

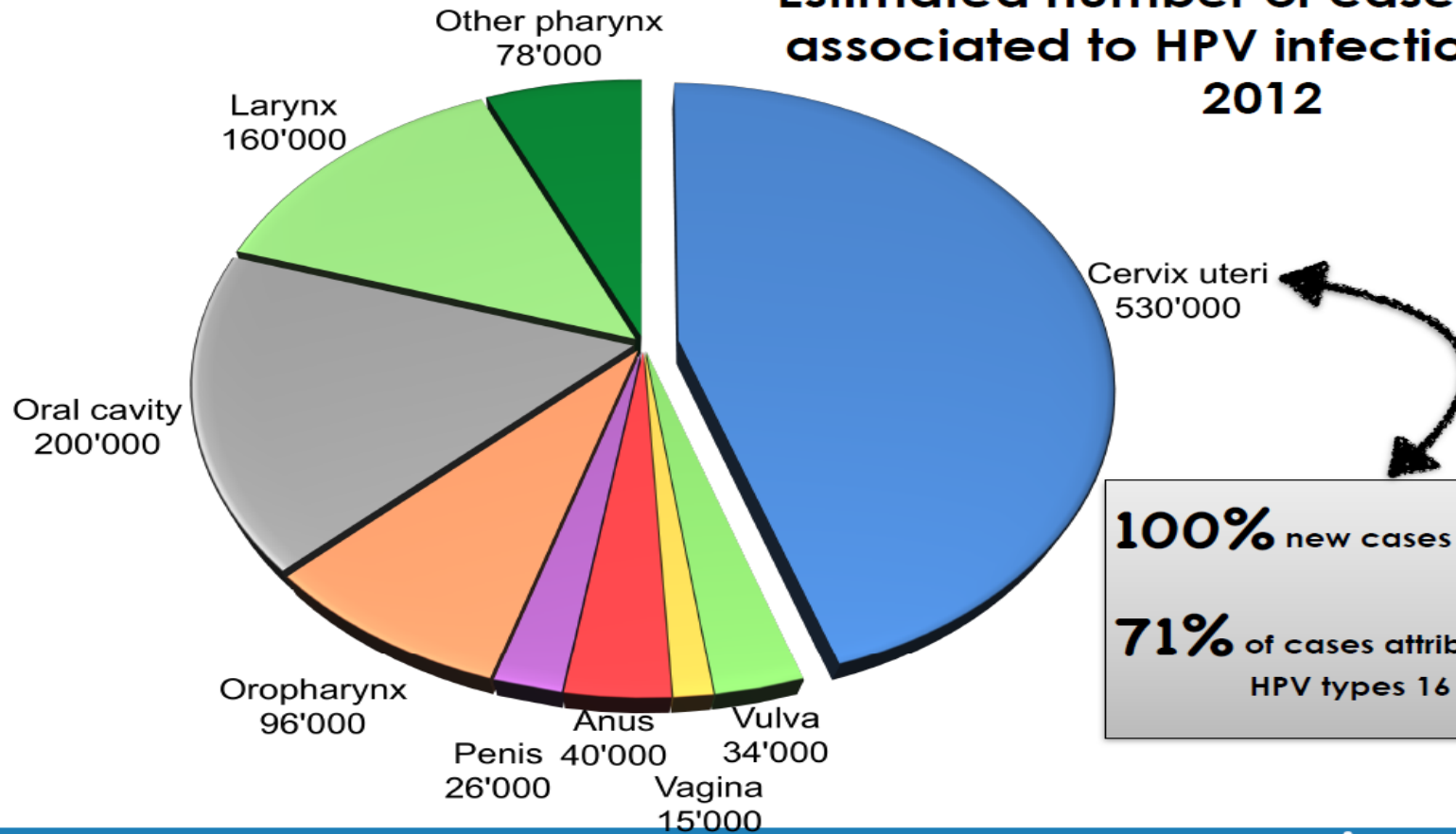
HPV: a Global and European overview



Robb Butler
Vaccine-preventable Diseases and Immunization Programme
WHO Regional Office for Europe
Copenhagen, Denmark



Estimated number of cases of cancer associated to HPV infection globally, 2012



100% new cases attributable to HPV

71% of cases attributable to HPV types 16 and 18



World Health Organization

HPV- and Cervical cancer prevalence

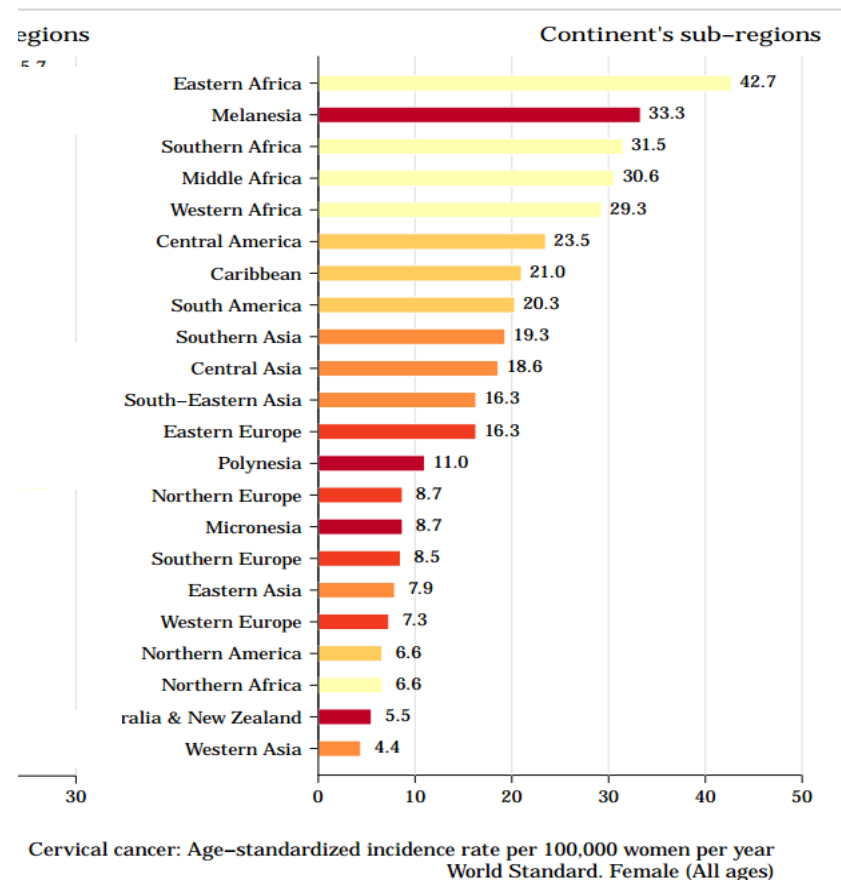
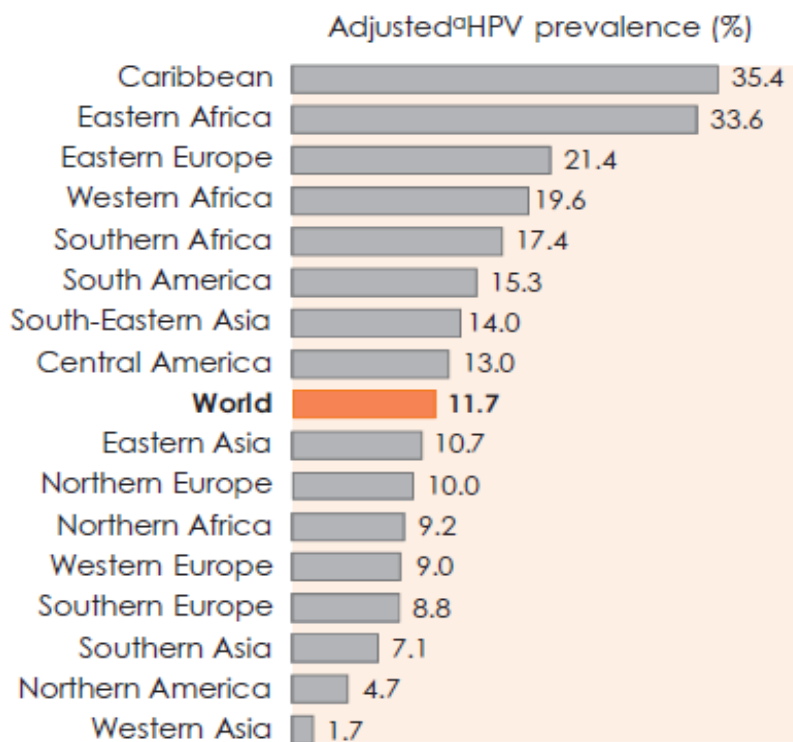


Figure 1. HPV prevalence among women with normal cytology: meta-analysis based on results from 1,016,719 women. ^aRegionally-adjusted HPV (see [1] for adjustment methodology). Redrawn from Bruni L *et al.* [1].

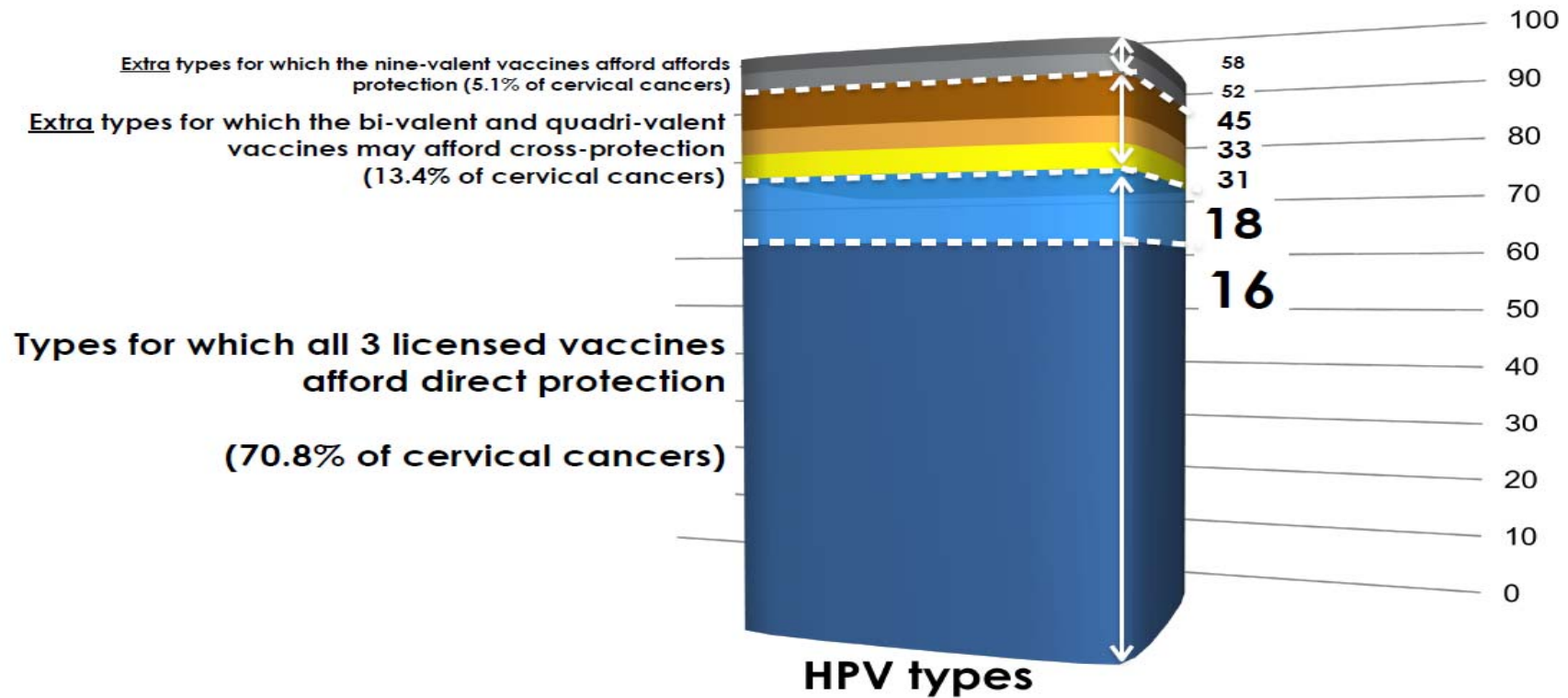
Cervical cancer: Age-standardized incidence rate per 100,000 women per year World Standard, Female (All ages)

Source: Forman et al., Vaccine 2012,

Vaccine Characteristics

Characteristics	Bivalent 2vVPH	Quadrivalent 4vVPH	9-valent 9vVPH
Commercial Name producer	Cervarix™, GSK	Gardasil™, Merck	Gardasil 9™, Merck
Types of virus like particles (VLP)	16 18	6 11 16 18	6 11 16 18 31 33 45 52 58
Dose of L1 protein	20/20 µg	20/40/40/20 µg	30/40/60/40 µg 20/20/20/20/20 µg
Adjuvant	ASO4 (500 µg aluminum hydroxide, 50 µg 3-O-deacylated-4'- monophosphoryl lipid A)	AAHS (225 µg amorphous aluminum hydroxyphosphate sulfate)	500 µg AAHS
Licensed schedules	0, 1, 6 month 0, 6 month	0, 2, 6 month 0, 6 month	0, 2, 6 month 0, 6 month

HPV types contribution to cervical cancer and protection offered by HPV vaccines



WHO Position

(www.who.int/imm)

- Reiterates the recommendation that HPV vaccines should be included in national immunization programmes

SAGE (Oct 2016) recommends:

Target: girls 9-14 years of age

2 doses

Interval min 6 months

No maximum interval (suggested until 12-15 months after first dose)

Multi-cohort of 9 -14 years of age (or the age of 18) at introduction

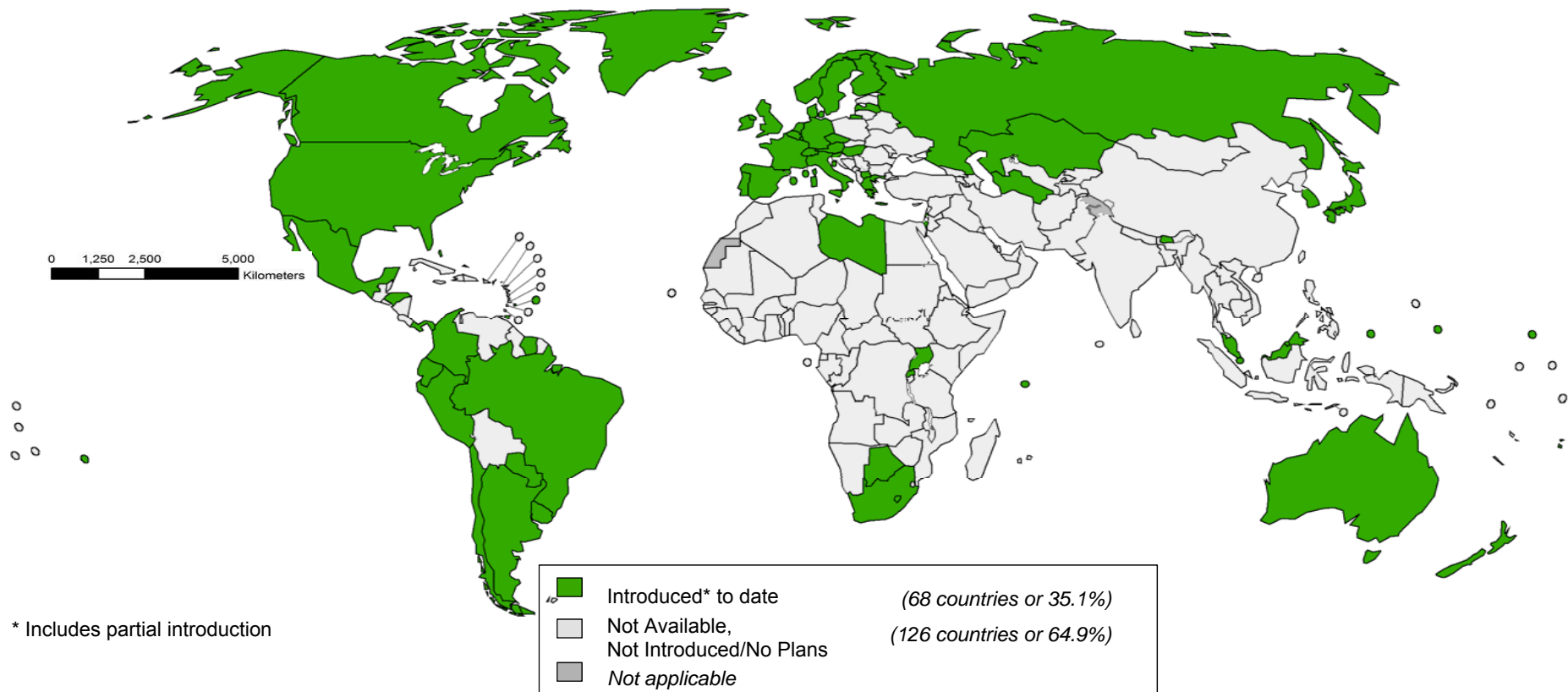
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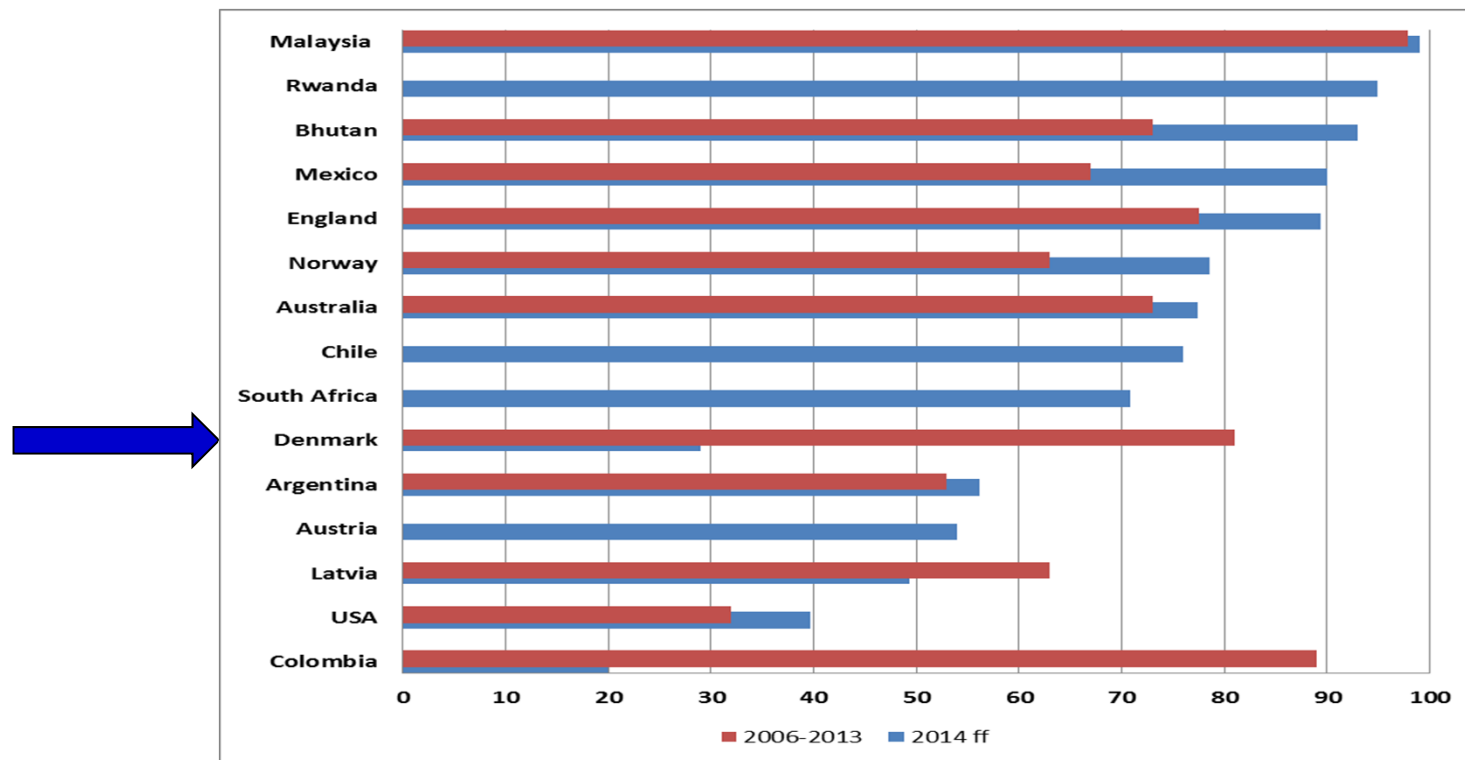
Countries with HPV vaccine in the national immunization programme



Data source: WHO/IVB Database, as of 10 January 2017
 Map production Immunization Vaccines and Biologicals (IVB), World Health Organization

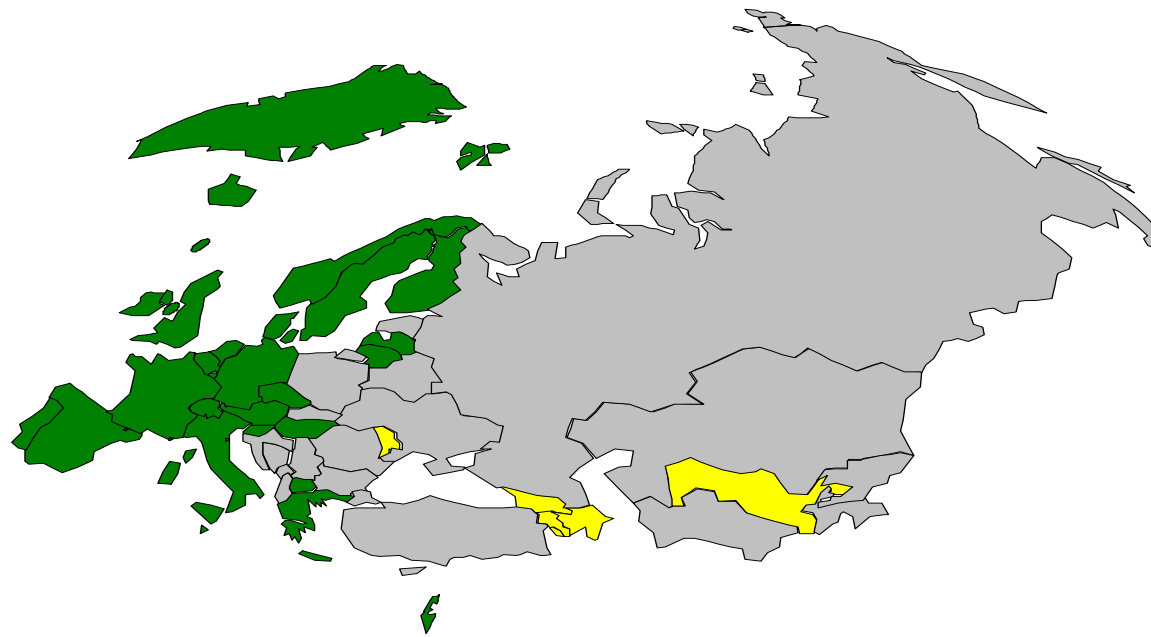
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. ©WHO 2017. All rights reserved.

Reported HPV coverage rates Selected countries & years in two time periods



Source: Brotherton et al. 2016

Introduction of HPV vaccine in WHO European Region, 2016

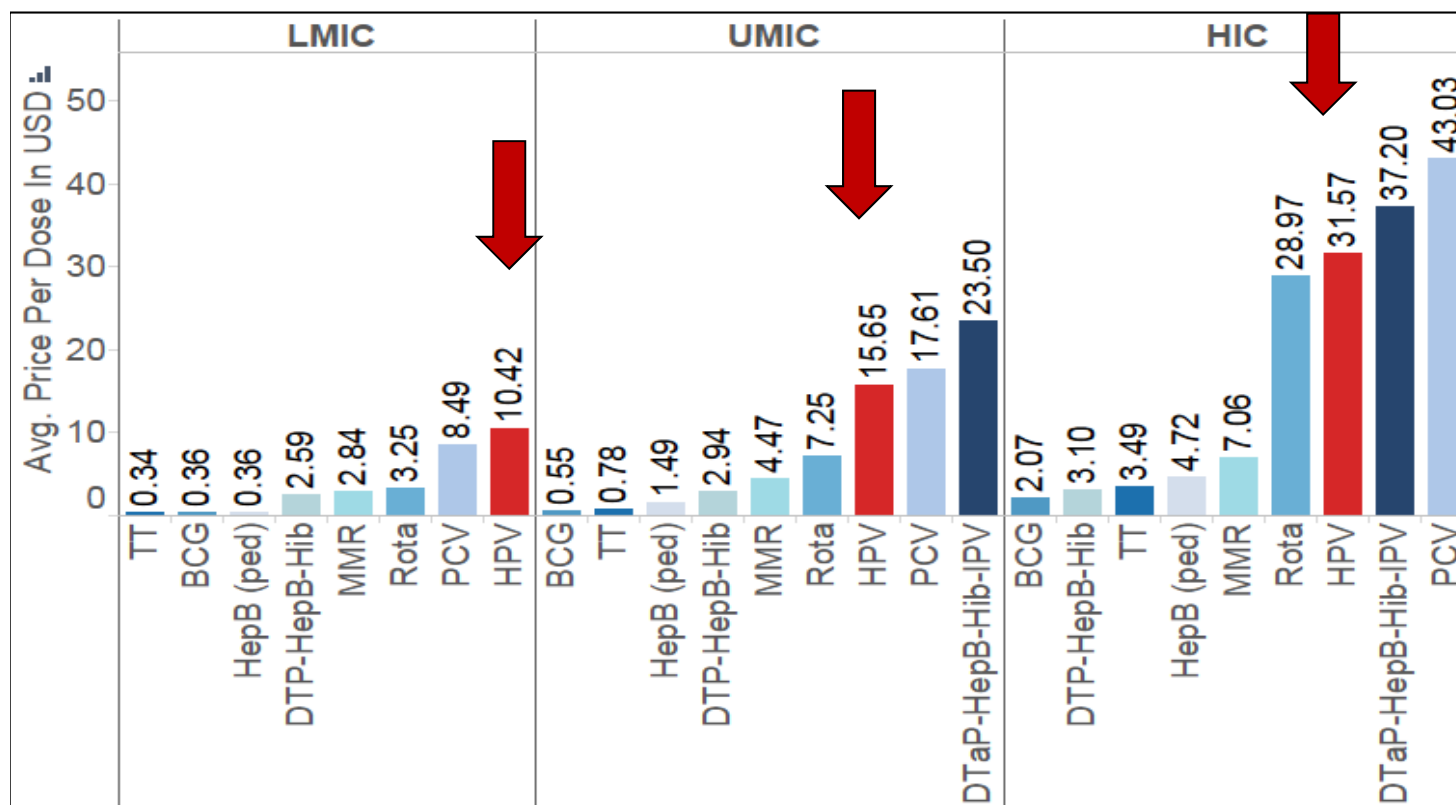


Data source: WHO/IVB Database, as of 30 January 2017
Map production Immunization Vaccines and Biologicals (IVB), World Health Organization

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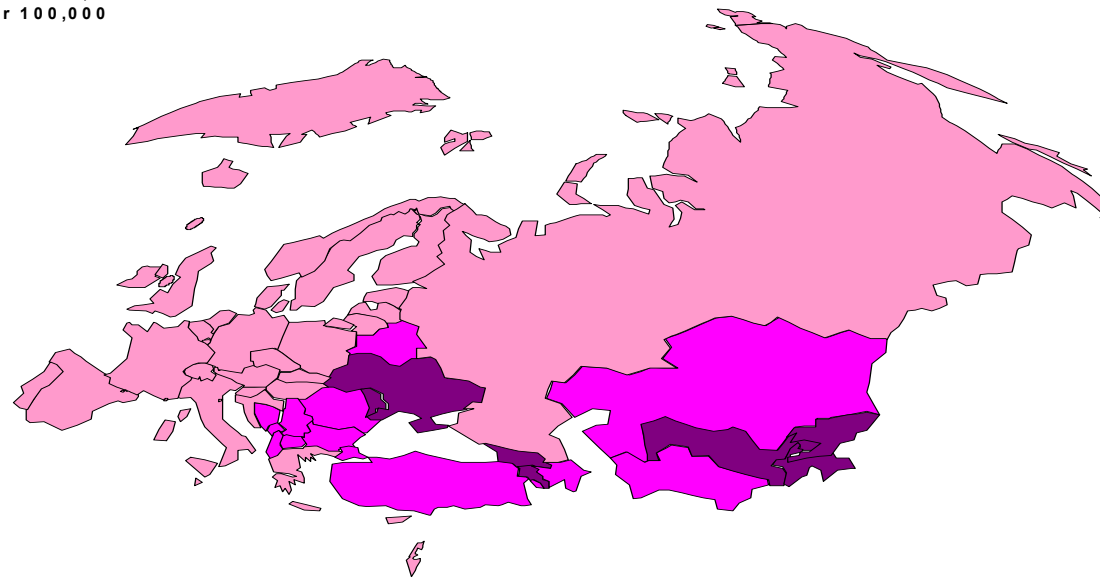
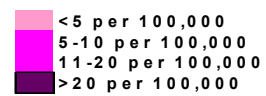
HPV vaccine is one of the most expensive vaccines across all income groups

Average price of selected vaccines by income group, USD 2015



Source: V3P database - www.who.int/immunization/v3p (extract on 16 Jan 2016).
 Note: Average price in USD for each vaccine type broken down by income level (vaccine type is color-coded). Price data is 2015 data (shared by countries in 2016). There are 50 countries sharing vaccine price information in the V3P database in 2016, including 15 countries reporting HPV price.

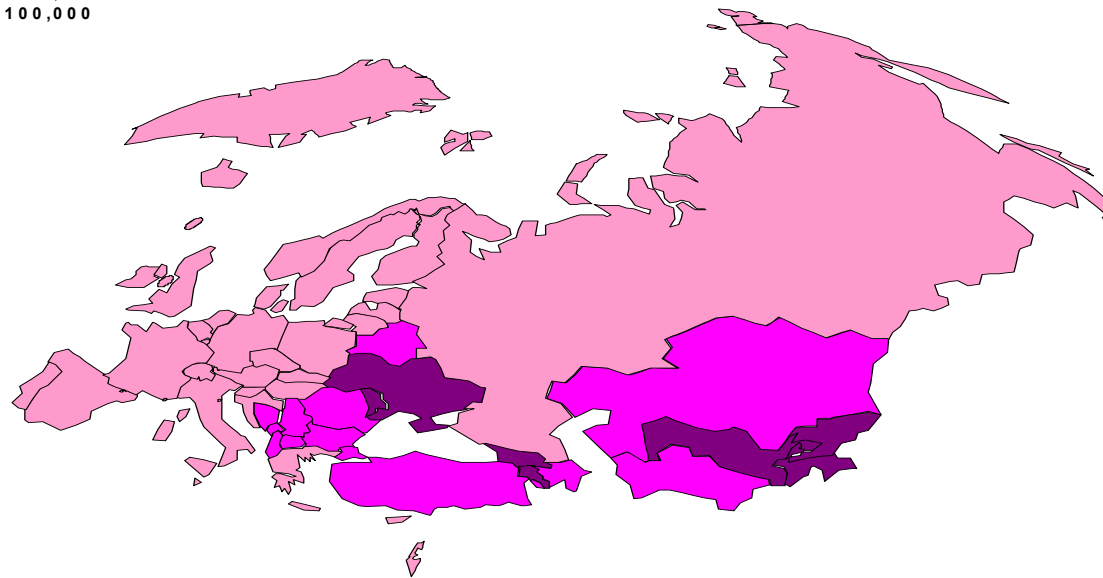
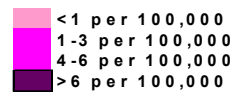
Cervical cancer incidence (age standardized rates per 100,000), WHO European Region, 2012



Source: International Agency for Research on Cancer, Globocan 2012



Cervical cancer mortality (age standardized rates per 100,000), WHO European Region, 2012



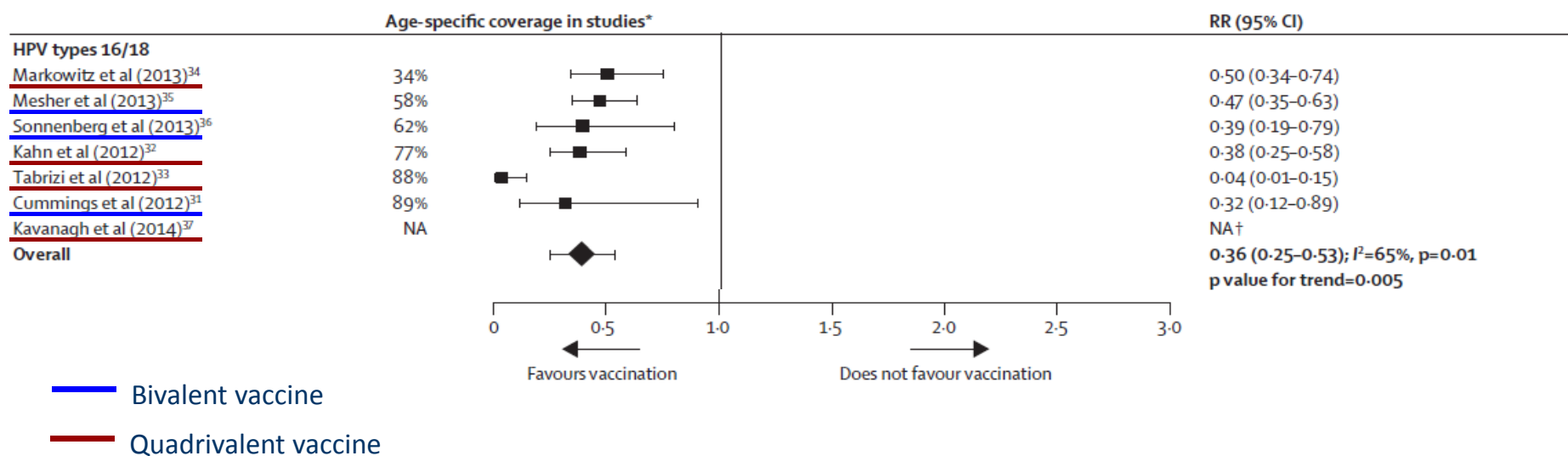
Source: International Agency for Research on Cancer, Globocan 2012



Early signs of Impact of vaccination

Prevalence of infections with HPV16/18 between periods before and after start of vaccination in 13–19 year olds

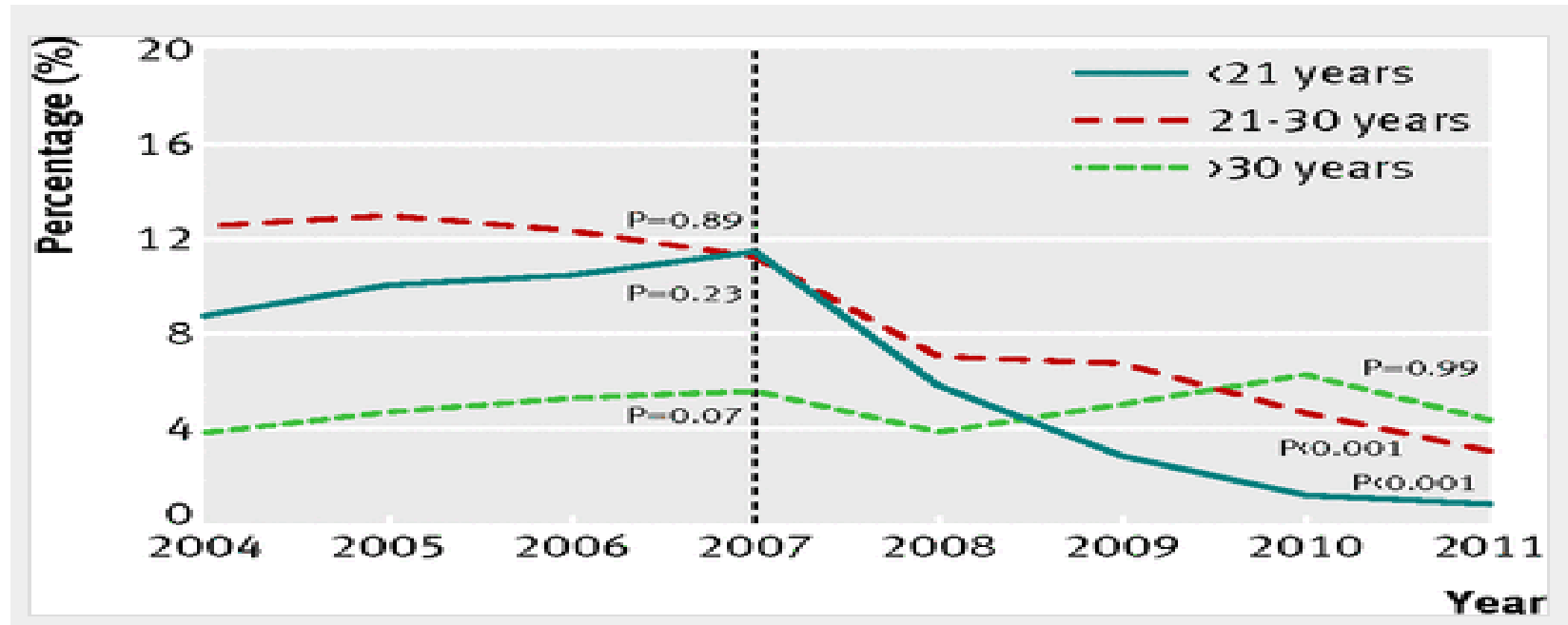
Systematic review and meta-analysis



Drolet et al., Lancet Infect Dis 2015, 15:565–80

HPV vaccine effectiveness against genital warts, Australia

Proportion of Australian born women diagnosed as having genital warts at first visit



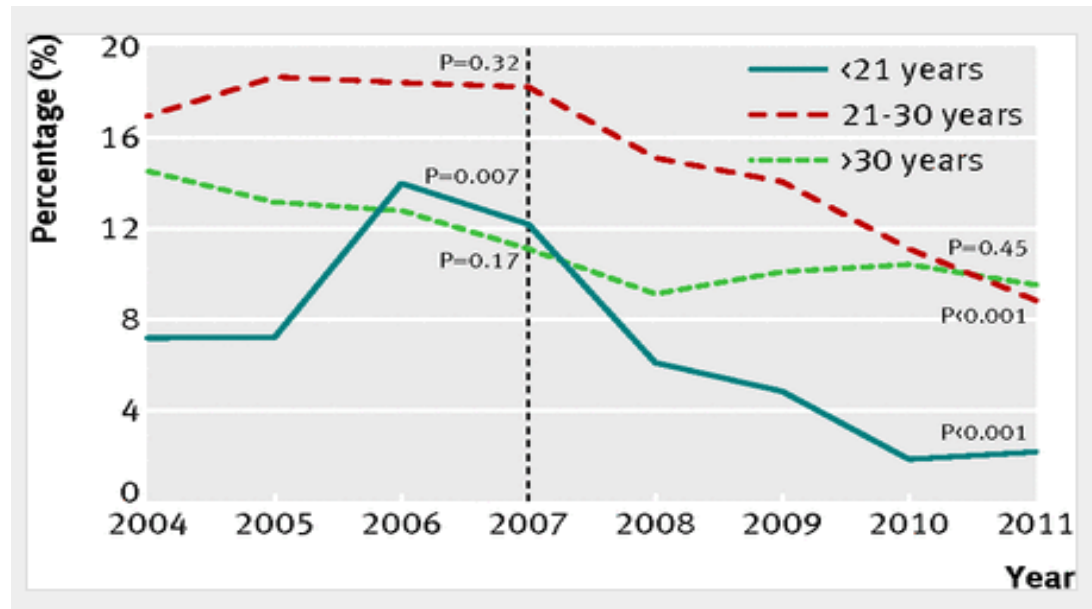
Females <21 years 92.6% decline post vaccination

Females 21-30 yrs 72.6% decline post vaccination

Ali et al., 2013

Herd immunity

Proportion of Australian born heterosexual men diagnosed as having genital warts at first visit



Males <21 years : 81.8% decline post vaccine introduction
Males 21-30 yrs : 51.1% decline post vaccine introduction

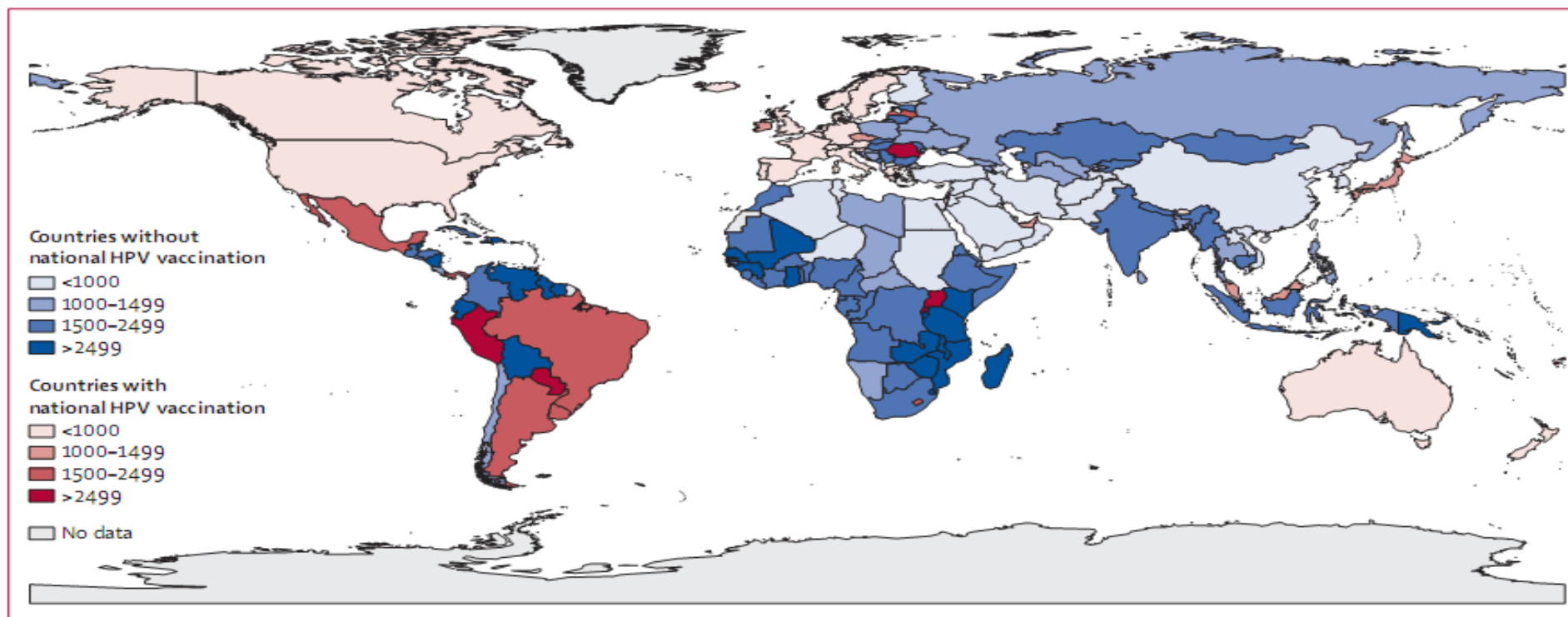
Ali et al., BMJ 2013

See also:

- Sando et al *Acta Derm Venereol* 2014
- Tabrizi and Brotherton et al, *Lancet Infect Dis* 2014
- Drolet et al, *Lancet Infect Dis*, 2015

Cervical cancers prevented per 100,000 vaccinated

PRIME&



- Vaccinating 80% of 12-year olds in 2012 would prevent 690,000 cervical cancer cases and 420,000 deaths over their lifetime.

HPV Vaccine Safety

March 12, 2014

As with all new vaccines, the safety of HPV vaccines is being closely monitored. The CDC recommends the use of HPV vaccines to reduce the risk of cervical cancer. The detection of pre-cancerous changes in the cervix is a key step in the prevention of cervical cancer. While safety issues are being investigated, the CDC continues to recommend the use of HPV vaccines.

The purpose of this review is to assess the safety of HPV vaccines. The immunization program is a result of increased awareness of the risks of cervical cancer.

To date, the GACVS has reviewed the following safety issues related to the HPV vaccine:

To date GACVS has reviewed the following safety issues related to the HPV vaccine :

- Adverse events coinciding with pregnancy
- Aluminium adjuvant used in the 4vHPV vaccine
- Syncope and anaphylaxis
- Venous thromboembolism and stroke ;
- Autoimmune conditions (MS and Guillain-Barre) and cerebral vasculitis
- Complex regional pain (CRPS) and / or other conditions of chronic pain syndrome.
- Postural orthostatic tachycardia syndrome (POTS)

HPV Vaccine Safety



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

5 November 2015
EMA/714950/2015

Review concludes evidence does not support that HPV vaccines cause CRPS or POTS

Reports of CRPS and POTS after HPV vaccination are consistent with what would be expected in this age group

WHO Global Advisory Committee on Vaccine Safety (GACVS)

22 January, 2016

Statement on the continued safety of HPV vaccination

- “The GACVS has systematically investigated safety concerns raised about HPV vaccines and has issued several reports in this regard.”
- “To date, GACVS has not found any safety issue that would alter its recommendations for the use of the vaccine.”
- “As GACVS has noted previously, policy decisions based on weak evidence, leading to lack of use of safe and effective vaccines, can result in real harm.”

GACVS and HPV Safety

- Next Review HPV Safety in June 2017
- New, [WHO Information Sheets on Observed Rates of Vaccine Reactions HPV vaccine](#) will be released soon
 - Graded – strength of evidence
 - by vaccine type



Global Vaccine Safety

Global Vaccine Safety

▶ Global Vaccine Safety Initiative

▼ Global Advisory Committee on Vaccine Safety

Topics

Committee reports









Reference documents and publications

Safety of human papillomavirus vaccines

Committee reports

- 22 January 2016 - Safety of HPV vaccines (from meeting of 2-3 December 2015)
- 14 February 2014 - Human papillomavirus vaccines safety (HPV) (from GACVS meeting of 11-12 December 2013)
- 19 July 2013 - Update on human papillomavirus vaccines (from meeting of 12-13 June 2013)
- 7 August 2009 - Safety of human papillomavirus vaccines (from meeting of 17-18 June 2009)
- 30 January 2009 - Safety of human papillomavirus vaccines (from meeting of 17-18 December 2008)
- 20 July 2007 - Safety of human papillomavirus vaccine (from meeting of 12-13 June 2007)

Statements

-  [GACVS Statement on Safety of HPV vaccines - 17 December 2015](#)
 pdf, 112kb
-  [GACVS Statement on the continued safety of HPV vaccination - 12 March 2014](#)
 pdf, 173kb
-  [GACVS Safety update on HPV Vaccines, Geneva - 17 December 2013](#)
 pdf, 19kb
-  [GACVS Safety update on HPV Vaccines - 13 June 2013](#)
 pdf, 230kb

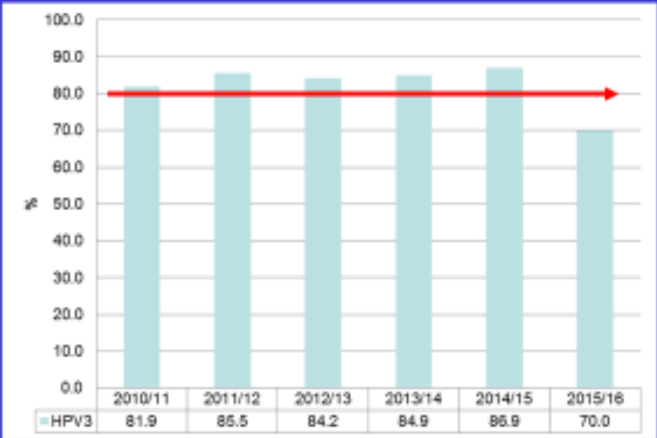
Page last updated: 22 January 2016

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Ireland

HPV vaccine uptake 2010/2011 - 2015/2016 Routine programme First years

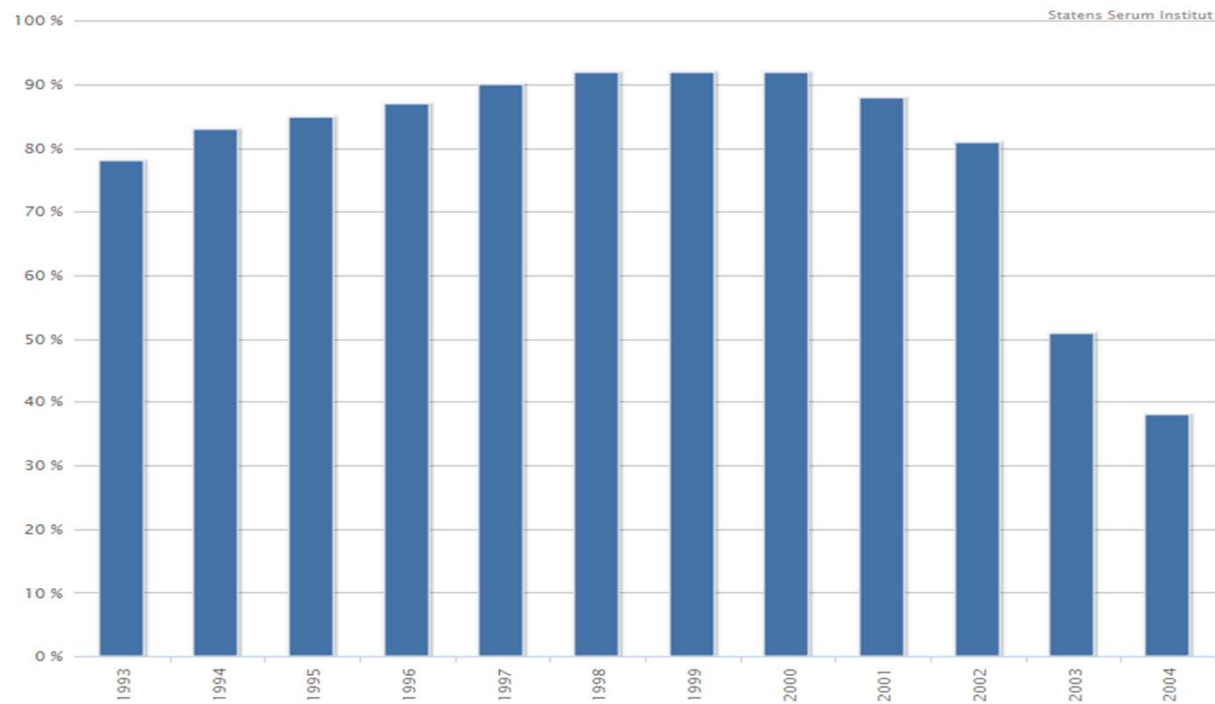


5000 more girls not vaccinated in 2015/16

Highest uptake achieved in 2014/15
Excellent cohort retention
97% girls who started dose 1 completed dose 2

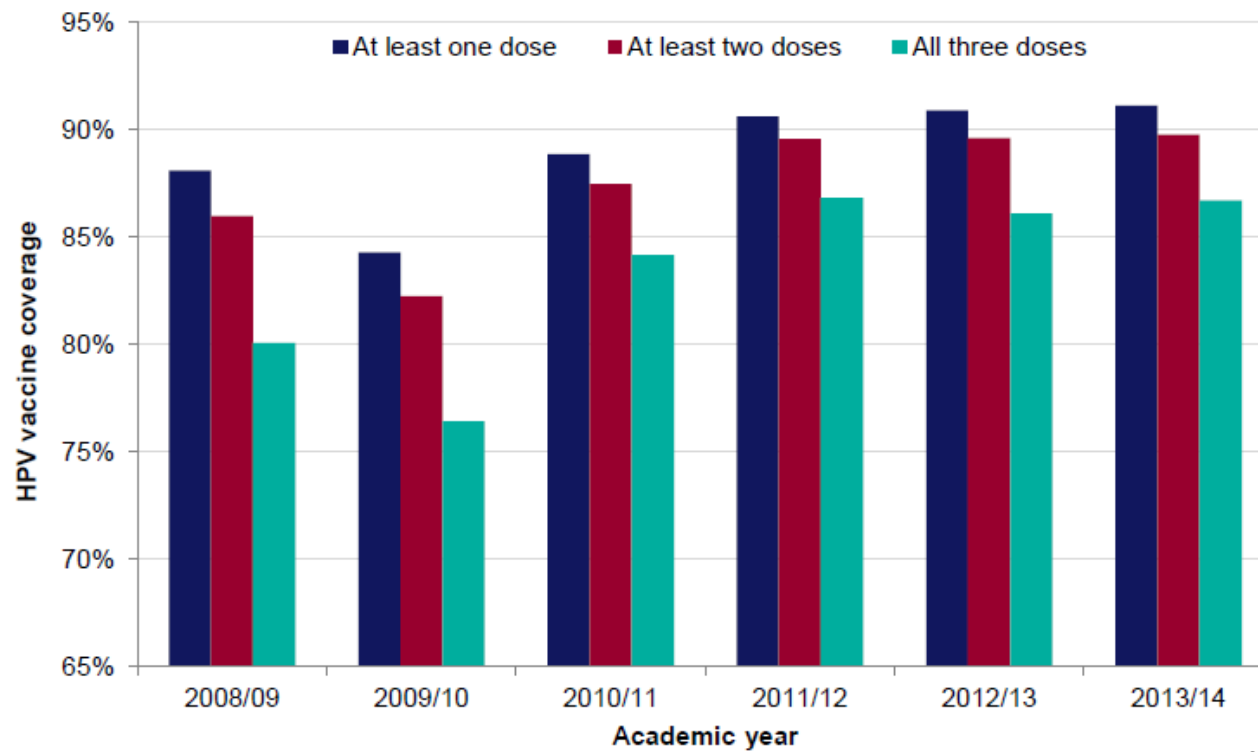


Current uptake for the first dose of the HPV vaccine



Source: Statens Serum Institut

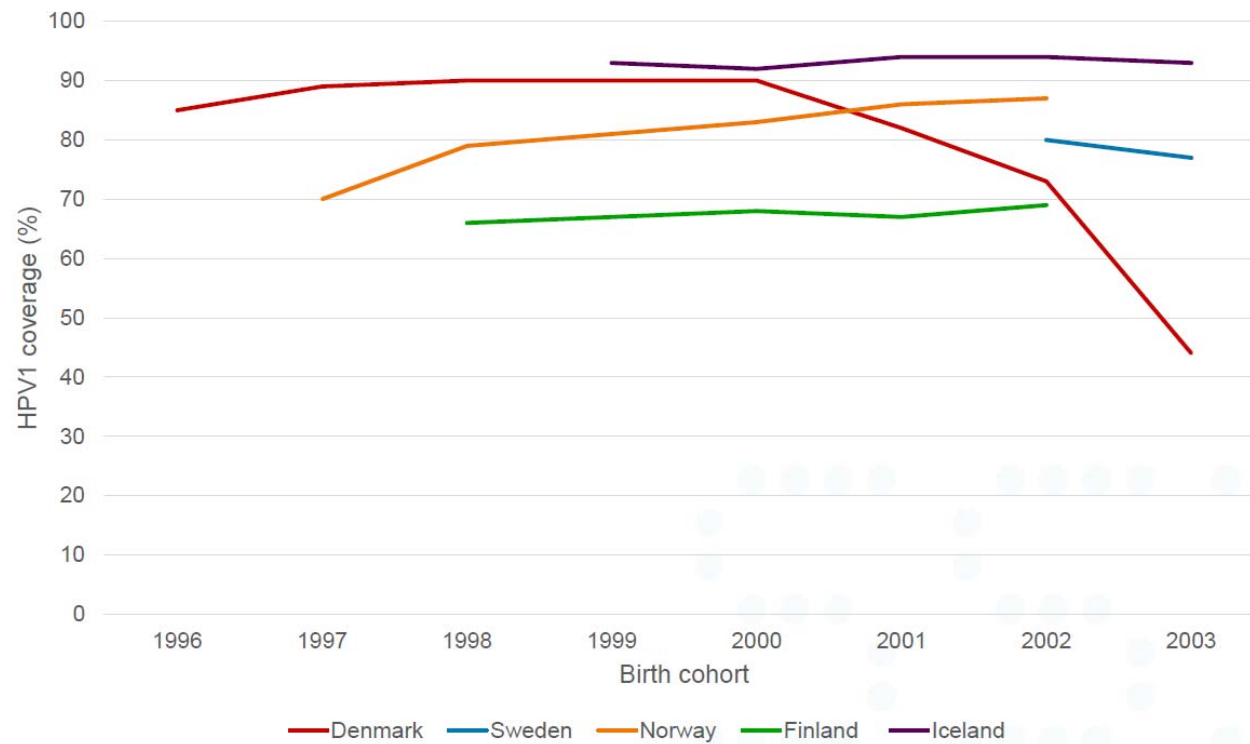
HPV vaccine coverage in 12-13 years girls, UNK



Source: Public Health England

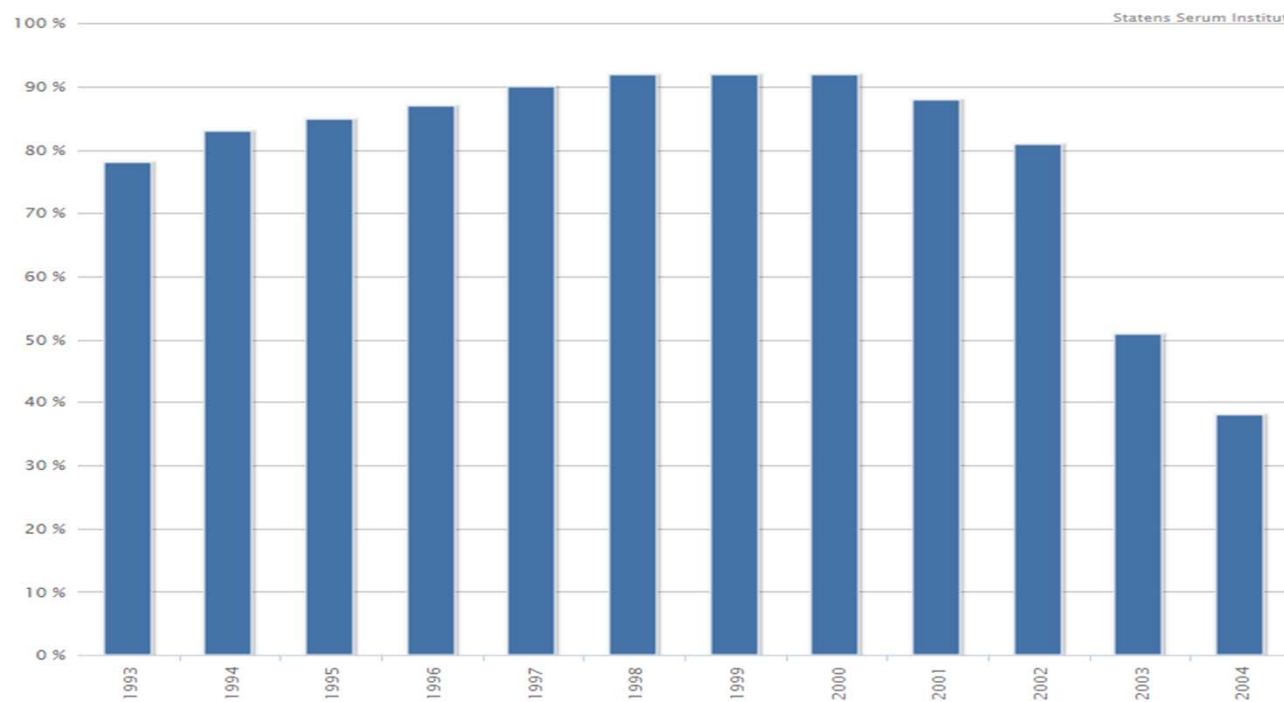


HPV 1 uptake in Nordic countries by birth cohort



Palle Valentiner-Branth, MD, PhD
Department of Infectious Disease Epidemiology
Statens Serum Institut, Denmark

Current uptake for the first dose of the HPV vaccine



Source: Statens Serum Institut

HPV vaccination in the Danish Childhood vaccination programme

2007: a national medical technology assessment recommends implementation of HPV vaccine for girls

2008: pre-introduction of the HPV vaccine, Gardasil in the Danish childhood vaccination programme for birth cohorts 1993-1995

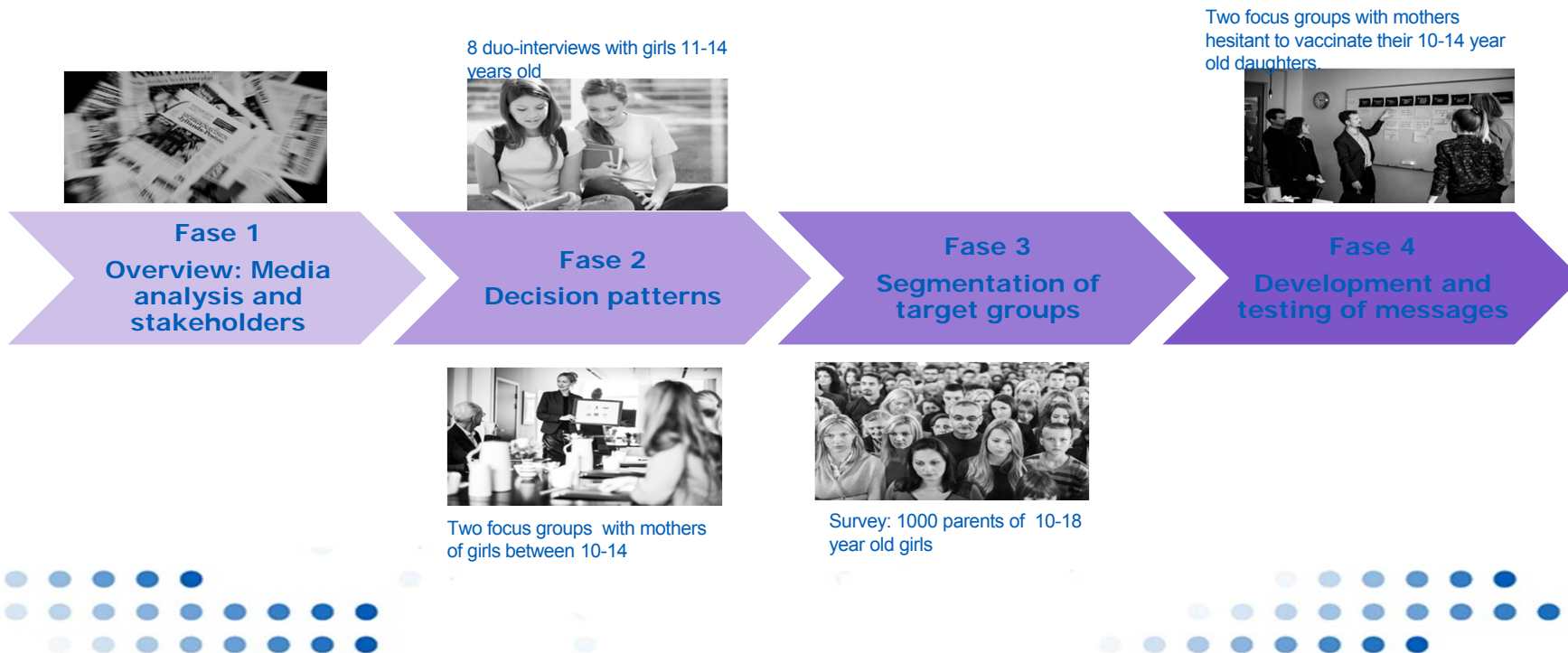
2009: full national implementation of the programme for age groups 12 to 15 years of age

2012-13: catch-up program for woman in birth cohorts 1985-1992

2014: two-dose HPV-vaccination program introduced for girls 12-13 years of age

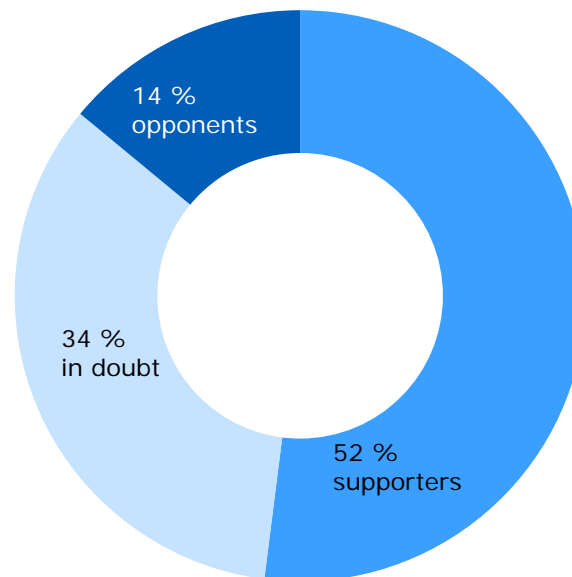
1st of February 2016: through the national procurement procedure, Danmark changes vaccine from Gardasil til Cervarix

Overview of the analysis



Segmentation of the target group

(daughters between 10 and 14)



What do mothers respond to?

- Statistics on the risk of cervical cancer vs. risk of side effects from HPV vaccination.
- Joint voice from authorities: No more side effect than other vaccines. The vaccine has been thoroughly tested worldwide.
- Girls can be infected with HPV the first time they have sex – postponing the decision about vaccination increases this risk.
- Mothers were not hesitant about the other vaccines in the programme – the HPV vaccine does not have more side effects.
- Referral to GP for clarification and advice.

Strategy 2016-2018

- A low intensive and ongoing information ‘campaign’ established on a digital platform consisting of a Facebook page and a website. The style is fact-based, informative and advisory
- The main target group are ”mothers is doubt”
- An network of stakeholders is behind the campaign, which has its own visual identity
- Along with the digital platform comes an ‘information package’ using the visual identity and consisting of leaflet and posters targeted parents and daughters as well as material targeted health professionals, primarily GP staff.



STOP LIVMODERHALSKRÆFT

Faktaark til sundhedsprofessionelle om HPV-vaccination

Om HPV

HPV smitter seksuelt, og mere end 80 % af alle seksuelt aktive vil på et tidspunkt i løbet af deres liv blive smittet med HPV. Omkring 4 ud af 10 unge danskere under 30 år er smittet med HPV netop nu.

- Kondom kan nedsætte risikoen for smitte, men beskytter ikke tilstrækkeligt, da virus også kan sidde på huden omkring kønsorganerne.
- Uden HPV-infektion får man ikke celledorandring, der kan udvikle sig til livmoderhalskræft.
- Hvert år får cirka 15.000 danske kvinder konstateret celledorandring – nogle kan udvikle sig til livmoderhalskræft. Hvert år får cirka 6.000 danske kvinder foretaget kegleoperationer for at fjerne forstadier til livmoderhalskræft.
- Hvert år rammes cirka 375 danske kvinder af livmoderhalskræft – mere end halvdelen er under 50 år.
- Danmark har Nordens højeste forekomst af livmoderhalskræft.
- I Danmark vil 1 ud af 100 kvinder få livmoderhalskræft på et tidspunkt i deres liv.

Forebyggelseseffekt ved vaccination: Med udgangspunkt i en fødselsårgang med 37.000 piger og en vaccinationstilslutning på 80 %, vil man kunne forebygge 207 tilfælde af livmoderhalskræft og 41 dødsfald i fødselsårgangen.

Om HPV-vaccination

- HPV-vaccination beskytter mod livmoderhalskræft, kræft i skeden, kræft i kvinders ydre kønsorganer og analkræft.
- Der findes cirka 15 typer af HPV, der kan forårsage livmoderhalskræft. HPV-vaccinen beskytter imod HPV-typerne 16 og 18, og disse to typer er skyld i 70 % af alle tilfælde af livmoderhalskræft.
- Sundhedsstyrelsen anbefaler HPV-vaccination til piger på 12 år. Piger under 15 kan nøjes med to doser Cervarix®, mens piger på 15 år og derover skal have tre.
- Knap 40 % af 15-årige har haft deres seksuelle debut, hvilket understreger vigtigheden af at blive vaccineret som 12-årig.
- Det anbefales, at man udleverer indlægseddelen til piger og forældre.
- Sundhedspersoner bør sætte sig ind i de kontraindikationer for HPV-vaccination, der fremgår af produktresuméet.
- Vaccinerne indeholder antigen og hjælpestoffer (eks. adjuvans). Blandt hjælpestofferne er aluminiumsalte, som er den adjuvans, der øger immunsystemets respons på vaccinen, så man er sikker på, at den virker. HPV-vacciner uden aluminium giver ikke et effektivt forsvar mod HPV. Aluminiumsate er sikre at anvende som hjælpestof, og man har brugt dem i små mængder i vacciner siden 1930'erne. De bruges i en lang række vacciner – også i de andre vacciner i børnevaccinationsprogrammet.
- WHO anbefaler HPV-vaccination i Europa er det kun Polen og Estland, der endnu ikke tilbyder HPV-vaccination.



HPV-vaccination forebygger livmoderhalskræft

Livmoderhalskræft skyldes HPV (human papilloma virus). HPV kan angripe cellerne i livmoderhalsen og give celledorandring, som kan udvikle sig til kræft. HPV-vaccinen beskytter imod HPV-typerne 16 og 18, der forårsager cirka 70 % af alle tilfælde af livmoderhalskræft.

Din datter kan blive smittet med HPV, første gang hun har sex.



Sundhedsstyrelsen, Kræftens Bekæmpelse og Lægeforeningen anbefaler, at piger bliver vaccineret, når de er 12 år. Vaccinen er gratis, indtil de fylder 18.

Læs mere på stophpv.dk

Vi bakker op om HPV-vaccination:

- Stations Serum Institut
- Lægemiddelstyrelsen
- Danske Regioner
- Lægemiddelkøberne
- Danske Selskab for Intern Medicin
- Praktiserende Lægers Organisation
- Danske Selskab for Obstetrik og Gynekologi
- Danske Selskab for Klinik Onkologi
- Danske Pædiatriske Selskab
- Regionale Sundhedsmyndigheder
- Regionale Sundhedsmyndigheder og Informationsmyndigheder
- Regionale Sundhedsmyndigheder og Obstetriske Sygeplejersker
- Ses & Søstrene
- Patientforeningen Kræft i Underlivet

Ved du nok om forebyggelse af livmoderhalskræft og HPV-vaccination?



HPV-vaccination er en del af det danske børnevaccinationsprogram og er gratis for piger mellem 12 og 17 år. Vi anbefaler, at piger vaccineres, når de fylder **12 år**

HPV er en smitsom virus, som kan give celledorandring, der kan udvikle sig til livmoderhalskræft. HPV-vaccination beskytter mod **70 %** af alle tilfælde af livmoderhalskræft

Ved du nok om forebyggelse af livmoderhalskræft og HPV-vaccination?

HPV overføres seksuelt, og kondom beskytter ikke tilstrækkeligt mod smitte. Omkring **80 %** af alle seksuelt aktive vil på et tidspunkt i deres liv blive smittet med HPV

Mere end **600.000** danskere er allerede HPV-vaccineret. Vaccinen er grundigt gennemtestet. Der er ingen videnskabelig dokumentation for, at den giver flere bivirkninger end andre vacciner

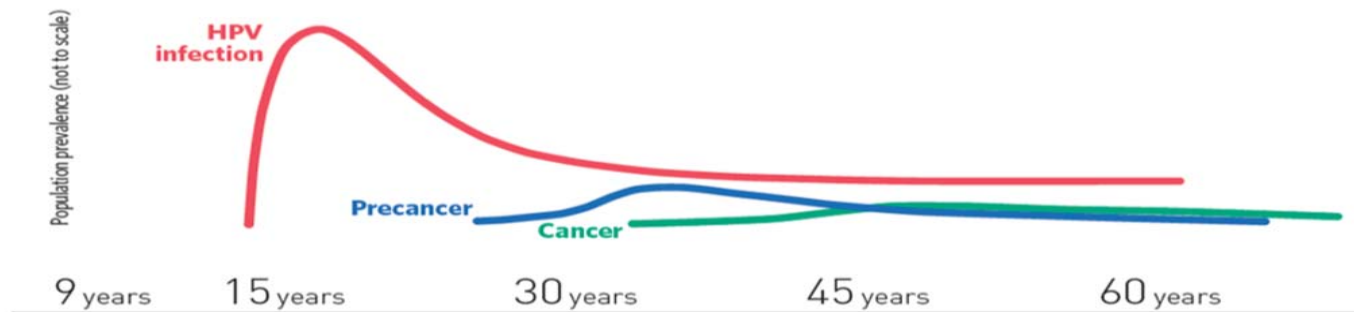
Hvert år får cirka **15.000** danske kvinder celledorandring – nogle udvikler sig til livmoderhalskræft. Hvert år får cirka **6.000** foretaget en operation for at fjerne celledorandringerne

Hvert år **375** danske kvinder ramt af livmoderhalskræft – også helt unge kvinder. Hvert år dør omkring **100** kvinder af sygdommen



Læs mere om HPV-vaccination på: stophpv.dk

Comprehensive Approach to Cervical Cancer Prevention and Control



INTEGRATION

PRIMARY PREVENTION
Girls 9-13 years

- HPV vaccination

Girls and boys, as appropriate

- Health information and warnings about tobacco use*
- Sexuality education tailored to age & culture
- Condom promotion/provision for those engaged in sexual activity
- Male circumcision

SECONDARY PREVENTION
Women >30 years of age
Screening and treatment as needed

- "Screen and treat" with low cost technology VIA followed by cryotherapy
- HPV testing for high risk HPV types (e.g. types 16, 18 and others)

TERTIARY PREVENTION
All women as needed
Treatment of invasive cancer at any age

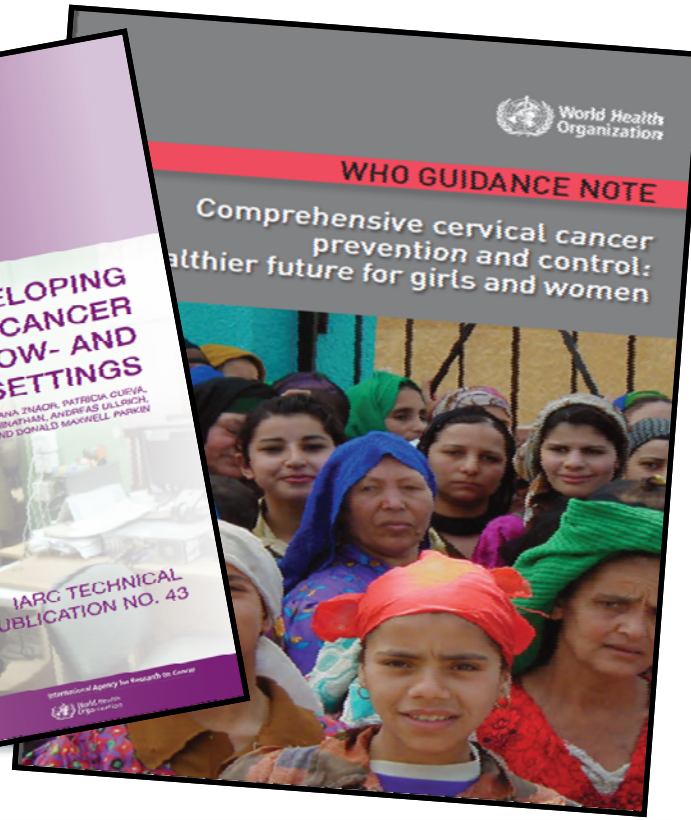
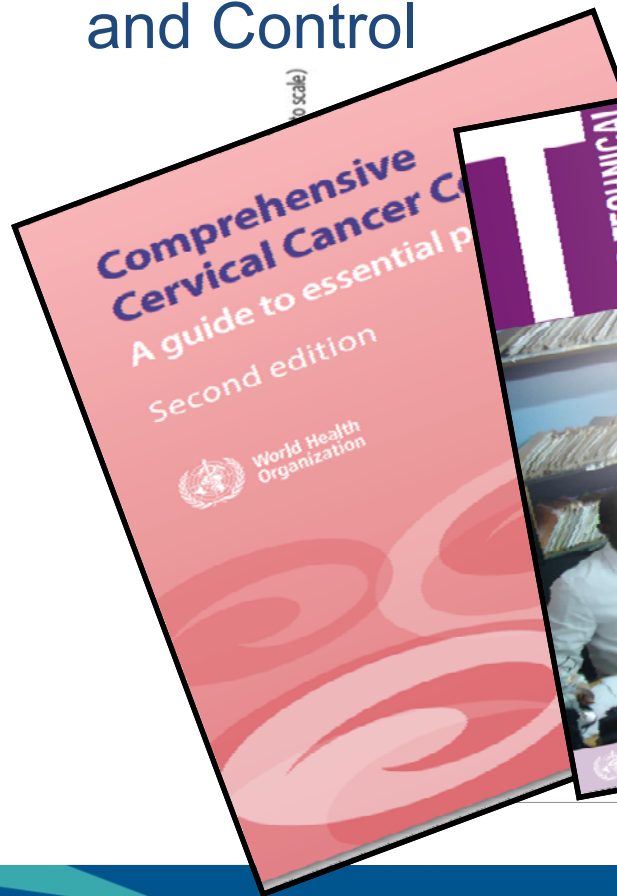
- Ablative surgery
- Radiotherapy
- Chemotherapy

* Tobacco use is an additional risk factor for cervical cancer.

INTEGRATION



Comprehensive Approach to Cervical Cancer Prevention and Control



WHO support to countries: *Science, knowledge and tools*



Policy & decision making



Planning & implementation



The United Nations Global Cervical Cancer Programme
End cervical cancer: prevent, treat, care



HPV Toolbox

Activities (by country)

Coordination TA Focal points

HPV Toolbox



Filtered Filter

34 of 34 rows met filter conditions

Developed by	Tool Name	Main use in TA phase:	Category	Language	Status
WHO	Scaling up HPV vaccine introduction	Planning introduction	Planning delivery strate	English	Final
WHO	La mise en echelle de l'introduction du vaccin PVH	Planning introduction	Planning delivery strate	French	Final
WHO	Fieldguide for formative research on HPV introduction	Planning Social Mobili	Social mobilization	English	Draft
WHO	HPV vaccine communication	Planning Social Mobili	Social mobilization	English	Final
WHO	Communication sur le vaccin anti PVH	Planning Social Mobili	Social mobilization	French	Final
WHO	Population estimates for 9-14 year olds, all countries, 2017	Planning introduction	Planning delivery strate	English	Final
WHO	School readiness assessment	Planning introduction	Planning delivery strate	English	Final
WHO	Guidance note on consent	Planning introduction	Planning delivery strate	English	Final
PATH LSHTM	HPV Lessons learned tool kit (abstracts, video etc)	n	nn	English	Final
Zambia	HPV vaccine fieldguide		JobAids	English	Country based resource
Zambia	Guidelines for vaccinators on HPV	n	JobAids	English	Country based resource
England	Guidance on consent	Planning introduction	Planning delivery strate	English	Country based resource
England	FAQ HPV vaccination	Planning introduction	Social mobilization	English	Country based resource
Ireland	HPV consent form	Planning introduction	Planning delivery strate	English	Country based resource
Palau	Integrated school health /HPV consent form	Planning introduction	Planning delivery strate	English	Country based resource
Seychelles	Consent form	Planning introduction	Planning delivery strate	English	Country based resource
UNICEF UNFPA WHO	Adolescent health assessment	Planning introduction	Integration	English	Final
UNICEF UNFPA WHO	Adolescent Health Assessment - Avaliação das Intervenções na	Planning introduction	Integration	Portuguese	Final
WHO	Training materials on HPV vaccination Gardasil	Planning introduction	Training	English	Final
WHO	Training materials on HPV vaccination Gardasil	Planning introduction	Training	French	Final
Seychelles	Leaflet FAQ for parents	Social Mobilization	Social mobilization	English	Country based resource
Seychelles	Leaflet FAQ for girls	Social Mobilization	Social mobilization	English	Country based resource
Zamba	Poster & Leaflet	Social Mobilization	Social mobilization	English	Country based resource
Zambia	Vaccination card	Planning introduction	Monitoring	English	Country based resource

EURO HPV crisis: facilitating inter-country collaboration

- Informal technical consultations, Copenhagen: October 2016 and June 2016
- *HPV group of peers* with bimonthly TCs: Denmark, Ireland, United Kingdom, Netherlands, Austria
- Ongoing technical support to Member States
- Q & As to be launched Q2 2017

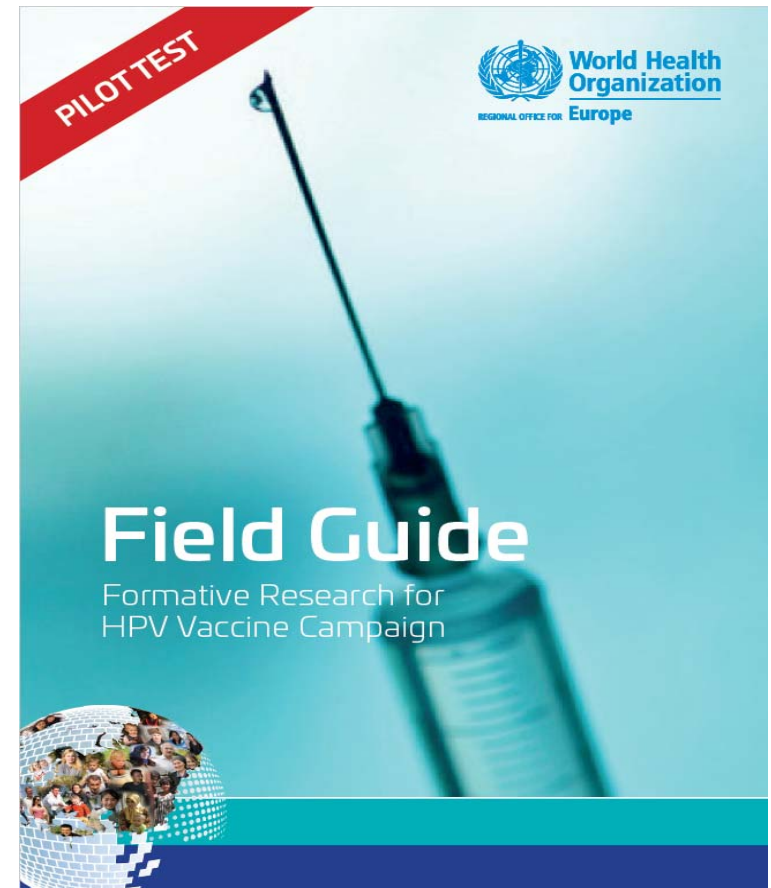
HPV introduction

Communication support package

Guidance on rapid qualitative research and communications strategy development:

- Training workshop, Belarus March 2017
- In-country technical support in Armenia, Moldova, Georgia

→ *More on comms this afternoon.....*





United Nations Inter-Agency Task Force on the Prevention and Control of Noncommunicable Diseases UNIATF



unicef 



UN WOMEN 

International Agency for Research on Cancer
World Health Organization



UNAIDS 

UN HABITAT 



United Nations System

Standing Committee on Nutrition



Thank you

<http://www.who.int/immunization/diseases/hpv/resources/en/>

butlerr@who.int

