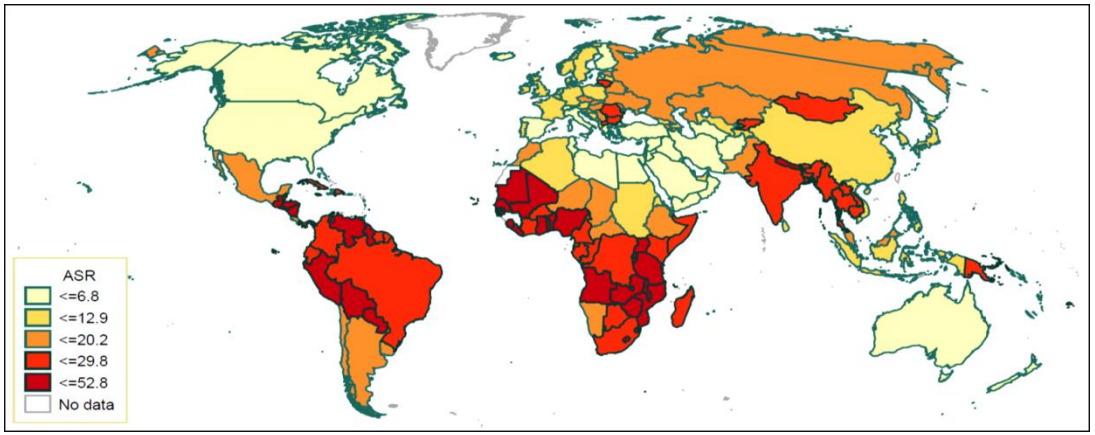
HPV vaccines and the future of cervical cancer prevention in Europe



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Potential conflict of interest

- Research and educational institutional grants:

  GSK, SPMSD, Merck, Qiagen
- Personal / speaking / travel grants:

  GSK, SPMSD, Merck, Qiagen, RMS

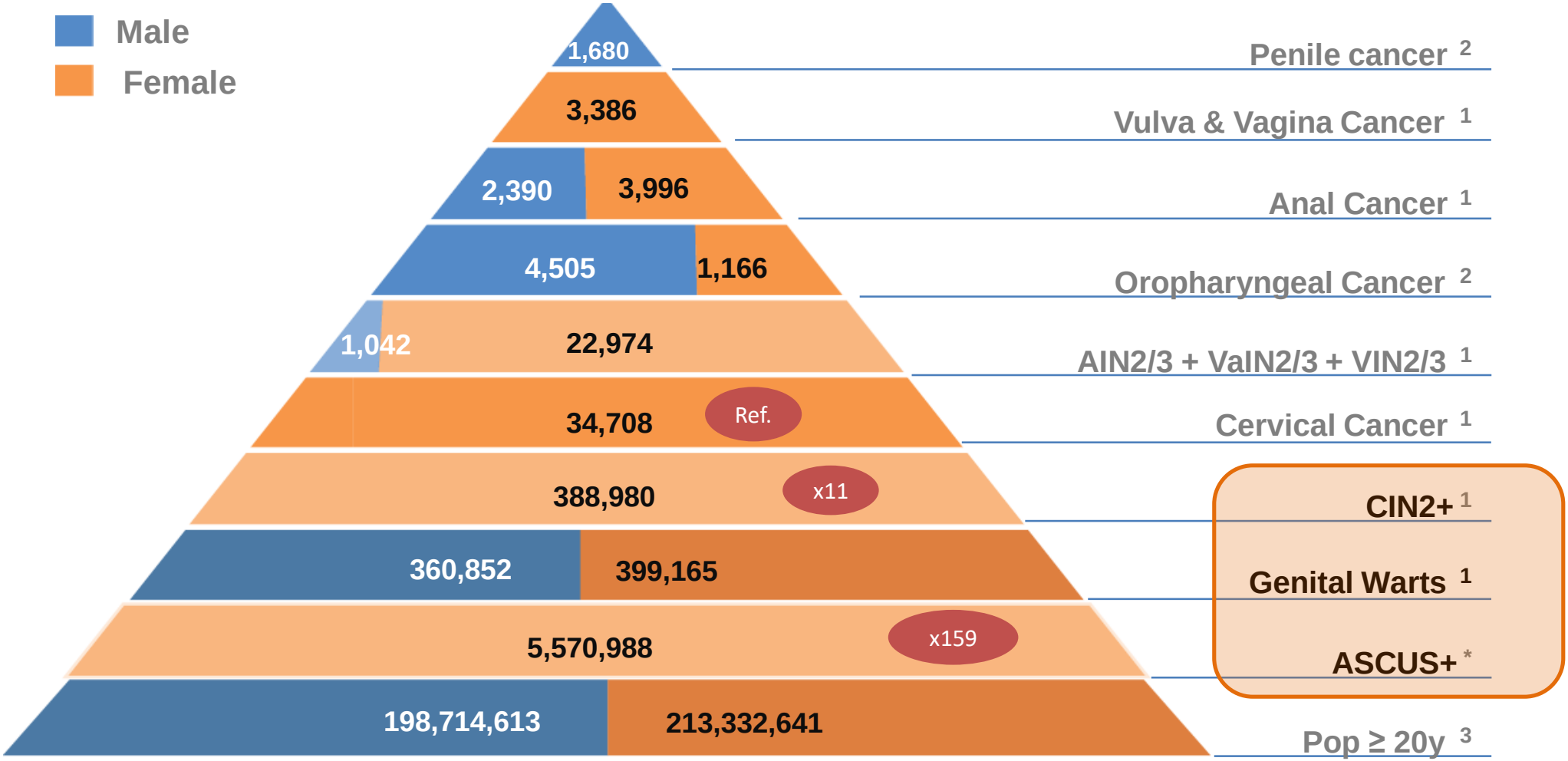
This presentation is the sole responsibility of the author

Agenda

- *Burden of HPV infections and disease in Europe*
- *Current strategies for prevention*

European Union (30 countries) HPV-Related Disease Burden:

Annual estimations of 52,000 Cancers and close to 6M precancerous lesions



(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. * Estimations assuming 3.5% of ASCUS+ among women aged 25-65 years. 1. Hartwig et al. submitted; 2. Forman et al .2012 Vaccine; 3. World Population Prospects 2012 Revision

Options to control cervical cancer

	SCREENING (PAP)[1–3]	SCREENING (HPV)	HPV 16/18 VACCINATION[3–6]
Target	Cervical cancer / pre- cancer		Cervical cancer / pre-cancer *& Interrupt Transmission*
Impact	Participant		Participant *+ Herd effect*
Number of interventions	***10…50+ tests lifetime***	***5+ tests lifetime***	3 / 2 doses no booster dose to date
Follow-up	***Local diagnostic & treatments network***		Phase IV studies in selected countries
Side effects	Mild / Obstetrics /over-diagnostics		Local/short-lived
Impact on other cancers	Limited / none		*Significant in all HPV-related cancers*

1. Kesic V, *et al*. *Cancer Epidemiol Biomarkers Prev* 2012; 21:1423–1433; 2. Anttila A, *et al*. *Eur J Cancer* 2009; 45:2649–2658; 3. Cuzick J, *et al. Vaccine* 2008; 26S:K29–K41; 4. EMA. *Cervarix*®, European Summary of Product Characteristics, 2013; 5. GSK. Clinical Study Register. 2013; 6. Downs LS Jr, *et al*. *Gynecol Oncol* 2010; 117:486–490.

The arrival of HPV screening

parameter	cytology	HPV tests
Sensitivity	50 - 70%	90-95%
Specificity	70 - 95%	90-92%
Reproducibility	Low	Very high
High throughput & Automation	Requires human resources Limited	High to very high Point of care technology
Coverage / Follow up / diagnostics / treatment	Required	Required
Logistics and cost	Difficult to comply	Technology calibrated to work in remote areas. Allows self-sampling

State of the opinion

- *In spite of screening proposals the burden of HPV infections and disease in Europe remains important notably in Eastern countries*
- *HPV screening is the technology of choice for secondary prevention*

Agenda

- *Achievements of 10 years of HPV vaccination*
  - Efficacy in Phase III
  - Worldwide Coverage
  - Predicted impact

HPV vaccines in 2017

bi-valent HPV vaccine (Cervarix)

16 *20µg*	**18** *20µg*	ASO4-AL

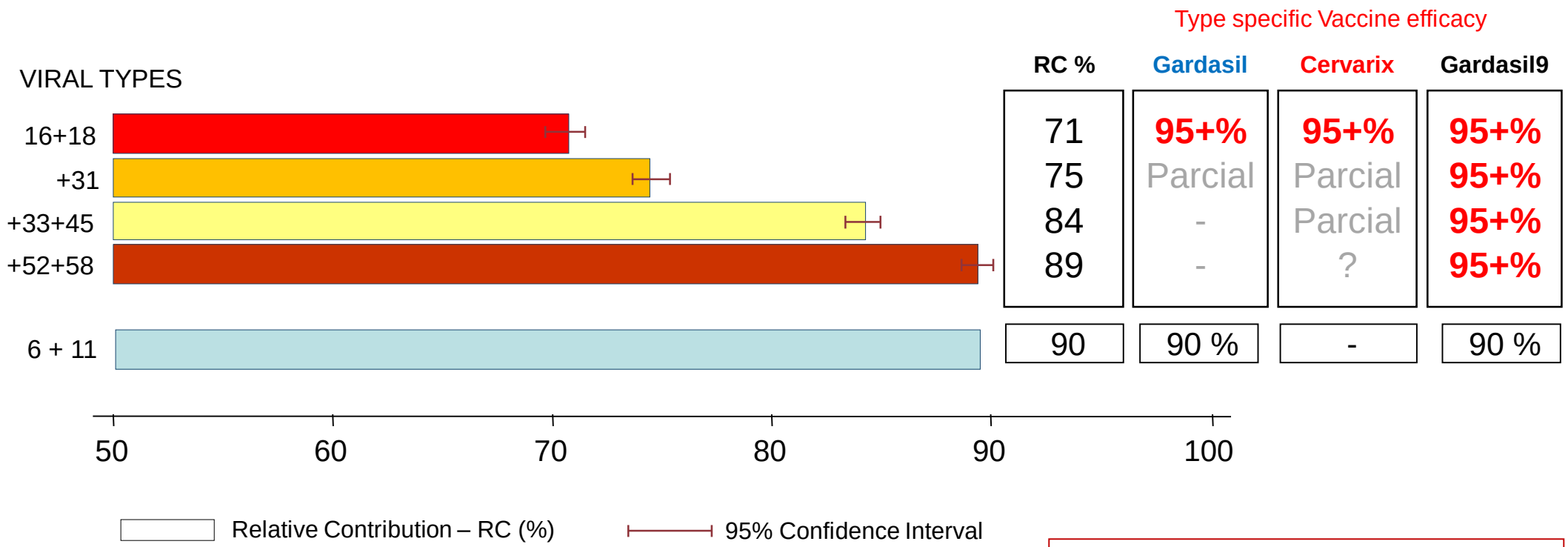
quadri-valent HPV vaccine (Gardasil)

6 *20µg*	**11** *40µg*	**16** *40µg*	**18** *20µg*	AAHS 250

nine-valent HPV vaccine (Gardasil 9)

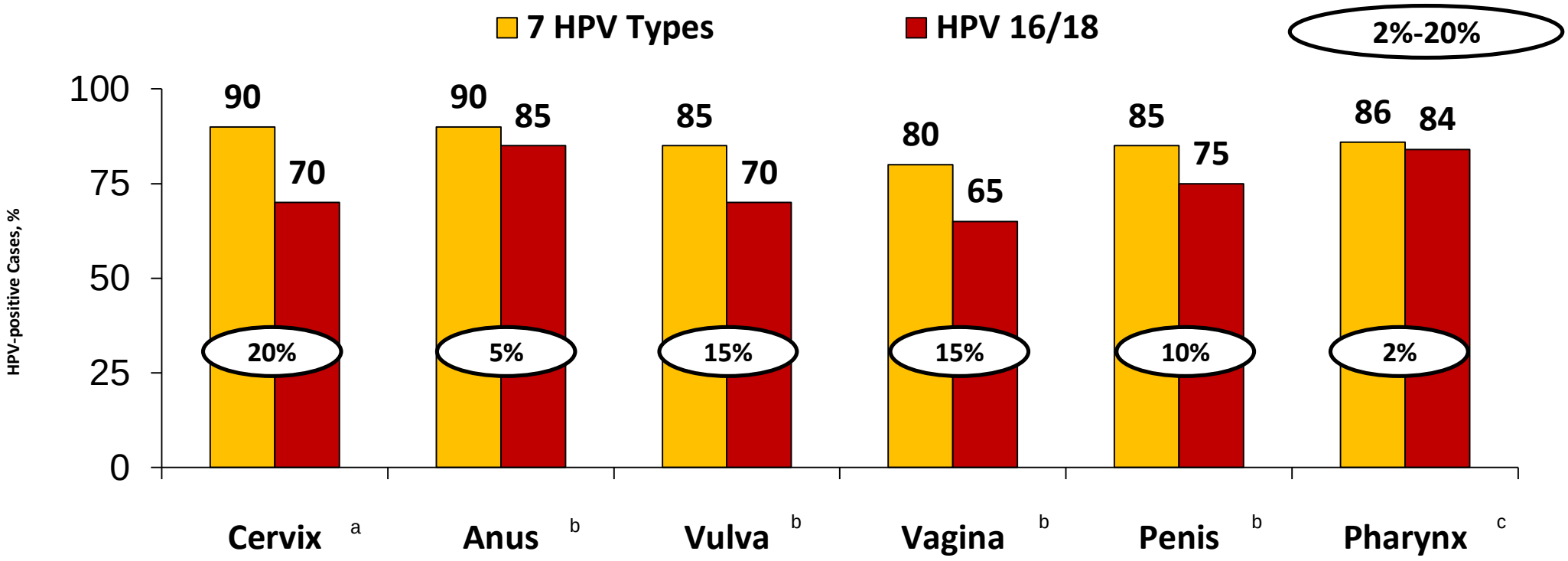
6 *30µg*	**11** *40µg*	**16** *60µg*	**18** *40µg*	**31** *20µg*	**33** *20µg*	**45** *20µg*	**52** *20µg*	**58** *20µg*	AAHS 500

HPV type-specific contribution to cervical cancer and potential for prevention of existing vaccines



de Sanjosé S et al. Lancet Oncol, 2010
Serrano B et al. Infect Ag Cancer, 2012
Schiller J et al Vaccine 30 S 5 2012
Lehtinen M et al. Nat Rev Clin Oncol. 10 2013

Relative contribution of the 7 and 2 Hr HPV Types to HPV positive cancer by organ site

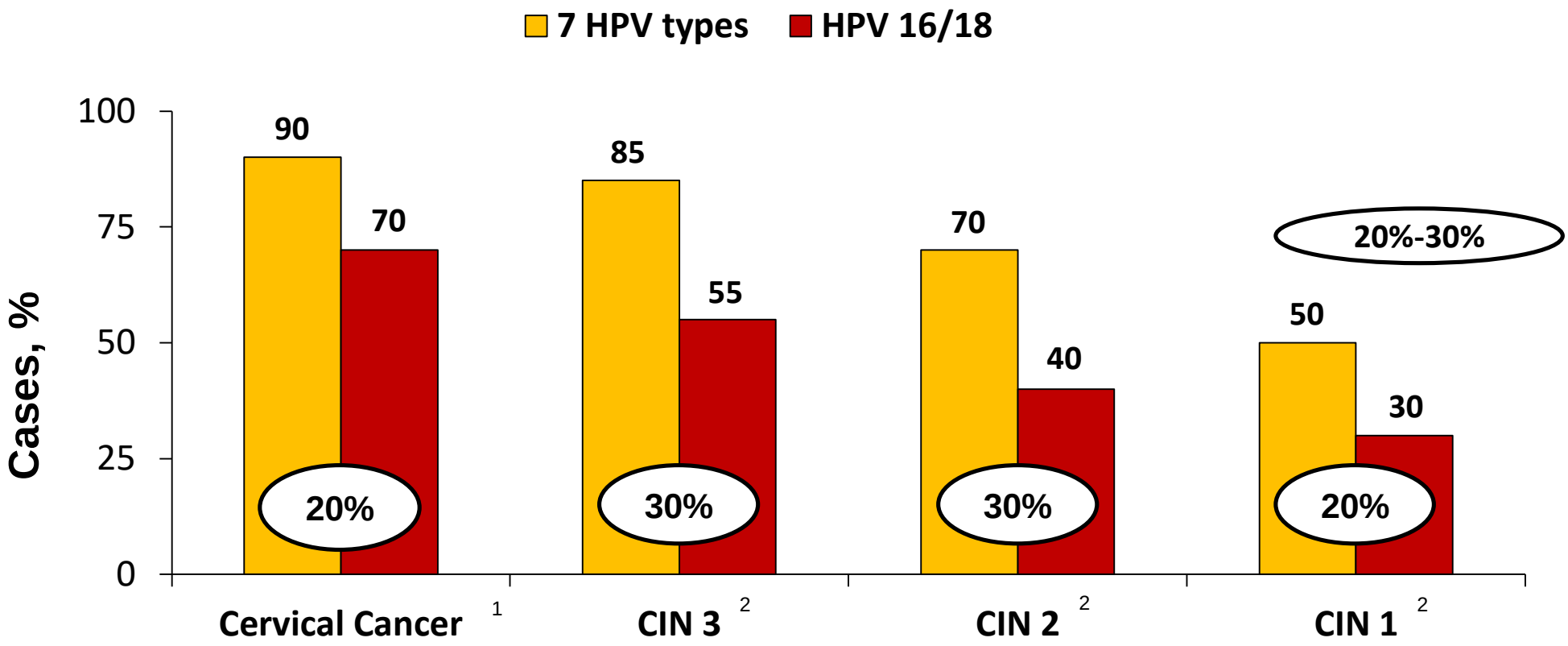


***HPV 6/11/16/18/31/33/45/52/58**

†Overall contribution of HPV in cases of cervical cancer (100%), anal cancer (88%), vulvar cancer (25%), vaginal cancer (70%), penile cancer (30%), and oropharyngeal cancer (26%). a. Serrano B, et al. *Infect Agent Cancer*. 2012;7:38.; b. Merck data on file.

c. Castellsague X, et al. Presented at: 28th International Papillomavirus Conference; November 30-December 6, 2012; San Juan, Puerto Rico.

Relative contribution of the 7 and 2 Hr HPV Types to HPV positive cancer by stage of cervical cancer



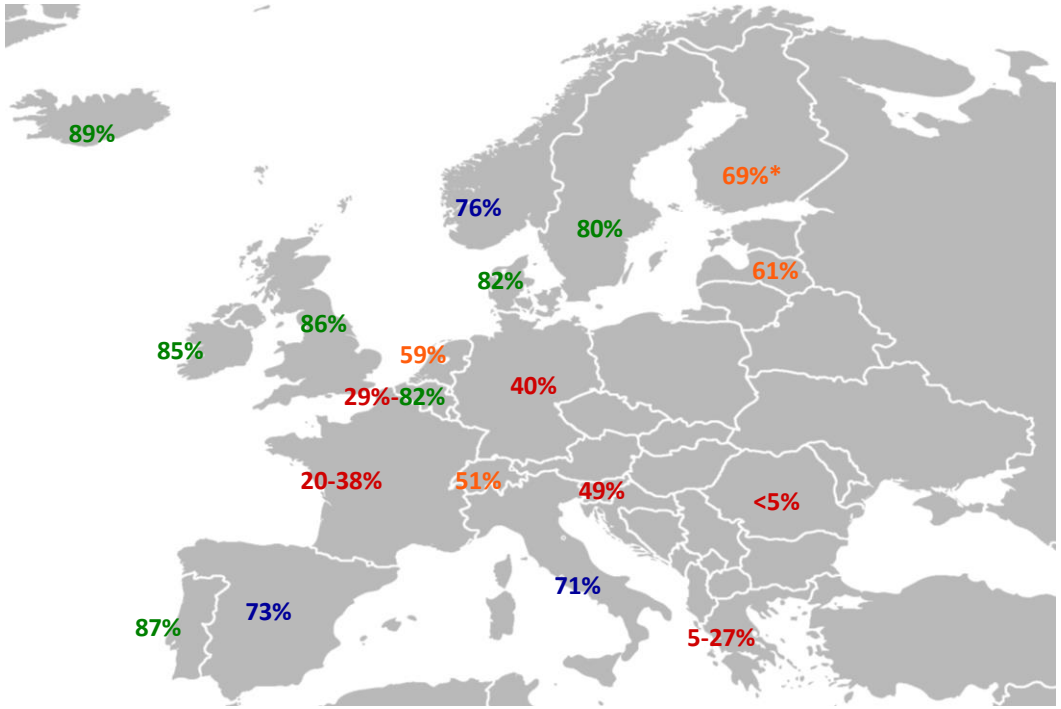
1. Serrano B, et al. *Infect Agent Cancer.* 2012;7:38. 2. Merck data on file.

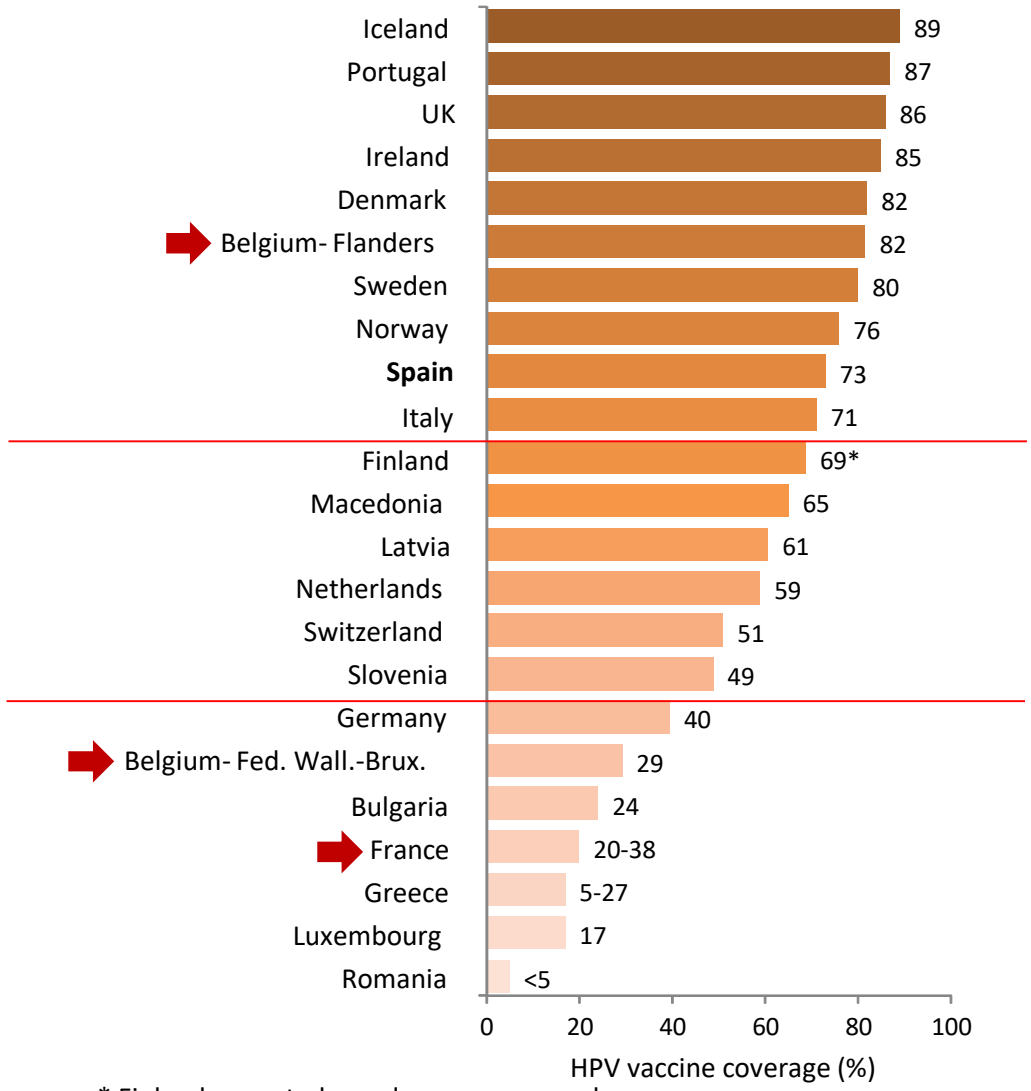
QUADRIVALENT HPV VACCINE EFFICACY STUDIES IN MEN

Vaccine efficacy against EGL, (mostly GW) in men	Vaccine efficacy against anal intraepithelial lesions in MSM
 **90.6% (70-98)**	 **77.5% (40-93)**
Giuliano *et al.* NEJM 2011 Per protocol cohorts	Palefsky *et al* . NEJM 2011 Per protocol cohorts

HPV VACCINATION COVERAGE IN EUROPE (FULL COURSE MOSTLY IN GIRLS 12-14)

Coverage of the last reported vaccinated cohort





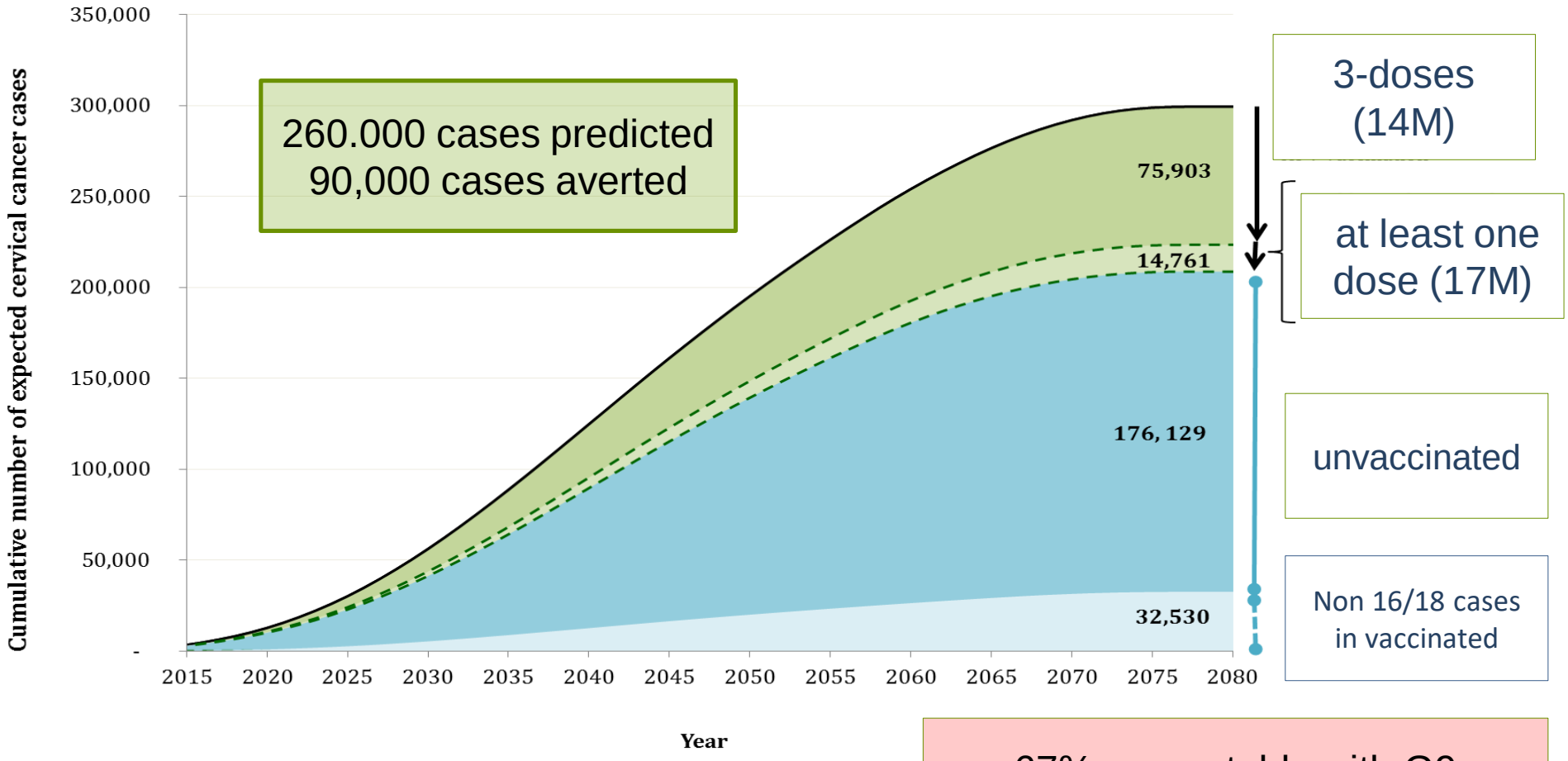
By 2015 23 countries from EU-28 have introduced HPV vaccines

* Finland: reported one dose coverage only

Updated November 2015

ESTIMATED INCIDENT CERVICAL CANCER AVERTED BEFORE AGE 75 YEARS IN THE *36 MILLION WOMEN EVER TARGETED* BY HPV VACCINATION PROGRAMMES in 2014

EUROPE



Based on Bruni 2016 Lancet Glob Health

State of the opinion

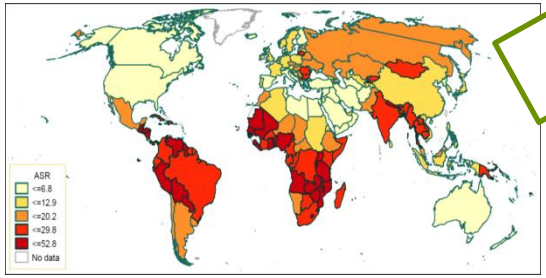
- *HPV vaccination is having a significant impact on infection and disease prevention*
- *Broad spectrum vaccines and gender neutral vaccination are the alternatives of choice in the most advanced countires*

HPV FASTER: Master concept

Women in middle age groups, found HPV negative and receiving a broad spectrum HPV vaccine (expected 90% protection against oncogenic HPV types) has a subsequent risk of cervical cancer extremely low

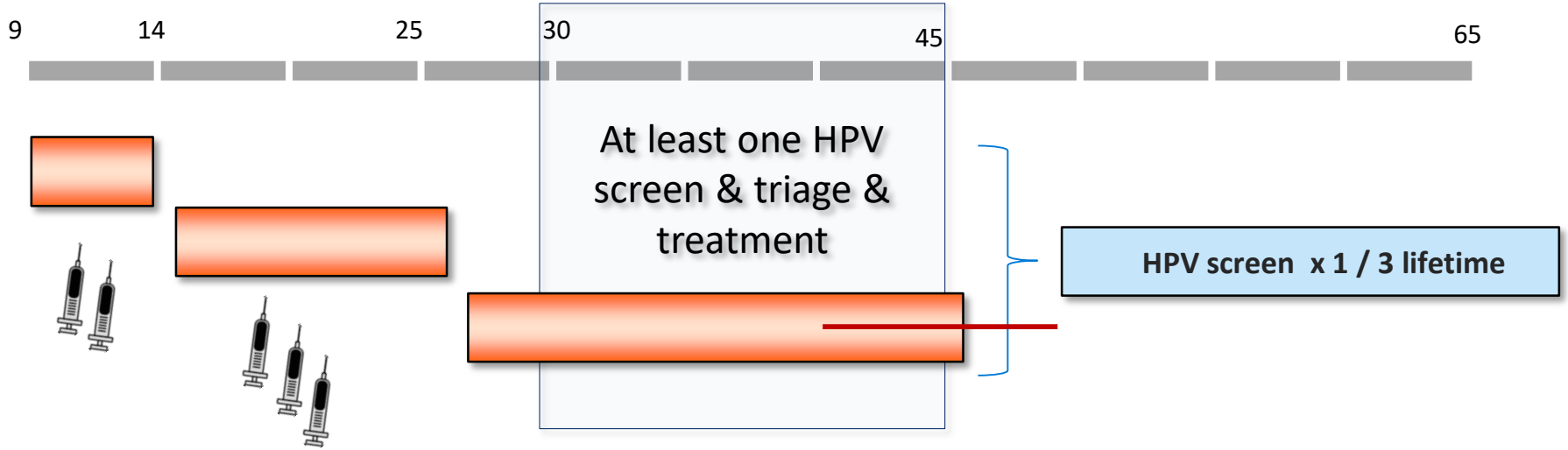
Under these risk estimates, the requirements for further screening are likely to be minimal (one / two lifetime) and necessarily HPV based (sensitivity 90%+)

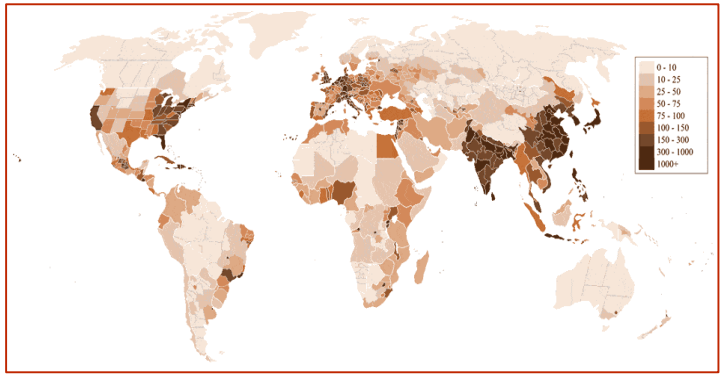
A choice



A unique chance

Proposed HPV FASTER initiative for countries in the planning phases (female program)



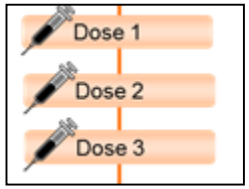


Exact age limits to be defined

HPV FASTER ISSUES : *1 DEVELOPED COUNTRIES*

Women 25-65

ONE HPV SCREENING & TREATMENT



At each round < 2 % follow up required

1 / 2 visits

X 5 / 7/ 10y

7 to 9 visits

At each round 5-10% follow up required

Women will recognize the right to receive and the Health Services will have the obligation to provide unbiased information on the value of vaccination and its implications for future screening

Conclusion

- In Europe HPV cancer prevention will include intelligent *combinations* of HPV vaccination and HPV based screening
- New protocols are being conceived and tested as we learn more on the potential of these technologies
  - Extension of vaccination to women in screening ages
  - Systematic vaccination of high risk groups
  - Less frequent screening, diagnostics and treatment events using HPV tests
  - Self sampling in screening programs