HPV vaccination

How to promote women’s health and prevent cancer with good screening strategies, hosted by NFOG

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Our presentation complies with FIGO's policy for declaration of good standing and conflict of interest disclosure;

We do not have a financial interest in any product or service related to my presentation;

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Learning objectives

1. To know the efficacy and effectiveness of HPV vaccines in trials and routine

2. Gain knowledge on the safety of the HPV vaccines

3. Learn strategies for vaccination program organization to achieve greater coverage and effect
HPV disease burden: Cancer

- **Cervix**: >99%
- **Anus**: 84.3%
- **Vagina**: 69.9%
- **Penis**: 47.0%
- **Vulva**: 40.4%
- **Oropharynx**: 35.6%
- **Oral Cavity**: 23.5%

Proportion of cancer specimens with HPV DNA
Age-standardized incidence rates of cervical cancer: Europe

Cervical cancer cases/year (2014): 58,373
Cervical cancer deaths/year (2014): 24,385
Women aged >15 years (2010): 328,457,000

1. ICO, Europe, 2014.
2. UN ESA population data, 2012.
HPV vaccination efficacy
Phase III trials with active follow-up

• FUTURE I/II (4-valent vaccine)*
• PATRICIA (2-valent vaccine)**
• Costa Rica HPV Vaccine Trial (CVT; 2-valent vaccine)***
• Broad Spectrum HPV Vaccine Study (9-valent vaccine)#

***Vaccine 2014;32:5087; #NEJM 2015;372:711; Lancet 2017 (Sept 5)
# Efficacy against HPV16/18 related CIN3+

## HPV naive*

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Control</th>
<th>VE (%)</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No./Total</td>
<td>No./Total</td>
<td></td>
</tr>
<tr>
<td>Quadrivalent</td>
<td>0/4,616</td>
<td>34/4,680</td>
<td>97.2 (91.5-99.4)</td>
</tr>
<tr>
<td>Bivalent</td>
<td>0/5,466</td>
<td>27/5,452</td>
<td>100 (85.5-100)</td>
</tr>
</tbody>
</table>

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## Intention-to-treat (ITT)**

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<tr>
<th>Vaccine</th>
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<tr>
<td>Quadrivalent</td>
<td>100/8,562</td>
<td>177/8,598</td>
<td>43.5 (27.3-56.2)</td>
</tr>
<tr>
<td>Bivalent</td>
<td>51/8,694</td>
<td>94/8,708</td>
<td>45.7 (22.9-62.2)</td>
</tr>
</tbody>
</table>

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VE=Vaccine efficacy; *HPV naive population: Subjects received at least 1 vaccination, were seroneg and DNA neg to vaccine types and DNA neg to 12 non-vaccine types and had normal Pap test; **All subjects who received at least 1 vaccination and had follow-up regardless of the presence of HPV infection or HPV-related disease at enrollment

Efficacy against any CIN3+

<table>
<thead>
<tr>
<th>HPV naive*</th>
<th>Vaccine</th>
<th>Control</th>
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<td></td>
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<tr>
<td>Quadrivalent</td>
<td>36/4,616</td>
<td>64/4,680</td>
<td>43.0 (13.0-63.2)</td>
<td></td>
</tr>
<tr>
<td>Bivalent</td>
<td>3/5,466</td>
<td>44/5,452</td>
<td>93.2 (78.9-98.7)</td>
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<td></td>
</tr>
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<td>158/8,708</td>
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Cross-protection

Overall vaccine efficacy

Efficacy against HPV 16/18

Efficacy against non-vaccine oncogenic types
Why differences in efficacy?

• No face-to-face comparison

• Baseline characteristics
  • The proportion of HPV-naive subjects was higher in PATRICIA
  • Baseline prevalence rates of HPV16/18 DNA and Pap abnormalities were lower in PATRICIA

• Adjuvant

• Endpoint definitions

• Colposcopy algorithms

FUTURE = Females United To Unilaterally Reduce Endo/Ectocervical disease;
PATRICIA = PApilloma TRIal Cervical cancer In young Adults;
A systematic review of 10 years of real-world experience

- >200 Million doses
- 129 countries; Vaccination programs in >60 countries
- Impact data: 58 reports from 9 countries
- Maximal reductions
  - \( \approx 90\% \) for genital warts
  - \( \approx 60\% \) for low-grade atypias
  - \( \approx 90\% \) for high-grade atypias
Effectiveness of qHPV vaccination on cervical cytological abnormalities

Australia was first!
Changes in the prevalence of human papillomavirus following a national bivalent human papillomavirus vaccination programme in Scotland: a 7-year cross-sectional study

Lancet Infectious Diseases Sept. 2017

Dr Kimberley Kavanagh, PhD, Kevin G Pollock, PhD, Kate Cuschieri, PhD, Tim Palmer, FRCPath, Ross L Cameron, MPH, Cameron Watt, BSc, Ramya Bhatia, PhD, Catherine Moore, MSc, Heather Cubie, PhD, Margaret Cruickshank, MD, Prof Chris Robertson, PhD
Pre- and post-vaccine HPV prevalence in 20 yo females

HPV 16/18 prevalence reduced from 30.0% (26.9, 33.1%) in 1988 cohort to 4.5% (3.5, 5.7%) in the 1995 cohort

HPV 31/33/45 prevalence reduced from 14.2% (12-16.7%) in the 1988 cohort to 2.6% (95% CI: 1.9-3.6%) in the 1995 cohort

Other HR-HPV - no significant changes

Kavanagh et al submitted
Impact of vaccination on CIN

(88% reduction)

(94% reduction)
Impact of HPV vaccine: Herd effect

HPV vaccination protects against invasive HPV-associated cancers

Luostarinen et al. *Int J Cancer*. 2018 May 15;142(10):2186-2187

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>HPV vaccinated women</th>
<th>Non-HPV vaccinated women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Person years</td>
<td>n</td>
</tr>
<tr>
<td>Cervix cancer</td>
<td>65,656</td>
<td>0</td>
</tr>
<tr>
<td>Vulva cancer</td>
<td>65,656</td>
<td>0</td>
</tr>
<tr>
<td>Oropharyngeal cancer</td>
<td>65,656</td>
<td>0</td>
</tr>
<tr>
<td>Other HPV cancersa</td>
<td>65,656</td>
<td>0</td>
</tr>
<tr>
<td>All HPV associated invasive cancers</td>
<td>65,656</td>
<td>0</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>65,656</td>
<td>2</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>65,656</td>
<td>1</td>
</tr>
<tr>
<td>Melanoma</td>
<td>65,656</td>
<td>3</td>
</tr>
<tr>
<td>Non-melanoma skin cancer</td>
<td>65,656</td>
<td>2</td>
</tr>
</tbody>
</table>
Overview of HPV vaccination in the Nordic countries

- HPV vaccination for girls is included in the childhood vaccine programs

- Vaccination of males
  - A decision has been made to vaccinate boys in Norway and Denmark
  - The decision to vaccinate boys is pending in Sweden and Finland

- Vaccines used differ across countries and are decided by national tenders
  - Cervarix – Finland, Norway
  - Gardasil4 – Sweden
  - Gardasil9 - Denmark

Map: [Nordic countries including Estonia](https://www.fig2018.org), by Jon Matti Sonberg
Effect of HPV vaccination

- Long tradition of evaluating HPV vaccines in the Nordic countries
  - Clinical trials: FUTURE and PATRICIA

- Continued evaluation of vaccine effect through population-based studies post-implementation of the vaccines

- Follow-up of vaccine effect and safety is possible through individual registration and linkage to other healthcare and population registries

  - In the research setting, personal identity numbers can be used to link information on vaccines received to cervical screening registries, patient registries, population registries, and prescription drug registries

  - Evaluation of disease endpoints (genital warts, cervical lesions), safety endpoints (potential side effects), and behavioral endpoints (do vaccinated women participate in screening?) made possible through such linkages
Vaccine safety – evidence from post-licensure studies

• Collaboration between researchers in Nordic Countries,

• The vaccine is **not associated with autoimmune, neurological or venous thromboembolic adverse events**, studied among nearly 1 million vaccinated or unvaccinated girls ages 10-17 (Arnheim-Dahlström et al., BMJ 2013)

• The **risk of developing multiple sclerosis (MS) and other demyelinating diseases is not higher** among girls and women (ages 10-44) who have been vaccinated compared to unvaccinated (Scheller et al., JAMA 2015)
RR for NOADs; Lehtinen et al: Human Vaccines Immunotherap 2016
Organization of vaccination programs and impact on coverage

- In Sweden, vaccination coverage by birth year has varied with the highest coverage achieved in the school-based, organized vaccination program
Key Messages

1. The HPV vaccines are very effective, they prevent HPV diseases including cancer

2. HPV vaccines are safe

3. Continued monitoring and evaluation of vaccine impact in population will be necessary to inform the intersection of vaccination and screening
Thank you for your attention