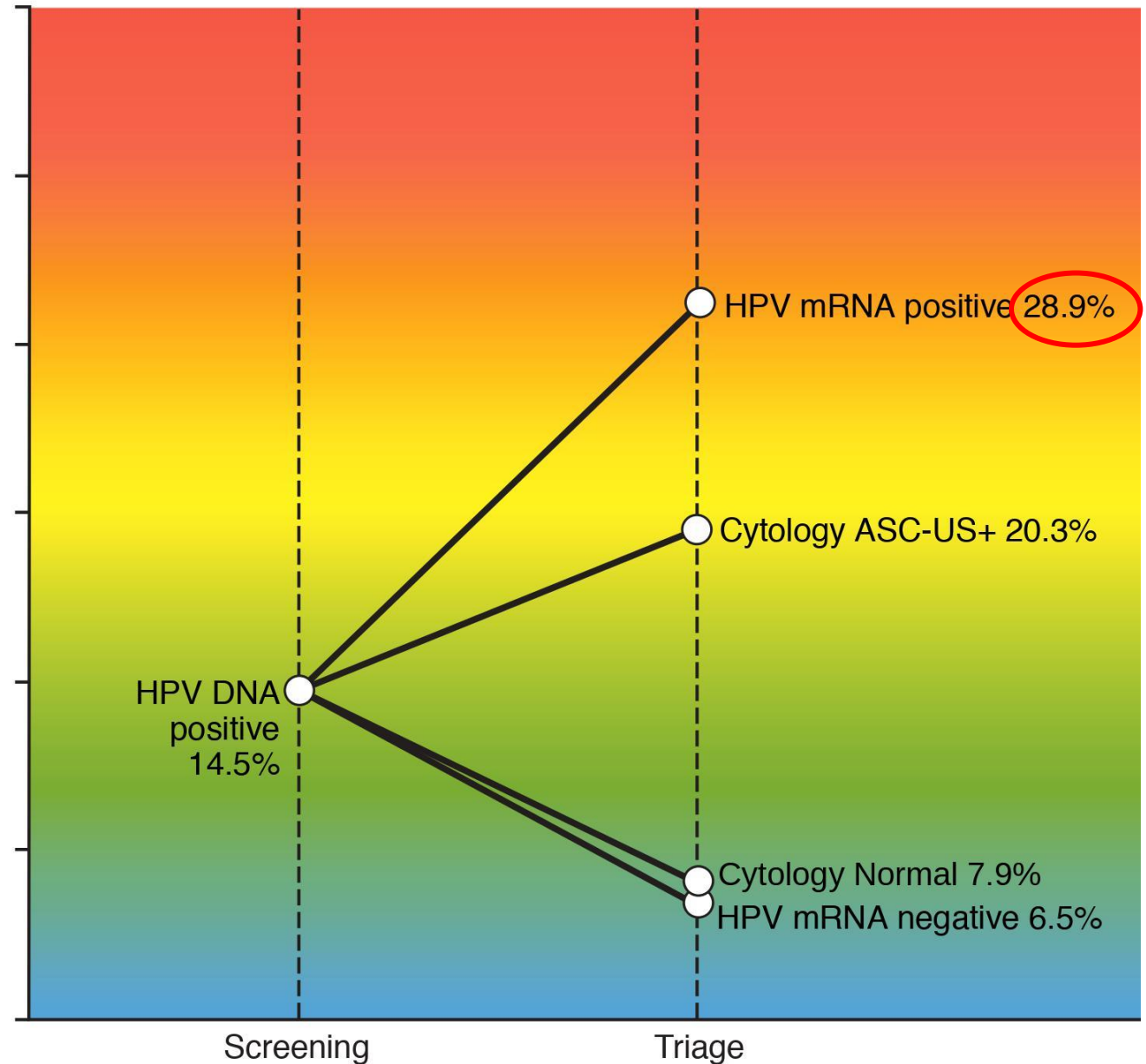
The number of colposcopies required per  $\geq$  CIN2 case detected

Triage strategy	Positives %	CIN2+ <sup>1</sup> n	Colposcopies <sup>2</sup> n	Colposcopies <sup>3</sup> per detected CIN2+
ASC-US+	53.4	145	713	4.9
HPV mRNA+	35.7	138	477	3.5

- (1) the number of CIN2+ cases detected by each strategy among the total 194 cases.
- (2) the estimated number of colposcopies to be performed if all test positives are scheduled to colpo.
- (3) the calculated number of colposcopies required to detect one case of CIN2+.

# Results 4. Risk of CIN2+ across screening tests

Increasing risk of high grade dysplasia (CIN2+) %



## Results 5.

### Absolute risk for CIN2+ per HPV DNA & mRNA genotype (Phase1)






HPV genotype	No. of infections	No. of CIN2+	Risk estimate (%)	95% CI
16_DNA	130	45	34.6	26.4 - 42.8
<b>16_mRNA</b>	73	39	<b>53.4</b>	42.0 - 64.9
18_DNA	39	9	23.1	9.9 - 36.3
<b>18_mRNA</b>	30	10	<b>33.1</b>	16.5 - 50.2
Other_12 DNA pool*	793	80	10.1	8.0 - 12.2
<b>Other_5 mRNA pool**</b>	235	49	20.9	15.7 - 26.0
31_mRNA	88	23	26.1	17.0 - 35.3
<b>33_mRNA</b>	28	14	<b>50.0</b>	31.5 - 68.5
45_mRNA	59	8	13.6	4.8 - 22.3
52_mRNA	59	14	23.7	12.9 - 34.6
58_mRNA	32	6	18.8	5.2 - 32.3

\*12 types DNA (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)

\*\* 5 types mRNA (31, 33, 45, 52, 58)

## Study Conclusions

The PreTect HPV-Proofer`7 test performance compared to LBC in triage of HPV-DNA positives:

		<b>mRNA vs. LBC</b>
<input type="checkbox"/> Specificity		70.3% vs. 50.3%
<input type="checkbox"/> PPV		28.9% vs. 20.3%
<input type="checkbox"/> Sensitivity		71.1% vs. 74.7%
<input type="checkbox"/> NPV		93.5% vs. 92.1%
<input type="checkbox"/> No. of colpo.		3.5 vs. 4.9

Using this biomarker as a threshold for referral to colposcopy may better balance the benefits and harms of screening, reducing over referrals.



## Take home messages

HPV DNA primary screening provides high sensitivity and improved prevention of CC

Risk stratification is required for accurate patient management of HPV DNA positive women

7 HPV-types are crucial  
HPV 16, 18, 31, 33, 45, 52, 58 cause 90% of CC

A 7-type HPV mRNA test might better balance benefits/harms of screening and allows self-sampling

A low mRNA positivity rate gives a low referral rate for colposcopy and might reduce over-treatment

An aerial night view of Tromsø, Norway, showing the city lights reflecting on the water and the Aurora Borealis in the sky. The city is illuminated with warm yellow and orange lights, while the surrounding mountains and water are in deep shadow. The Aurora Borealis is a vibrant green, appearing as a large, ethereal shape in the dark sky above the city.

*Tromsø*  
the Gateway to the Arctic

Thank you for your attention!