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

- Cervix uteri: 530,000
- 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 1,016,718 women. *Regionally-adjusted HPV (see [1] for adjustment methodology). Redrawn from Bruni L et al. [1].

Source: Forman et al., Vaccine 2012,
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Bivalent 2vVPH</th>
<th>Quadrivalent 4vVPH</th>
<th>9-valent 9vVPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Name producer</td>
<td>Cervarix™, GSK</td>
<td>Gardasil™, Merck</td>
<td>Gardasil 9™, Merck</td>
</tr>
<tr>
<td>Types of virus like particles (VLP)</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Dose of L1 protein</td>
<td>20/20 µg</td>
<td>20/40/40/20 µg</td>
<td>30/40/60/40 µg, 20/20/60/20/20 µg</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>ASO4 (500 µg aluminum hydroxide, 50 µg 3-O-deacylated-4′-monophosphoryl lipid A)</td>
<td>AAHS (225 µg amorphous aluminum hydroxyphosphate sulfate)</td>
<td>500 µg AAHS</td>
</tr>
<tr>
<td>Licensed schedules</td>
<td>0, 1, 6 month 0, 6 month</td>
<td>0, 2, 6 month 0, 6 month</td>
<td>0, 2, 6 month 0, 6 month</td>
</tr>
</tbody>
</table>

Herrero et al., Lancet Oncol 2015, 16:e206–16
HPV types contribution to cervical cancer and protection offered by HPV vaccines

- Extra types for which the nine-valent vaccines afford protection (5.1% of cervical cancers)
- Extra types for which the bi-valent and quadri-valent vaccines may afford cross-protection (13.4% of cervical cancers)
- Types for which all 3 licensed vaccines afford direct protection (70.8% of cervical cancers)

World Health Organization
WHO Position Paper on HPV Vaccines

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

Focuses on cervical cancer but considers other cancers and diseases preventable by HPV vaccines.

Incorporates 9-valent HPV vaccine and provides guidance on vaccine choice.

Recommends different vaccination strategies, including multiple age cohorts of girls.

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
Countries with HPV vaccine in the national immunization programme

Introduced* to date (68 countries or 35.1%)
Not Available, Not Introduced/No Plans (126 countries or 64.9%)

* Includes partial introduction

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 be no 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
HPV vaccine is one of the most expensive vaccines across all income groups

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

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

Ali et al., BMJ 2013
Vaccinating 80% of 12-year olds in 2012 would prevent 690,000 cervical cancer cases and 420,000 deaths over their lifetime.
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

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
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
Ireland

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
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

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

**Fase 1**
Overview: Media analysis and stakeholders

- 8 duo-interviews with girls 11-14 years old

**Fase 2**
Decision patterns

- Two focus groups with mothers of girls between 10-14

**Fase 3**
Segmentation of target groups

- Survey: 1000 parents of 10-18 year old girls

**Fase 4**
Development and testing of messages

- Two focus groups with mothers hesitant to vaccinate their 10-14 year old daughters
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.
Comprehensive Approach to Cervical Cancer Prevention and Control

**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

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

**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
Comprehensive Approach to Cervical Cancer Prevention and Control
WHO support to countries: 
Science, knowledge and tools
<table>
<thead>
<tr>
<th>Developed by</th>
<th>Tool Name</th>
<th>Main use in TA phase</th>
<th>Category</th>
<th>Language</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO</td>
<td>Scaling up HPV vaccine introduction</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>La mise en echelle de l’introduction du vaccin PVH</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>French</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>Fieldguide for formative research on HPV introduction</td>
<td>Planning Social Mobilization</td>
<td>Social mobilization</td>
<td>English</td>
<td>Draft</td>
</tr>
<tr>
<td>WHO</td>
<td>HPV vaccine communication</td>
<td>Planning Social Mobilization</td>
<td>Social mobilization</td>
<td>English</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>Communication sur le vaccin anti PVH</td>
<td>Planning Social Mobilization</td>
<td>Social mobilization</td>
<td>French</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>Population estimates for 9-14 year olds, all countries, 2017</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>School readiness assessment</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>Guidance note on consent</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Final</td>
</tr>
<tr>
<td>PATH LSHTM</td>
<td>HPV Lessons learned tool kit (abstracts, video etc)</td>
<td>n</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Final</td>
</tr>
<tr>
<td>Zambia</td>
<td>HPV vaccine fieldguide</td>
<td>n</td>
<td>JobAids</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>Zambia</td>
<td>Guidelines for vaccinators on HPV</td>
<td>n</td>
<td>JobAids</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>England</td>
<td>Guidance on consent</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>England</td>
<td>FAQ HPV vaccination</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>Ireland</td>
<td>HPV consent form</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>Palau</td>
<td>Integrated school health / HPV consent form</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>Seychelles</td>
<td>Consent form</td>
<td>Planning introduction</td>
<td>Planning delivery strategy</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>UNICEF UNFPA WHO</td>
<td>Adolescent health assessment</td>
<td>Planning introduction</td>
<td>Integration</td>
<td>Portuguese</td>
<td>Final</td>
</tr>
<tr>
<td>UNICEF UNFPA WHO</td>
<td>Adolescent Health Assessment - Avaliação das Intervenções</td>
<td>Planning introduction</td>
<td>Integration</td>
<td>Portuguese</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>Training materials on HPV vaccination Gardasil</td>
<td>Planning introduction</td>
<td>Training</td>
<td>English</td>
<td>Final</td>
</tr>
<tr>
<td>WHO</td>
<td>Training materials on HPV vaccination Gardasil</td>
<td>Planning introduction</td>
<td>Training</td>
<td>French</td>
<td>Final</td>
</tr>
<tr>
<td>Seychelles</td>
<td>Leaflet FAQ for parents</td>
<td>Planning introduction</td>
<td>Social Mobilization</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>Seychelles</td>
<td>Leaflet FAQ for girls</td>
<td>Planning introduction</td>
<td>Social Mobilization</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>Zambia</td>
<td>Poster &amp; Leaflet</td>
<td>Planning introduction</td>
<td>Social Mobilization</td>
<td>English</td>
<td>Country based resource</td>
</tr>
<tr>
<td>Zambia</td>
<td>Vaccination card</td>
<td>Planning introduction</td>
<td>Monitoring</td>
<td>English</td>
<td>Country based resource</td>
</tr>
</tbody>
</table>
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......
Thank you

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

butlerr@who.int