XIII INTERNATIONAL WORKSHOP ON LOWER GENITAL TRACT PATHOLOGY
HPV Disease and Cervical Cancer: Summing Up
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DETECTION OF CIN2+ IN WOMEN WITH NORMAL CYTOLOGY - THE ADDED VALUE OF A 3-TYPE HPV E6/E7 MRNA TEST

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No conflicts of interests to declare

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Background

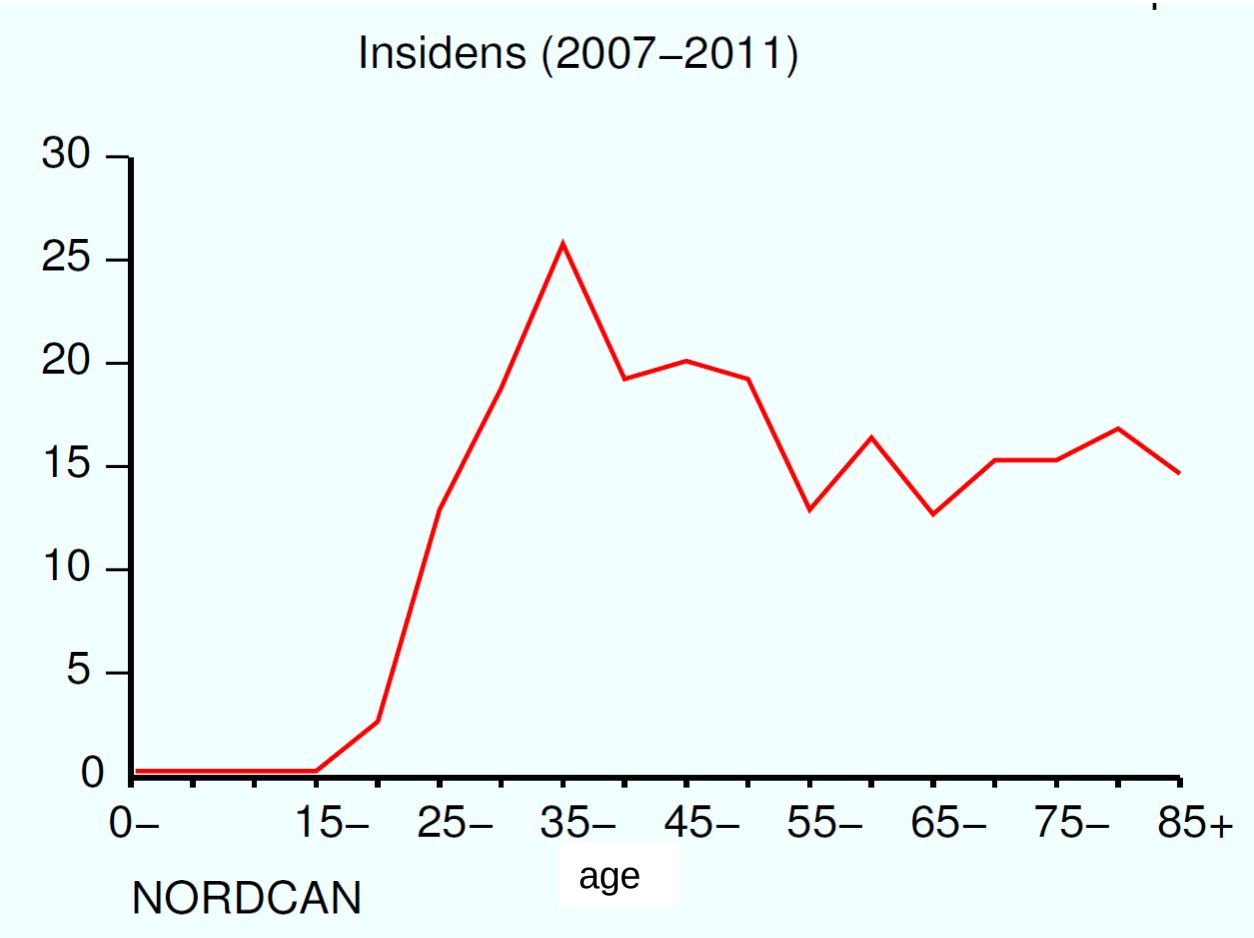
Cervical cancer in Norway is peaking at 35 years

Cervical cytology has limited sensitivity and reproducibility with a limited impact of reducing cervical cancer in women < 40 years

Twenty-five percent of all women diagnosed with cervical cancer had normal cytology within 3 years of cancer diagnosis

A 3-type HPV mRNA test has high specificity and low positivity rate compared to a 14-type HPV DNA test

Cervical cancer in Norway



Quality assurance of cytology
Possible methods

Rescreen all?

Rescreen a random sample?

Retrospective audit of cancer cases with normal cytology?

Test samples by another detection method and re-screen test positive cases?

Objectives

- To assess if a 3-type HPV mRNA test can increase detection rate of CIN2+ among women < 40 years
- To evaluate the potential reduction of false negative PAP smears
- Rescreen all normal PAP smears with HPV mRNA positive result
- Assess the additional workload of implementing HPV mRNA test as quality assurance of normal cytology

Methods

The study was initiated by Department of Pathology, Ålesund Hospital starting in 2013 with follow up through 2017.

Cytology: Bethesda system: Conventional PAP

Histology: CIN classification Outcome:CIN2+

HPV mRNA: PreTect SEE

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

Study Design

- Women age 25-39 years attending national screening program at Ålesund Hospital, Norway
- Quality assurance of «normal» Pap smears with 3-type HPV mRNA test
- Re-screening of all «normal» Pap smears with a positive HPV mRNA test
- All women with revised cytology diagnosis are followed up according national guidelines

Selection of study population

Database (SymPathy)		
	Women	Women
	n	N
01.01.2000-30.09.2014		**47,926**
No smear after 04.04.2013	34,129	
Age index smear:14-24y	195	
40-92y	8,555	
Total	43,179	
Eligible study participation 25-39 yrs		**4,747**
CIN1+ before index	339	
HSIL before index	42	
Normal smears before index		
	381	
Study population		**4,366**

Primary and revised cytology/ HPV mRNA results

Normal		ASC-US	LSIL	HSIL	ASC-H	AGUS	ACIS	Total
No mRNA*	HPV mRNA PreTect SEE							
n	n	n	n	n	n	n	n	N
2 407	1 444	366	80	35	32	1	1	4 366
55.1%	33.1%	8.4%	1.8%	0.8%	0.7%	0.02%	0.02%	100.0%
Rescreening HPV mRNA+		**Revised Cyt diagn**						
PreTect SEE (+)	27	23	1		2	1		
	1.9%							
* No sample available								

Cytology and HPV mRNA positive versus histology

	SEE (+)	ASC-US/ LSIL	HSIL
	N=27	N=446	N=69
No follow-up	2	74	6
Normal	11	301	28
CIN 1	6	3	1
CIN 2	2	11	1
CIN 3	6	56	33
Sq CC	0	1	0
CIN 2+	32% (8/25)	18.3% (68/372)	54% (34/63)

Estimated change in detection rates of CIN2+

	Normal Not mRNA tested	Normal PreTect SEE (+)	ASC-US/ LSIL	HSIL	Total
	N=2 407	N=1 444	N=446	N=69	N=4 366
CIN2+	*13.3 (0.55%)*	8 (0.55%)	68	34	123
CIN3+	*10.1 (0.42%)*	6 (0.42%)	57	33	106
			CIN2+ = 2.34% (102/4366) (95% CI: 1.9-2.8%)		
	CIN2+ = 2.82% (123.3/4 366) (95% CI: 2.3-3.3%)				

Summary

Low HPV mRNA positive rate = 1.9% in women with normal cytology

1/3 of all HPV mRNA positive among women with normal cytology had CIN2+

Estimated 20.9% increase in detection rate for CIN2+

Conclusions

It is possible to increase screening sensitivity by adding a 3-type HPV mRNA test in women with normal cytology

The low HPV mRNA positivity rate results in low re-screening rate

The more CIN2+ cases treated in first screening round => less cancers in next screening round


THANK YOU!