



Primary Cervical Cancer Screening with a 5-type HPV E6/E7 mRNA test: Results of 10 years follow-up

Sørbye SW¹, Rad A², Skjeldestad FE²

University Hospital of North Norway

No conflicts of interests to declare



Background

HPV DNA testing offers better protection from cervical cancer than cytology, but at the cost of substantially more false-positive tests and low-grade CIN diagnoses

HPV DNA primary screening in women 25-33 years will lead to huge challenges when as many as 30% of young women will have a positive HPV DNA-test

HPV E6/E7 mRNA detects the overexpression of E6 and E7 and is more specific than a test that detects the presence of viral DNA

Objectives

Assess the performance of a 5-type HPV mRNA test in primary screening

Estimate cumulative risk of CIN3+ after 42 - 78 - 120 months of follow-up

Evaluate if HPV E6/E7 mRNA test is suitable in women 25-33 years

Evaluate the risk of CIN3+ in women with negative HPV mRNA test

Methods

The study was initiated by Clinical Pathology, University Hospital of North Norway starting in 2003 with follow up until 2015.

Follow-up: cytology/ histology data from the Norwegian Cancer Registry (NCR).

Cytology: Bethesda system PAP/LBC (ThinPrep)

Histology: CIN classification

HPV testing: PreTect HPV-Proofer

Individual genotyping of HPV E6/E7 mRNA 16, 18, 31, 33 and 45

Study population

Women attending national screening progr (2003-2004)

**Total
N=19,153**

- In 2003-2004, 19,153 women in Norway were tested with HPV mRNA test in primary and secondary screening
- Follow-up: Cytology every 3 years through 2015

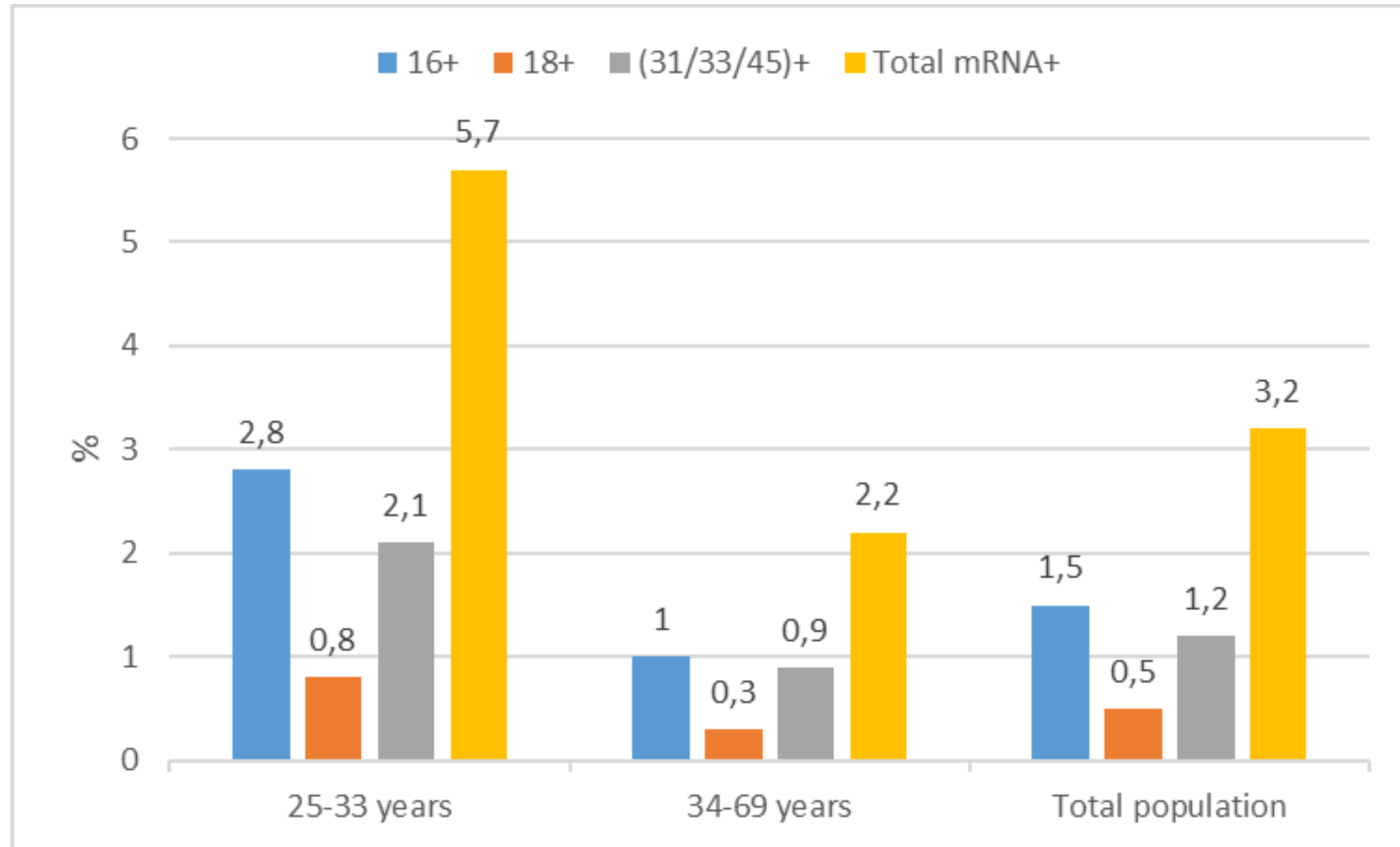
**Excluded
N=9,571**

- By Age < 25y and > 69y
- By Abnormal/Unsatisfactory/No Cytology
- By Biopsy with previous CIN1+

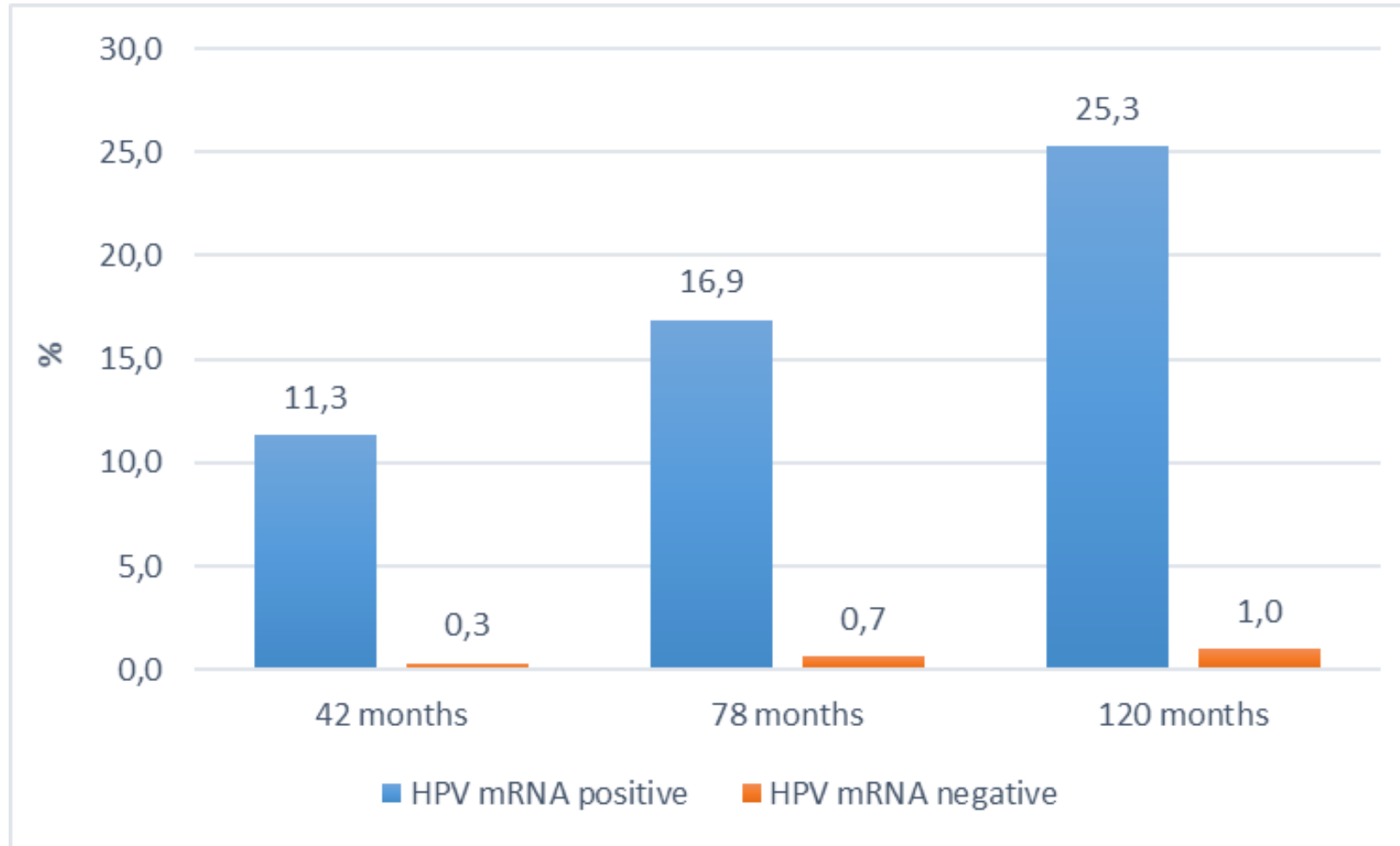
**Valid
N=9,582**

- Eligible: 9,582 women 25-69 yrs, resembling primary screening
- 25-33y: 27.2% (n=2,610)
- 34-69y: 72.8% (n=6,972)

HPV mRNA prevalence by age

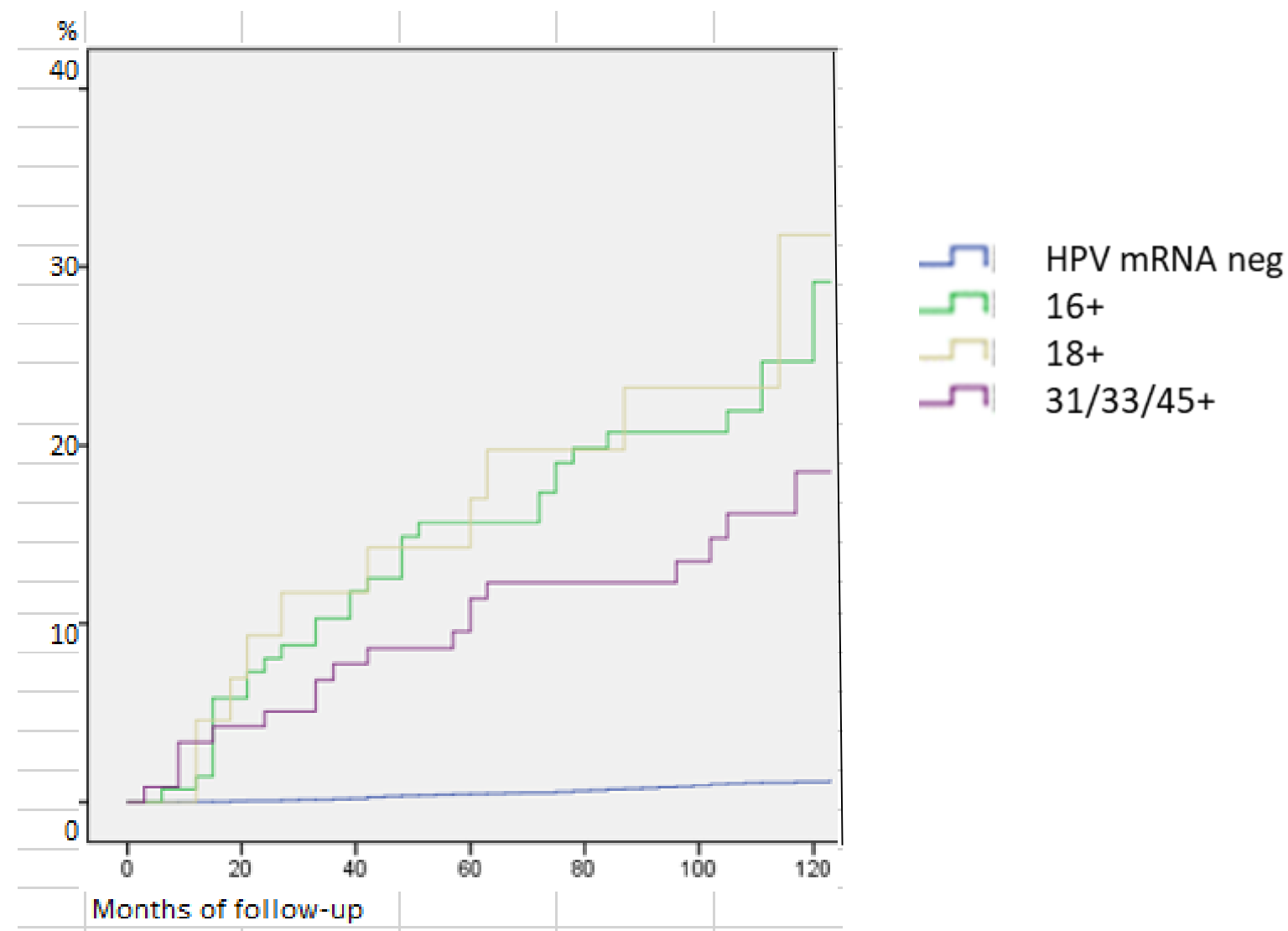


Cumulative risk of CIN3+ at 3.5 – 6.5 – 10 years follow-up

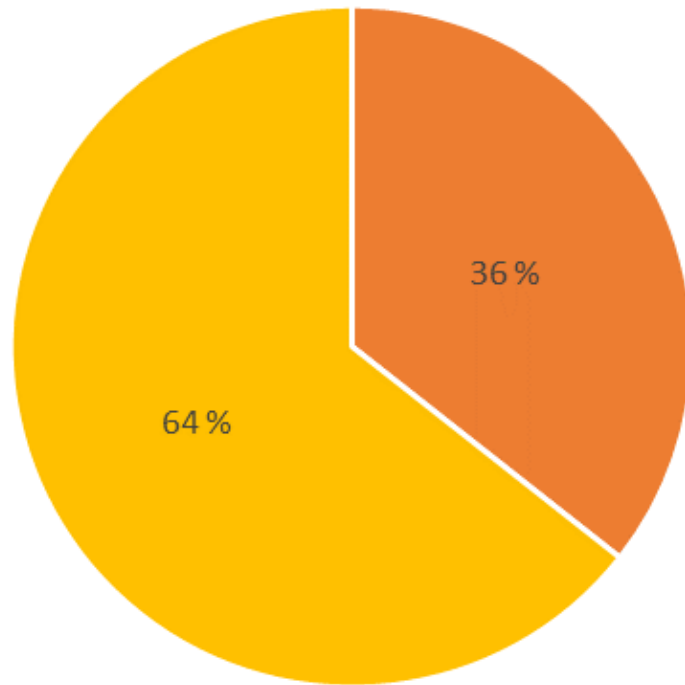


Cumulative risk of CIN3+ by HPV mRNA genotypes

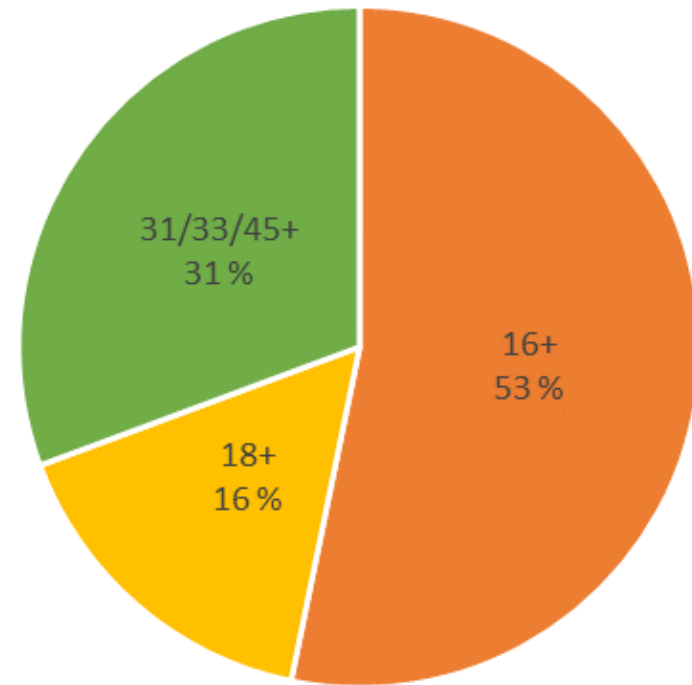
25.3% overall risk mRNA pos / 0.99% risk mRNA neg



CIN3+ cases by age/ HPV mRNA genotypes



■ 25-33 ■ 34-69



■ 16+ ■ 18+ ■ 31/33/45+

Summary

- PreTect HPV-Proofer positivity rate by age: (25-69): **3.2%**
(25-33): 5.7%
(34-69): 2.2%
- 10-years risk of CIN3+ for HPV mRNA positive women: **25.3%**
 - Age 25-33 had significantly higher cumulative risk of CIN3+ than 34-69
 - No differences in cumulative risk of CIN3+ by HPV mRNA types
- 10-years risk of CIN3+ for HPV mRNA negative women: **0.99%**

Conclusions

- ✓ Screening for cervical cancer should minimize harm and maximize benefit by detecting as many true positives and as few false negative as possible
- ✓ PreTect HPV-Proofer positive women in primary screening have a significant elevated risk of CIN3+ and can be referred directly to colposcopy and biopsy without cytology triage
- ✓ Low HPV mRNA positivity rate in screening population implies low referral rates and reduced risk of over-treatment
- ✓ PreTect HPV-Proofer negative women have low risk of CIN3+ and may return to screening at 5 years interval