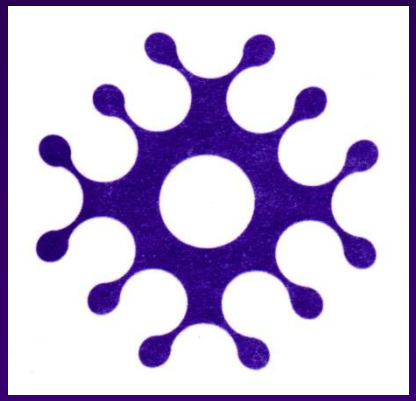
Overview of challenges at the level of HPV-based cervical cancer screening



Mario Poljak

Institute of Microbiology and Immunology
Faculty of Medicine, University of Ljubljana, Slovenia

Do we have reliable baseline data about cervical cancer screening practices in Europe ?

European Journal of Cancer (2015) 51, 950–968

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Cervical cancer screening in Europe: Quality assurance and organisation of programmes

K. Miriam Elfström [a], Lisen Arnheim-Dahlström [a], Lawrence von Karsa [b], Joakim Dillner [a,c,*]

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[b] *Quality Assurance Group, Early Detection and Prevention Section, International Agency for Research on Cancer, 150 Cours Albert Thomas, 69372 Lyon CEDEX 08, France*
[c] *Department of Laboratory Medicine, Karolinska Institutet, 141 83 Stockholm, Sweden*

Data collection – response status

Country	Response	Data submitted
Austria	X	X
Belgium	X	X
Bulgaria	X	
Cyprus		
Czech Republic	X	X
Denmark	X	
England	X	X
Estonia	X	X
Finland	X	X
France	X	X
Germany	x	X
Greece	X	X
Hungary	X	X
Iceland	X	X
Ireland	X	X
Italy	X	X
Latvia	X	X

Country	Response	Data submitted
Liechtenstein	X	X
Lithuania	X	X
Luxembourg	X	X
Malta	X	X
Northern Ireland		
Norway	X	X
Netherlands	X	X
Poland	X	X
Portugal	X	
Romania	X	X
Scotland	X	
Slovakia		
Slovenia	X	X
Spain	X	X
Sweden	X	X
Switzerland	X	X
Wales		

Responses have been received from both individual program/research/key informant contacts as well as ministries of health in some countries.
Data submitted is all or partial depending on the country

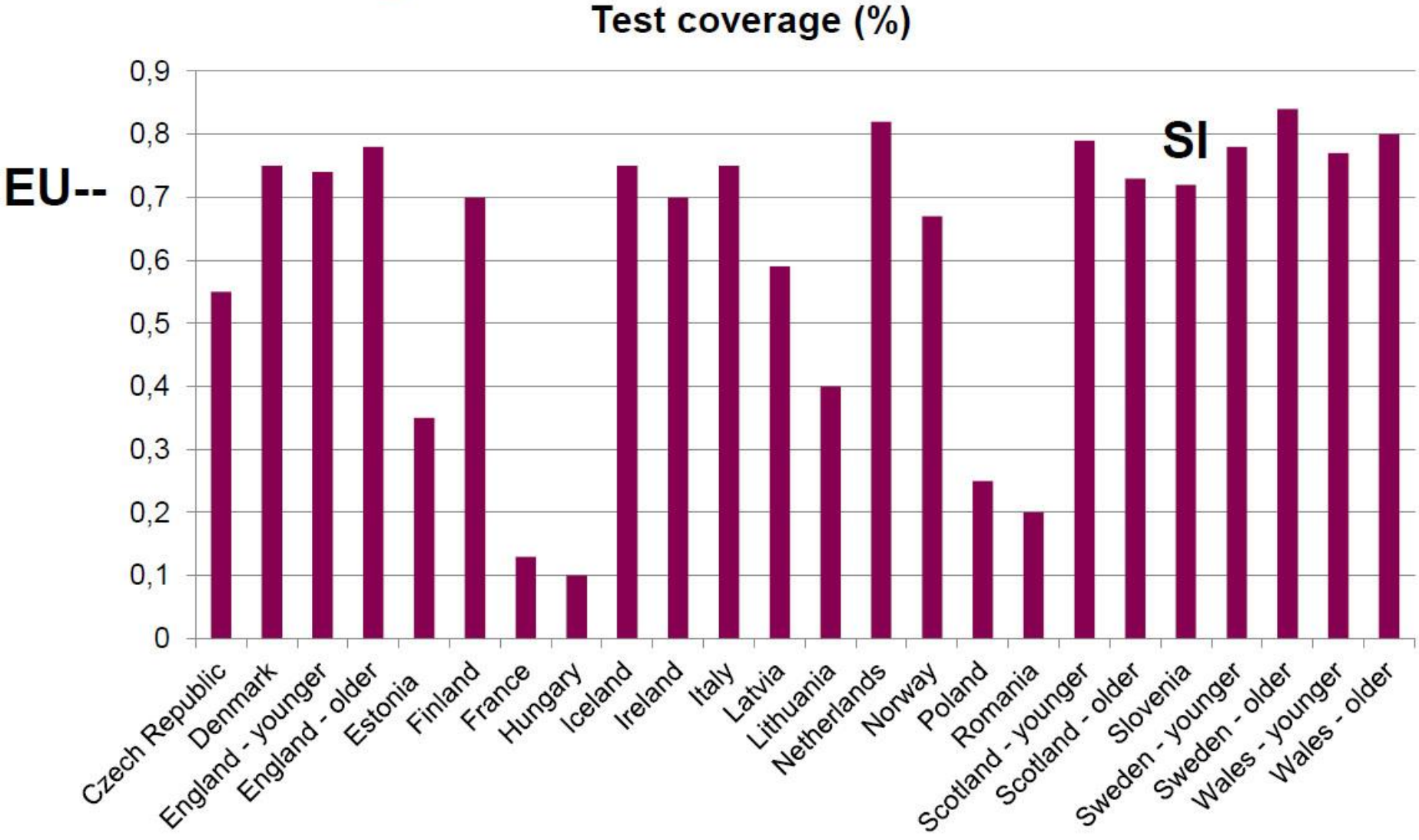
Results – Screening programme details

Karolinska Institutet

Country	Exam interval & age-range	Further eligibility criteria	Financing source	Co-payment
Czech Republic	1 year	All adult women	Public health insurance	No
England	3 years (ages 25 - 49) 5 years (ages 50 - 64)	Women with a cervix in situ	Primary Care Trusts through the Department of Health	No
Estonia	5 years (ages 30 - 59)	Women with health insurance	Health Insurance Fund	No
Finland	5 years (ages 30 - 60)	Some regional variation in age-range	Municipality health care budget	No
France	3 years (ages 25-65)	Women with a cervix in situ & have had intercourse	Health Insurance Plan, Ministry of Health, National Cancer Institute	Unknown
Hungary	3 years (ages 25 - 65)	Women who have not participated in opportunistic screening	Health Ministry, National Health Insurance Fund Administration	No
Iceland	2 years (ages 20-39) 4 years (ages 40-69)		Department of Welfare	Yes
Ireland	3 years (ages 25 - 44) 5 years (ages 45 - 60)	Immunosuppressed women start at age 20	Department of Health	No
Italy	3 years cytology 5 years HPV (ages 25 - 64)	Opportunistic screening, women with other health concerns excluded	Regional health funds	No
Latvia	3 years (ages 25 - 70)		Health Care budget	Yes
Liechtenstein	2.5 years (older than 17)		Governmental funding	No
Lithuania	3 years (ages 25-60)		National Health Insurance Fund	No
Netherlands	5 years (ages 30 - 60)	Women with a cervix in situ, no recent smear for other indications, not currently pregnant	Ministry of Health, Welfare, and Sport	No
Norway	3 years (ages 25 - 70)	Women with a cervix in situ, no recent opportunistic smear		Yes
Poland	3 years (ages 25 - 59)	Women with a cervix in situ, have an identify card, and proof of health insurance	National Healthcare Fund	No
Romania	5 years (ages 25 - 64)		Ministry of Health	No
Slovenia SI	**3 years (ages 20 - 64)**		**Health Insurance Institute of Slovenia**	**No** SI
Sweden	3 years (ages 23 - 50) 5 years (ages 50 - 60)		Regional health funds	Varies by region

Results – Test coverage

Screening interval as used in different countries

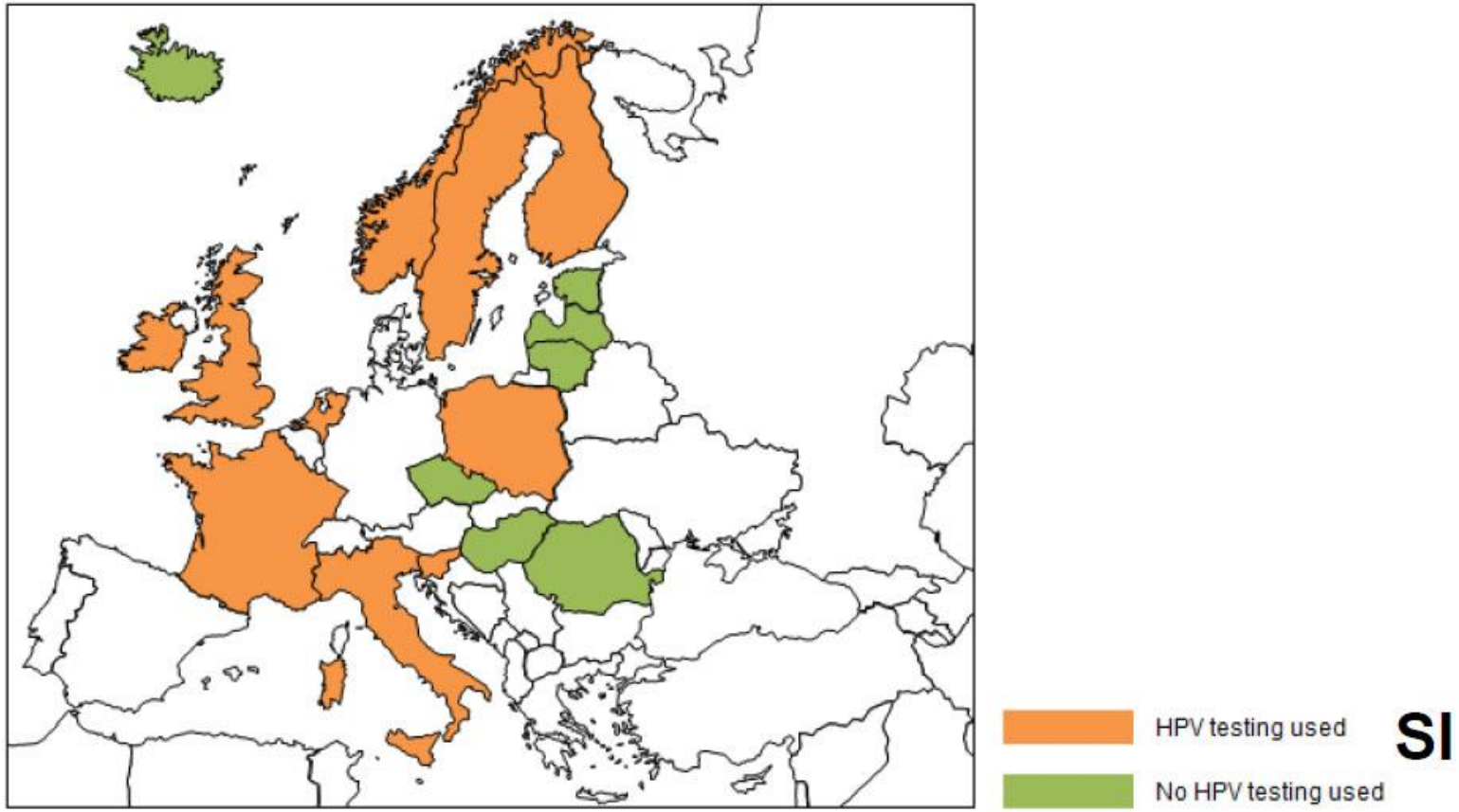


Hungary

- implemented organized national cervical cancer screening in 2004
- low coverage of target population in organized settings (10%)
- more than 60% attendance outside the organized program

- public perception of screening service quality

Results – Use of HPV testing in organized programmes



Results – Specific uses of HPV testing

Country	Primary HPV testing	HPV with cytology (co-testing)	Triage of cytology	Triage of cytology - LSIL	Triage of cytology - ASCUS	Test of cure
Belgium	No	Yes	Yes	No	Yes	Yes
England	No	No	Yes	Yes	Yes	Yes
Finland	Yes	No	Yes	No	Yes	Yes
France	No	No	Yes	No	Yes	No
Ireland	No	No	No	No	No	Yes
Italy	Yes	No	Yes	Yes	Yes	Yes
Liechtenstein	Yes	Yes	Yes	No	No	No
Netherlands	Yes	No	Yes	No	No	No
Poland	No	No	Yes	Yes	Yes	No
Slovenia	No	No	Yes	Yes	Yes	Yes
Sweden	Yes	No	Yes	Yes	Yes	Yes

Yes
No

ICO MONOGRAPH SERIES ON HPV AND DISEASE PREVENTION

ICO: Institut Català d'Oncologia
http://ico.gencat.cat

Generalitat de Catalunya
Departament de Salut

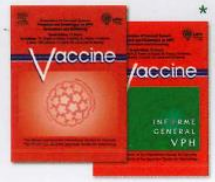
ICO Institut Català d'Oncologia

WHO/ICO HPV information centre

2006
Vol 24, Suppl 3

2007
Vol 25, Suppl 3

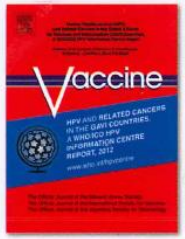
2008
Vol 26, Suppl 10



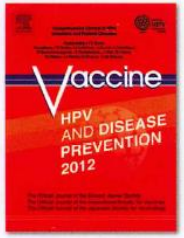
Vol 26, Suppl 11

Vol 26, Suppl 12

2012
Vol 30, Suppl 4



Vol 30, Suppl 5



2013
Vol 31, Suppl 1

Vol 31, Suppl 2

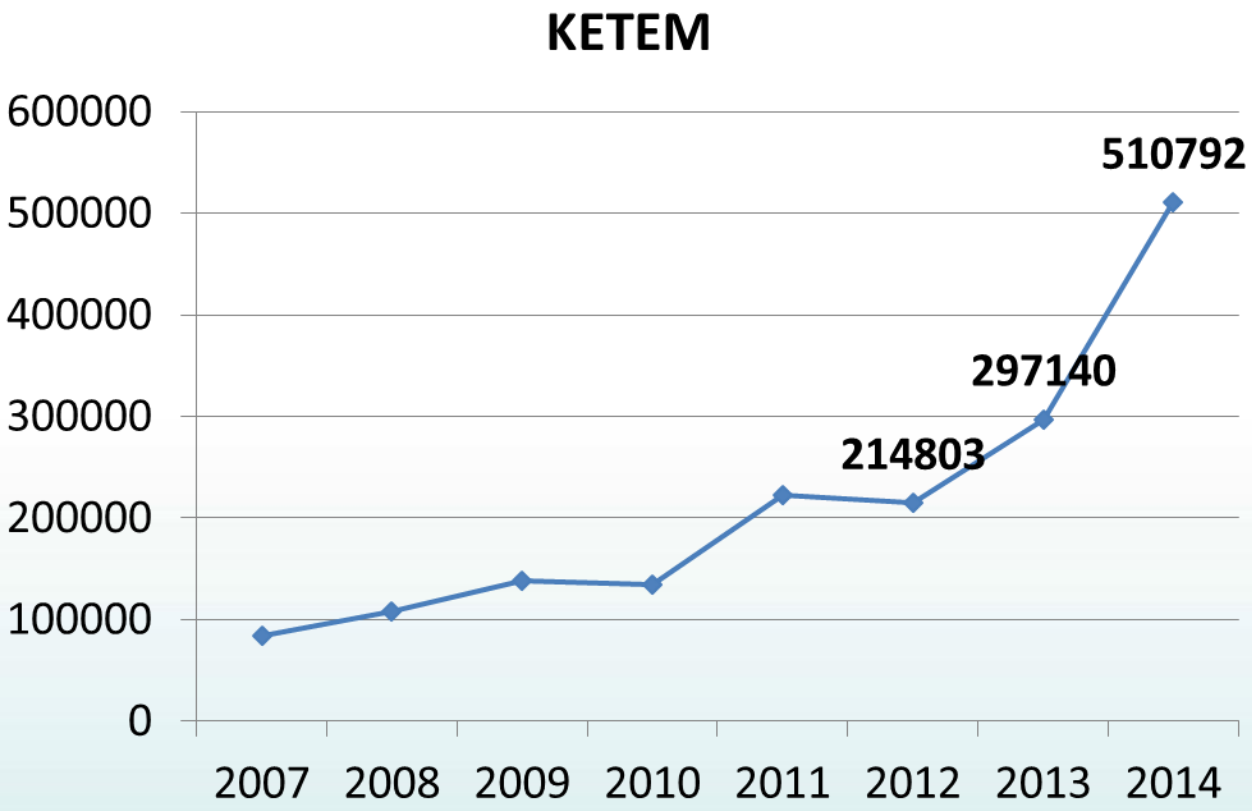
Vol 31, Suppl 3

Vol 31, Suppl 4

* Spanish * Japanese * Chinese * French * Russian

T.C. Sağlık Bakanlığı
Türkiye Halk Sağlığı Kurumu

Results
Population Based Cancer Screening



Volume 31, Supplement 7, 31 December 2013 ISSN 0264-410X

ELSEVIER

WHO/ICO HPV information centre

Comprehensive Control of HPV Infections and Related Diseases in the Central and Eastern Europe and Central Asia Region

Guest Editor: F.X. Bosch
Co-Editors: M. Poljak, S.I. Rogovskaya, X. Castellsagué, M. Brotons and S. Syrjänen

Vaccine

HPV AND DISEASE PREVENTION 2013

CENTRAL AND EASTERN EUROPE AND CENTRAL ASIA REPORT

28 countries included in the regional report

"Comprehensive Control of HPV Infections and Related Diseases in the Central and Eastern Europe and Central Asia Region"

Questionnaire on cervical cancer screening practices in the Central and Eastern Europe

Coordinators of the project: Prof. Xavier Bosch, MD, PhD; Prof. Mario Poljak, MD, PhD

Purpose of the Questionnaire: collected data will be used for the preparation of the chapter »Cervical cancer screening practices and current status of HPV vaccination implementation in the Central and Eastern Europe« in the HPV Monograph »Eastern and Central Europe and Central Asia report« which is planned to be published in the late 2012 as a supplement of Vaccine journal and will represent the main source of data concerning cervical cancer screening and HPV vaccination practices in the region.

Name:	
Country:	
Institution:	
Position:	
Contact details (e-mail, telephone, fax number):	

No.	Question	Reply (PLEASE FILL IN OR HIGHLIGHT THE ANSWER(S))
Cervical cancer basic data and organization of cervical cancer screening (FOR ALL COUNTRIES)		
1.	Does cervical cancer represent a significant public health problem in your country?	Yes, No
2.	Is there a national or regional cancer registry established in your country?	--Yes, national --Yes, regional --No
3.	Do you collect epidemiological data on cervical cancer on national or regional level and if yes, which data?	--Yes, national --Yes, regional --No
		--crude incidence rates --age-standardized incidence rates --crude mortality rates --age-standardized mortality rates

Vaccine 31S (2013) H46–H58

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Human Papillomavirus Prevalence and Type-Distribution, Cervical Cancer Screening Practices and Current Status of Vaccination Implementation in Russian Federation, the Western Countries of the former Soviet Union, Caucasus Region and Central Asia

Svetlana I. Rogovskaya[a,*], Irina P. Shabalova[b], Irina V. Mikheeva[c], Galina N. Minkina[d], Nataly M. Podzolkova[a], Olga Y. Shipulina[e], Said N. Sultanov[f], Iren A. Kosenko[g], Maria Brotons[h], Nina Buttmann[i], Myassa Dartell[j], Marc Arbyn[k,l], Stina Syrjänen[m], Mario Poljak[n]

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[f] Research Centre of Obstetrics and Gynecology of Ministry of Health, Tashkent, Uzbekistan
[g] Department of Oncogynecology, Research Centre of Oncology of Ministry of Health, Minsk, Belarus
[h] Institut d'Investigació Biomèdica de Bellvitge - Bellvitge Biomedical Research Institute (IDIBELL), Unit of Infections and Cancer (UNIC), Cancer Epidemiology Research Program (CERP), Institut Català d'Oncologia - Catalan Institute of Oncology (ICO), L'Hospitalet de Llobregat, Barcelona, Spain
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[j] Department of International Health, University of Copenhagen, Copenhagen, Denmark
[k] Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium
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[m] Department of Oral Pathology and Oral Radiology, Institute of Dentistry and Medicine Research Laboratory, University of Turku, Turku, Finland
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Vaccine 31S (2013) H59–H70

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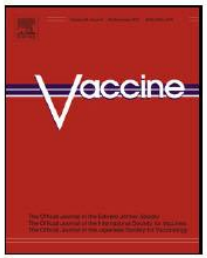
journal homepage: www.elsevier.com/locate/vaccine



Review

Human Papillomavirus Prevalence and Type-Distribution, Cervical Cancer Screening Practices and Current Status of Vaccination Implementation in Central and Eastern Europe

Mario Poljak[a,*], Katja Seme[a], Polona J. Maver[a], Boštjan J. Kocjan[a], Kate S. Cuschieri[b], Svetlana I. Rogovskaya[c], Marc Arbyn[d,e], Stina Syrjänen[f]

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[b] *Specialist Virology Centre, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom*
[c] *Department of Obstetrics and Gynecology, Russian Medical Academy of Post-Graduate Education, Moscow, Russia*
[d] *Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium*
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[f] *Department of Oral Pathology and Oral Radiology, Institute of Dentistry and Medicine Research Laboratory, University of Turku, Turku, Finland*

Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2013;22:7-19
doi: 10.2478/v10162-012-0025-0

Cervical cancer screening practices in central and eastern Europe in 2012

Polona J. Maver[1], Katja Seme[1], Tina Korać[1], Goran Dimitrov[2], Lajos Döbrőssy[3], Ludmila Engele[4], Ermina Iljazović[5], Vesna Kesić[6], Petya Kostova[7], Dragan Lauševič[8], Anita Maurina[9], Florian A. Nicula[10], Yulia Panayotova[11], Maja Primic Žakelj[12], Alenka Repše Fokter[13], Ewa Romejko-Wolniewicz[14], Giedrė Smailytė[15], Ofelia Şuteu[10], Joanna Świderska-Kiec[14], Ruth Tachezy[16], Zdravka Valerianova[7], Piret Veerus[17], Ilze Vīberga[18], Ariana Znaor[19], Pavol Zubor[20], Mario Poljak[1] ✉

Abstract

The burden of cervical cancer in central and eastern Europe is generally higher compared to western or northern Europe due to a history of mostly opportunistic cervical cancer screening practices and due to the strong influence of political and economic changes in post-communist transition. This article describes the current cervical cancer screening practices, organizational plans for the future, and main obstacles that need to be overcome in 16 countries in central and eastern Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia and The former Yugoslav Republic of Macedonia. Unfortunately, only a few countries have managed to establish an organized and well-functioning cervical cancer screening program in recent years, whereas most countries in the region are still struggling with implementation-related issues of organized cervical cancer screening. Encouragingly, even in the countries where only opportunistic screening is performed, well-prepared plans and strategies have been established for switching to organized screening in the near future.

Received: 20 February 2013 | **Returned for modification:** 10 March 2013 | **Accepted:** 15 March 2013

Oportunistic cervical cancer screening in Central/Eastern Europe

- opportunistic screening with poor return
- over-screening and under-screening
- relatively high coverage in women below 40 and poor coverage in older women
- the first steps towards organized screening already taken
- several pilot programs; switch to organized screening program planned for near future

- lack of financial resources
- not high on political agenda
- country specific problems: population registry lacking (BiH)

Do we have reliable baseline data about cervical cancer screening practices in Europe ?

HPV !!!

HPV test ?

2010

EXPERT REVIEWS

Commercially available assays for multiplex detection of alpha human papillomaviruses

Expert Rev. Anti Infect. Ther. 8(10), 1139–1162 (2010)

Mario Poljak[†1] and Boštjan J Kocjan[1]

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[†]*Author for correspondence:*
Tel.: +38 615 437 453
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mario.poljak@mf.uni-lj.si

Five main groups of commercial assays for the multiplex detection of alpha human papillomaviruses (HPVs) are currently available. DNA-based screening assays, which test for the presence of 13–14 HPVs without determination of HPV type, have been the standard for HPV detection in the last decade. Assays that combine testing for 14 HPVs and HPV-16 and HPV-18 genotyping are a potential future standard for HPV detection. The clinical value of HPV genotyping assays has still not been finally determined. Recently, one of the mRNA-based assays showed equal clinical sensitivity but higher clinical specificity for CIN2+/CIN3+ in comparison with the validated DNA-based assay. *In situ* hybridization assays are too laborious and have insufficient clinical sensitivity to be used in routine screening. Automation, price reduction and improvement of clinical specificity are the main goals for the future development of HPV assays.

KEYWORDS: cervical cancer • diagnosis • HPV • human papillomaviruses • PCR

2012

Vaccine 30S (2012) F100–F106

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Nucleic Acid Tests for the Detection of Alpha Human Papillomaviruses

Mario Poljak[a,*], Jack Cuzick[b], Boštjan J. Kocjan[a], Thomas Iftner[c], Joakim Dillner[d], Marc Arbyn[e]

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[d] *Departments of Laboratory Medicine, Medical Epidemiology & Biostatistics, Karolinska Institute, Stockholm, Sweden*
[e] *Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium*

G Model
JCV-3467; No. of Pages 11

ARTICLE IN PRESS

Journal of Clinical Virology xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Virology

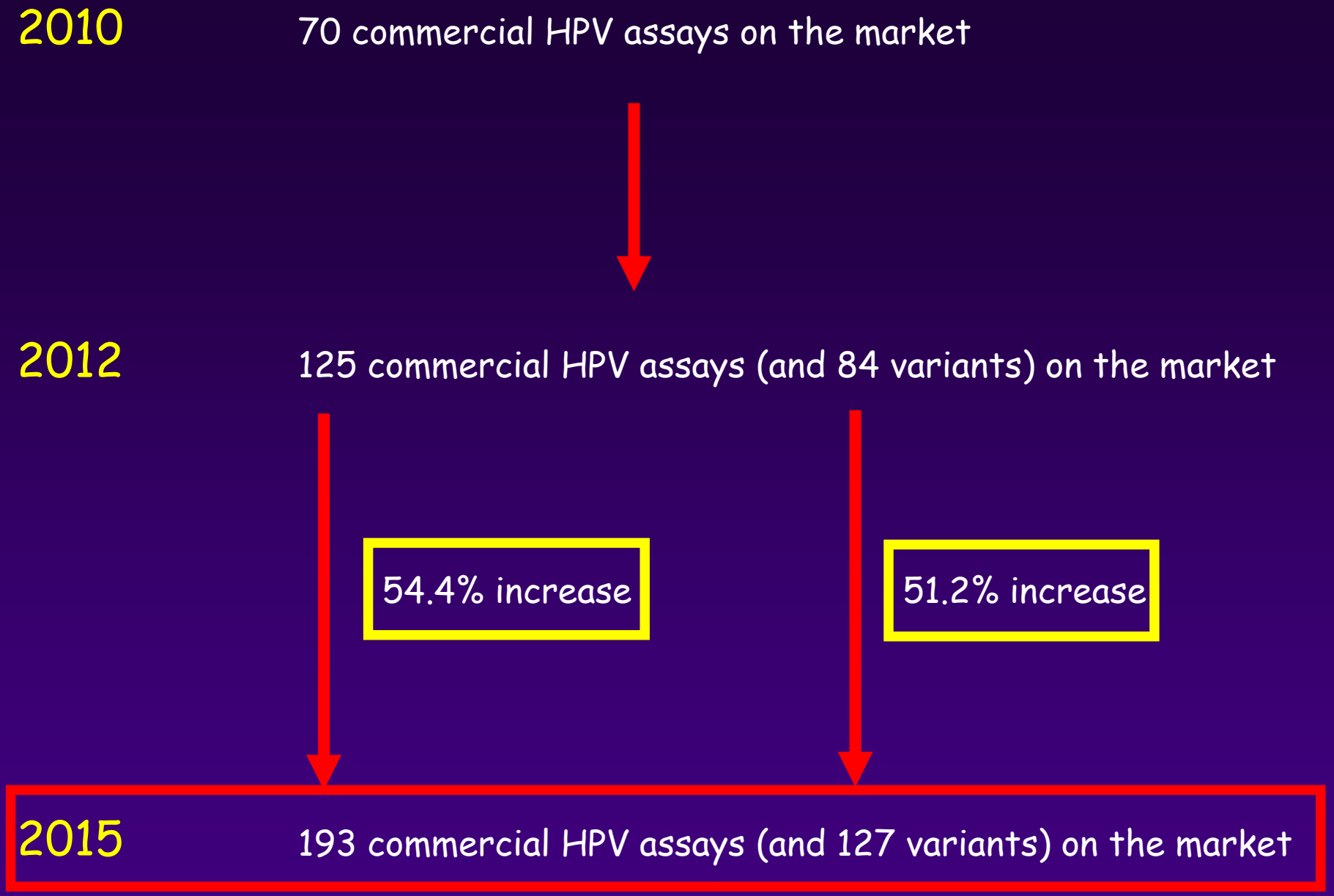
journal homepage: www.elsevier.com/locate/jcv

Review

Commercially available molecular tests for human papillomaviruses (HPV): 2015 update

Mario Poljak*, Boštjan J. Kocjan, Anja Oštrbenk, Katja Seme

Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia


2010
70 commercial HPV assays on the market
2012
125 commercial HPV assays (and 84 variants) on the market
54.4% increase
51.2% increase
2015
193 commercial HPV assays (and 127 variants) on the market

Test vs. test variant

particular HPV test was considered a variant if it was technologically identical or very similar to the original test but targeted different HPV type(s)

HPV TS 16 PCR-DEIA (Labo Bio-medical Products, Ev Rijswijk, Netherlands)

HPV TS 18 PCR-DEIA

HPV TS 31 PCR-DEIA

HPV TS 45 PCR-DEIA

Table 1
hr-HPV DNA screening tests present on the market in August 2015.

Tests targeting IARC-2009 hr-HPV types plus HPV66 and/or HPV68
Hybrid Capture 2 (HC2) HPV DNA Test (Qiagen Gaithersburg, Inc., MD, USA)
EIA kit HPV GP HR (Diassay, Ev Rijswijk, The Netherlands)
Cervista HPV HR Test (Hologic, Madison, WI, USA)
CareHPV Test (Qiagen Gaithersburg, Inc., MD, USA)
Amplicor HPV Test (Roche Molecular Systems Inc., Alameda, CA, USA)
13 High-risk HPV Real-time PCR Kit (Hybribio, Beijing, China)
Biorad Dx HR-HPV Auto Assay (Bio-Rad, Hercules, CA, USA)
Tests targeting IARC-2009 hr-HPV types only
HPV High Risk Screen Real-TM Quant (Sacace, Como, Italy; Nuclear Laser Medicine S.R.L., Milano, Italy)
HPV High Risk Screen Real-TM Quant 2 x (Sacace, Como, Italy; Nuclear Laser Medicine S.R.L., Milano, Italy)
AmpliSens HPV HCR screen-titre-FRT PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli, Bratislava, Slovak Republic) and 1 variant
Tests targeting IARC-2009 hr-HPV types and additional alpha-HPV types
HPV-Risk assay (Self-Screen BV, Amsterdam, The Netherlands)
Seeplex HPV4A ACE Screening (Seegene, Seoul, Korea)
Urine-Based HPV (High and Low Risk) PCR Detection Kit (Norgen, Thorold, Canada)
STD Kit (Autoimmun Diagnostika GmbH, Strassberg, Germany)
AmpliSens HPV HCR screen-Eph PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli, Bratislava, Slovak Republic) and 1 variant
HPV-DNA Assay Kit (Tofema, Seoul, Korea)
PapilloScreen (GeneMatrix Co., Seoul, Korea)
HPV Screen PCR Kit (BioCore, Seoul, Korea)
AmpliQuality HPV-SM (AB Analitica, Padova, Italy)
AmpliQuality HPV-HS Bio (AB Analitica, Padova, Italy)
Human Papilloma Virus (HPV Common/double check) (Genekam Biotechnology, Duisburg, Germany)
BIOPAP Kit (Biotools, Nave, Spain)
High-risk human papillomavirus DNA Diagnostic kit (Sansure Biotech Inc., Changsha, Hunan, China)
Tests targeting a subset of IARC-2009 hr-HPV types
HPV High Risk Screen (Sacace, Como, Italy; Nuclear Laser Medicine S.R.L., Milano, Italy)
AmpliSens HPV HCR screen-FEP PCR kit (3x) (Federal State Institution of Science, Moscow, Russia; Ecoli, Bratislava, Slovak Republic)
HPV Total & High Risk (Clonit, Milano, Italy)
Absolute HPV HR Test (BioSewoom, Seoul, Korea)
HPV Screening (Clonit, Milano, Italy)
Cancer Molecular Marker TEST (GoodGene, Seoul, Korea)

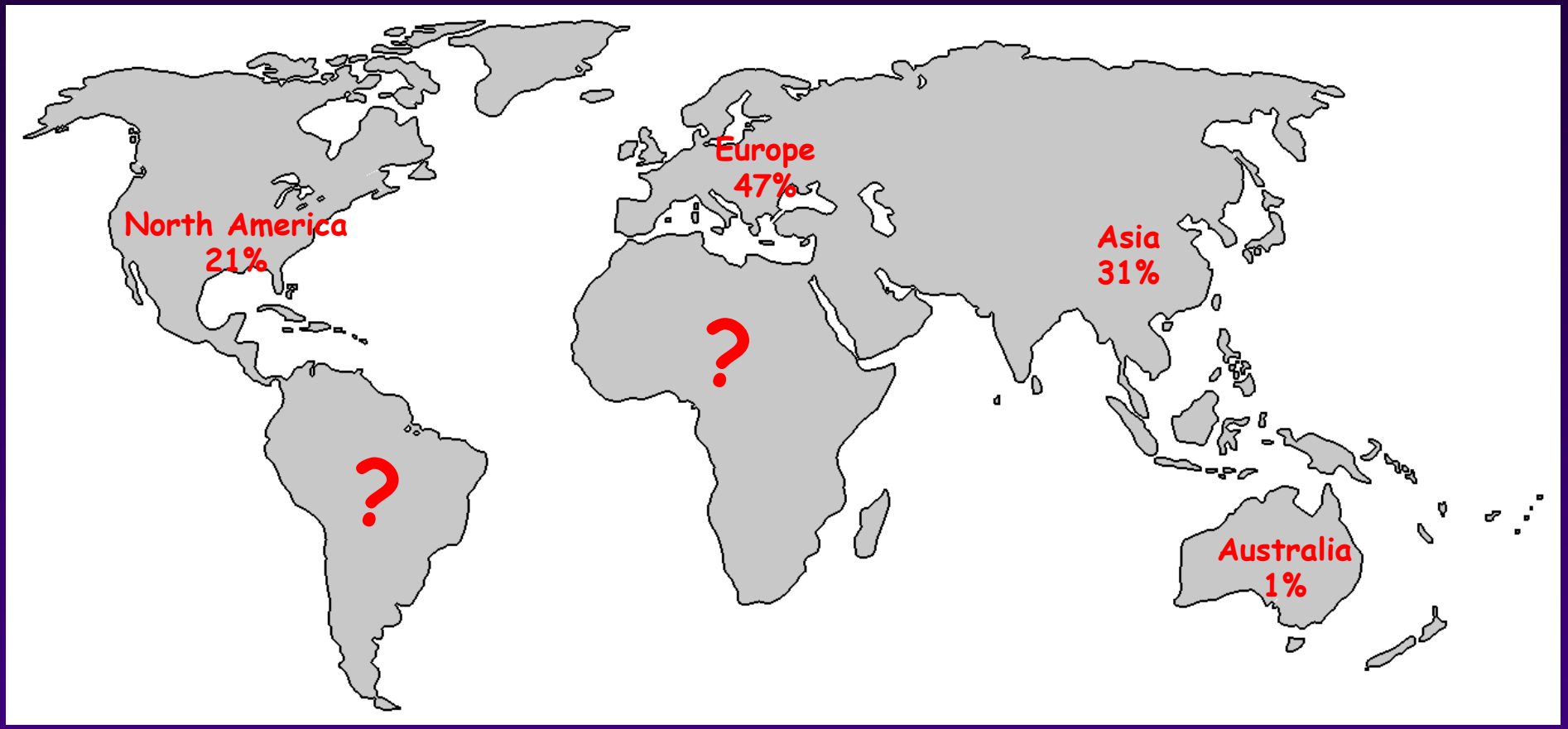
Surprising finding: extensive intra-manufacturer dynamics

companies are constantly changing the design and names of their tests, resulting in delayed and non-updated data presented on vendors' webpages

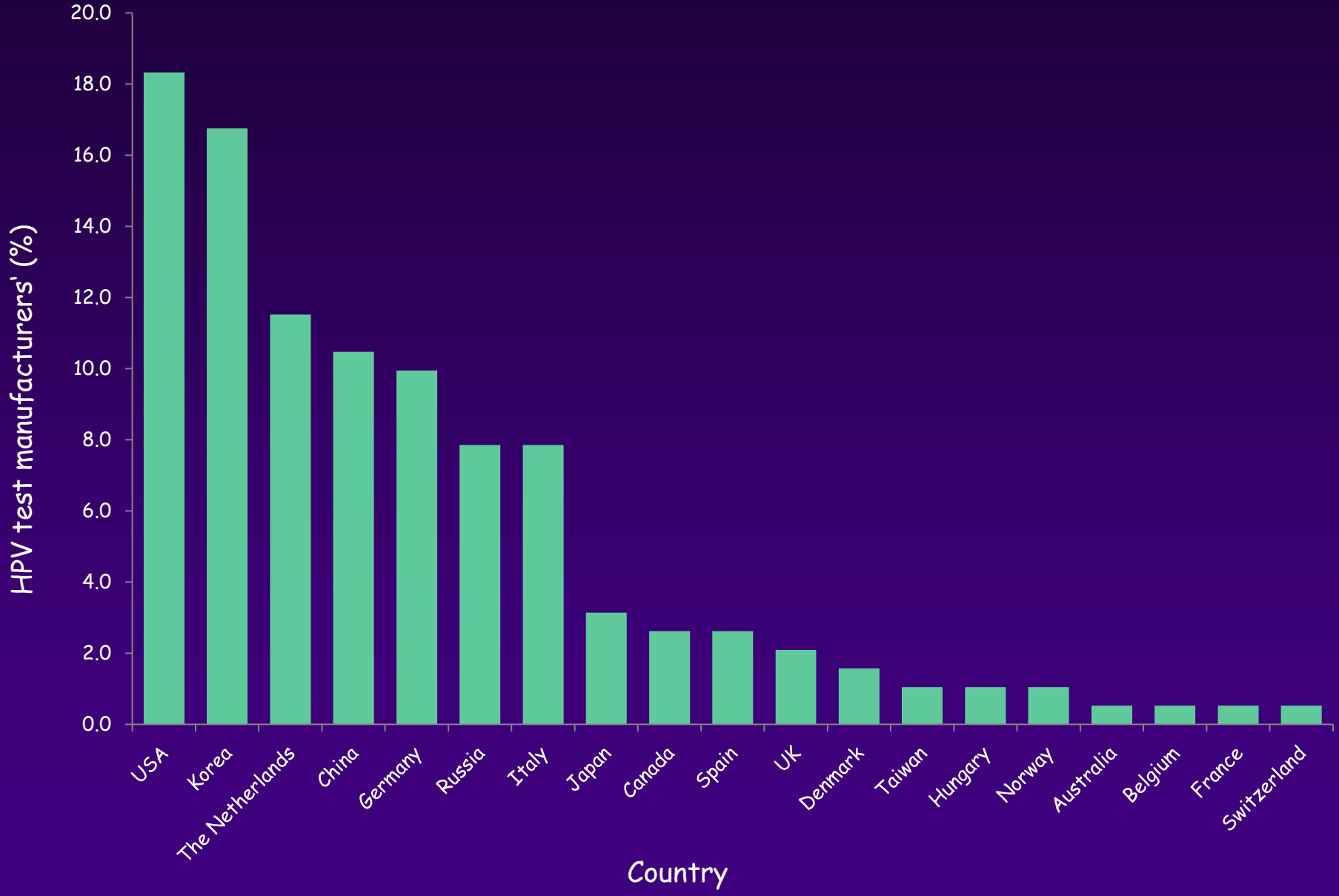
one cannot simply rely on data presented on the manufacturers' official homepages or in scientific publications, but must complement this information with repeated contacts with responsible people in several diagnostic companies, mainly those not regularly present at major HPV-related national and international conferences

finding the "right" and longstanding person in a particular company to address questions to and obtain reliable data from is the main challenge in building a database of HPV tests

Manufacturers' distribution by continent according to the number of different HPV tests currently on the market



Manufacturers' distribution by country according to the number of different HPV tests currently on the market



- 110/193 (57%) of HPV tests with at least one publication
- dramatical improvement from 2012 (25% vs. 57%)

BUT

- only 69/193 (35.7%) of HPV tests with published performance evaluation (analytical and/or clinical)
- 41/193 HPV tests only cross-sectional descriptive studies - no data for key test performance characteristics (sensitivity, specificity, reproducibility)

- "test A versus test B" approach with no reference standard
- ad hoc collections of heterogeneous clinical samples without follow-up
- various target population (including several non-genital)

Int. J. Cancer: **124,** 516–520 (2009)

FAST TRACK

Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women 30 years and older

Chris J.L.M. Meijer[1]*, Johannes Berkhof[2], Philip E. Castle[3], Albertus T. Hesselink[1], Eduardo L. Franco[4], Guglielmo Ronco[5], Marc Arbyn[6,7], F. Xavier Bosch[8], Jack Cuzick[9], Joakim Dillner[10], Daniëlle A.M. Heideman[1] and Peter J.F. Snijders[1]

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[7]*ECCG (European Cooperation on Development and Implementation of Cancer Screening and Prevention Guidelines), IARC, Lyon, France*
[8]*Servei d'epidemiologia, Institut Catala d'Oncologia (ICO), Hospitalet del llobregat, Barcelona, Spain*
[9]*Queen Mary's School of Medicine and Dentistry and Cancer Research UK, London, United Kingdom*
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Which high-risk HPV assays fulfil criteria for use in primary cervical cancer screening?

M. Arbyn[1], P. J. F. Snijders[2], C. J. L. M. Meijer[2], J. Berkhof[3], K. Cuschieri[4], B. J. Kocjan[5] and M. Poljak[5]

1) *Unit of Cancer Epidemiology and Belgian Cancer Centre, Scientific Institute of Public Health, Brussels, Belgium,* 2) *Department of Pathology,* 3) *Department of Clinical Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, The Netherlands,* 4) *Scottish HPV Reference Laboratory, Royal Infirmary of Edinburgh, Edinburgh, Scotland, UK and* 5) *Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*

Clin Microbiol Infect 2015; **21:** 817–826

Longitudinal data ?

Hybrid Capture 2 (hc2) HPV DNA Test (Qiagen)

EIA kit HPV GP GP5+/6+ HR

cobas 4800 HPV Test (Roche)

APTIMA HPV Assay (Hologic, Gen-Probe)

RealTime High Risk HPV test (Abbott)

Conclusions

- 193+ commercial HPV assays (and 127+ variants) on the market
- 2 + 9 HPV assays fulfil cross-sectional criteria for primary screening
- 2 + 3 HPV assays have at least 36+ months longitudinal data

future of inventory of commercial HPV tests ?

Routine use of HPV DNA testing

Primary screening

Do we have clear guideline recommending HPV-based primary screening in Europe ?

Papillomavirus Research 2015; doi:10.1016/j.pvr.2015.06.006.

European guidelines for quality assurance in cervical cancer screening. Summary of the supplements on HPV screening and vaccination

Lawrence von Karsa [a,*], Marc Arbyn [b], Hugo De Vuyst [c], Joakim Dillner [d], Lena Dillner [e], Silvia Franceschi [f], Julietta Patnick [g], Guglielmo Ronco [h], Nereo Segnan [h], Eero Suonio [a], Sven Törnberg [i], Ahti Anttila [j]

Suitability of HPV primary testing for use in cervical cancer screening programmes

Primary testing for oncogenic HPV can be used in an organized, population-based programme for cervical cancer screening (**I-A**) provided the other recommendations in this supplement are followed (**VI-A**). Primary testing for oncogenic HPV outside an organized population-based programme is not recommended (**VI-E**).

Avoidance of co-testing (HPV and cytology primary testing) at any given age

Only one primary test (either cytology or testing for oncogenic HPV) should be used (at any given age in cervical cancer screening (see also Rec. 1.3–1.7) (**II-A**).

Age at which to start HPV primary testing in cervical cancer screening programmes

Routine HPV primary screening can begin at age 35 years or above (**I-A**).

Routine HPV primary screening should not begin under age 30 years (**I-E**).

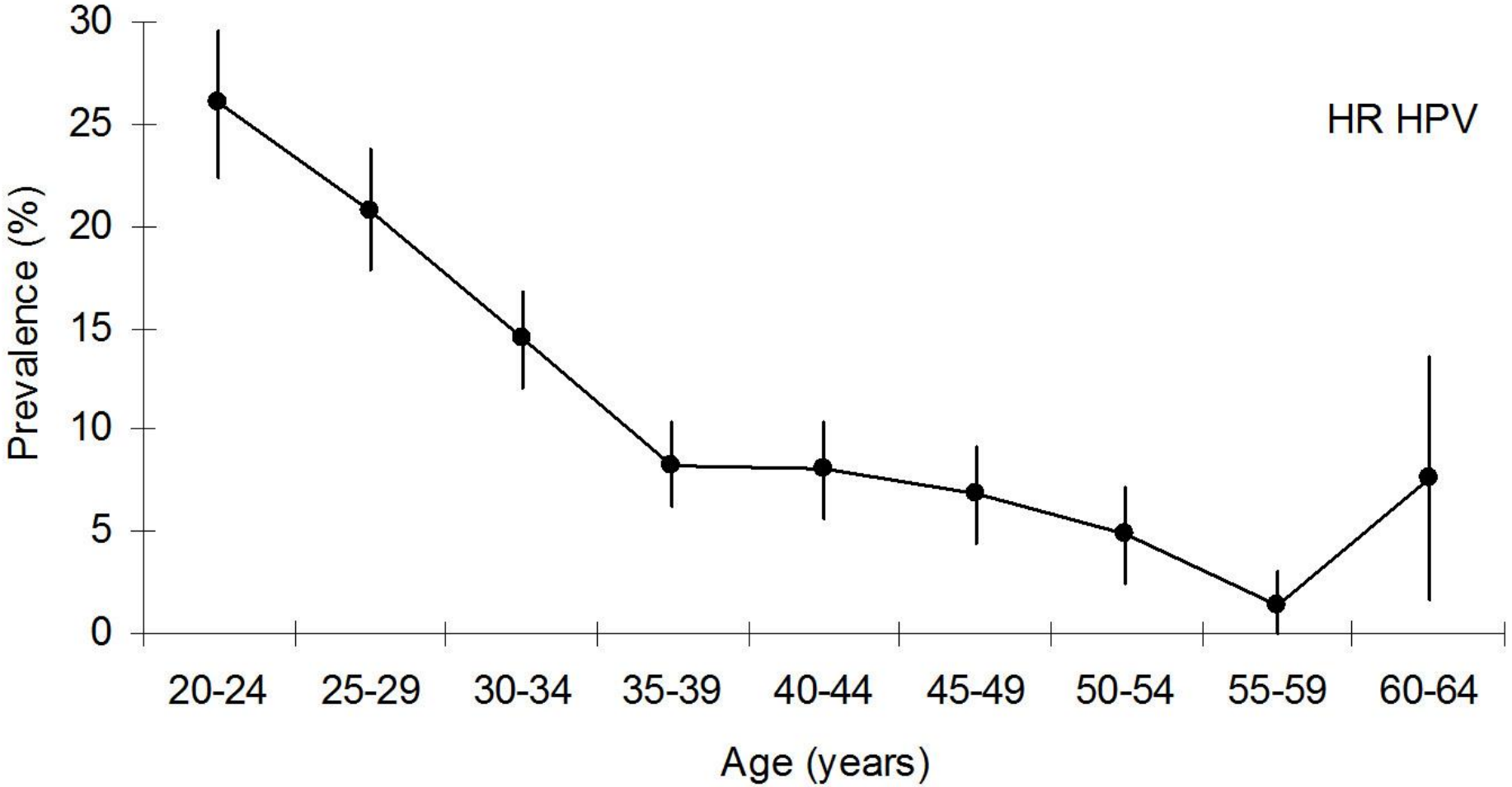
Routine use of HPV DNA testing

Primary screening

reduced specificity of HPV DNA testing

requires appropriate triage

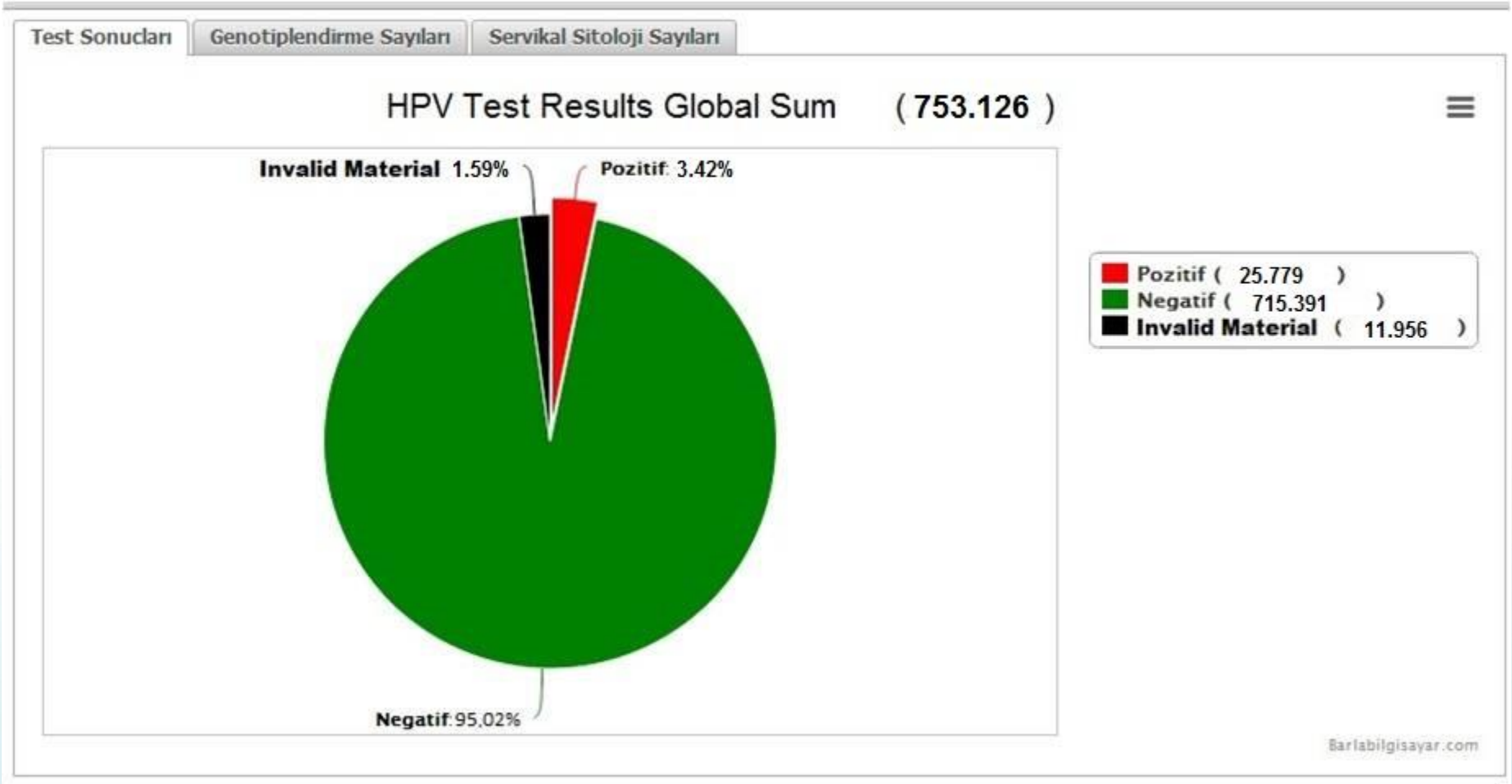
Prevalence of infection with 14 hr-HPV types with 95% confidence intervals according to age among 4,431 women screened for cervical cancer, Slovenia, 2010



Učakar V, Poljak M, Klavs I. Vaccine 2012; 30: 116-120.

T.C. Sağlık Bakanlığı
Türkiye Halk Sağlığı Kurumu

HR-HPV (+)



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Secondary testing - Cytology triage

Women testing positive for oncogenic HPV at primary screening should be tested without delay for cervical cytology (cytology triage) (**I-A**).

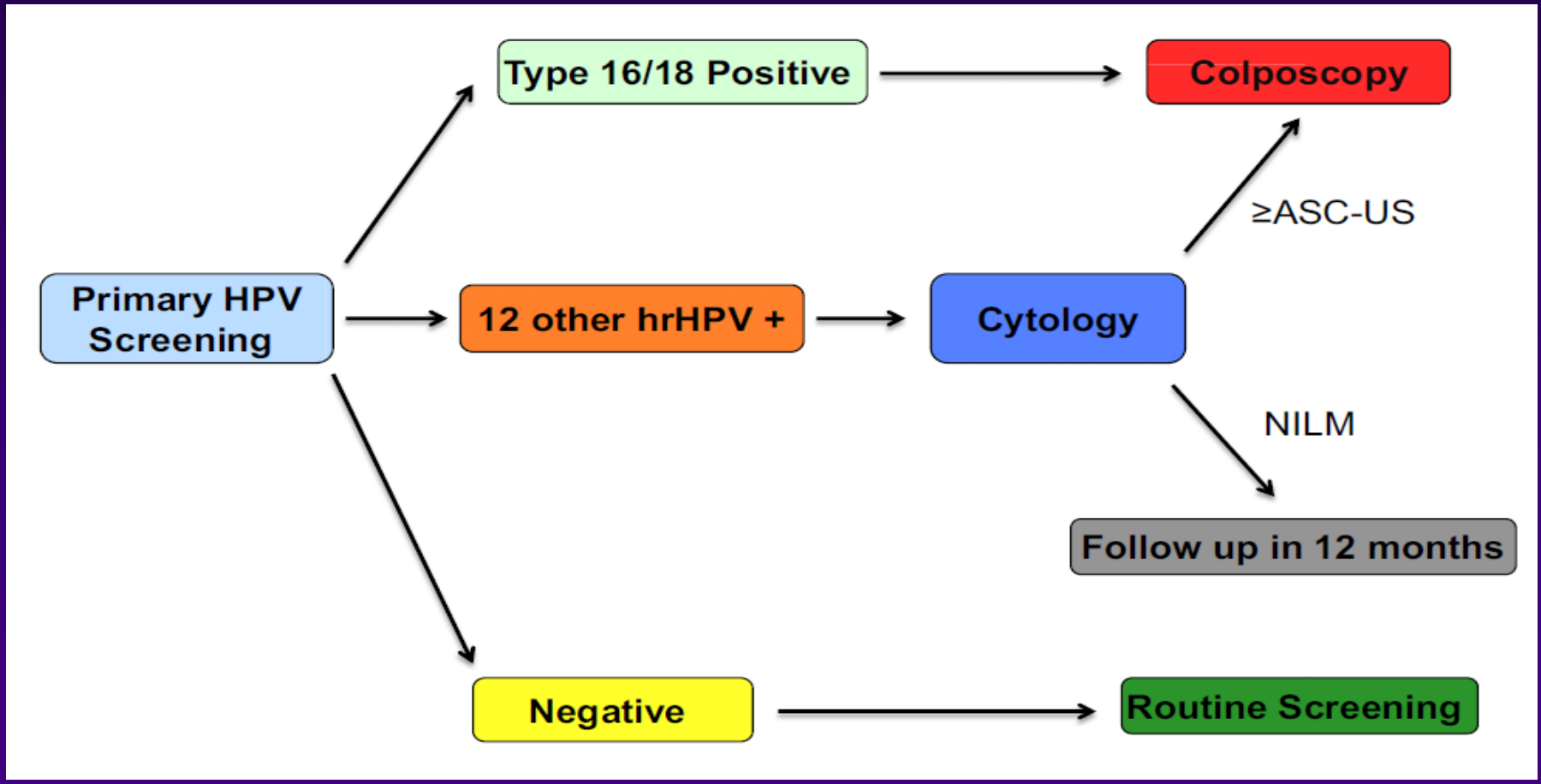
Women who have negative cytology at triage after a positive initial HPV primary test in a screening episode should be followed up by re-testing after an interval shorter than the regular screening interval, but after at least 6-12 months (**VI-A**).

Clinical Commentary

Use of primary high-risk human papillomavirus testing for cervical cancer screening: Interim clinical guidance ☆

Gynecol Oncol 2015; 136:178-82

Warner K. Huh [a,*], Kevin A. Ault [b], David Chelmow [c], Diane D. Davey [d], Robert A. Goulart [e], Francisco A.R. Garcia [f], Walter K. Kinney [g], L. Stewart Massad [h], Edward J. Mayeaux [i], Debbie Saslow [j], Mark Schiffman [k,1], Nicolas Wentzensen [k,1], Herschel W. Lawson [l], Mark H. Einstein [m]



Routine use of HPV DNA testing
Progression markers

- HPV 16 (18, 45, 31…..other priority hr-HPVs)
- HPV viral load ?
- HPV E6/E7 mRNA
- p16
- p16/Ki-67 dual-staining
- FISH markers
- TOP2A and MCM2 staining
- gene methylation

Before we start…

performing local HPV genotype distribution studies in women with normal cytology, HSIL and/or cervical cancer prior implementation of primary HPV screening is not necessary any more – use available regional data

performing additional local evaluation of already clinically validated HPV tests (other than feasibility studies) prior implementation is not necessary any more for any of the approved indications of HPV testing (including primary HPV screening) – use available general and regional data

do not complicate and reinvent wheel, trust more experienced colleagues and their results

Fighting against wrong perception

- more genotypes = better HPV test

- higher price = better HPV test

- manufacturers' rumors (bizarre case reports, biased evacuations, L1 deletion story…)

- long screening rounds are unsafe (even with shorter rounds they missed Ca…)

- lobbies (cytologists, gynecologists, colposcopists…new role for all should be identify)

- experiment serving diagnostic companies

- general mistrust in the ineffective public health system

Existing gaps in knowledge and areas of research interest

If HPV testing is adopted for women ages 30+ (35+), what screening options should be recommended for younger women ?

Self-collected sample based sceening for all ?

One stop shop screening test ?

What is the role (if any) of HPV viral load as a clinical tool ?

Is the balance between lower accuracy and higher coverage acceptable ?

Algorithm management versus risk stratification ?

Can healthcare providers learn and apply risk stratification via multiple biomarker testing as part of practice guidelines? Is it cost-effective ?

primary and secondary prevention (HPV vaccination and screening) are not mutually exclusive, but act synergistically by intervening at different points in the natural history of cervical cancer, and currently imply actions in women of different ages

adequately combined, two prevention options have the potential dramatically to reduce cervical cancer incidence and mortality; no other neoplastic disease can currently rival the magnitude of this potential

BUT

two powerful prevention strategies remain apparently unconnected and no country has yet adopted different screening policies for vaccinated and unvaccinated women