



HPV vaccines

Updated results in 2018



F X Bosch
IDIBELL / ICO
Rumania 2018

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

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

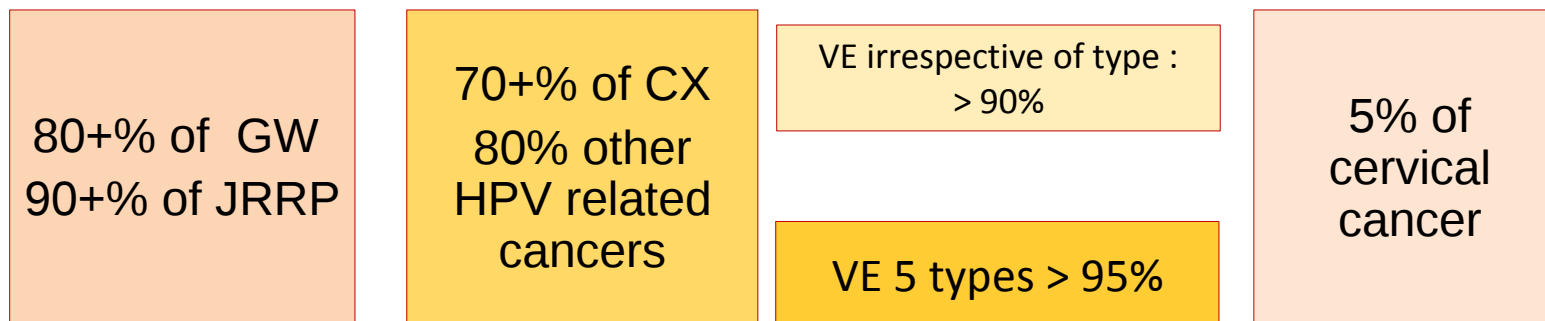
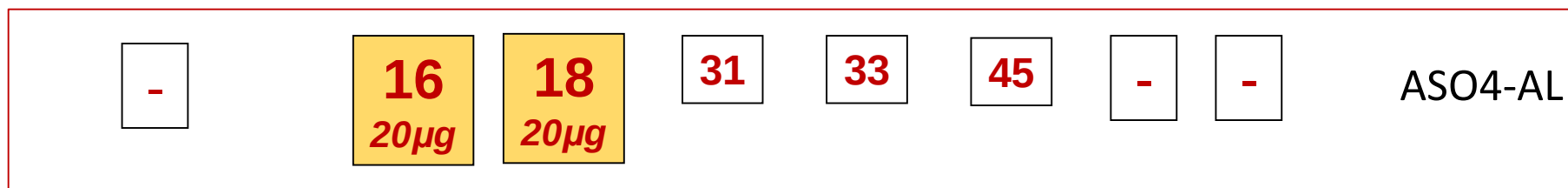
58
20µg

AAHS 500

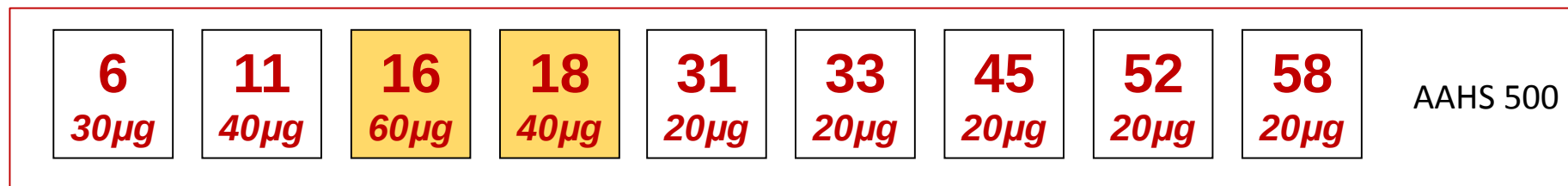
HPV vaccines in 2017+



bi-valent HPV vaccine (Cervarix)

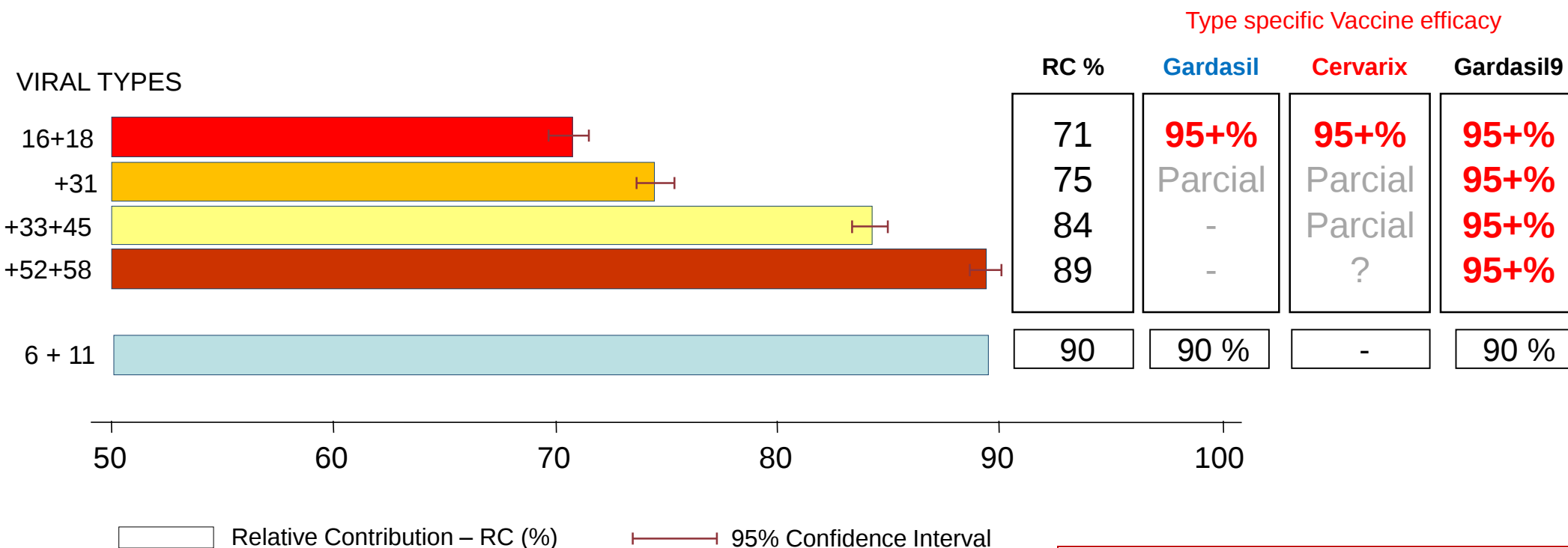


nine-valent HPV vaccine (Gardasil 9)



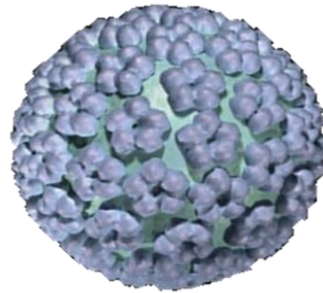


HPV type-specific contribution to cervical cancer and potential for prevention of existing vaccines



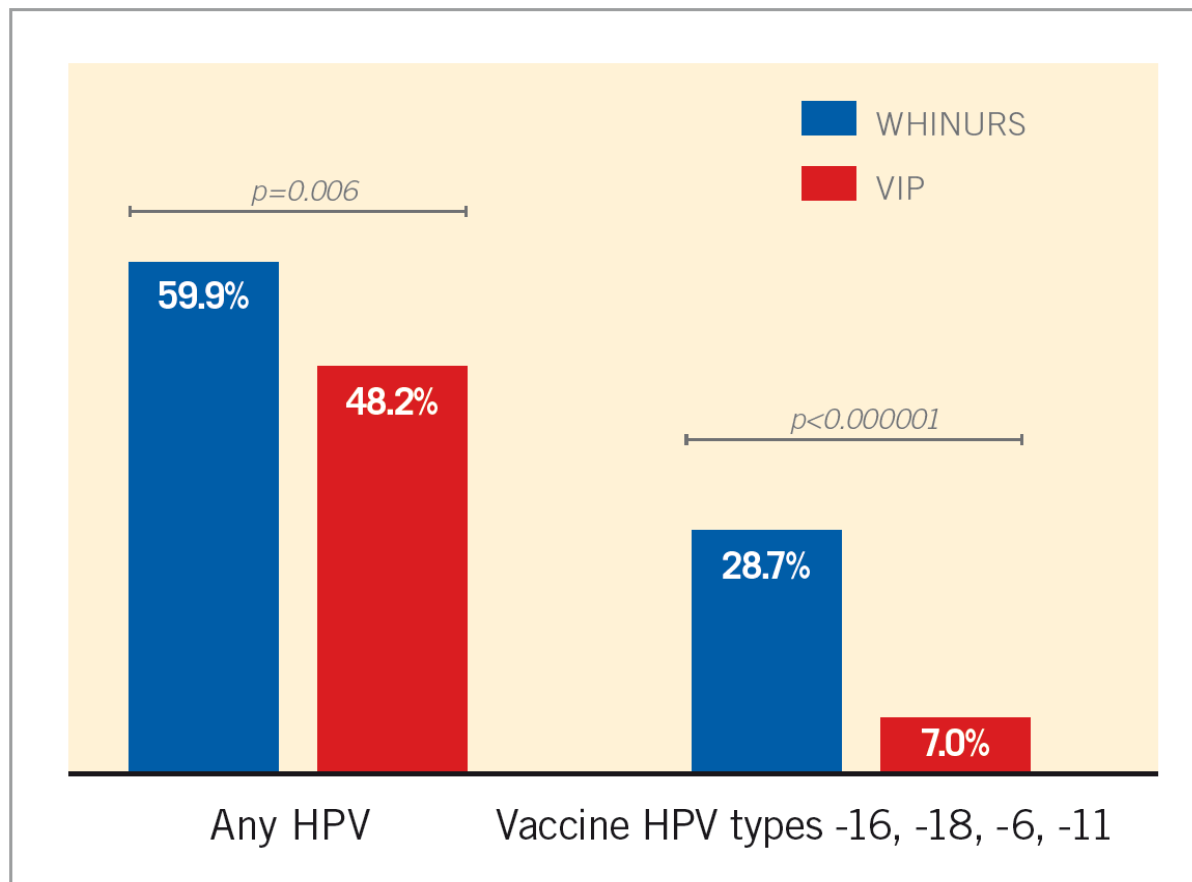
de Sanjosé S et al. Lancet Oncol, 2010
Serrano B et al. Infect Ag Cancer, 2012
Schiller J et al Vaccine 30 S 5 2012
Lehtinen M et al. Nat Rev Clin Oncol. 10 2013

POPULATION STUDIES: OUTCOME HPV INFECTIONS



Prevalence surveys in Australia
Vaccination in 2007 + up to age 26 with 70% coverage for the
three dose regime

DIFFERENCES IN HPV PREVALENCE BETWEEN PRE (WHINURS) AND POST VACCINATION (VIP) PERIODS



Tabrizi S., HPV TODAY 28/29 2013

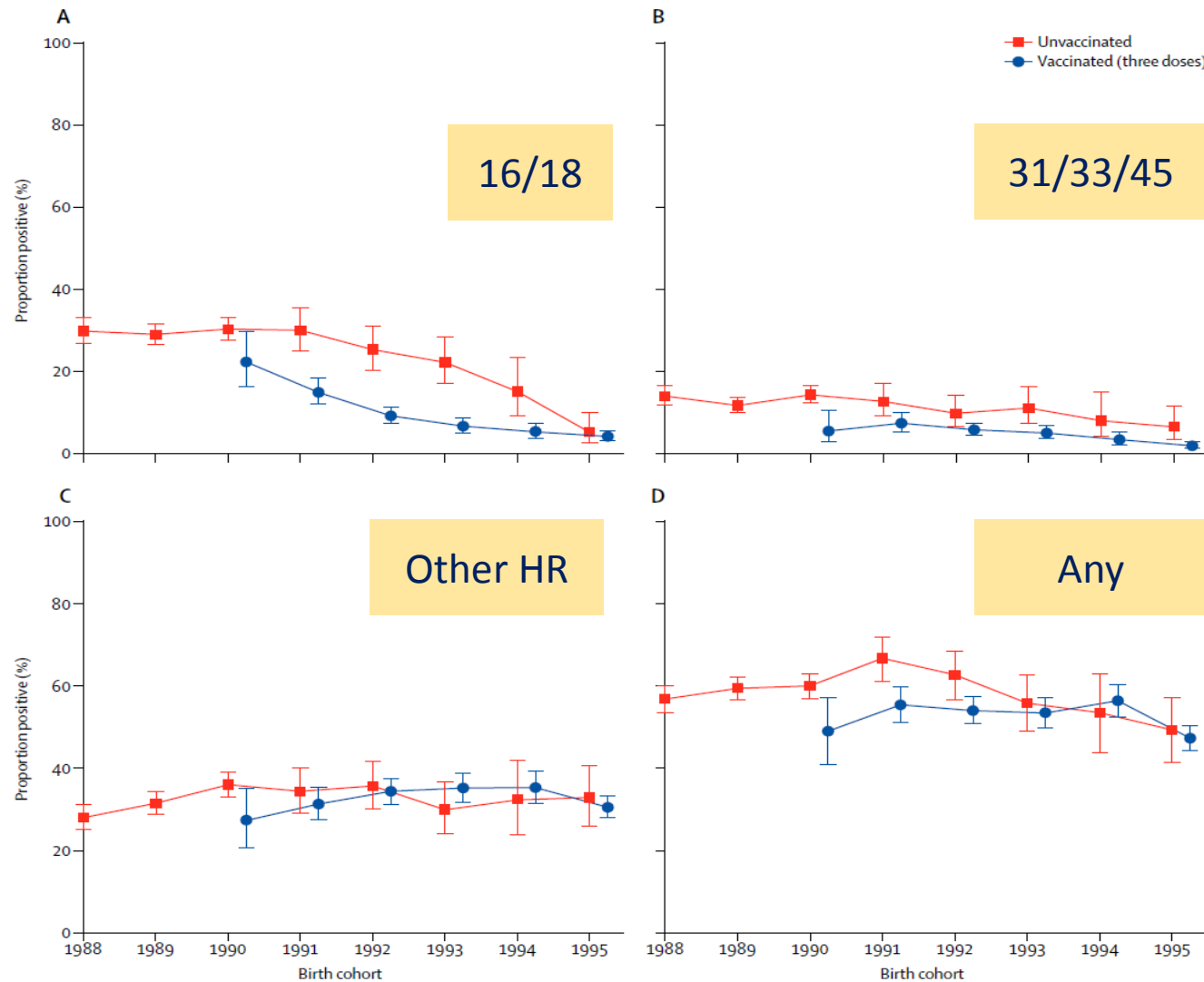
Changes in the prevalence of human papillomavirus following a national bivalent human papillomavirus vaccination programme in Scotland: a 7-year cross-sectional study



Kimberley Kavanagh, Kevin G Pollock, Kate Cuschieri, Tim Palmer, Ross L Cameron, Cameron Watt, Ramya Bhatia, Catherine Moore, Heather Cubie, Margaret Cruickshank, Chris Robertson



Impact of vaccination on the prevalence of human papillomavirus (HPV) by birth cohort 1988–1995



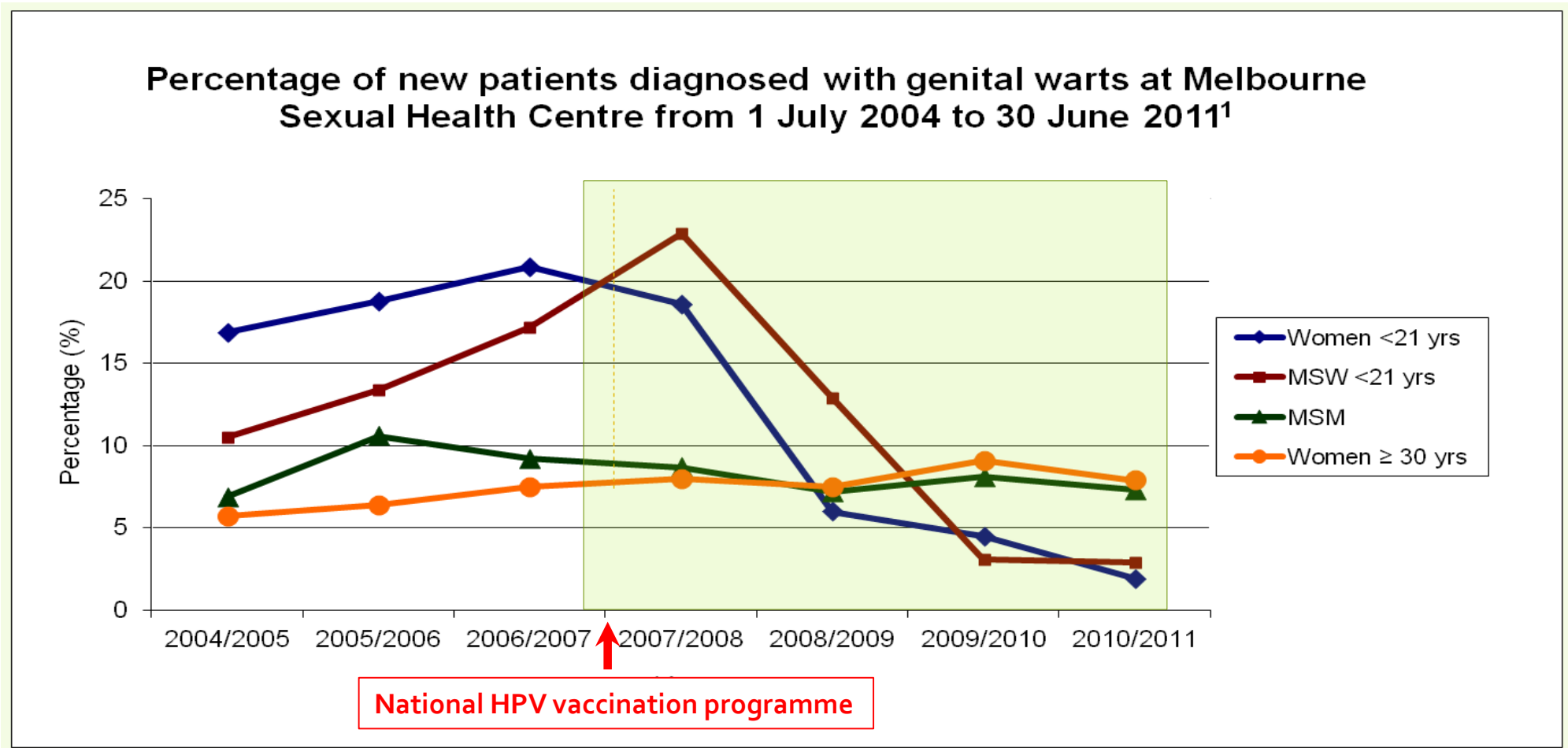
K.Kavanagh et al Lancet Inf Dis 2017



Outcome: Genital warts HPV 6/11



AUSTRALIA: POPULATION IMPACT ESTIMATES ON GENITAL WARTS



Declines in under 21 years of age: women from **18.6% to 1.9%** heterosexual men from **22.9% to 2.9%**
 Around 93% reduction of GW – consistent with results in other countries

OUTCOME: CIN 2/3 - CARCINOMA IN SITU



Largely consistent for both vaccines

Decline in CIN 2+ in Australia by age (2002-2014)now impacting up to 30 years

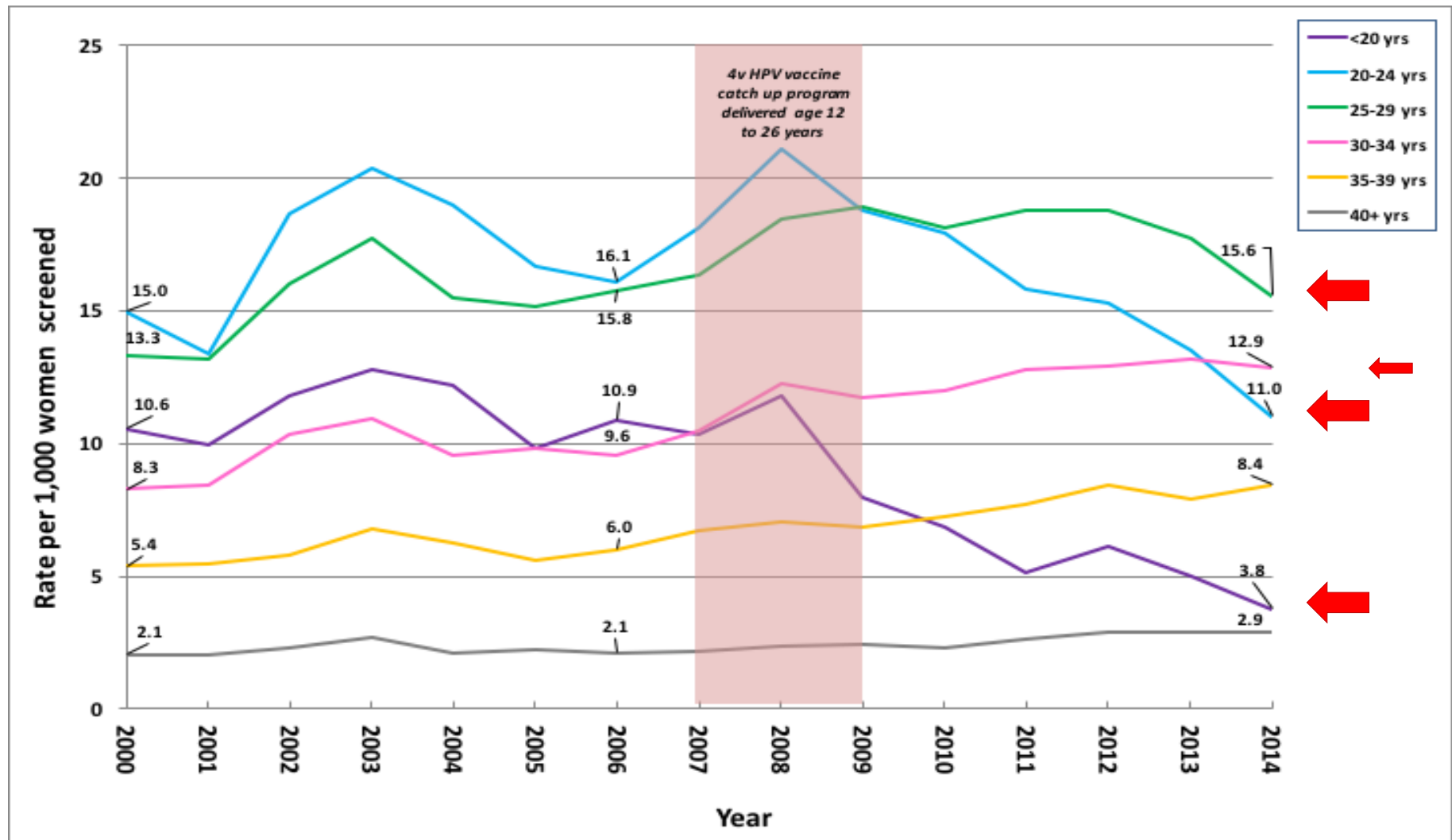
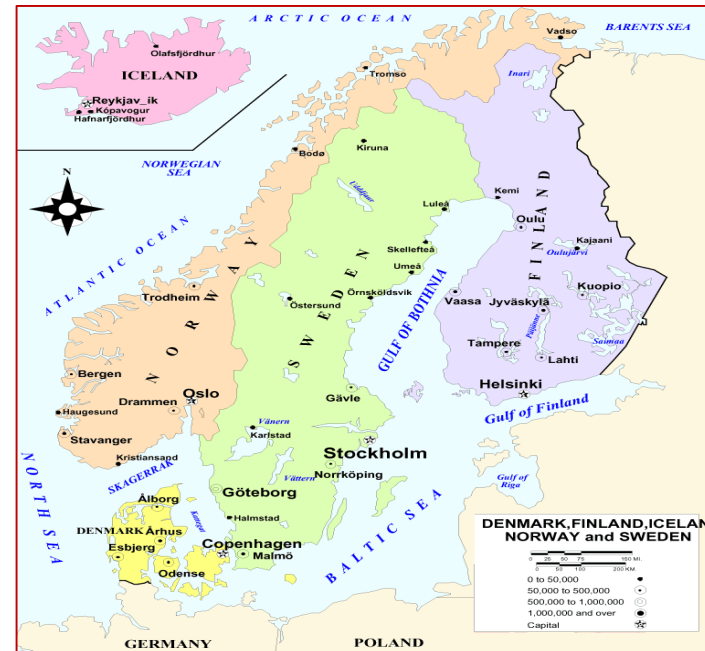


Figure 1: Trends in prevalence rates of high grade histologically confirmed cervical abnormalities (CIN2+)* diagnosed in Victorian women, Australia, by age group, 2000-2014

Source: Brotherton et al. Med J Aust 2016



Population impact on cervical cancer incidence: the nordic countries registration control



Cohorts recruited into Phase III trials (both vaccines) passively followed
up by the network of cancer registration

Finland: Incidence of cancer in girls aged 14-17 by HPV vaccination status
Vaccinated 9,500 & Non-vaccinated 18,000



Cancer site	Vaccinated women. Number and Rates(10x5) <i>66,000 person years</i>		Non vaccinated women Number and Rates (10x5) <i>124,000 person years</i>	
Cervix	0		8	6.4 (3.2-13)
Vulva	0		1	
Oropharynx	0		1	
Anal / Vaginal	0		0	
All HPV related	0		10	8.0 (4.3-15)
Vaccine efficacy estimates: 100% (95% CI 16-100)				
Breast	2	3.0 (0.8-12)	10	8.0 (4.3-15)
Thyroid	1	1.5 (0.2-11)	9	7.2 (3.8-14)
Melanoma	3	4.6 (1.5-14)	13	10.5 (6.1-18)
Other skin	2	3.0 (0.8-12)	3	2.4 (0.8-7.5)

Luostarinen T. et al IJC 2018

Vaccine balance over safety Weight of the evidence



Sore arm
Fainting from vaccination

All suspected claims have been
declared inconsistent after
careful examination

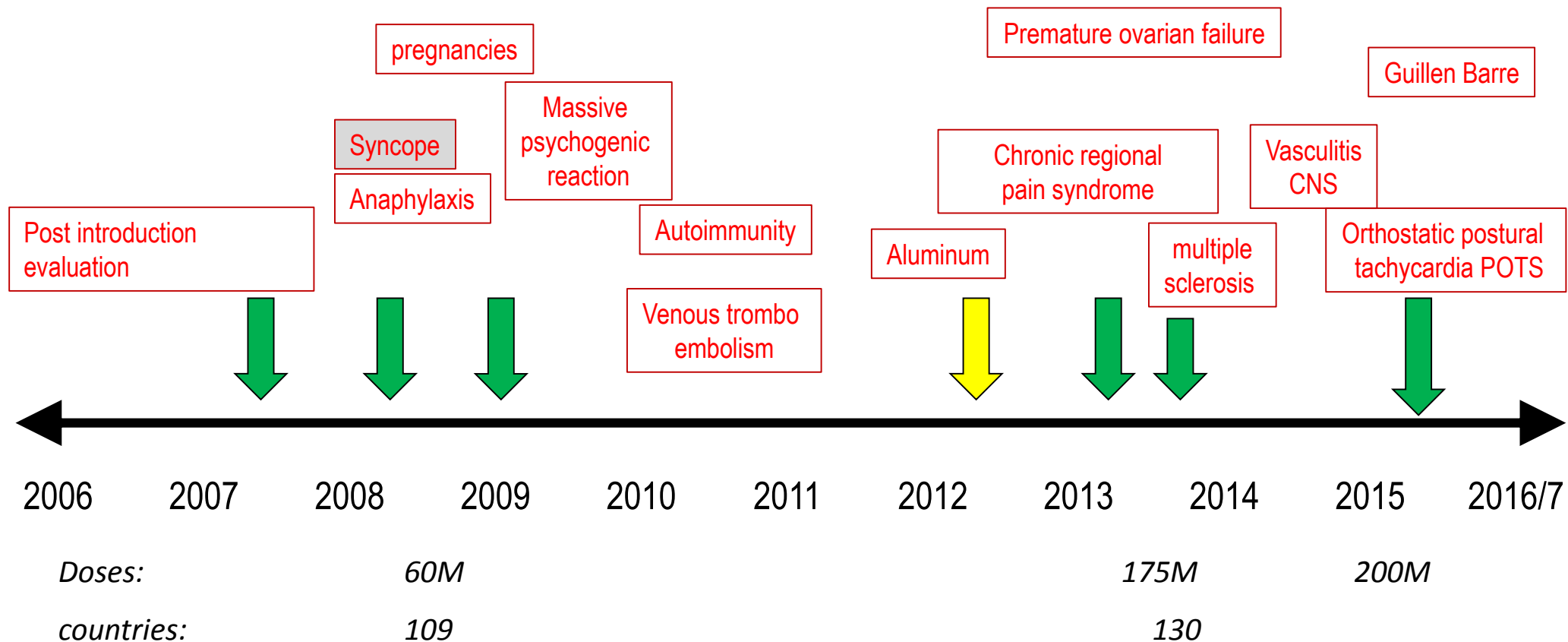
Recognizing that the risk “0”
does not exist in biology



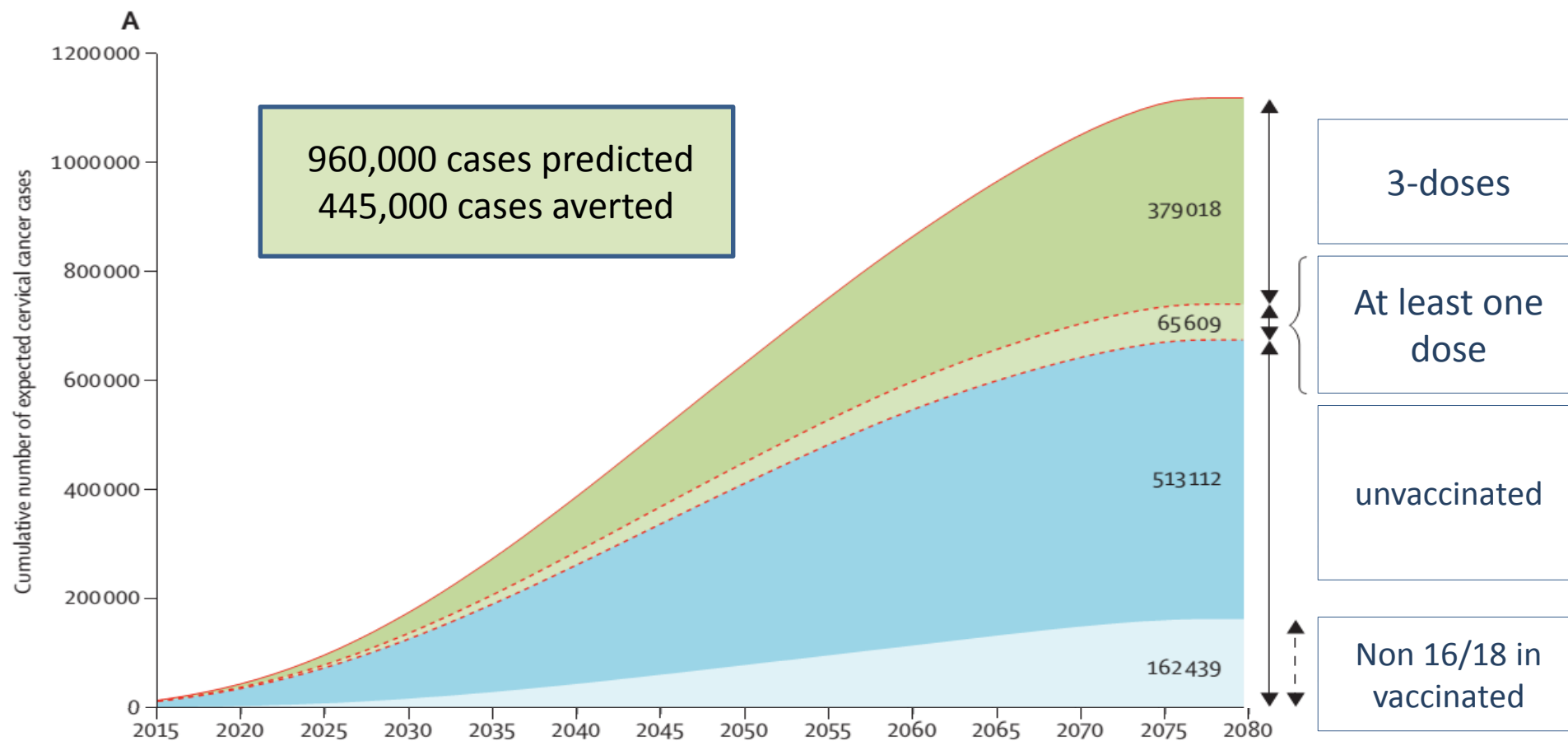
Over **100,000** subjects in RCT
Over **240 M** doses distributed
Estimated **60M** vaccinated
8 WHO reviews on safety
62 countries (**30 in Europe**)
introduced routine HPV
vaccination
13+ countries introduced male
vaccination...

**OVERWHELMING and
UNANIME SUPPORT OF THE
VACCINATION PROGRAM**

Reports of the Global Advisory Committee on Vaccination Safety (GACVS) & Strategic Advisory Group of Experts in immunization (SAGE) in relation to the HPV vaccine



ESTIMATED INCIDENT CERVICAL CANCER AVERTED BEFORE AGE 75 YEARS IN **118 MILLION** WOMEN EVER TARGETED BY HPV VACCINATION PROGRAMMES BY THE END OF 2014



Bruni 2016 Lancet Glob Health

MALE HPV VACCINATION:

Further increase protection of women by interrupting transmission
Protect vaccinated males against HPV-induced cancers



Herd protection is lost when individuals leave the herd...

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 <i>et al.</i> NEJM 2011 Per protocol cohorts	Palefsky <i>et al.</i> NEJM 2011 Per protocol cohorts

COST BENEFIT BALANCE: GENERAL CONSIDERATIONS

Women only

- Highest burden of severe disease is in women
- High cost of the vaccine
- Herd protection may be sufficient for both genders if high female vaccination rates are achieved (*requires stable heterosexual populations*)

Include males

- Recognition of the HPV etiology of significant number of cancers in males
- Impact of GW's & global burden of disease / health services requirements
- Trends in sexual practices in many countries. MSM, high risk groups
- Interrupting the transmission chain to other partners
- *Powerful herd effects and program resilience if both genders are included*



Australia, US, Canada, Austria, Italy, Argentina... 13+ countries



prospects

- Vaccination of girls will *continue and expand* under the two dose regimes (i.e. GAVI countries)
 - *One-dose* regime
 - Vaccination of *boys*
 - Vaccination of *middle aged women*
 - Vaccination of *high risk groups*
- *Elimination of cervical cancer* is being proposed as part of the new edition of the WHO's millennium goals

