EUROGIN 2022

7-Type HPV mRNA test in triage of HPV DNA positive women

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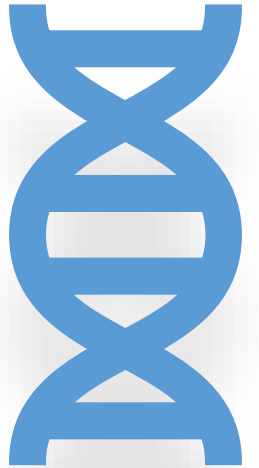

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Disclosures

- SWS has nothing to disclose
- PreTect AS has provided HPV mRNA kits and testing FOC

HPV-based screening- a recommended public health policy

- 99.7% of all cases of cervical cancer are caused by HPV
- HPV DNA test in primary screening improves prevention of cervical cancer
- Prolongs test interval for screen negatives compared to cytology
- Molecular testing is objective, reproduceable and allows use of self-collected samples which may increase access to screening

Primary HPV-DNA challenges

- Generates a lot of screen positives (5-20%)
- Not to be used in young women < 30 years
- Most women with a positive HPV-DNA test do not have clinically significant disease
- HPV DNA assays with 14 genotypes have a lower specificity compared with Pap smears
- Substantial increased number of biopsies
- Effective **Triage & Risk stratification** is crucial to avoid unnecessary follow-up

Triage
A risk-based approach

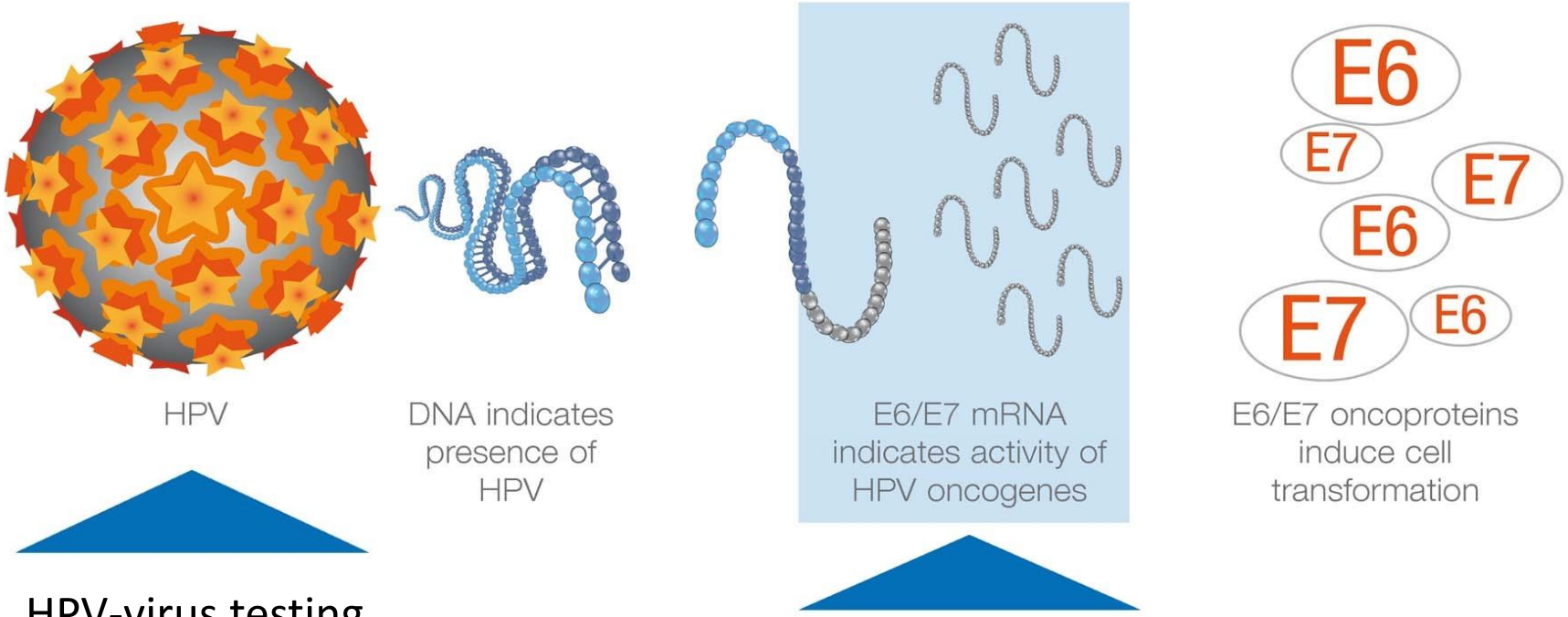
- 90% of HPV infections are harmless
- To more accurately identify the women who are warranted for colposcopy by discriminating among the HPV infections
- To reduce unnecessary interventions and risk of overtreatment
- Requires a highly specific test, detecting as few false positives as possible

Triage by Cytology

- PAP technology from 1920
- Relies on subjective skills
- Poor reproducibility
- Low sensitivity (50-60%)
- Low specificity
- Knowledge of HPV-status affects interpretation
- Difficulties detecting adenocarcinomas
- Not compatible with self-collected samples

The Cause of Cervical Cancer

Different Prevention Concepts



HPV-virus testing identifies a harmless condition

E6/E7 mRNA identifies a high risk condition

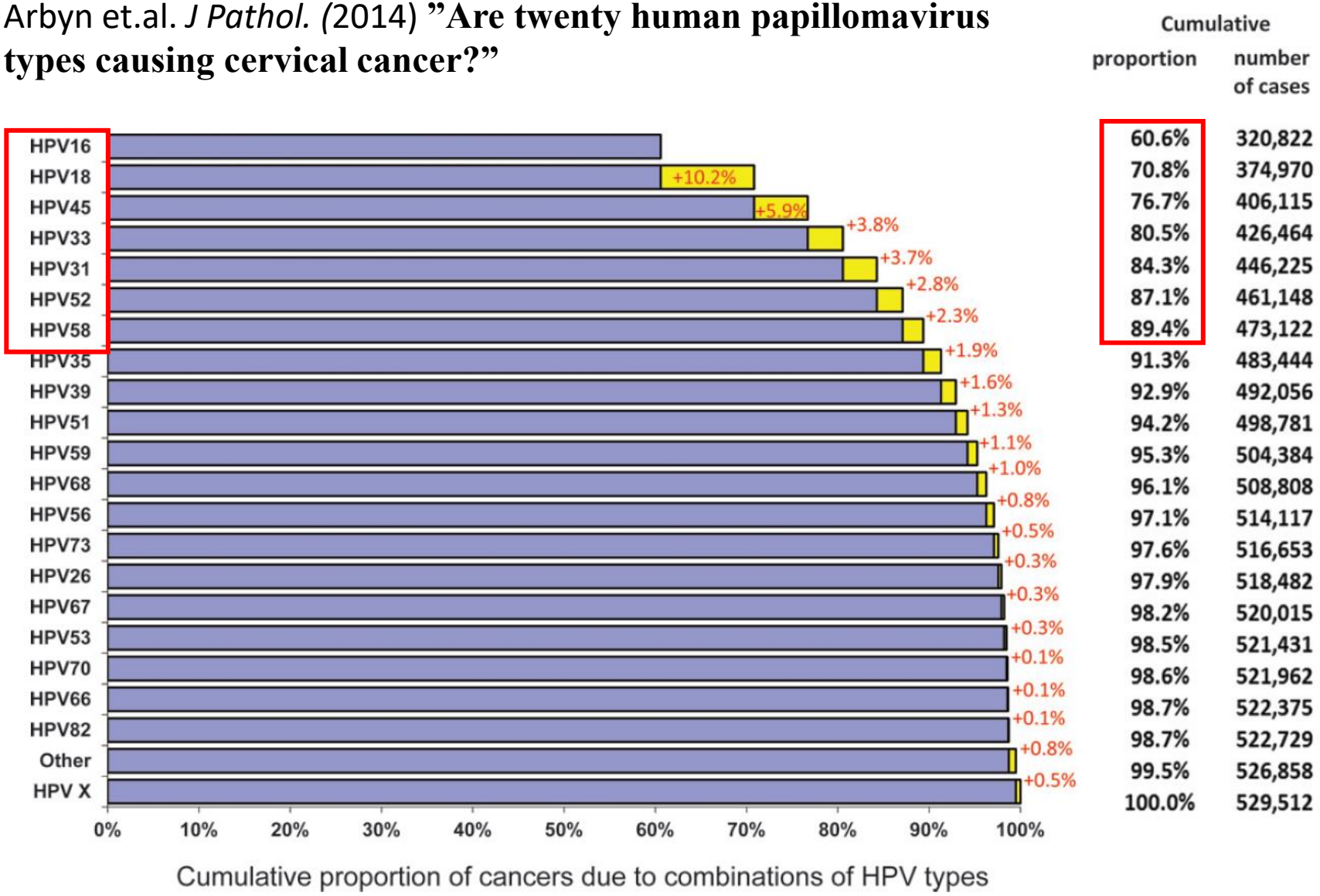
Triage by Biomarkers E6/E7 mRNA

- Detects HPV mRNA E6/E7; precursors of the oncoproteins known to disturb normal cell cycle control
- Genotypes the 7 most prevalent HPV-types causing cervical cancer (HPV 16, 18, 31, 33, 45, 52 and 58)
- Holds a high clinical specificity and positive predictive value (PPV) for CIN2+
- Holds low positivity rate in general population (only 1/3 of HPV-DNA positives)
- Identifies the women at increased risk for future abnormalities; warranted for immediate colposcopy and biopsy

How many HPV-types to screen for?

- Only a few HPV genotypes are highly associated with cervical cancer and require the most aggressive management, whereas others carry a lower risk of disease
  - HPV 16 and 18 cause 70% of all cases of cervical cancer
  - 7 HPV-types (16, 18, 31, 33, 45, 52 and 58) cause 90% of all cases of cervical cancer
- The 7 genotypes are covered by the 9-valent HPV vaccine; documented to enable high level of protection

Arbyn et.al. *J Pathol. (*2014) **"Are twenty human papillomavirus types causing cervical cancer?"**



Cumulative proportion	Cumulative number of cases
60.6%	320,822
70.8%	374,970
76.7%	406,115
80.5%	426,464
84.3%	446,225
87.1%	461,148
89.4%	473,122
91.3%	483,444
92.9%	492,056
94.2%	498,781
95.3%	504,384
96.1%	508,808
97.1%	514,117
97.6%	516,653
97.9%	518,482
98.2%	520,015
98.5%	521,431
98.6%	521,962
98.7%	522,375
98.7%	522,729
99.5%	526,858
100.0%	529,512

STUDY: *7-TYPE HPV mRNA test in triage of HPV DNA positive women*

Department of Clinical Pathology,
University Hospital of North Norway
2019-2021

Primary HPV screening
-> women 34-69 yrs.
-> HPV DNA test: Roche Cobas 4800

Triage of all DNA positives by
-> Cervical Cytology
-> 7-type HPV mRNA test:
PreTect HPV-Proofer`7

Study endpoint:
-> Histologically confirmed CIN2+

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Preliminary study results:

"A 7-type E6/E7 mRNA-test in triage of HPV DNA positive women attending primary screening"

Unpublished data, UNN, Norway

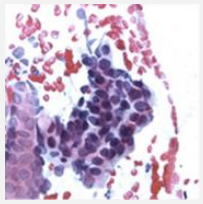
16,729 women enrolled 2019-2021

5.0% HPV DNA**+** (836/16,729)

Triage by Cytology and mRNA E6/E7

55.0% (460/836): Cytology**+** (ASC-US+)

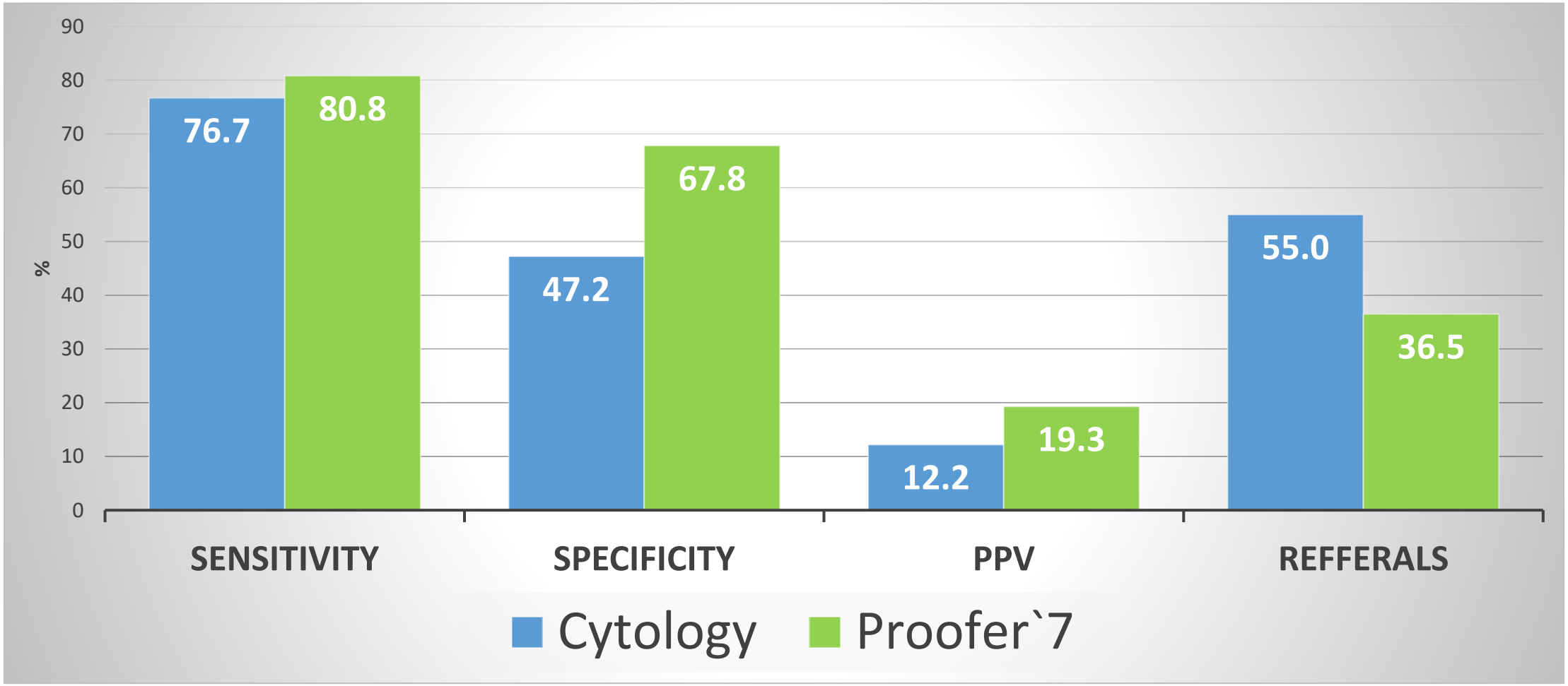
36.5% (305/836): E6/E7 mRNA`7**+**



31.1% (260/836) biopsy

8.7% (73/836) CIN2+

Test performance CIN2+



Unpublished data University Hospital North Norway 2019-2021

- The 7-type HPV mRNA test had significant **higher specificity and PPV** for detection of CIN2+ than cervical cytology in triage of HPV-DNA positive women
- A **low positivity rate** of the triage test can be translated into a **low referral rate** to colposcopy which is very appealing in a triage setting

Take home messages

HPV DNA test provides high sensitivity and improved prevention of Cervical Cancer

7 HPV-types are crucial

HPV 16, 18, 31, 33, 45, 52, 58 cause 90% of CC

Triage of HPV DNA positives

Risk stratification is required for accurate patient management-

7-type mRNA might balance benefits/harms

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

Thank you for your attention!