

HPV Testing & Screening Current Status & Future Screening HPV





Why HPV Screening Which Problems What Methods

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Female population pyramid by income



Age Standardized Incidence of Cervical Cancer (Rate per 100.000 women/year)



- >560.000 new cases, >270.000 deaths/year
- 85% cases in developing countries (no prevention)
- Most common cancer-related deaths in women in some countries
- Loss of many life years of mothers, grandmothers

Cervical Cancer by Human Papillomaviruses



55 nm HPV Particle 1/20.000 mm)

Papillomaviridae PV in every vertebrate species 203 HPV types cutanous/mucosal types

ca. 20 "high-risk" HPV in 99.7% cervical cancers

ca. 18 "low-risk" HPV in 90% genital warts

Oncoproteins E6 and E7 mandatory for cellular transformation

Worldwide ea. Year 560.000 Cxca, ? Premalignant stages 50.000 oral Ca



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http://cvc.dfci.harvard.edu/hpv/HTML/classification.html

Progression from Infection to Cervical Cancer



Sensitivity and Specificity of HPV Test vs Cytology



HPV Test: high Sensitivity but low Specificity for true disease



Cervical Cancer prevention in Germany Trends of Incidence and Mortality



Invasive CxCa after initial Screening in RCTs in 2nd Round

176 464 women aged 20–64 years were randomly assigned to HPV-based (experimental arm) or cytology-based (control arm) screening in **Sweden** (Swedescreen), **The Netherlands** (POBASCAM), **England** (ARTISTIC), and **Italy** (NTCC). Followed up for a median of 6.5 years (**1 214 415 person-years**) and identified **107 invasive cervical carcinomas**



Higher sensitivity results in therapy and lower CxCa incidence in follow up

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Ronco et al., Lancet 2014; 383: 524-32

>220 commercially available HPV Tests

Testsystem	Firma	Bemerkung	FDA	Но	chri	isik	o- (fet	t)/	mö	glici	he H	loch	risi	ko-I	HPV	-Ту	pei	n [§] :									Zahi HR- Typen
		Signal Amplification		16	18	26	30	31	33	34	35	39	45	51	52	53	56	58	59	66	67 (58	69	70	73	82	85	
Cervista HPV 16/18	Hologic	Invader [®] Chem.	2009																									2
Cervista HPV HR	Holog	[®] Chem.	2009																									(14)
hc2 HPV DNA Test	🗫 nroh	C Capture 2																										(13)
hc2 High-Risk HPV-DNA Test		Capture 2	2003																									(13)
digene HPV Genotyping PS Test ¹⁾	ÇIAGEN	Hybrid Capture 2																										3
		PCR		16	18	26	30	31	33	34	35	39	45	51	52	53	56	58	59	66	67 (58	69	70	73	82	85	
HPV Easy-Typing Kit	ALD Autoimmun Dia.	PCR / Line Blot																										3 (10)
f-HPV typing	Nimagen (Genomed)	multiplex PCR																										13
AMPLICOR HPV Test	Roche	PCR / 96er Platte																										13
cobas [®] HPV Test	Roche	rt-PCR	2011																									2 (12)
RealTime HR HPV	Abbott	rt-PCR																										2 (12)
Xpert HPV	Cepheid	PCR / Kartusche																										3 (11)
BD Onclarity HPV-Test	Becton Dickinson	rt-PCR																										6 (8)
ProDect Chip HPV typing	bcs E																											14
HPV Genotypes 14 Real-TM Quant		DCP _																										14
HPV		, I ON $_$																										17
PapilloCheck	greiner and and																											18
Anyplex [™] II HPV28 Detection	Seegene	rt-PCR / cyclic CMTA																										20
HPV Direct Flow Chip	nedac	PCR / Chip																										20
INNO-LiPA HPV Genotyp. Extra	Fujirebio	PCR / Line Blot																										20
CLART HPV2	Genomica	PCR / Microarray																										20
Linear Array HPV Genotyp.	Roche	PCR / Line Blot																										21
Infiniti HPV Genotyping Assay	AutoGenomics	Microarray																										24
		NASBA / TMA		16	18	26	30	31	33	34	35	39	45	51	52	53	56	58	59	66	67 (58	69	70	73	82	85	
NucliSens EasyQ HPV		E6E7 mRNA																										5
APTIMA HPV-Test		E6E7 mRNA	2011																									(14)
APTIMA HPV 16 18/45 genotype ²⁾	Holog	E6E7 mRNA	2012																									1 (2)
OncoE6TM Cervical Test	Arbo Drof	teral flow																										2
		ein																										
1) zur Genotypisierung HC2 hr HPV DNA-positiver mobeli					= DNA-Typisierung = Proteinnachweis								5															
2) zur Genotypisierung APTIMA HPV-positiver Proben					= Sonde vorhanden, aber keine individuelle Typisierung																							
				= FDA (Food and Drug Administration, USA) zugelassen (Jahr)																								

CIN2+ after HPV Genotype Persistence



Elfgren et al., 2016

CIN 3 Risk when HPV16/18+ by Cobas Roche HPV-Test



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The Special Situation in Low Resource Countries

- No screening program established yet
- Cytology capacity marginal, subjective and training intensive
- Colposcopy and treatment availability
- Quality control issues
- Difficult to reach populations: geographical, information, trust
- No financial and human resources available
- No knowledge of disease
- No knowledge of epidemiology
- No knowledge of acceptance, cultural barriers

WHO:

"If a country has not established Cytology, it should start with HPV testing"



20%-50% in ca. 25 year old

5%-30% in >40 year old

Esp. in Oceania and SS Africa



High HPV prevalence poses problem for HPV testing => Need for triaging

ICO HPV Information Center



-25 25-34 35-44 45-54 55-64 65+ Age group (years)

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Referral to Colposcopy in the Era of HPV Primary Screening





courtsey T. Agorastos



Screening and Adequate Triage of HPV 16/18 Positives

Oncoprotein E6 Cervical Test (Biomarker for Progression)

- Lateral flow Immunoassay Test
- Detection of HPV16 and 18 (typing)
- 15 samples in <3 h (hands on time appx. 2 h)

•	Sensitivity	for CIN3+	53.5%					
		for CervixCa	91.7%					
•	Specificity	for CIN3+	98.9%					
•	PPV	for CIN3+	40.8%					
•	NPV	for CIN3+	99.37%					

⇒ High specificity for disease
⇒ Simple robust technology
⇒ Low resource settings



Zhao et al., 2013

Positivity by Disease Stage





Biomarker for high-grade and progressive Dysplasia



Only truely progressive dysplasia expresses detectable amount of HPV Oncoprotein

Self-sampling and AVE6 cervical test: MorocOncoE6



12,23 Mio women >15 years

- 3,5% Screening Rate
- (4,6% urban/1,9% rural)
- 2258 CxCa (2014)
- 1076 deaths
- CxCa Incidence: 20/100.000/year
- 2nd most frequent cancer

Lalla Salma Foundation, MoH, Hassan II University, Cancer Centre National screening program: VIA

AIM: Feasibility of access and motivation, VIA, AVE6 biomarker test, self-sampling, HPV Test/Histology (reference)

7 Centre de Santé: 4 urban; 3 rural 2 Centre de Référence: Casablanca, Tanger

Planned/recruited (4 months) 216 sampled and biopsied 20 CxCa (enrich cases) ALL PARTICIPATED IN SELF-SAMPLING

VIA+: 31] True disease? OncoE6+: 6 J Follow up effort and cost!

Annually Screened Women by Age in Morocco



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WHO ICO Fact sheet Morocco 2017

Solving the screening problem in LMIC countries by HPV testing?

- Accessibility of women in an organized system for screening, enhancement by self-sampling
- Low barriers, wide coverage, sufficient financing
- Adequate test for given situation, genotyping
- HPV screening test efficacy depends on HPV prevalence
- Biomarker tests with high disease specificity seem favorable



Rwanda vaccinated 90% eligible girls against HPV!