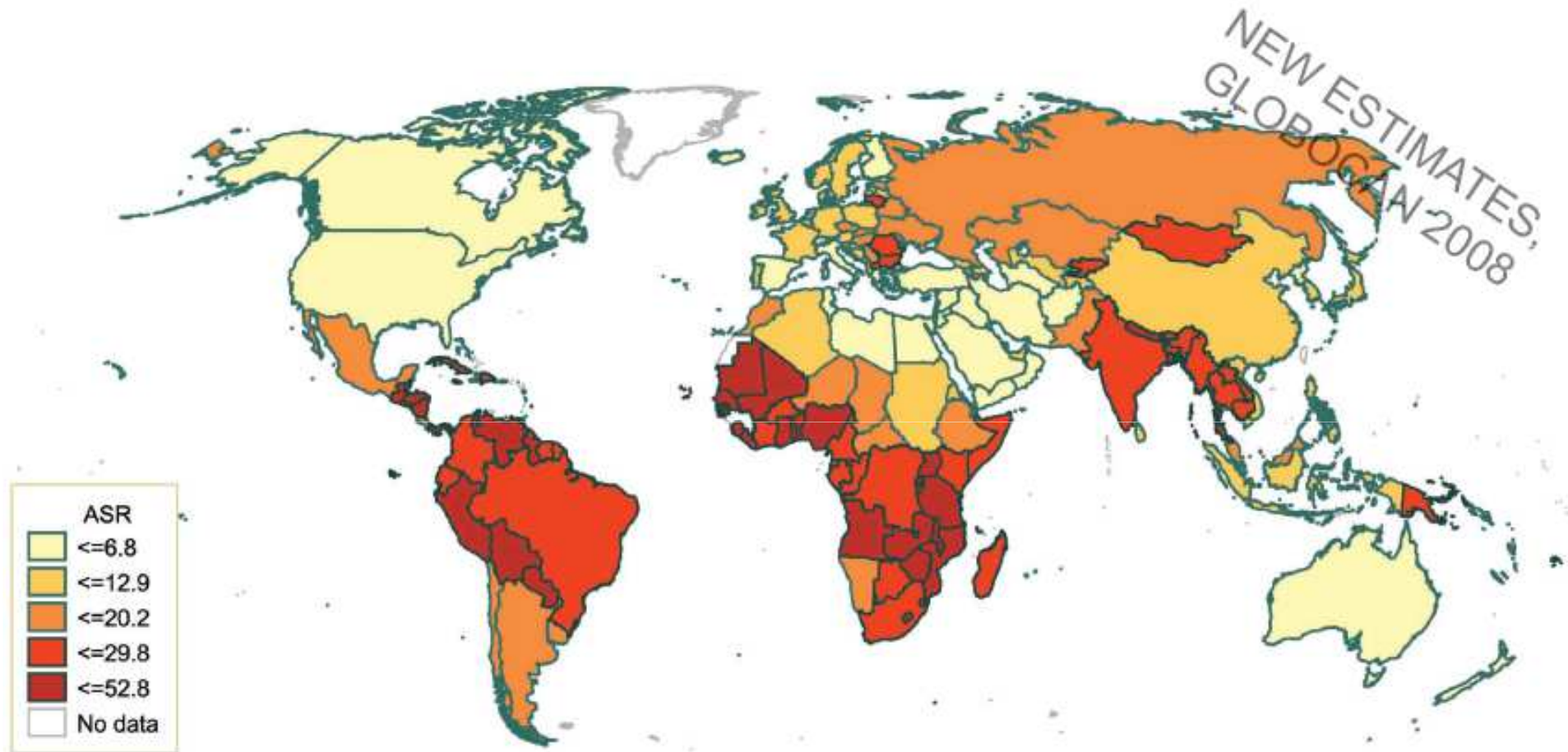


# Wissenswertes über die *HPV-Impfung*

Elmar A. Joura

Universitätsklinik für Frauenheilkunde, AKH Wien

# World age-standardized incidence rates of cervical cancer

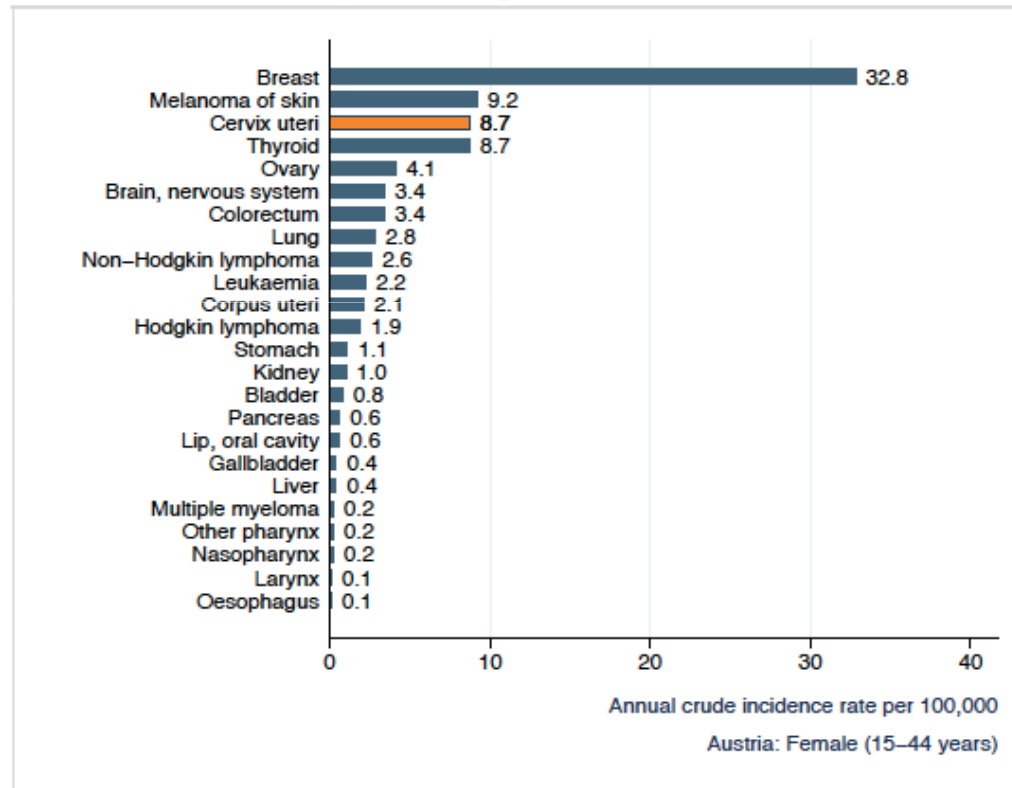


ASR, age-standardized incidence rate; Rates per 100,000 women per year.  
Data sources: IARC, Globocan 2008.

# Cervical Cancer Austria <45a

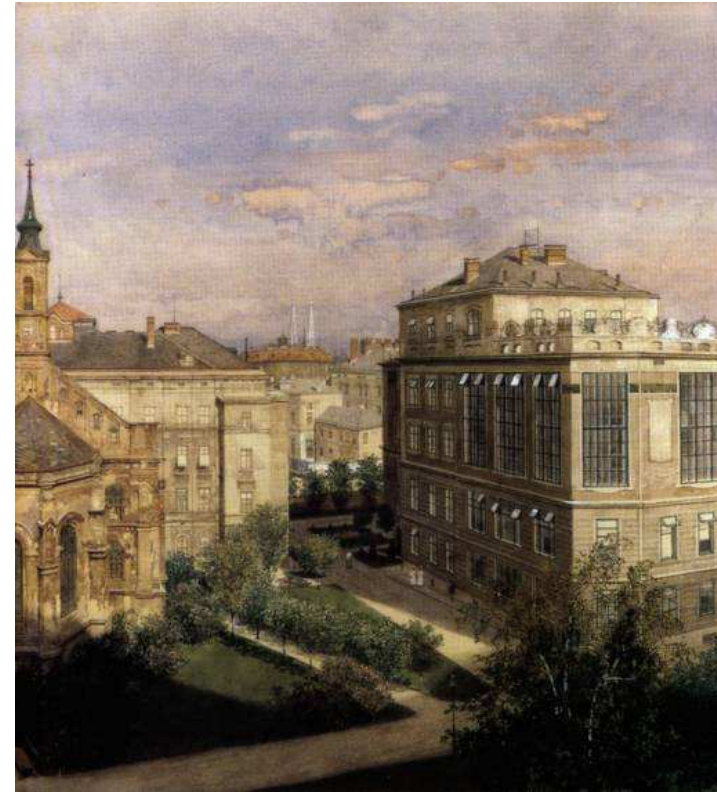
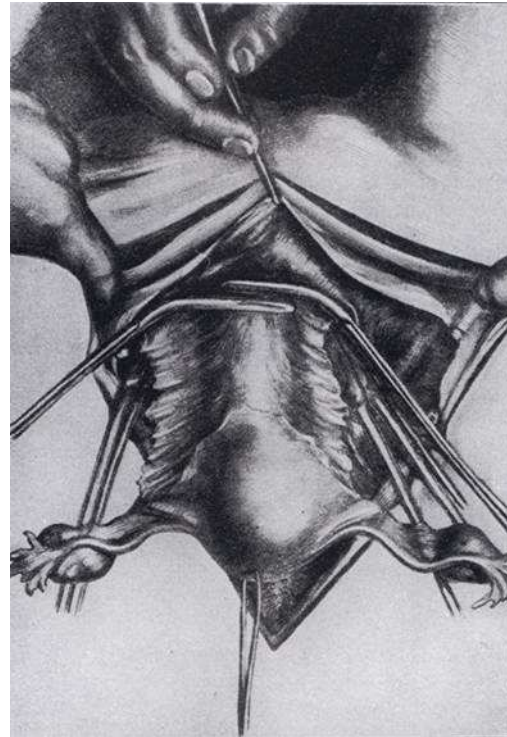


Figure 5: Age-specific cervical cancer incidence compared to age-specific incidence of other cancers among women 15-44 years of age in Austria



Data sources:  
IARC, Globocan 2008. Age-specific data from GLOBOCAN 2008 were obtained from IARC, personal communication.  
For specific estimation methodology refer to [http://globocan.iarc.fr/DataSource\\_and\\_methods.asp](http://globocan.iarc.fr/DataSource_and_methods.asp).

# 1897 Ernst Wertheim



# Nobelpreis für Medizin und Biologie 2008

## Harald zur Hausen



*Proc. Natl. Acad. Sci. USA*  
Vol. 80, pp. 560–563, January 1983  
Medical Sciences

### Human papillomavirus types 6 and 11 DNA sequences in genital and laryngeal papillomas and in some cervical cancers

(molecular cloning/blot hybridization/perinatal infection/genital cancer)

LUTZ GISSMANN\*, LUTZ WÖLNIK†, HANS IKENBERG\*, URSULA KOLDOVSKY‡, HANS GEORG SCHNÜRCH‡, AND HARALD ZUR HAUSEN\*

\*Institut für Virologie, Zentrum für Hygiene, Universität Freiburg, Hermann-Herder-Strasse 11, 7800 Freiburg, Federal Republic of Germany; †Universitäts-Frauenklinik, Pilgrimstein 3, 3550 Marburg, Federal Republic of Germany; and ‡Universitäts-Frauenklinik, Mohrenstrasse, 4000 Düsseldorf, Federal Republic of Germany

Communicated by Gertrude Henle, October 13, 1982

**ABSTRACT** Human genital tumors as well as recurrent laryngeal papillomas were analyzed for the presence of human papillomavirus (HPV) 6 and HPV 11 sequences. HPV 11 DNA was found in 7 of 14 laryngeal papillomas; in the 7 other tumors no HPV DNA was demonstrated. HPV 11 DNA was also found in all five atypical condylomata of the cervix included in this study. Condylomata acuminata mainly contained HPV 6 DNA. From 63 biopsy specimens, 41 clearly harbored HPV 6 DNA and 13 harbored HPV 11 DNA. In three tumors accurate typing was impossible, and in six additional ones neither HPV 6 nor HPV 11 DNA could be demonstrated. The data support a genital origin of laryngeal papillomavirus infections. In 4 of 24 malignant tumors, HPV 11 DNA or related sequences were demonstrated; 2 of the 4 were biopsy specimens from invasive cancer, and the other 2 originated from carcinomata *in situ*. A possible role of this or related papillomavirus types in the induction of malignant genital tumors remains to be elucidated.

#### MATERIALS AND METHODS

**Extraction of Cellular DNA.** Biopsy materials were examined histologically and stored at  $-20^{\circ}\text{C}$  or  $-70^{\circ}\text{C}$  until further processing. Extraction of cellular DNA was done as described (6).

**Labeling of HPV DNA.** HPV 6 DNA has been cloned into pBR322 in two fragments representing approximately one-third and two-thirds of the total genome, respectively (5). HPV 11 DNA, which has been identified from a genomic library of laryngeal papilloma constructed in  $\lambda$  L47 (7), was subcloned in pBR322 at the single *Bam*HI site.

Both DNAs were prepared as described (10) and labeled with deoxynucleotide [ $\alpha$ - $^{32}\text{P}$ ]triphosphate by the nick-translation procedure to a specific activity of  $>10^8$  cpm/ $\mu\text{g}$  (6).

**Blot Hybridization.** About 10  $\mu\text{g}$  of papilloma DNA was cleaved with restriction enzyme; the products were separated

# FUTURE I Studie (Phase III)

---

- ▶ quadrivalente HPV- Impfstoff
  - ▶ größtes europäisches Studienzentrum
  - ▶ erste Probandin außerhalb der USA 6/2002
- ▶ 22. September 2006 Zulassung durch die EMEA
- ▶ **30. September 2006**
  - ▶ **I. HPV Impfung in Europa**



12.8.2013

---



Die HPV- Impfung wird ab Februar 2014 für alle in Österreich lebenden Kinder in der vierten Schulstufe (vollendetes neuntes Lebensjahr) kostenfrei im Rahmen des bestehenden Schulimpfprogramms angeboten

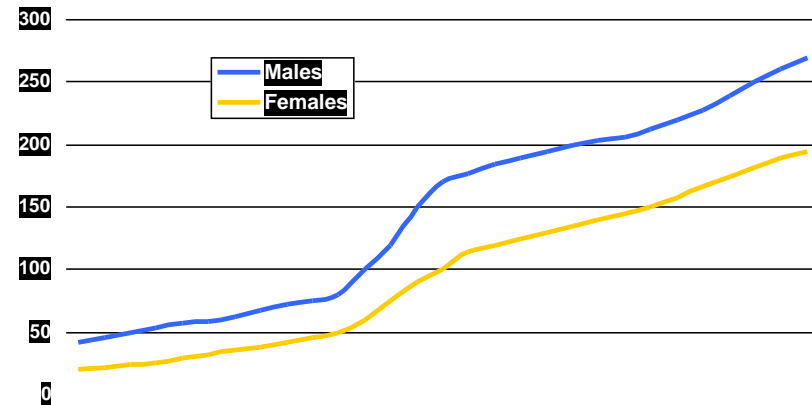
---

# HPV- Impfung für Buben?

## ▶ Condylome

♂ > ♀

- ▶ Risikofaktor für die Partnerin (RR 10!)
- ▶ Herdenimmunität





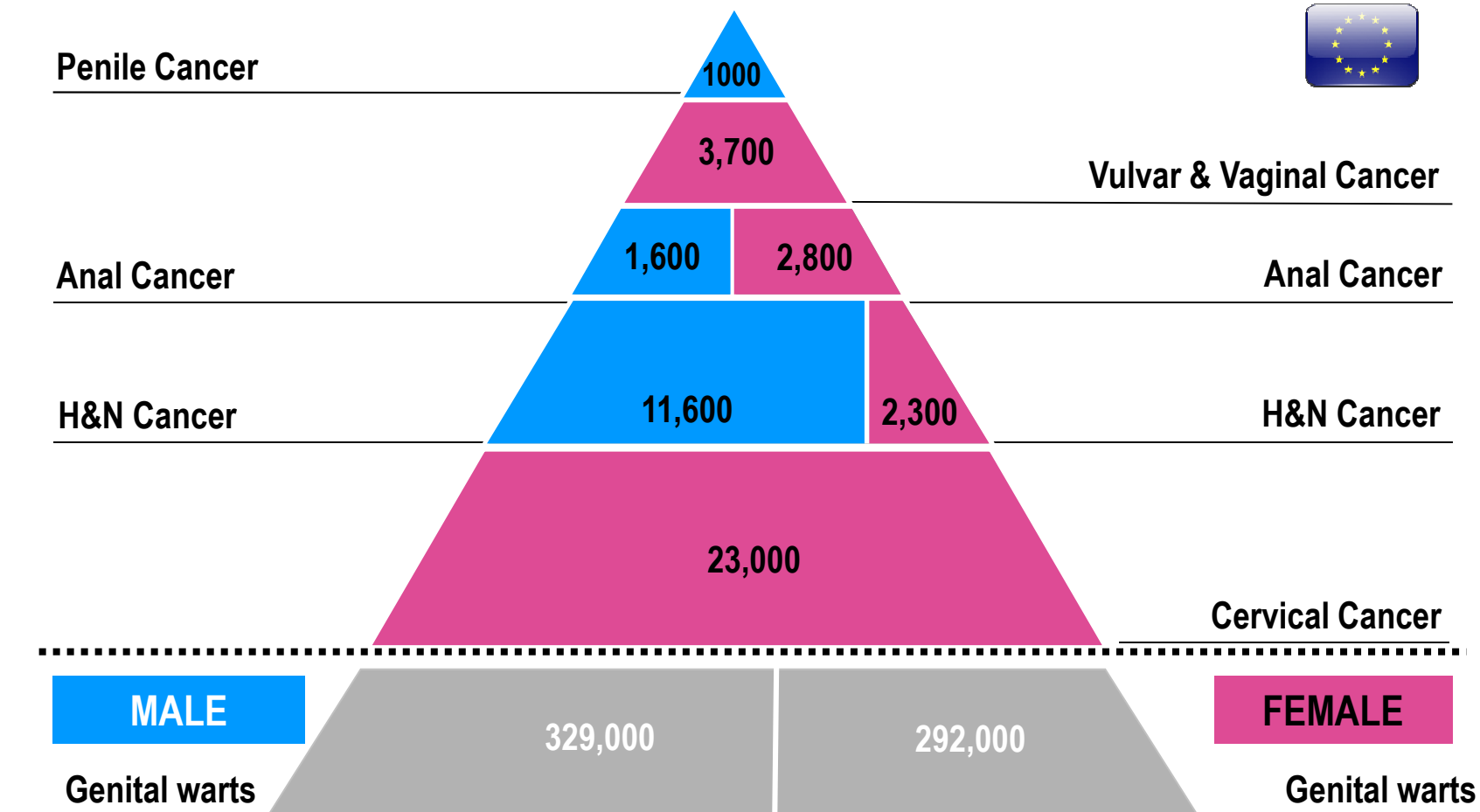
# HPV- assoziierte Karzinome Männer USA 2004-8

---

- ▶ **9400 Karzinome Oropharynx**
- ▶ **1700 Analkarzinome**
  - ▶ 2/100.000
  - ▶ 35/100.000 MSM (HIV-)
- ▶ **1000 Peniskarzinome**
  - ▶ Frauen
    - ▶ 12000 Zervixkarzinome
    - ▶ 3900 Vulva/Vaginalkarzinome
    - ▶ 3100 Analkarzinome
    - ▶ 2400 Oropharynx



# HPV - Related Cancers in Men and Women



Annual new cancers and genital warts cases related to HPV 6, 11, 16 and/or 18 in Males and Females in Europe

Annual number of new cancer cases calculated based on crude incidence rates from IARC database (1998-2002) and population estimate Eurostat 2008; estimate Globocan 2008 for cervical cancer; published HPV prevalence rates were applied (for Europe, when available) Genital warts estimates based on incidence rates in UK, HPA 2007

# Libby Trickett – „*I did it*“

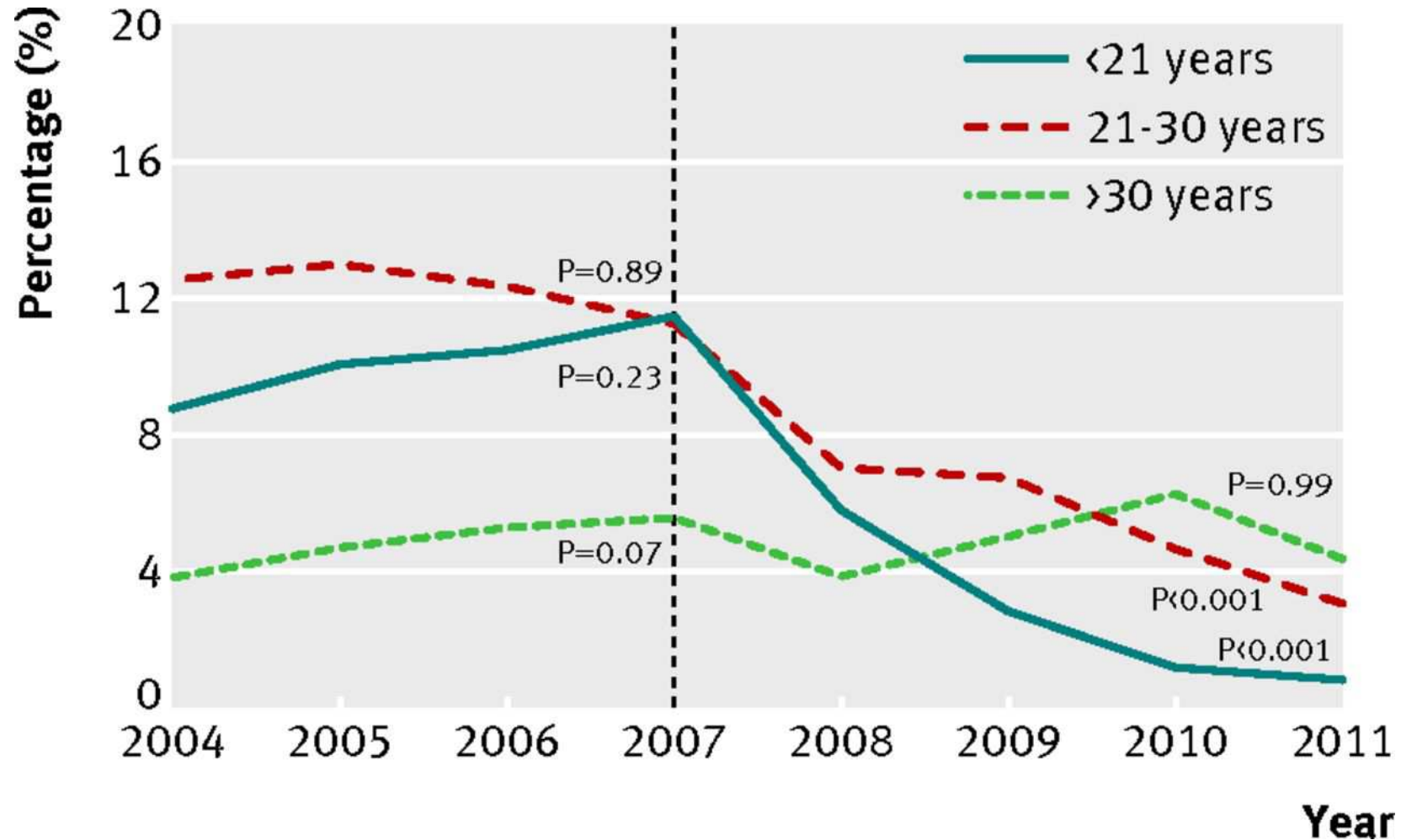
---



---

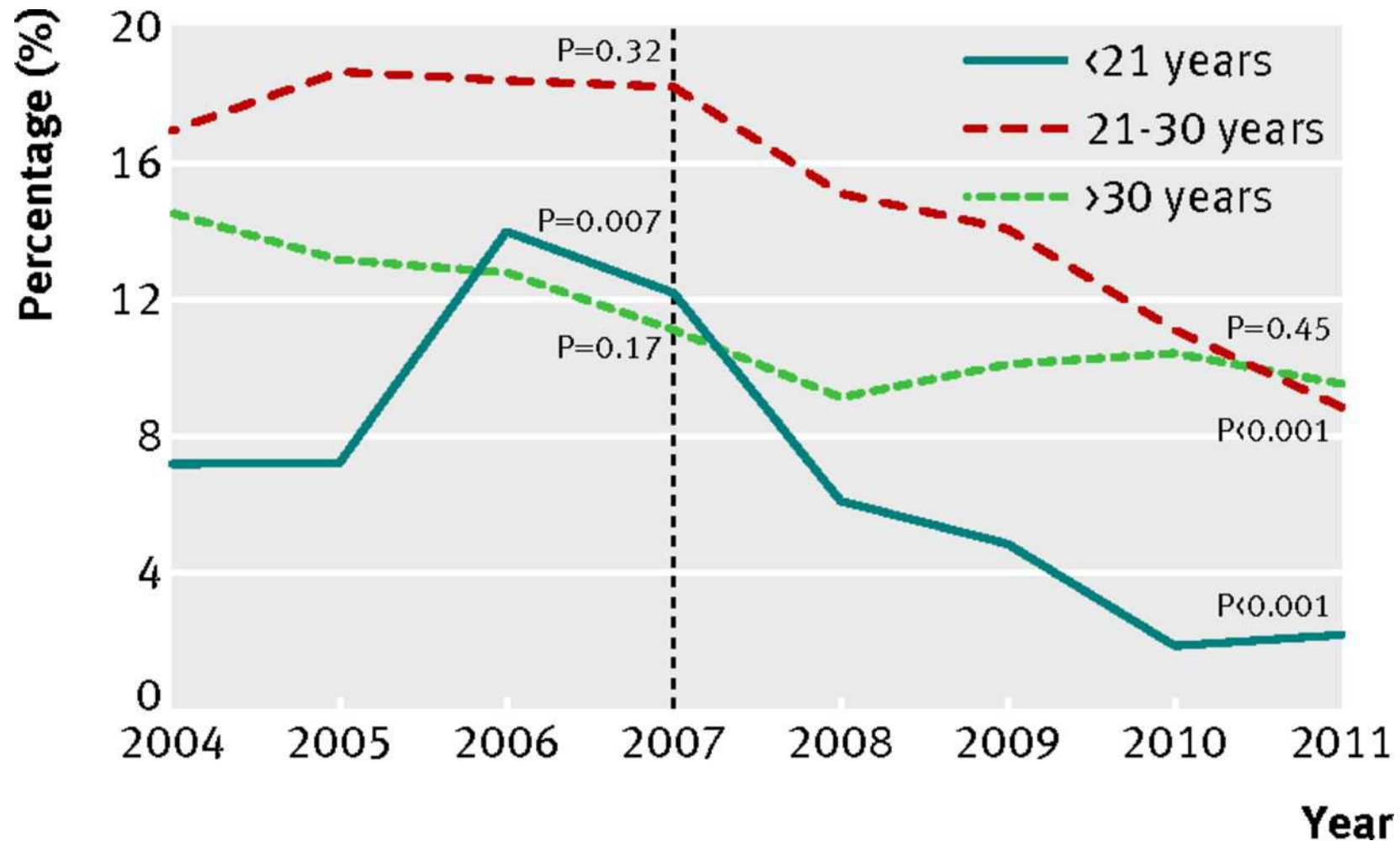
▶ Olympic Gold Medalist - Athens 2004 - Beijing 2008 - London 2012 - WR 100m freestyle

**Fig 1 Proportion of Australian born women diagnosed as having genital warts at first visit, by age group, 2004-11.**



Ali H et al. BMJ 2013;346:bmj.f2032

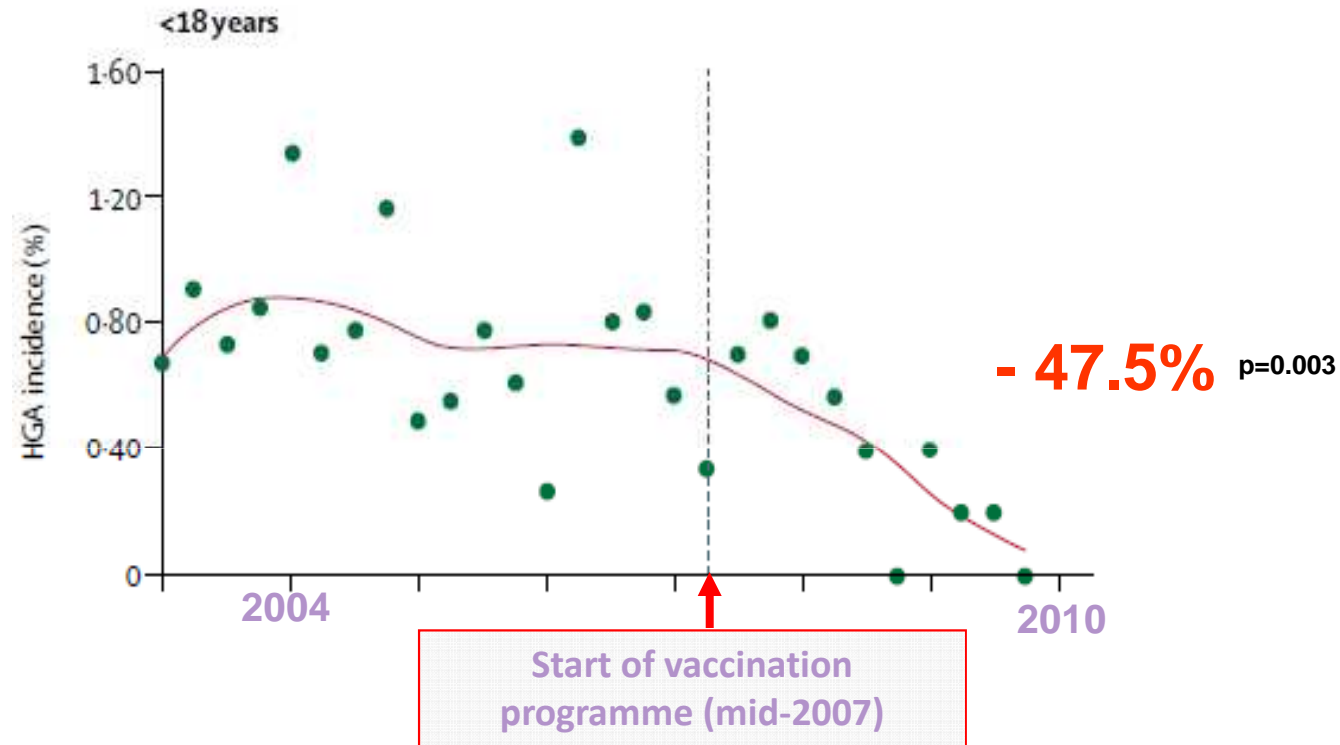
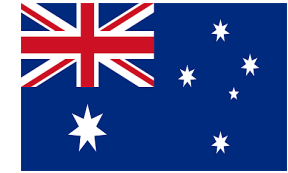
**Fig 3 Proportion of Australian born heterosexual men diagnosed as having genital warts at first visit, by age group, 2004-11.**



Ali H et al. BMJ 2013;346:bmj.f2032

# Impact in Australia

## Cervical high-grade abnormalities (HGA)



- ▶ A relative reduction of ~50% was observed in this age group, post vaccination vs. pre vaccination, barely 3 years after the introduction and the trend continues<sup>1</sup>
- ▶ Similar early trends have been observed in the US on abnormal Pap smears<sup>2</sup>

1. Brotherton J et al. Lancet 2011

2. Gross et al. J Pediatr Adolesc Gynecol 2010

# Rwanda



**Table 1. Cumulative human papillomavirus vaccination coverage, by vaccination round, Rwanda, 2011**

Coverage	Round 1	Round 2	Round 3
Girls vaccinated in school, no.	91 752	89 704	88 927
Girls vaccinated outside school, no.	2 136	3 066	3 180
Total no. of girls vaccinated	93 888	92 770	92 107
<b>Cumulative coverage (%)</b>	<b>95.04</b>	<b>93.90</b>	<b>93.23</b>

# Sexuelle Übertragung

---

- ▶ *State Sen. George Runner of California :*
- ▶ „American money would be much better spent on other types of vaccines, since cervical cancer is a result of lifestyle choices“





# The New York Times

OCTOBER 15, 2012, 12:01 AM | 99 Comments

## HPV Vaccine Doesn't Alter Sexual Behavior, Study Finds

By ANAHAD O'CONNOR



Joe Raedle/Getty Images

 FACEBOOK

 TWITTER

 GOOGLE+

 SAVE

Coni Butler, an accountant in Austin, Tex., and a devout Catholic, encourages her three children to remain celibate before marriage. But that did not stop her from getting them vaccinated against human papillomavirus, or HPV, a sexually transmitted disease that raises the risk of some cancers.

# Statistik Austria 2009

## HPV 16/18

	Inzidenz	HPV 16/18*
CX	<b>394</b>	295
Vulva	<b>128</b>	38
Vagina	<b>26</b>	10
Anus	<b>80</b>	66
Kopf/Hals	<b>273</b>	68
<i>Frauen gesamt</i>	<b>901</b>	477
Penis	<b>58</b>	17
Anus	<b>49</b>	40
Kopf/Hals	<b>851</b>	212
<i>Männer gesamt</i>	<b>958</b>	269
<b>Gesamt</b>	<b>1859</b>	<b>746</b>

\* Estimation

# Impfplan 2014 - [www.bmg.gv.at](http://www.bmg.gv.at)

## Schulkinder

Alter→ ↓Impfung	7. Jahr	8. Jahr	9. Jahr	10. Jahr	11. Jahr	12. Jahr	13. Jahr	14. Jahr.	15. Jahr
<b>Diphtherie (dip)</b> <b>Tetanus (TET)</b> <b>Pertussis (PEA)</b> <b>Poliomyelitis (IPV)</b>	4-fach						3-fach (dip+TET+PEA) für Kinder, die vorher nur eine dip+Tet+IPV Imp- fung erhalten haben		
<b>Hepatitis B (HBV)</b>	Grundimmunisierung (0/1/6 Monate) oder Auffrischung								
<b>Mumps</b> <b>Masern (MMR)</b> <b>Röteln</b>	MMR (Nachholen bei Kindern, die keine oder nur eine Impfung erhalten haben und nicht immun sind)								
<b>Meningokokken (MEC4)</b>						MEC4			
<b>Humane Papillo- maviren (HPV)</b>			2 x HPV (0/6 Monate)			3 x HPV <sup>1</sup> (ab vollendetem 12 LJ)			

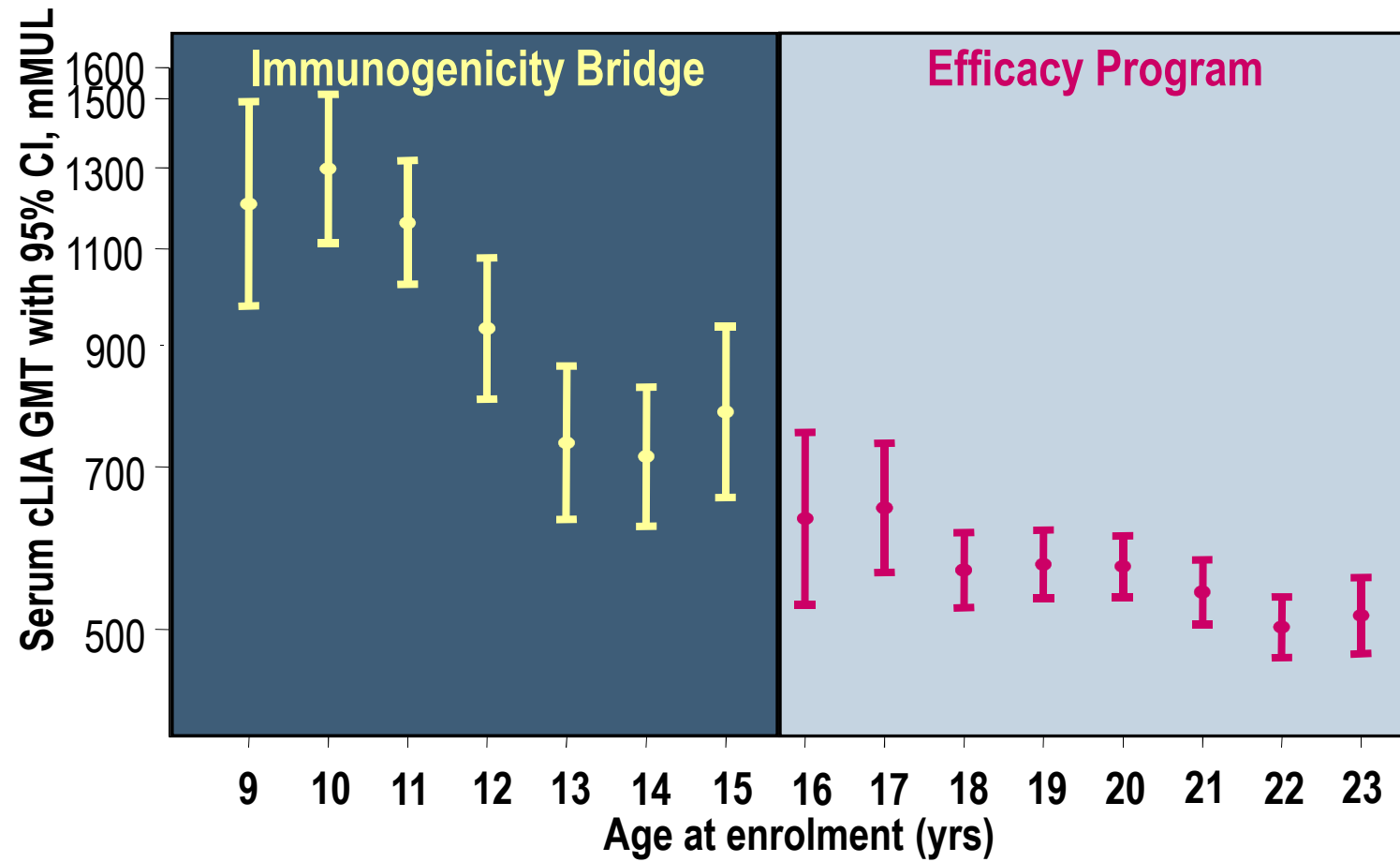
Impfkalender des Gratskinderimpfprogramms für Schulkinder

- ▶ Die 1. Teilimpfung im Herbst 2014 in Schulen (4. Schulstufe)
    - ▶ Die 2. Teilimpfung 2015, 6 Monate nach der Erstimpfung im gleichen Schuljahr
  - ▶ ab 2/ 2014 an den öffentlichen Impfstellen der Bundesländer
    - ▶ kostenlos ab dem vollendeten 9. Lebensjahr bis zum vollendeten 12.
  - ▶ Catch-up Impfungen zum vergünstigten Selbstkostenpreis
    - ▶ Kinder bis zum vollendeten Lebensjahr | 5. Lebensjahr.
  - ▶ öffentlichen Impfungen in einigen Bundesländern im Auftrag der Länder im privaten Bereich
- 

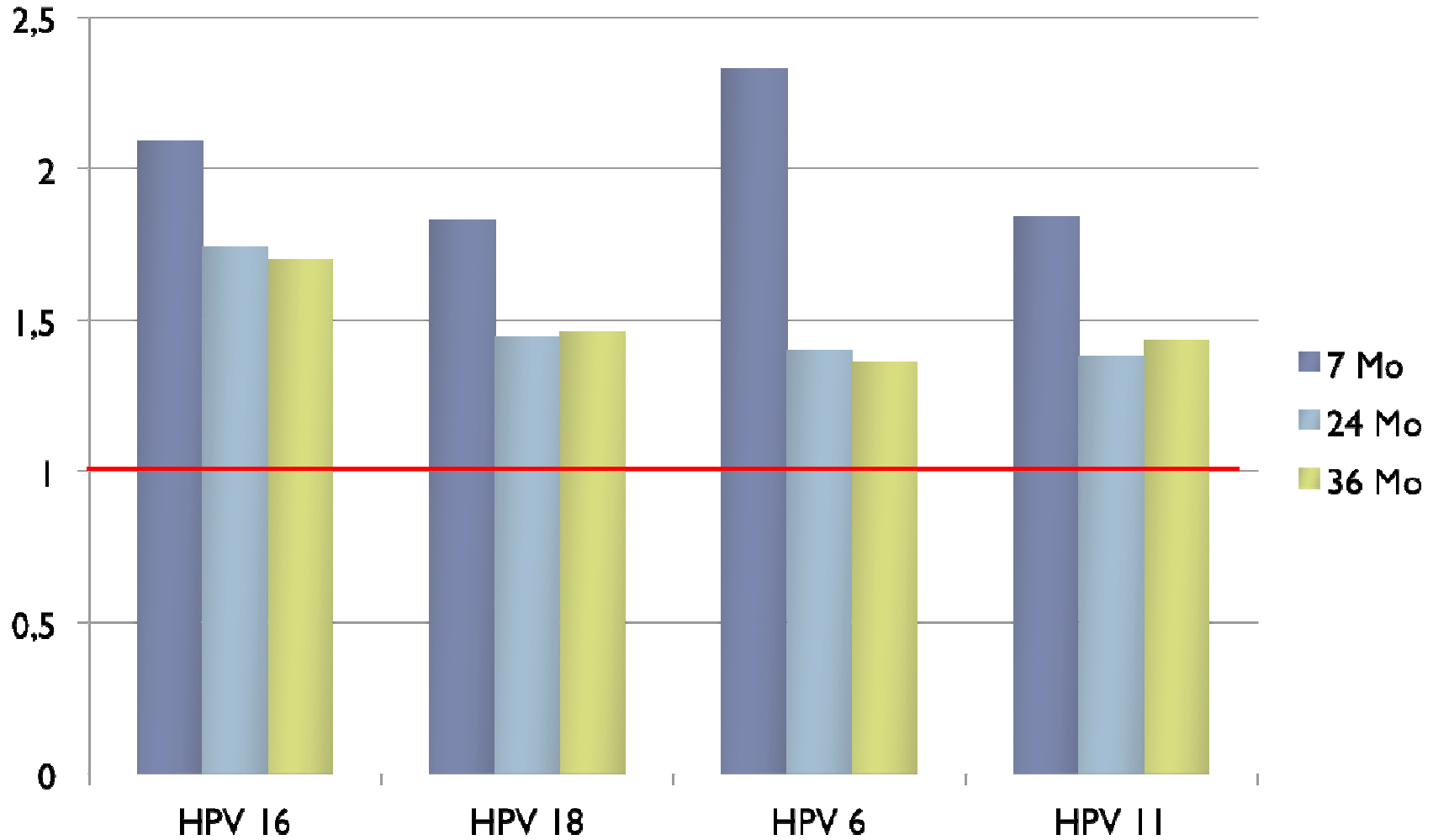


# Immunogenität

Block SL, et al. Pediatrics 2006



# qHPV GMT ratio 9-13 yo 2 dose vs 16-26 yo 3 dose



*Dobson et al. JAMA 2013*

# Global Advisory Committee on Vaccine Safety (GAVCS)<sup>1</sup>



- ▶ **2007:** Reviewed newly licensed qHPV vaccine safety: No safety profile concerns
- ▶ **2008:** Reviewed data related to large-scale use of qHPV vaccine and data on postlicensure surveillance.
- ▶ **2009:** Reviewed postmarketing surveillance studies and 3 reports from independent investigators.
- ▶ **2013:** With more than 175 million doses distributed worldwide, it continues to be reassured by the safety profile of the available HPV vaccines
- ▶ **2014:** GACVS has not found any safety issue that would alter any of the current recommendations for the use of the vaccine.
- ▶ No increase in risk of autoimmune diseases including MS.

<sup>a</sup>Studies focused on syncope, hypersensitivity, anaphylaxis, and central demyelinating diseases.  
qHPV=quadrivalent human papillomavirus; WHO=World Health Organization.

1. World Health Organization (WHO). *Wkly Epidemiol Rec.* 2009;84:37–40. Weekly epidemiological record Relevé épidémiologique hebdomadaire 14 FEBRUARY 2014, 89th YEAR / 14 FÉVRIER 2014, 89e ANNÉE

# Conclusio

---

- ▶ HPV löst viele Erkrankungen aus!
- ▶ HPV Impfprogramme sind wirksam
  - ▶ Durchimpfungsrate
  - ▶ Je jünger desto effektiver
- ▶ Rascher Rückgang von Erkrankungen
- ▶ Österreich
  - ▶ Geschlechtsneutrale Impfung ✓
  - ▶ Impfalter von 9-10 ideal ✓
  - ▶ 2-Dosen nur im Kinderimpfprogramm!
- ▶ Eltern und Schulärzte sind der Schlüssel zum Erfolg!

