HPV

It takes 2 to Tango once, twice or 3 times?

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Back to the Whiteboard ?
Everything under control?

Estimated Annual New HPV-Related Disease Cases in Males and Females in Europe

- Penile cancer
- Vulvar & vaginal cancer
- Anal cancer
- Head & neck cancers
- VIN 2/3, VaIN 2/3, AIN 2/3
- Cervical cancer
- CIN2+
- Genital warts

How good did we perform?

- Secondary Prevention = screening
- Primary Prevention = vaccination
Primary Prevention = vaccination

- VLP vaccines
- Available since 2006
- Reimbursement policy started in 2007
- Nona-valent vaccination is reimbursed since June 2017
- Coverage 91.2% in Flanders
HPV- vaccination

Cervarix: 68.86€ (R)

Gardasil 4: 118.18€ (R)

Gardasil 9: 134.7€ (R)
Worldwide Prevention?

• Ranking cervical cancer:
  • nº4 on the globe
  • nº 2 in the 3rd world

• > 250.000.000 vaccination doses in 10 y -> prevents
  500.000 cancers in the coming 80 years

• ImaGYNations: a FIGIJ plan with a goal

HPV Vaccine in a National Immunization Program, by Year of Introduction

The Lancet Global Health 2016 4, e453-e463 DOI: (10.1016/S2214-109X(16)30099-7)
Countries with HPV vaccine in the national immunization programme

Data source: WHO/IVB Database, as of 14 April 2017
Map production Immunization Vaccines and Biologicals (IVB), World Health Organization

* Includes partial introduction

- **Introduced* to date** (71 countries or 36.6%)
- **Not Available, Not Introduced/No Plans** (123 countries or 63.4%)
- **Not applicable**
“A lie can run round the world before the truth has got its boots on”

• Grimaldi et al, 2017: exposure to HPV vaccines was not associated with AD
• Jefferson and Jorgenson, 2016: HPV vaccines and autonomic dysfunction, a review
Safety profile

• Rate of **clinical adverse events generally similar** in the vaccines groups

• Higher frequency of injection-site AEs with 9vHPV vaccine (related to higher amounts of VLP and adjuvant)

• Most were of mild or moderate intensity

• Cumulatively, the estimated number of marketed 9vHPV vaccine doses distributed worldwide to **Q1 2017** was approximately **24 million doses** based on the available data (9 Million in -US, 15 Million ex-US)

AE=adverse event.
How can we do better?

Can we go sooner?

Can we go broader?

Can we go less?
Can we go sooner?

- There is evidence for mother to child transmission
- Mother / Father / child transmission is a reality
- Before the age of 9 is not yet an indication, Belgium starts at 12
- Timing should be optimal
Can we go broader?

• Gender neutral vaccination policy can stop viral circulation

• Most cost effective catch up: boys and girls between 12 & 14 y (Garland 2010)

• Worldwide 15 countries are gender neutral:
  Australia, South Korea, UK, USA, Canada, Argentina, Austria, Italy, …

• With a coverage < 50% boys vaccination is mandatory
  (Cummings et al., 2012; Arbyn et al., 2012; Canfell et al., 2011).
Can we go less?

• Shall we **stick to 1, 2 or 3 doses?**
  • The standard before 15 years is 2 doses, after 15 years is 3 doses
  • Between 9 and 13 years 1 dose might be ok, but no data on long term protection
  • Immunodepression and high risk profiles need 3 doses
How can we do better?

Before the age of 12?

Gender neutral?

How many types?

Stick to 1, 2 or 3 doses?
How can we do better?

Before the age of 12?
How can we do better?

Gender neutral?
How can we do better?

How many types?
Multityping... so far so good what are we looking at?
HPV prevalence by age category

HPV positivity gradually increasing with age
Overall prevalence = 15,7%
39,0% = multiple HPV infections

Ref: High frequency of genital HPV infections and related cervical dysplasia In adolescent girls in Belgium Eur J Cancer Prev.2014, Merckx et al
Genotyping of HPV in ado’s

The most frequently observed HR-HPV types were:

- HPV**16** (16.7%)
- HPV**51** (14.6%)
- HPV**66** (10.4%)
- HPV**31** (9.9%)
- HPV**39** (9.1%)

Type replacement can not be excluded

Can we go broader?

New emerging human papillomavirus types in the era of nonavalent vaccination.

G. Bogani 1, D. Recalcati 1, F. Martinelli 1, A. Ditto 1, M. Signorelli 1, A. Indini 1, D. Lorusso 1, F. Raspagliesi 1

1National Cancer Institute, Gynecologic Oncology, Milan, Italy

Feb 28-Mar 4 2017 -

31st International Papillomavirus Conference & Clinical Workshop (HPV 2017)

Further studies are needed in order to test a possible cross protection of 9vHPV against HPV53, 51 and 66
82% of high-grade pre-cancerous lesions in EU related to the 9 types included in Gardasil 9

Relative contribution of the 9 and 4 HPV types included in HPV9 and HPV4 in precancerous Lesions (among HPV+)

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Gardasil</th>
<th>HPV9</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN2+</td>
<td>45.5</td>
<td>82.3</td>
</tr>
<tr>
<td>VIN2/3</td>
<td>82.2</td>
<td>94.4</td>
</tr>
<tr>
<td>VaIN2/3</td>
<td>64.1</td>
<td>77.6</td>
</tr>
<tr>
<td>AlIN2/3</td>
<td>75.4</td>
<td>81.5</td>
</tr>
</tbody>
</table>

* all HG pre-cancerous lesions

- cervical, vulvar, vaginal, anal

Hartwig, papillomavirus research, 2015
89% of HPV+ cancers in EU related to the 7 oncogenic HPV types: HPV16/18/31/33/45/52/58

- Cervical cancer
- Vulvar cancer
- Vaginal cancer
- Anal cancer

Hartwig, papillomavirus research, 2015
Actual insight of cross-protection with available HPV vaccines

- Clinical and public health decisions about HPV vaccine should be based on the proven and consistently high efficacy against HPV types included in the vaccine to ensure broad and long term protection.

How can we do better?

Stick to 1, 2 or 3 doses?
Hello’s and goodbye’s

• Under 15 y goodbye to the 3 dose
• Any individual after 15 y and in case of immune problems keeps the 3 dose
• Hello to a 2 dose from 9 y onward to 15 y, +/- 12 months apart
• Interchangeability is a possible option
• One dose is depending on SAGE’s “let’s go… let’s gain…”
Even thinking beyond...

- Cost effectiveness after 30 y
- Hr HPV positiveness after 30 asks for further research
- Sex workers
- Sexual abuse
Sexual abuse In need for guidance

• Childhood sexual abuse is a mediator of ano-genital HPV transmission

• Once abuse occurred it leads to more risky behavior

• The correlation between onset of sex at early age and the higher risk of HPV infection supports a need for public health messages about the vaccination.
The sad truth is:
“in the sexual abuse guideline HPV is left behind”
Prevalence of sexual assault in children?

- Although the exact prevalence is unknown, 12-40% of children are victims of childhood sexual abuse.
- Approximately 1/5 of women has experienced childhood sexual abuse. The mean age is 12 years.
- Victims represent all cultural, racial, and economic groups.
Sexual abuse occurs before the age of HPV vaccination

- Success depends on the timing of vaccination, especially before and even after unplanned exposure
- Child sex abuse is a call for protection
Take home messages

• HPV calls for optimal timing of protection
• Ongoing of different HPV types exposure is a challenge
• Which is the **lucky number**? 9!
0,1,2,3 ..... 9 is your lucky number
“An ounce of prevention is worth a pound of cure”
There is no need as strong in childhood as protection