

# CERVICAL CANCER SCREENING WITH HPV DNA: UP TO DATE INFO FROM EUROPE

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X	No, nothing to disclose
	Yes, please specify:

<i>CompanyName</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify)</i>
Example: company XYZ	X		X		X			



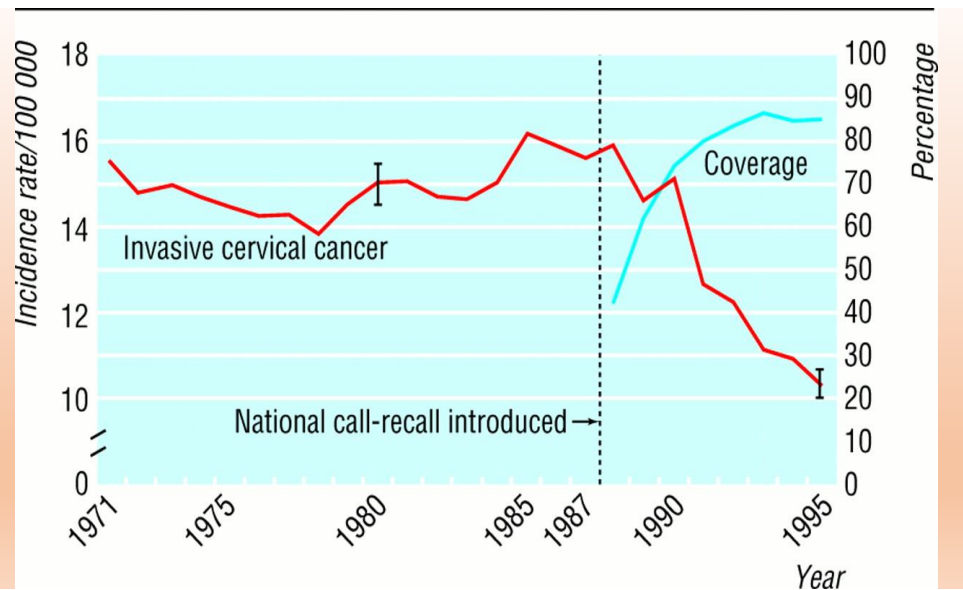
# Cervical Cancer Globally

- ✓ Half Million New Cases
- ✓ 50% Mortality
- ✓ >90-99.7 % HPV Related
- ✓ Preventable Cancer
  - ✓ HPV Vaccination, Smoking Cessation
- ✓ Early Detection is Possible
  - ✓ VIA-VILI / Smear / HPV / Combination / Others
  - ✓ WHO
- ✓ Eradicable Cancer



# Cervical Cancer Last Century

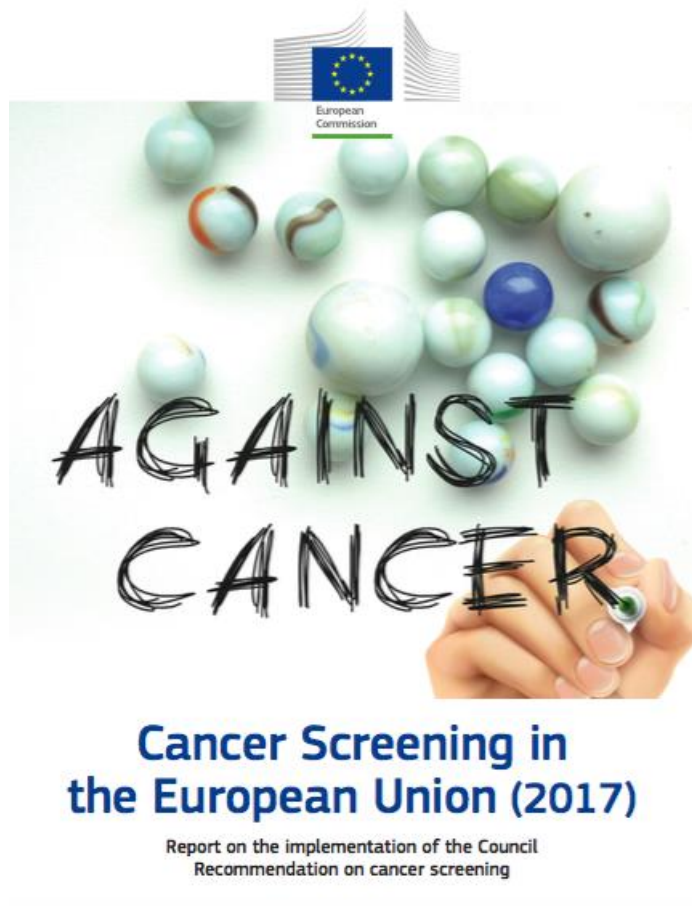
## UK National Screening Programme



- ✓ Cytology based screening programs have reduced more than 75% of incidence and mortality from cervical cancer in the last 50 years.
- ✓ Especially in developed countries.
- ✓ However, **only 12** countries have succeeded in EUROPE (2017).
- ✓ And still cervical cancer mortality does not decrease any more **even in most developed** countries.



# Current Status



## Second Report on Cancer Screening in EU

### ➤ Main collaborating institutions

- International Agency for Research on Cancer, Lyon, France (coordination)
- CPO Piemonte, University Hospital "Città della Salute e della Scienza" CPO, Turin, Italy
- Finnish Cancer Registry, Mass Screening Registry, Helsinki, Finland

### ➤ Over 80 Data providers from all 28 EU Member States

## Data Provider's Workshop (22 Member States Participating) – 16-17 Feb, 2016; IARC



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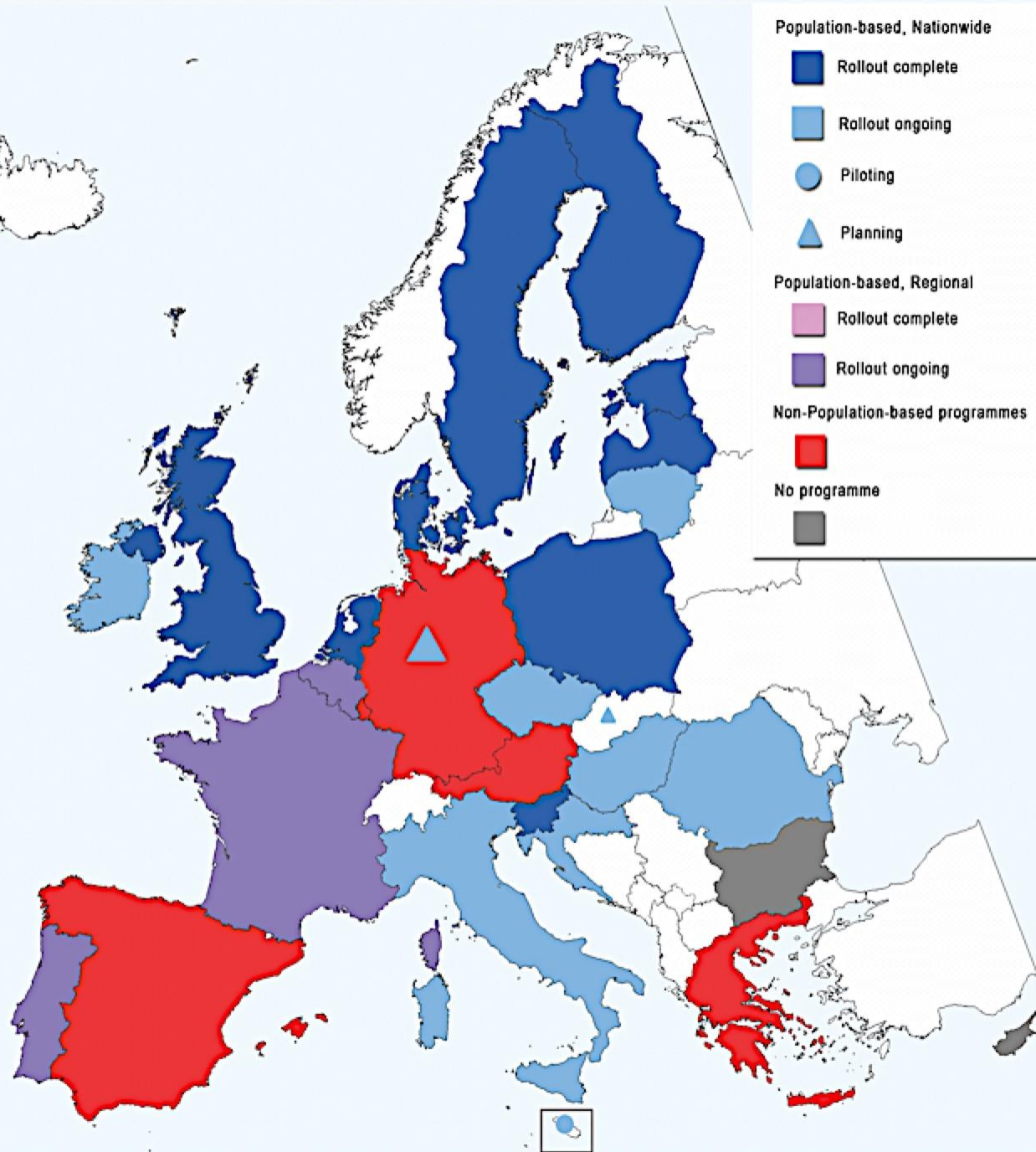


# Cervical Screening Programs in EU

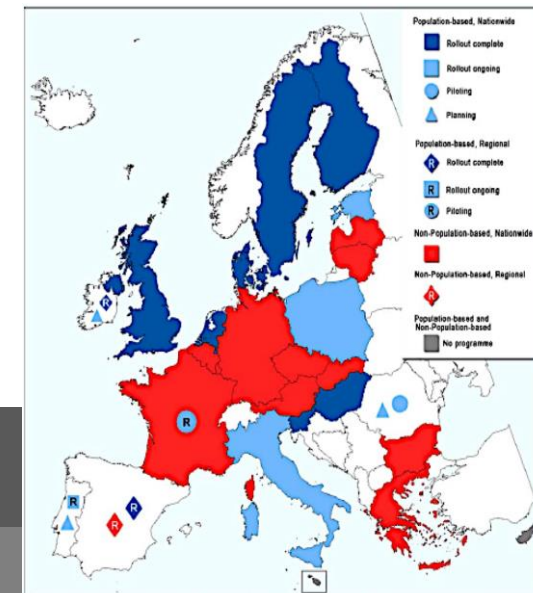
	1 <sup>st</sup> Report 2008	2 <sup>nd</sup> Report 2016
<b>Population based program</b>	<b>13</b>	<b>22</b>
• Rollout complete	7	12
• Rollout ongoing	3	7
• Pilot	1	1
• Planning	2	2
<b>Non-population based program</b>	<b>12</b>	<b>4</b>
<b>No program</b>	<b>2</b>	<b>2</b>



# Cervical Cancer Screening Programs in the EU 2016



## First Report



# Target Ages and Screening Intervals of EU

	Pop based program	Target age	Screening interval	HPV Test
Austria	✗	18 & above	1	
Belgium	✓	25 – 64	3	
Bulgaria	✗	NA	NA	
Croatia	✓	25 - 64	3	
Cyprus	✗	NA	NA	
Czech Rep	✓	15 & above	1	
Denmark	✓	23 - 65	3	60 – 65 (5 yr int)
Estonia	✓	30 - 59	5	
Finland	✓	30 - 34	5	
France	✓	25 - 64	3	
Germany	✓	20 & above	1	
Greece	✗	Sexual onset	NA	
Hungary	✓	25 - 65	3	
Ireland	✓	25 - 60	3 (25-44); 5 (45-60)	
Italy	✓	25 - 64	3	
Latvia	✓	25 – 69	3	
Lithuania	✓	25 - 59	3	
Luxembourg	✗	18 & above	1	
Malta	✓	25 – 64	3	30-64 (co-test)
Netherlands	✓	30 - 64	5	
Poland	✓	25 - 59	3	30-59 (co-test)
Portugal	✓	20 - 59	3	
Romania	✓	25 - 64	5	
Slovak Rep	✓	23 - 64	Yrly x 2; then 3 yrly	
Slovenia	✓	20 - 64	Yrly x 2; then 3 yrly	
Spain	✗	25 - 64	3 <i>Unpublished data; Not to be quoted</i>	
Sweden	✓	23 - 60	3 (23-50); 5 (51-60)	
UK	✓	25-64	3 (25-59); 5 (60-64)	





# Cytology Based Screening: International Problems



## ✓ Scientific Problems

- A single Pap-Test has a very low sensitivity for CIN2+ lesions
- Pap-Test has a high false negative rate
- Reproducibility of Pap-Test is low
- Pap-Test is less effective in detecting adenocarcinoma of cervix

## ✓ Organisational Problems

- It is a very difficult and complex service to provide.



# HPV DNA As a New SCREENING TOOL

## 20 Years Research Summary: Sensitivity and Specifity

- ✓ HPV Tests Are More Sensitive (2006)
- ✓ Low Specifity may cause unnecessary colposcopies
  - Can Be Compensated With Additional Tirage Tests and age for Screening >30 years
  - HPV Genotyping, Reflex Cytlogy, Cytology Stainings with p16 with or without Ki-67, Methylation Profiles

	<b>Sensitivity</b>	<b>Specifity</b>
<b>Cytology</b>	<b>53%</b>	<b>97%</b>
<b>HPV test</b>	<b>96%</b>	<b>92%</b>

1) Mayrand MH et al. Int J Cancer 2006 119;615-623, 2) PALMS STUDY, Cancer Cytopathol, 2015 3) Ikenberg, JNCI, 2013 4) Cuzick, PVR 2016



# HPV DNA As a New SCREENING TOOL

## 20 Years Research Summary: Co-Test or Alone ?

After 2012, Guidelines Has Changed

Comparison	Target	Relative Sensitivity	Relative Specificity	Trial Numbers
Cyto + HPV vs. Only HPV	CIN2+	1,05	0,95	10
Cyto + HPV vs. Only HPV	CIN3+	1,02	0,93	6

M. Arbyn et al. / Vaccine 30S (2012) F88–F99



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# HPV DNA As a New SCREENING TOOL

## 20 Years Research Summary: Negative Predictivity

### Articles



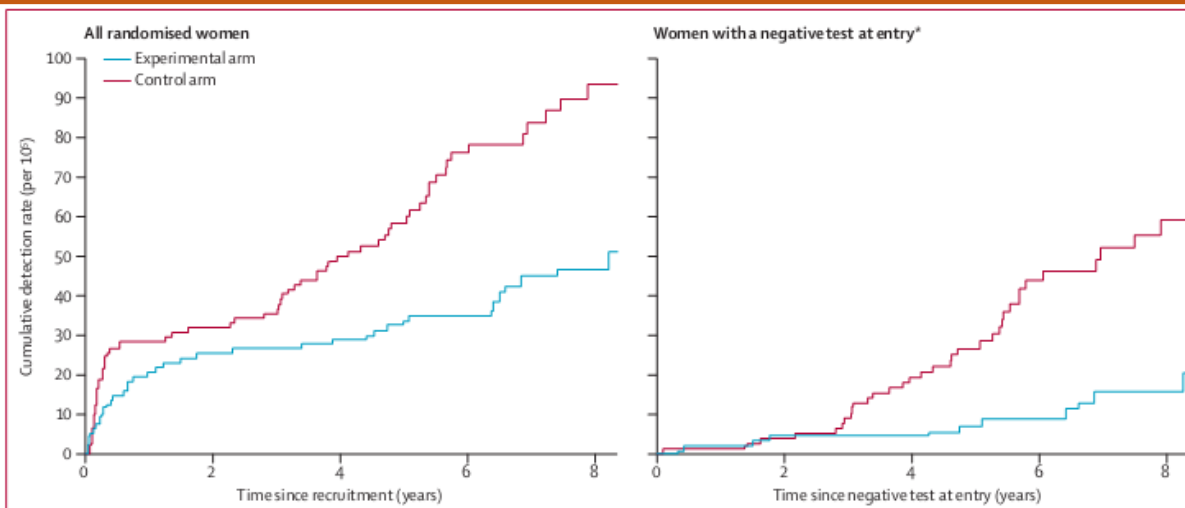
**Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials**

**Lancet**  
**2014**

*Guglielmo Ronco, Joakim Dillner, K Miriam Elfström, Sara Tunesi, Peter J F Snijders, Marc Arbyn, Henry Kitchener, Nereo Segnan, Clare Gilham, Paolo Giorgi-Rossi, Johannes Berkhof, Julian Peto, Chris J LM Meijer, and the International HPV screening working group\**

### ✓ Cumulative Cervical Cancer Incidences for negative initial tests:

	3,5 years	5,5 years
Negative cytology;	15.4 / 10 <sup>5</sup>	36.0 / 10 <sup>5</sup>
Negative HPV test;	4.6 / 10 <sup>5</sup>	8.7 / 10 <sup>5</sup>





# European Guidelines and All International Guidelines Has Changed

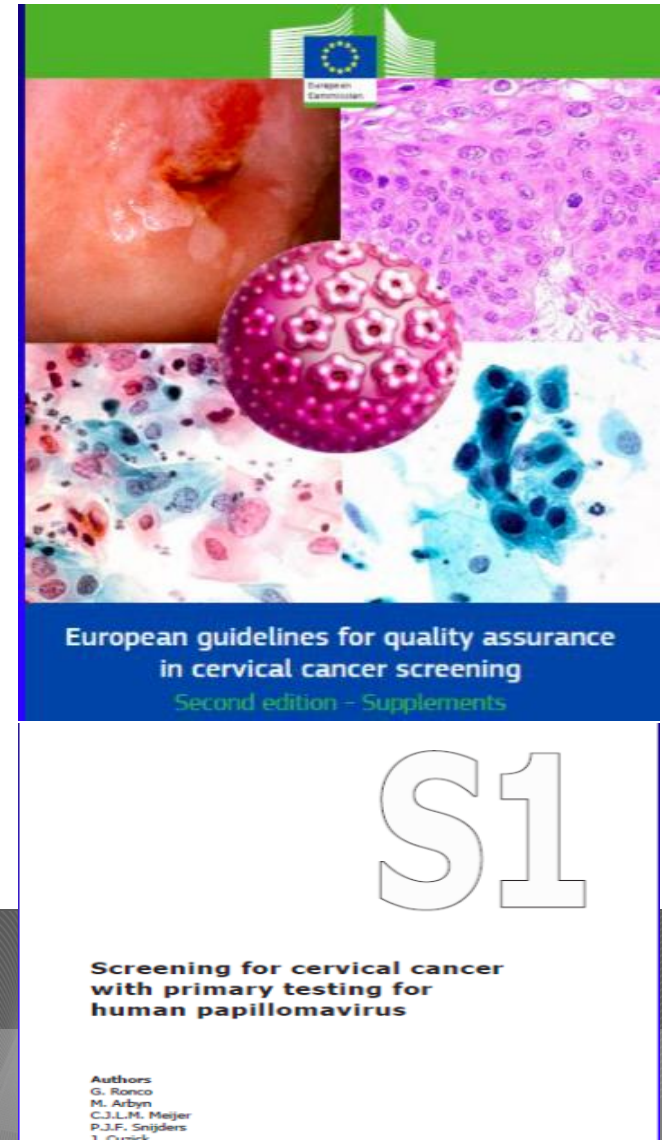
## ✓ EU 2008 Guidelines

- More data is needed to recommend HPV DNA for primary screening

## ✓ EU 2012 Guidelines Supplement

- HPV DNA can be used alone for primary cervical carcinoma screening

## ✓ FDA, EFC, ASCCP, SGO



# HPV DNA in Europe

- ✓ Turkey
- ✓ Netherlands
- ✓ Italy : Currently 8 regions, all regions by 2018
- ✓ Denmark, Poland, Malta, Switzerland, Norway
- ✓ 2017/2018: England, Denmark, Germany ....



# On the Pipeline for HPV DNA Screening



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# Point of Care / Convenience Testing

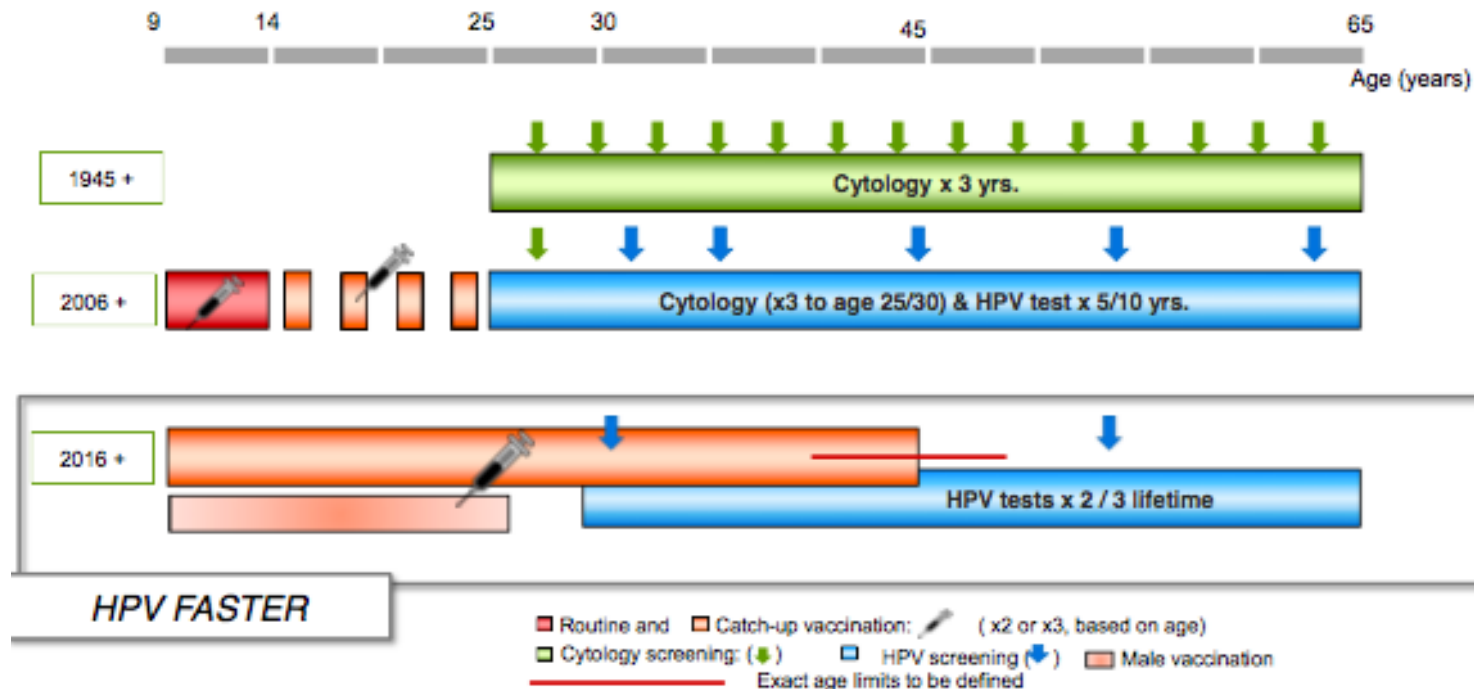
- ✓ 9 Regular Kits
  - Cepheid-X-pert
  - Qiagen Care HPV
  - Urine-Trovagen
- ✓ Oncoproteins-E6/E7
  - Arbovita
  - Oncohealth
- ✓ Self HPV Sampling
  - Similar accuracy to clinician collected samples with validated PCR based kits





# HPV Faster

Current cervical cancer preventive strategies (simplified)  
and proposed HPV FASTER initiative



# Screening in Post-Vaccination Era

- ✓ Some form of cervical screening will be needed for the foreseeable future
- ✓ Lower prevalence of CIN2+ due to lack of HPV vaccine type induced lesions
- ✓ Decreased sensitivity for cytology
  - Rare abnormalities, lack of experience and lack of concentration
- ✓ Decreased PPV for cytology
  - False positives will not change but true positives will decrease
- ✓ Objective, automated methods of HPV screening will be more important for low prevalence setting
- ✓ Cost effectiveness of screening will decrease
  - Further benefits are likely to accrue by combining HPV Vaccination in older women with HPV Screening-HPV Faster
  - This should be compensated with longer screening intervals



# CASE STUDY with HPV DNA SCREENING

## TURKEY



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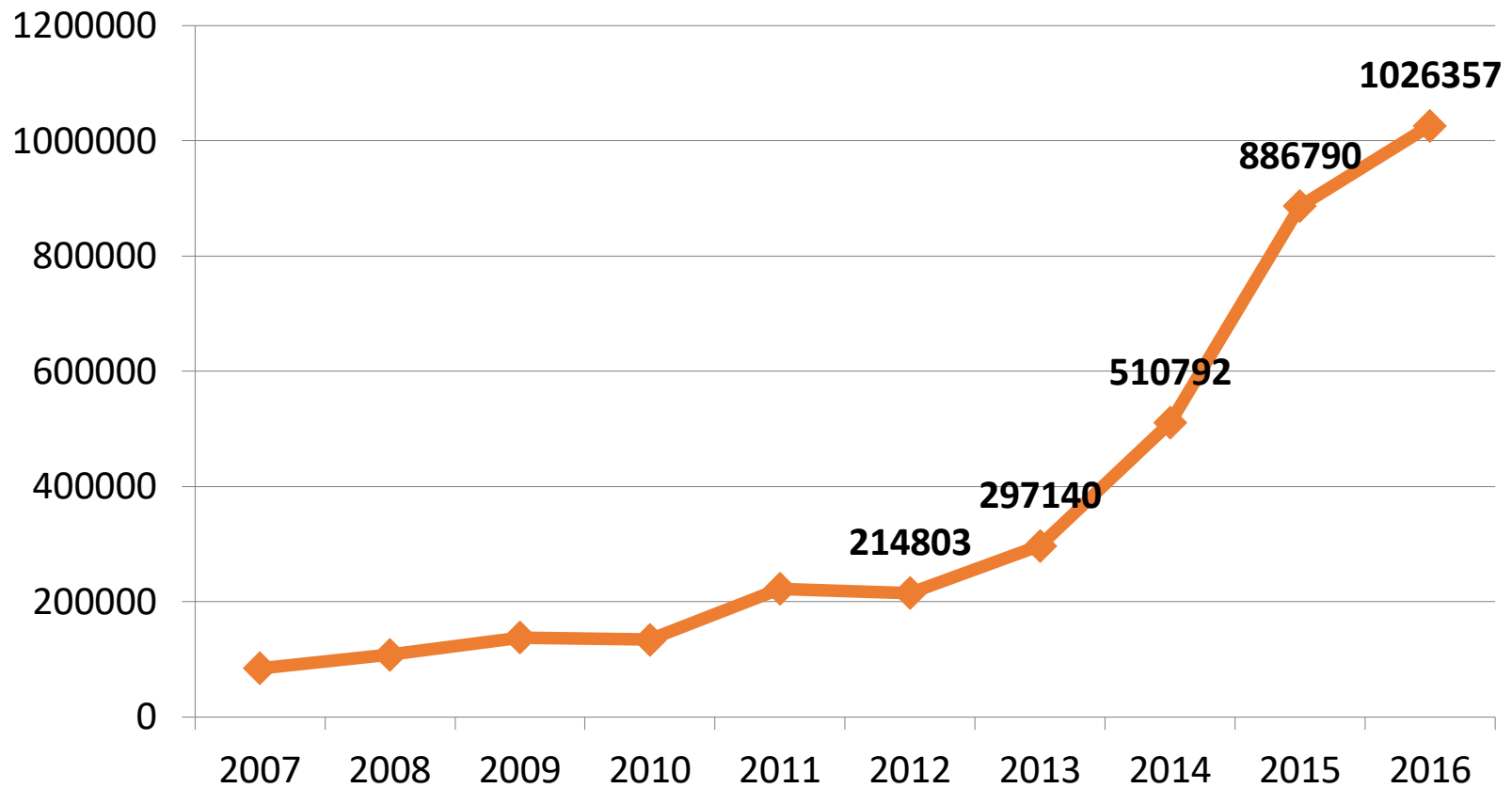
# Why HPV For Turkey ?

- ✓ For Screening Program Directors
  - Higher sensitivity
  - High Negative Predictive Value and Longer Screening Intervals
  - Low HPV positivity (low prevalence)
- ✓ For Academicians
  - Manpower advantage
  - Central quality control and automatisisation
- ✓ For Ladies
  - Shortening the time to final diagnosis
  - Self-testing ability for future a new test for ladies attention

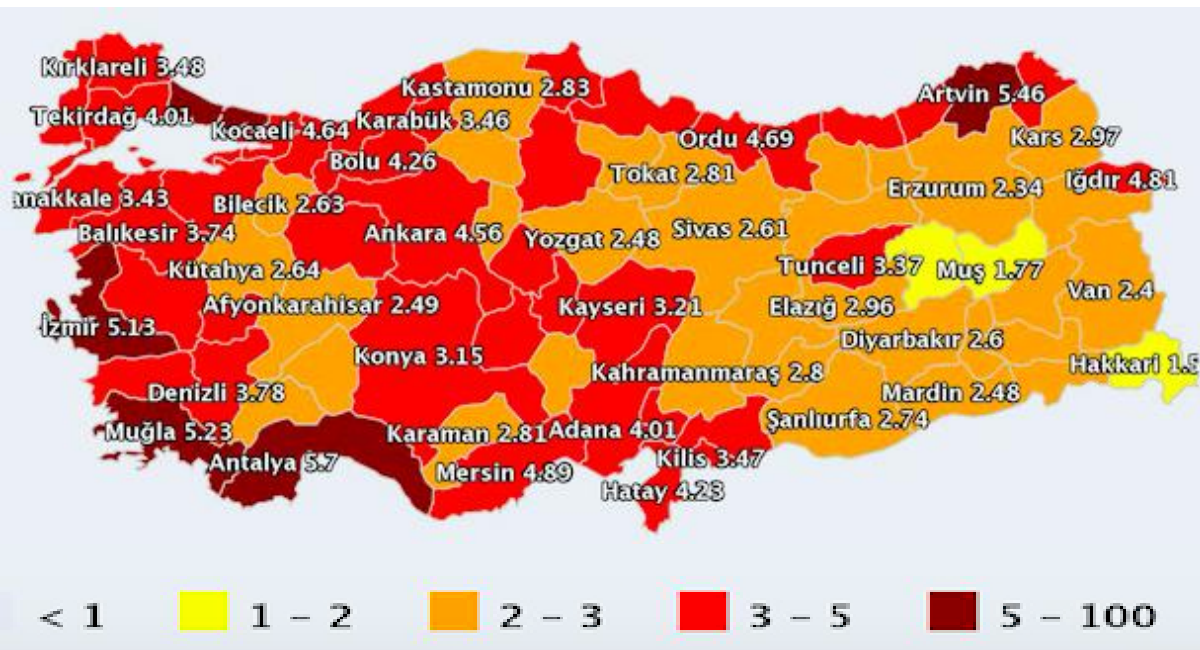




# Results: Population Based Cancer Screening



# Turkish HPV Geno-Map



- ✓ A total of 2,800,000 were screened by HPV test.
- ✓ Approximately 24,000 cancer cases were prevented (Except ASC-US)
- ✓ HPV Mapping of Turkey



# Challenges

- ✓ Resistance of cyto-pathology experts
- ✓ HPV is a sexually transmitted disease
- ✓ Resistance of GP for screening
- ✓ GP and nurses were not well trained for HPV
- ✓ HPV vaccination was not available
- ✓ Questions about adult vaccinations
- ✓ Colposcopy trainings quality



Thank you for your attention



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