

HPV

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

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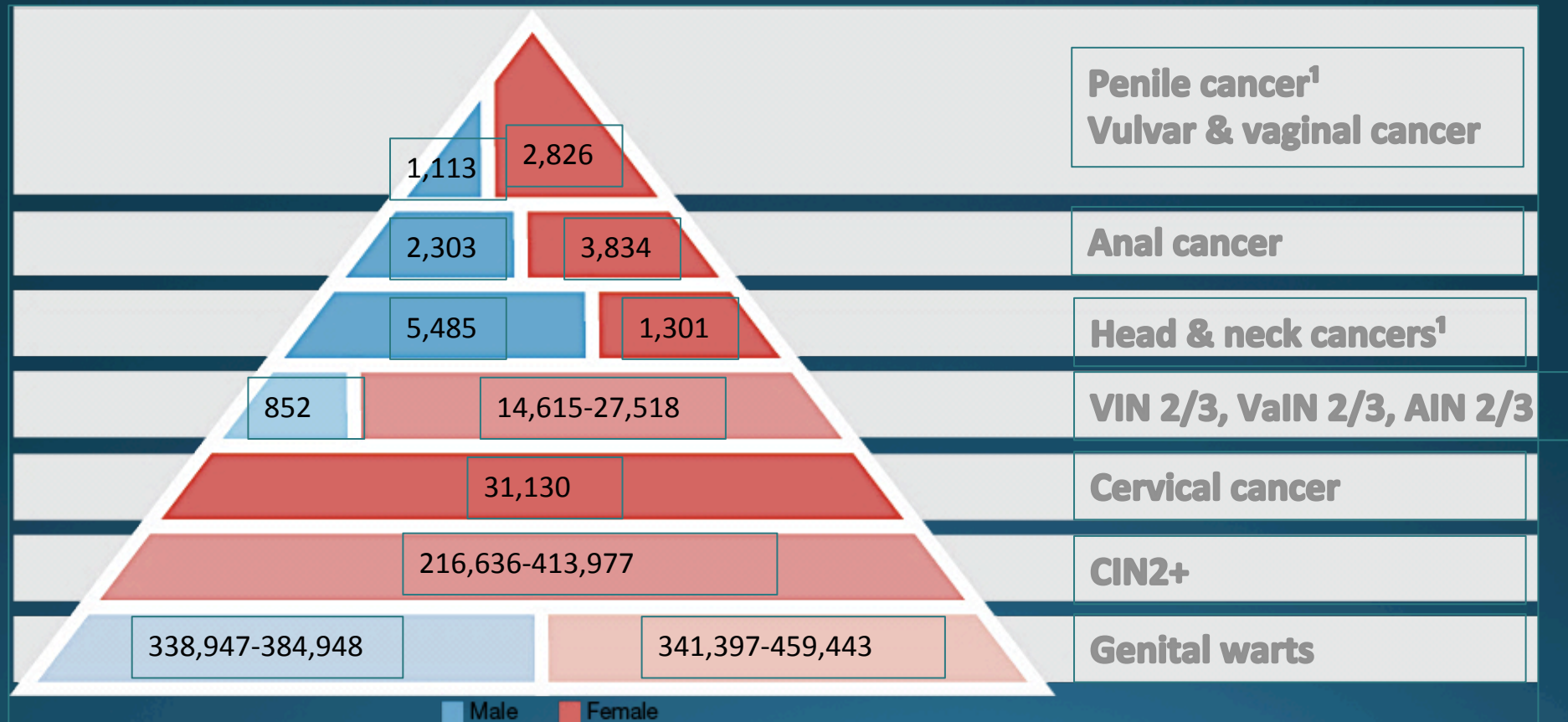


Back to the Whiteboard ?



Everything under control?

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



Europe: 30 countries from European Medicines Agency (Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Slovakia, Spain, Sweden, UK) + Switzerland. *

Hartwig S. et al. Infect Agent Cancer 2017;12:19.

How good did we perform?

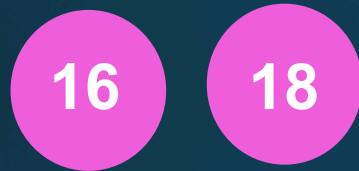
- Secondary Prevention = screening
- Primary Prevention = vaccination

Primary Prevention = vaccination

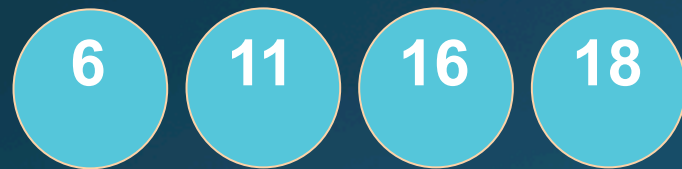
- VLP vaccines
- Available since 2006
- Reimbursement policy started in 2007
- Nona-valent vaccination is reimbursed since June 2017
- Coverage 91,2% in Flanders

HPV- vaccination

Cervarix: 68.86€ (R)



Gardasil 4: 118.18€ (R)



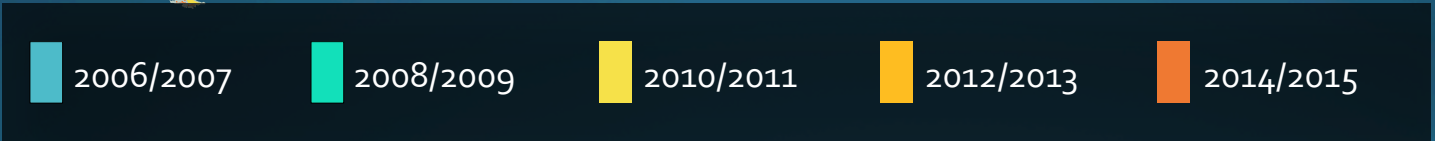
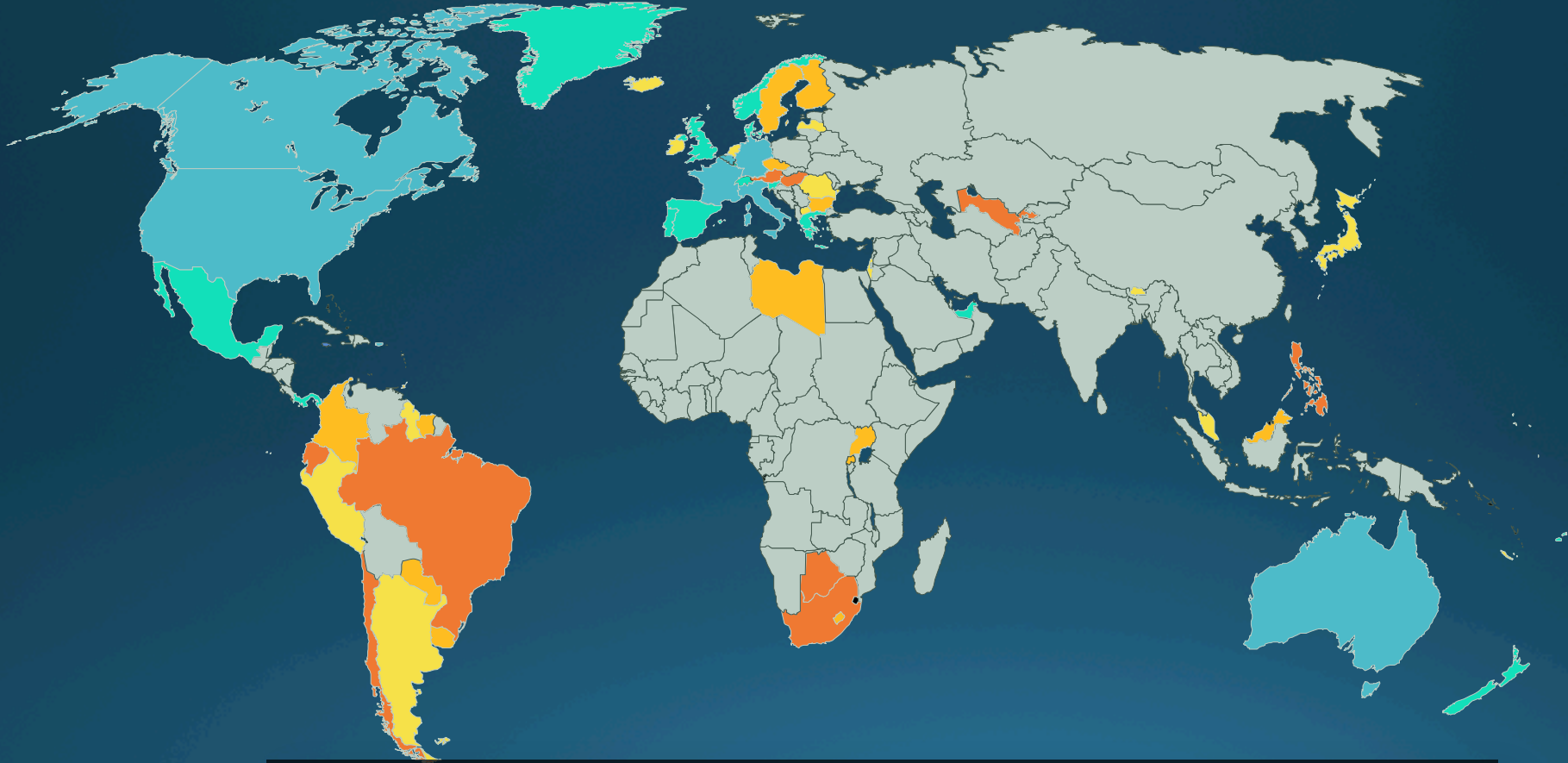
Gardasil 9: :134.7€ (R)



Worldwide Prevention ?

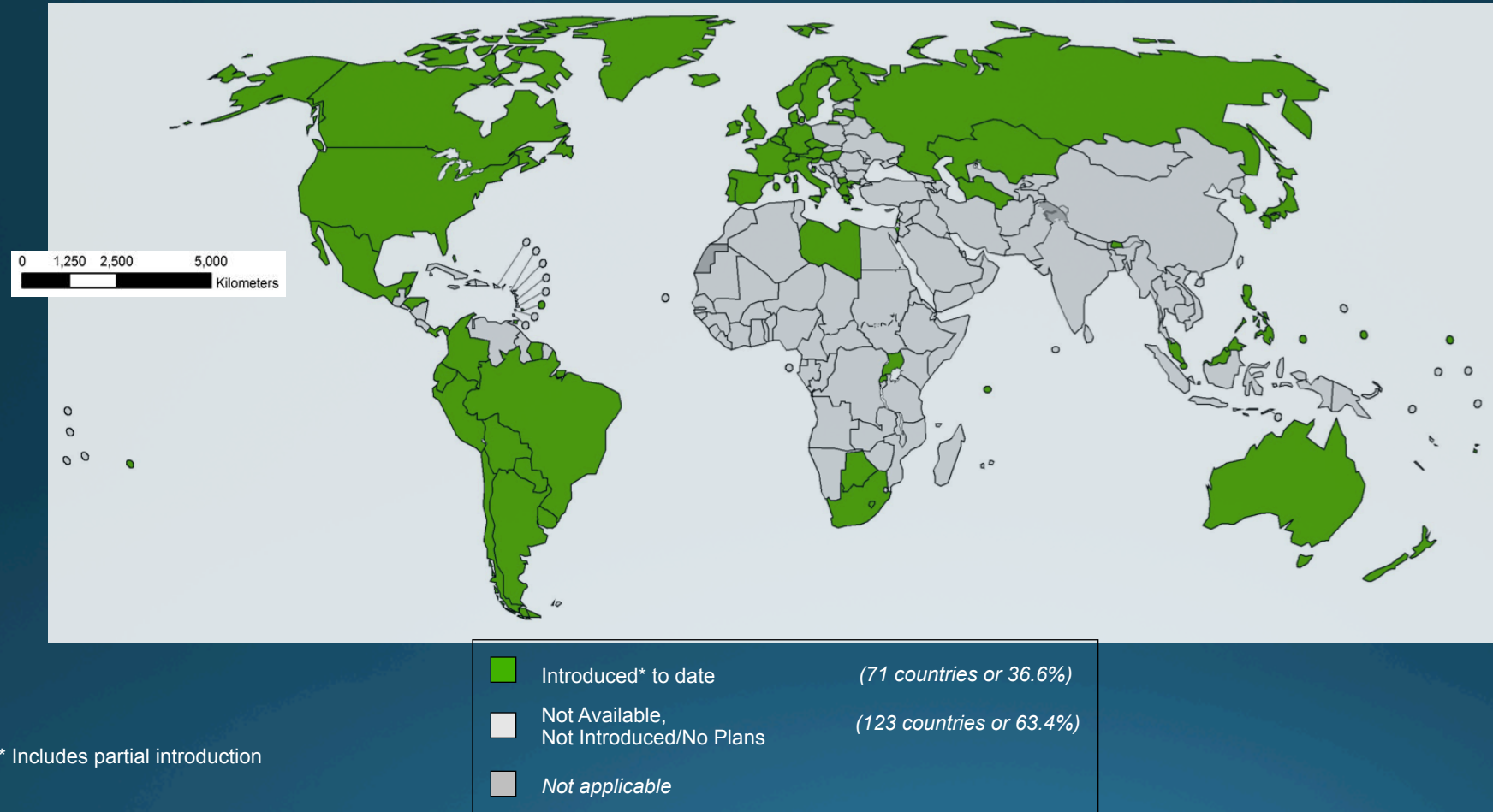
- Ranking cervical cancer:
 - n°4 on the globe
 - n° 2 in the 3rd world
- > 250.000.000 vaccination doses in 10 y -> prevents 500.000 cancers in the coming 80 years
- ImaGYNations: a FIGI plan with a goal

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



“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

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Journal of Autoimmunity xxx (2017) 1–7

Contents lists available at ScienceDirect

 **Journal of Autoimmunity**

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



Risk of autoimmune diseases and human papilloma virus (HPV) vaccines: Six years of case-referent surveillance

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)

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?

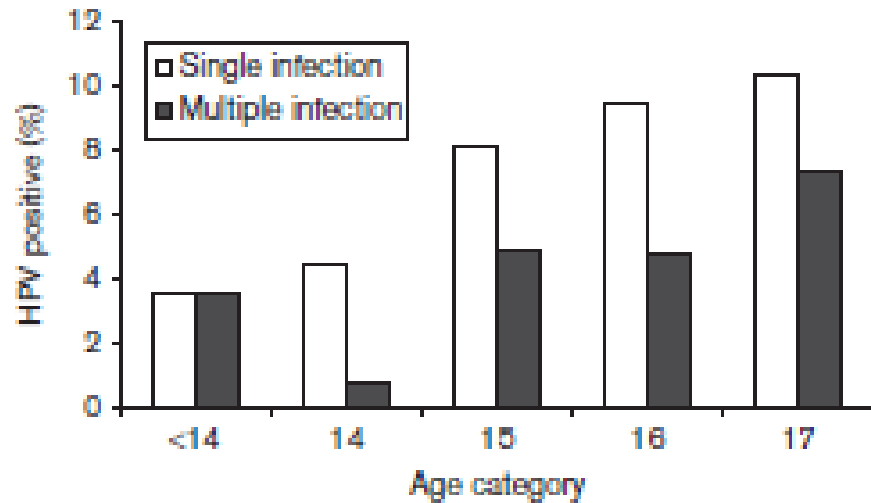
Gender neutral ?

How can we do better?

How many types ?

Multityping... so far so good what
are we looking at ?

HPV prevalence by age category



High-risk human papillomavirus-positive girls as a function of age (single and multiple infections). HPV, human papillomavirus.

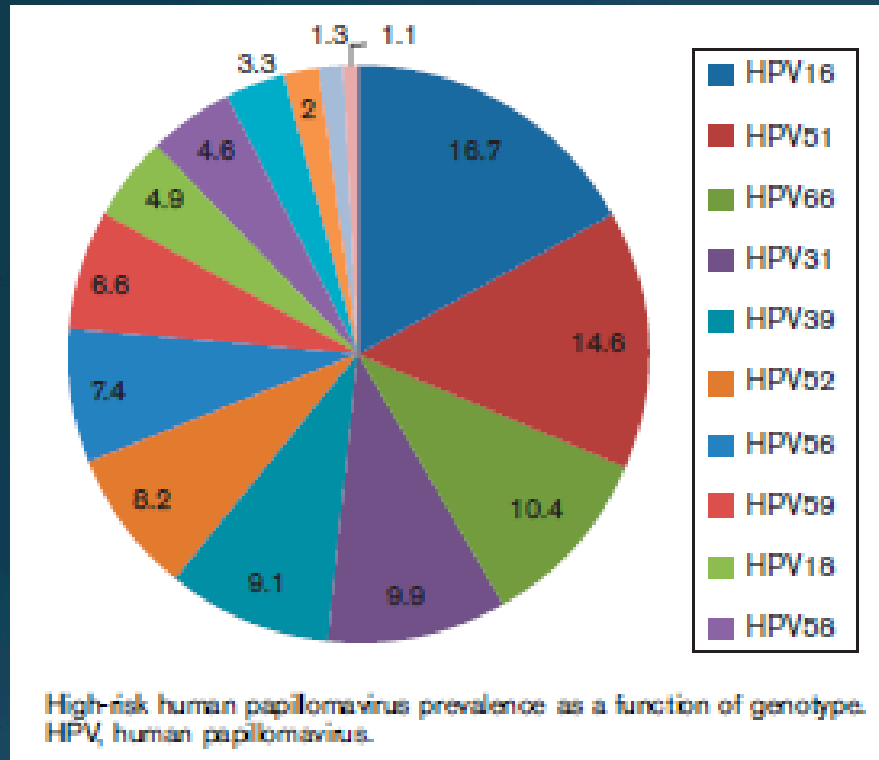
Retrospective descriptive study of :4180
<18 y old youngsters
(2006 to 2012)
Mainly opportunistic cervical screening

HPV positivity gradually increasing with age

Overall prevalence = 15,7%

39,0% = multiple HPV infections

Genotyping of HPV in ado's



The most frequently observed HR-HPV types were:

- HPV16 (16.7%)
- HPV51 (14.6%)
- HPV66 (10.4%)
- HPV31 (9.9%)
- HPV39 (9.1%)

Type replacement can not be excluded

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

Can we go broader?



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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

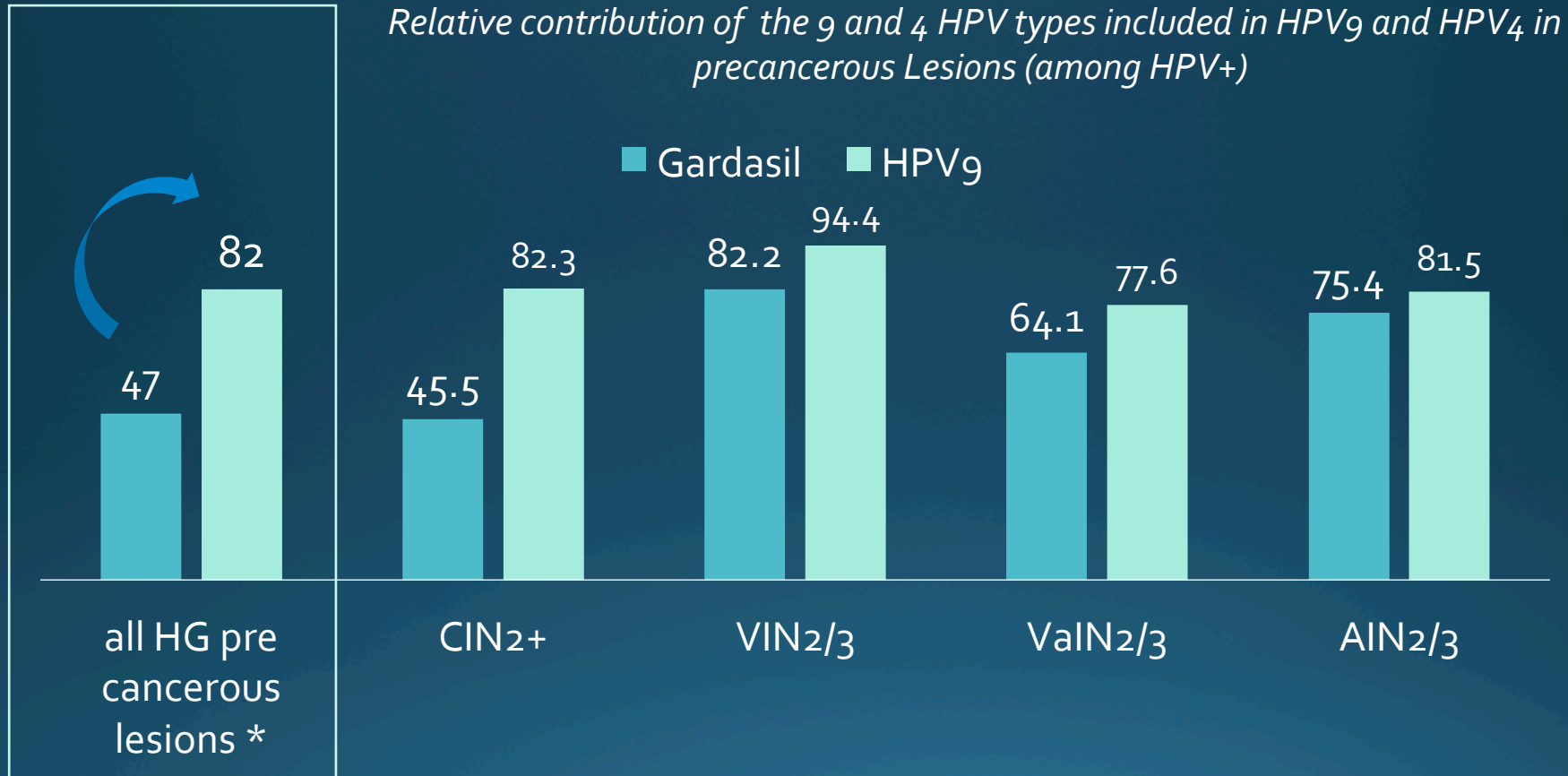
1National Cancer Institute, Gynecologic Oncology, Milan, Italy

Feb 28-Mar 4 2017 -

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

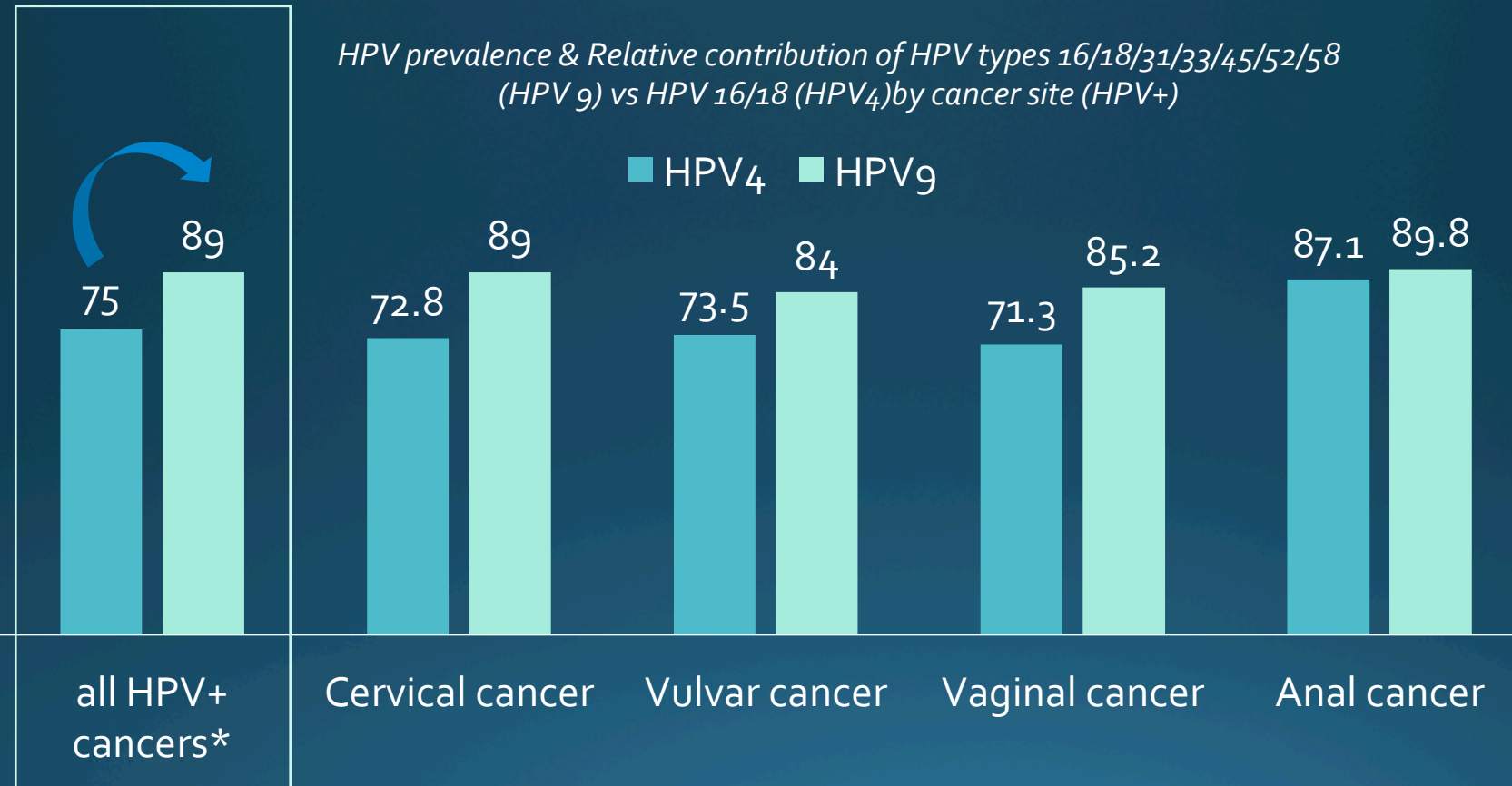
Further studies are needed in order to test a possible cross protection of **9vHPV** against HPV53, 51 and 66

82% of high-grade pre-cancerous lesions in EU related to the 9 types included in Gardasil 9



• cervical, vulvar, vaginal, anal

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



• cervical, vulvar, vaginal, anal

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.

- Ref Tanton et al Human papillomavirus (HPV) in young women in Britain: Population based evidence of the effectiveness of the bivalent immunization program and burden of 4-valent and 9-valent vaccine types. Papillomavirus Res 2017.
- Ref Woestenbergh et al No evidence for cross-protection of the HPV-16/18 vaccine against HPV-6/11 positivity in female STI clinic visitors. J Infection 2017.

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 "lets go... lets 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.

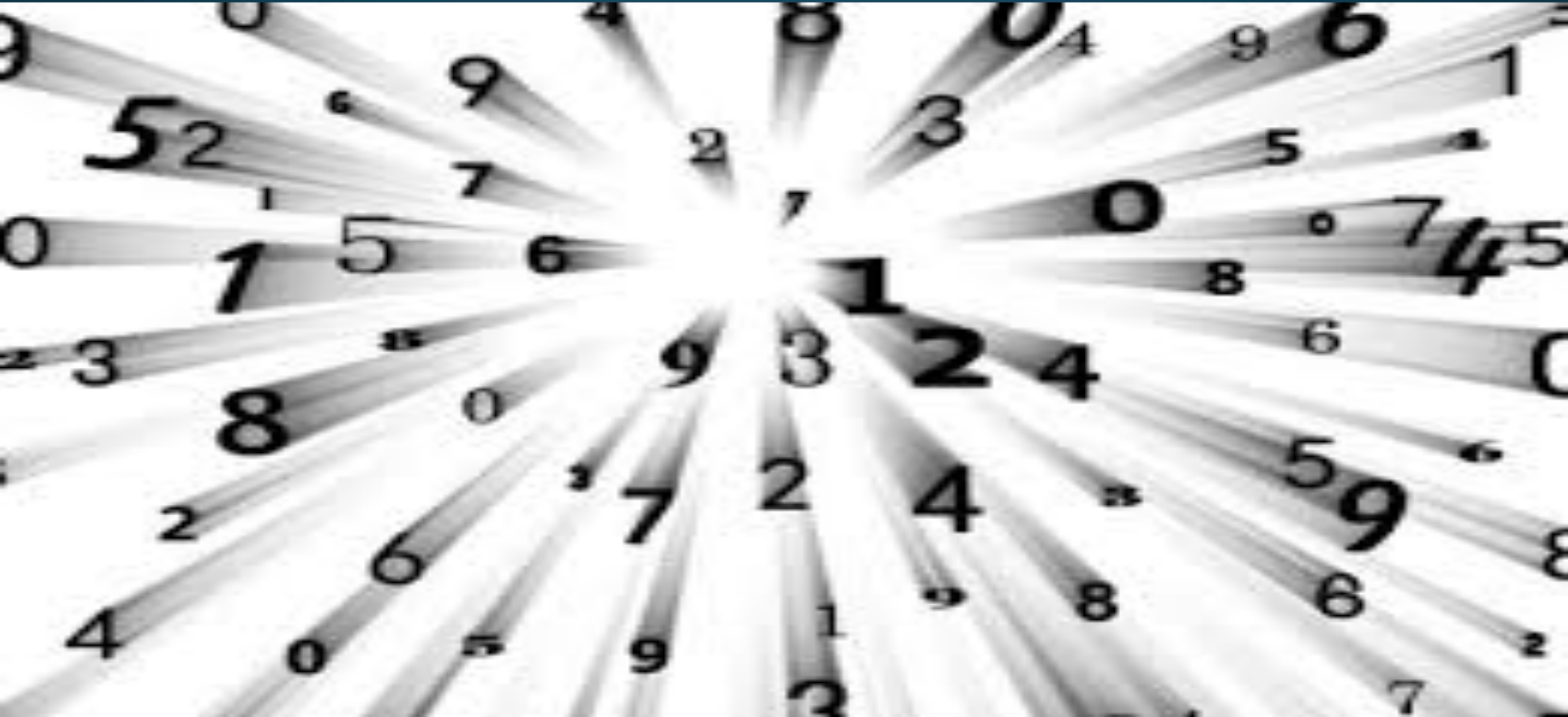
Sexual abuse occurs before the age of HPV vaccination

- 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



