



# Epidemiology of HPV Infection

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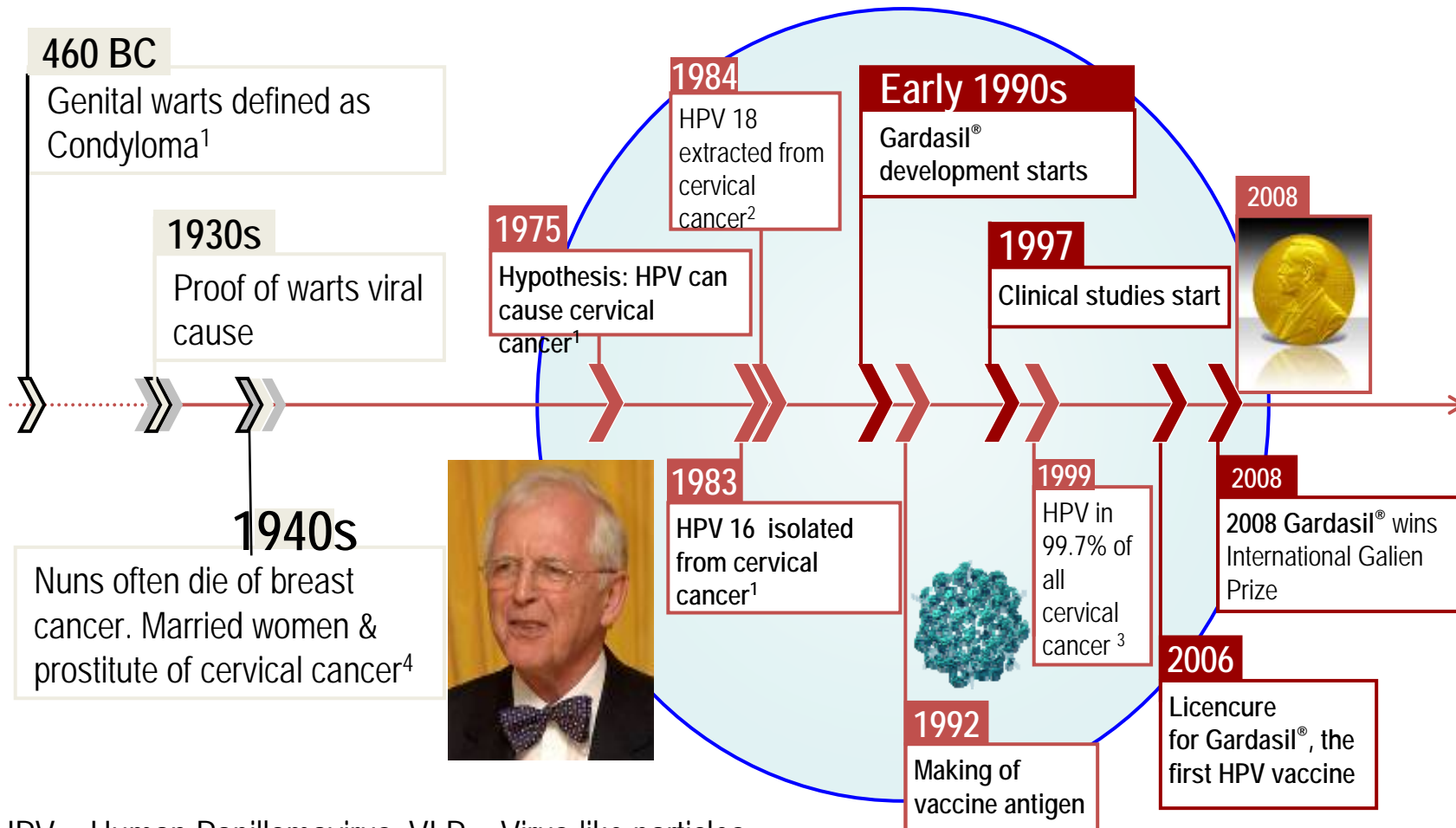
**HSE-HPSC**



# Genital HPVs- Quick Facts

- Most common sexually transmitted infection
- Usually symptom-free and spontaneously cleared
- Causes genital warts, cervical, penile, anal and other genital cancers
- Cervical cancer is a leading cause cancer-related death in women
- Globally and annually
  - > 500,000 women diagnosed cervical cancer; > 250,000 women die from cervical cancer (80% developing countries)
- **Cervical cancer is preventable**

# The HPV story...



HPV = Human Papillomavirus; VLP = Virus-like particles

1. Syrjänen and Syrjänen, Wiley & Sons, Chichester; 2000. p.1-10;
2. Zur Hausen H. Nat Rev Cancer 2002;2:342-350
3. Walboomers J et al. J Pathol 1999; 189: 12-19.
4. Rigoni-Stern A. *Gior Servire Progr Pathol Terap.* 1842;2:507-517.



# HPV Epidemiology- overview

- Reservoir Human
- Transmission Direct contact, usually sexual
- Temporal pattern None
- Communicability Presumed to be high



# HPV Clinical Features

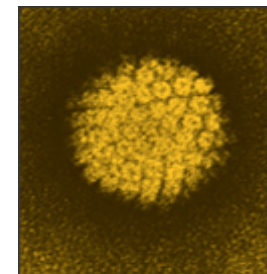
- Most HPV infections are asymptomatic and result in no clinical disease
- Clinical manifestations of HPV infection include:
  - anogenital warts
  - recurrent respiratory papillomatosis
  - cervical cancer precursors (cervical intraepithelial neoplasia, CIN)
  - Cancer (cervical, anal, vaginal, vulvar, penile, and some head and neck cancer)



# Human papillomavirus (HPV)

- DNA viruses
- > 100 different types
- ~ 40 types affect the genital area
- Affect skin and mucous membranes of upper respiratory and anogenital tracts
- Exist in host in active or latent form.

Electron micrograph of human papillomavirus. Courtesy of NCI.  
1986





## Transmission

- Through vaginal, oral or anal sexual intercourse
- Genital contact with an infected person
- Non-sexual transmission from mother to baby in period immediately before and after birth



## Factors Associated with Acquisition of HPV Infection in Women

- Young age (less than 25 years)
- Increasing number of sex partners
- Early age at first sexual intercourse (16 years or younger)
- Male partner has (or has had) multiple sex partners





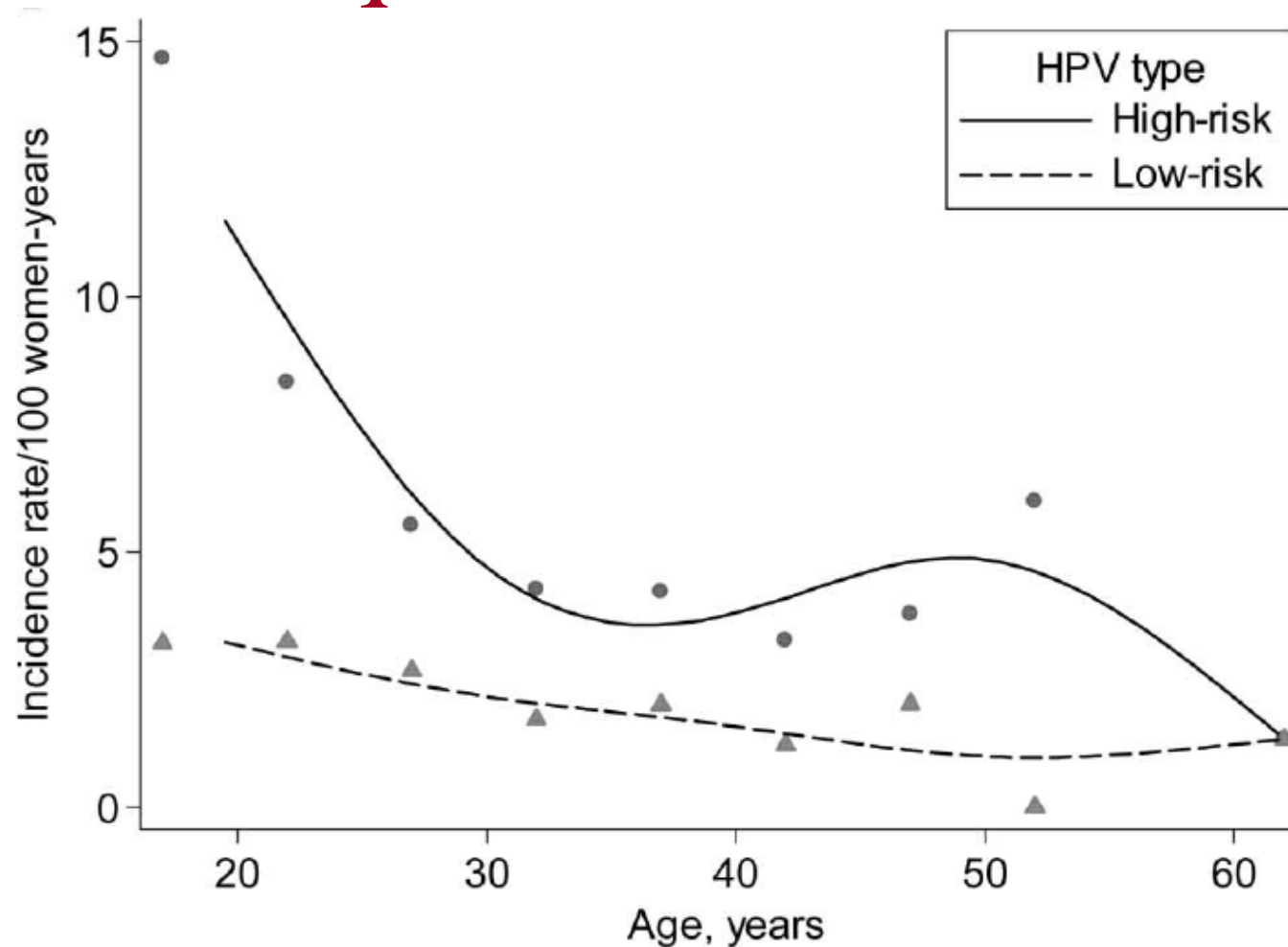
## Clan survey 2003

### Age of sexual onset and number of sexual partners of Irish men and women in lifetime

	Males	Females	Total
<b>Age at first sexual intercourse</b>	%	%	%
Under 14 years	3.4	1.8	2.4
15-16 years	26.8	21.9	23.8
17 years or older	69.8	76.3	73.7
<b>Number of sexual partners</b>			
1-3 people	58.0	71.3	66.1
4-5 people	14.6	13.7	14.1
6 or more people	27.4	15.0	19.9

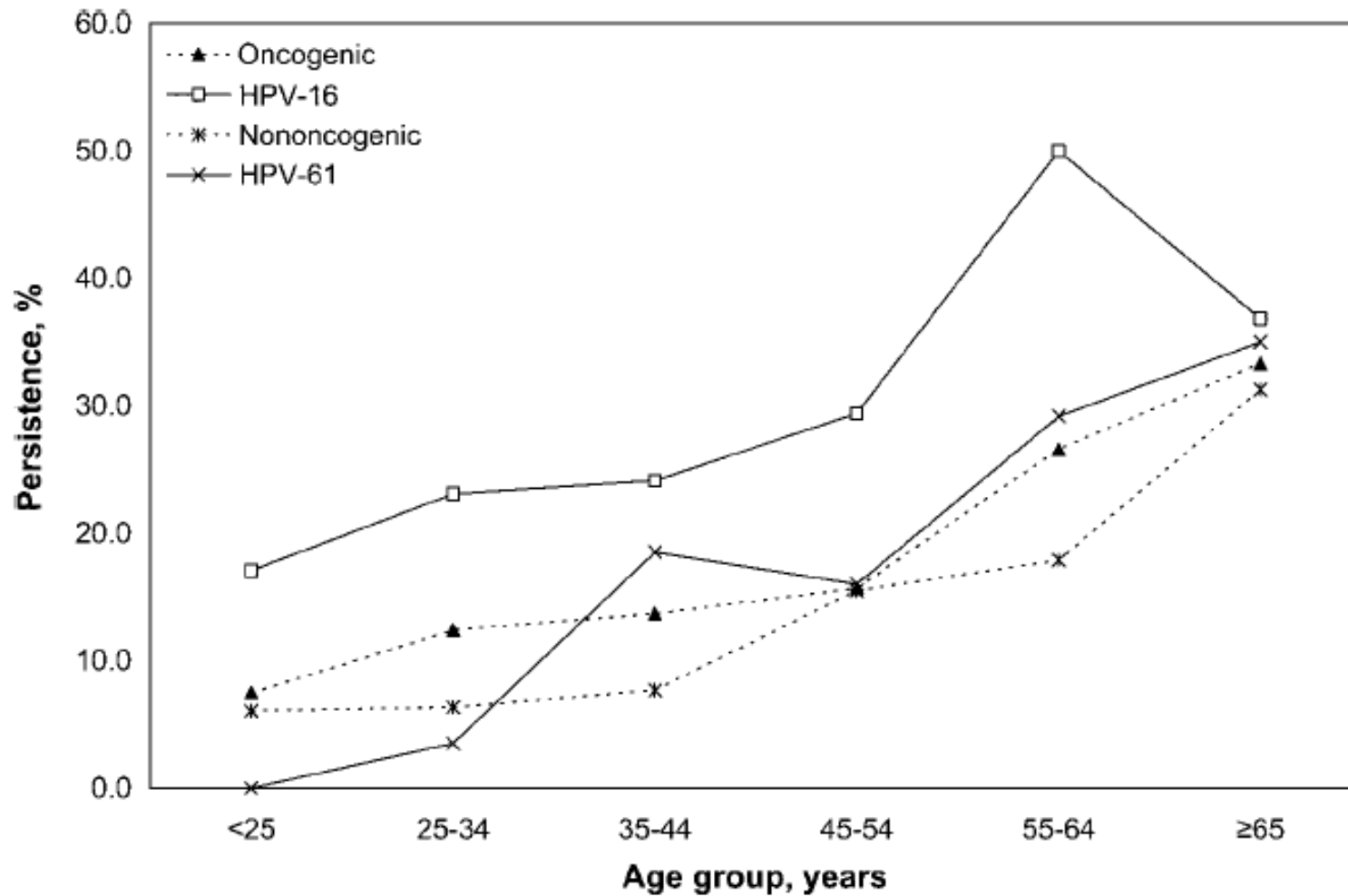


# HPV acquisition

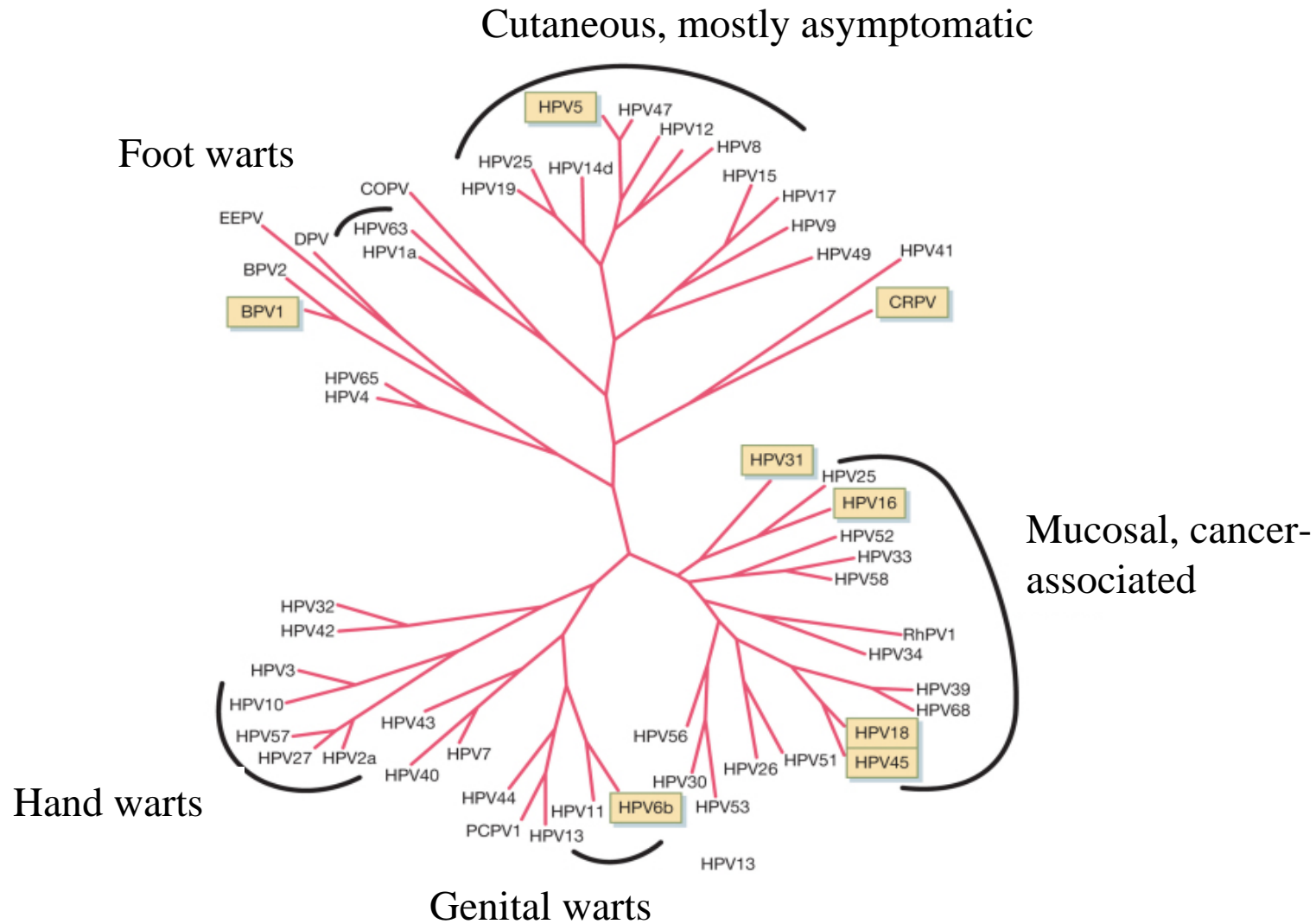




# HPV Persistence



# Taxonomy of papillomaviruses



Source: Vaccines. 5<sup>th</sup> edition. Courtesy de Villiers et al. 2004



# Classification of risk by HPV type

Classification	HPV Types
High-risk (HR) or carcinogenic	<b>16, 18</b> , 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66
Possibly carcinogenic (not proven)	26, 68, 73, 82
Low-risk (LR)	<b>6, 11</b> , 40, 42, 43, 44, 54, 61, 70, 72, 81, 89

Gardasil vaccine includes types **16,18, 6,11** (bolded)



<b>Type of Cancer</b>	<b>Papillomavirus types involved</b>	<b>Percentage of cases HPV-positive (%)</b>
<b>Cervical</b>	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66	>95
<b>Vulval: Basaloid</b>	16, 18	>50
<b>Warty</b>	16, 18	>50
<b>Keratinising</b>	16	<10
<b>Penile: Basaloid</b>	16, 18	>50
<b>Warty</b>	16, 18	>50
<b>Keratinising</b>	16	<10
<b>Vaginal</b>	16,18	>50
<b>Anal</b>	16, 18	>70
<b>Oral cavity and tonsils</b>	16, 18, 33	~25
<b>Nail bed</b>	16	~75



# Global burden of HPV related diseases



## HPV distribution by geographical region (%)

	HPV 16 (%)	HR HPV (other than HPV16) (%)	LR HPV (%)
Sub-Saharan Africa	3.2	14.6	13.6
Asia	1.7	3.7	4.2
South America	2.9	6.8	6.0
Europe	1.5	2.3	1.9

Source: Parkin et al. Int J Cancer 2006.





## Global Burden of High Risk (HR) HPV Disease

Site	AF (%)	Attributable cancers	% all cancers
Cervix	100	492,800	4.5
Penis	40	10,500	0.1
Vulva, vagina	40	16,000	0.2
Anus	90	27,400	0.2
Mouth	3	8,200	0.1
Oro pharynx	12	6,300	0.1
<b>All sites</b>		<b>561,200</b>	<b>5.2</b>



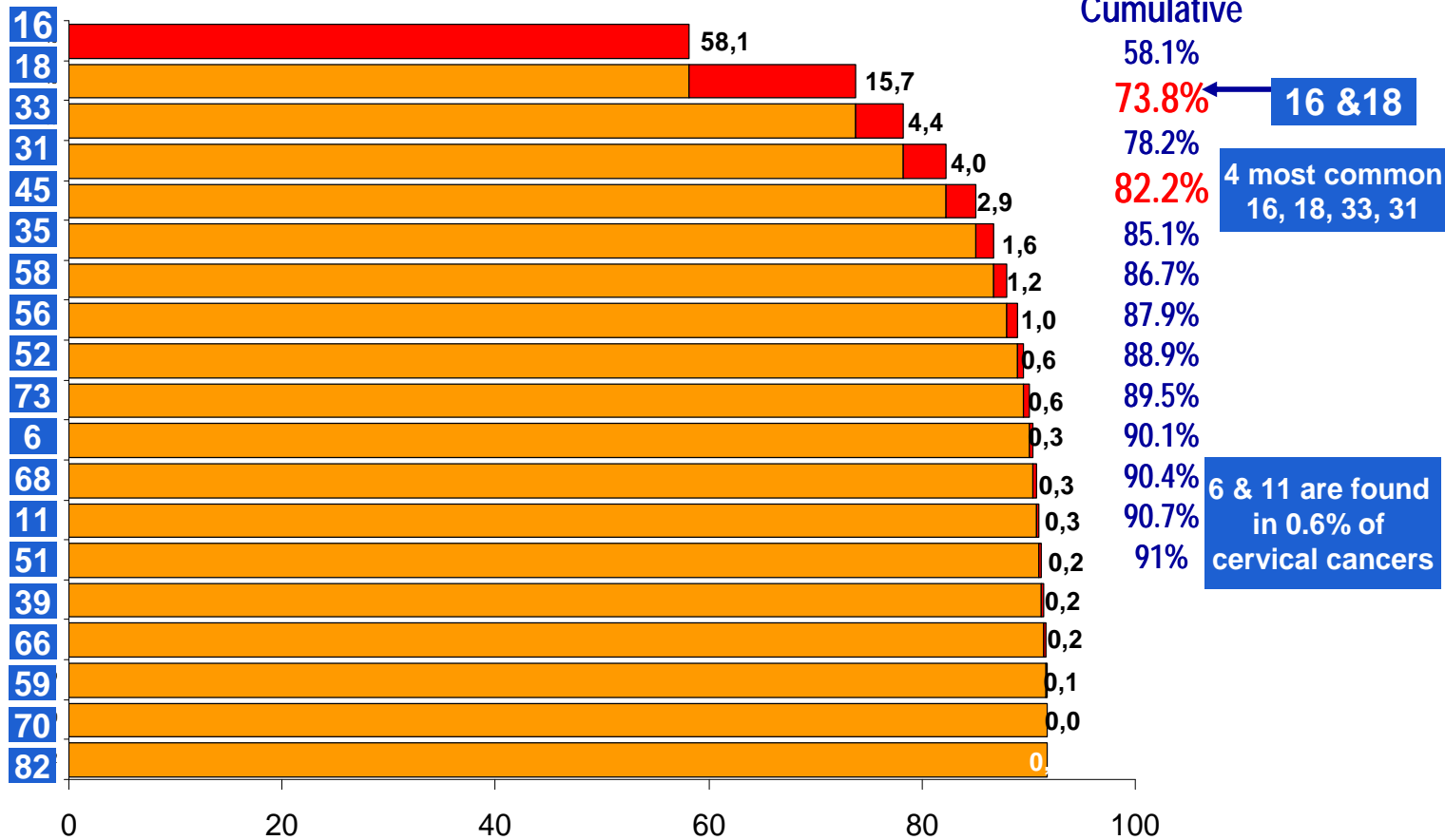
## Proportion of cancers attributable to HPV

Cervical cancer	100%
Cancer of vagina	91–94%
Cancer of anus	88–94%
Cancer of vulva	40%
Cancer of penis	40%
Cancer of pharynx	25%
Cancer of oral cavity	10%



## Human Papillomavirus types 6,11,16,18 in 73.8% of Cervical Cancers in Europe<sup>1</sup>

HPV type prevalence in Cervical carcinomas\* in Europe (% of all HPV+ cases treated)



\*Squamous cell carcinomas and Adenocarcinomas

N=4737 cases

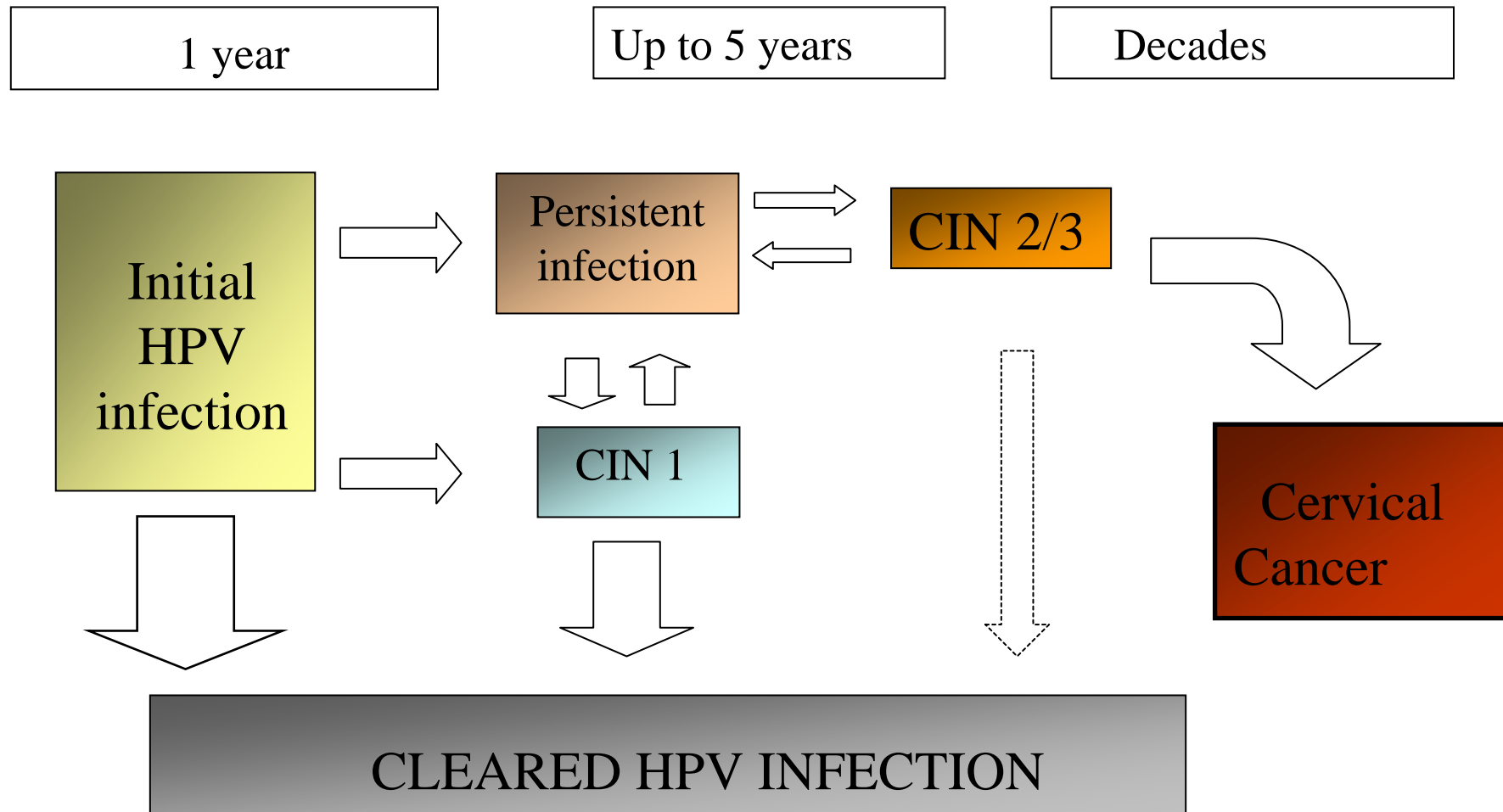
1:Smith JS, Lindsay L, Hoots B et al. Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: A meta-analysis update. *Int J Cancer* 2007;April.



# HPV – Cancer of the Cervix



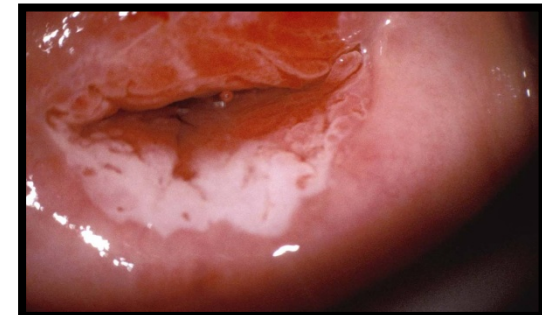
# HPV infection- natural history





# Development of Cervical Cancer

- **Cervical Intraepithelial Neoplasia (CIN) 1**
  - abnormal cells occupy lower third of epithelium
  
- **Cervical Intraepithelial Neoplasia (CIN) 2/3**
  - abnormal cells occupy lower two thirds to full thickness of epithelium





# Burden of Disease

In Ireland



# Cervical cancer in Ireland



- ~ 72 women deaths from cervical cancer annuallyear
  - Mean age at death; 56 years
  - Mean age at diagnosis; 44 years
- ~3,100 women living with cervical cancer <sup>1</sup>
- **In 2007 there were:**
  - **286 Cervical cancer cases** <sup>2</sup>
  - 59% of which were under the age of 39
  - **81 Cervical cancer deaths** <sup>2</sup>

1. National Cancer Registry Ireland, (unpublished analysis, 2007).

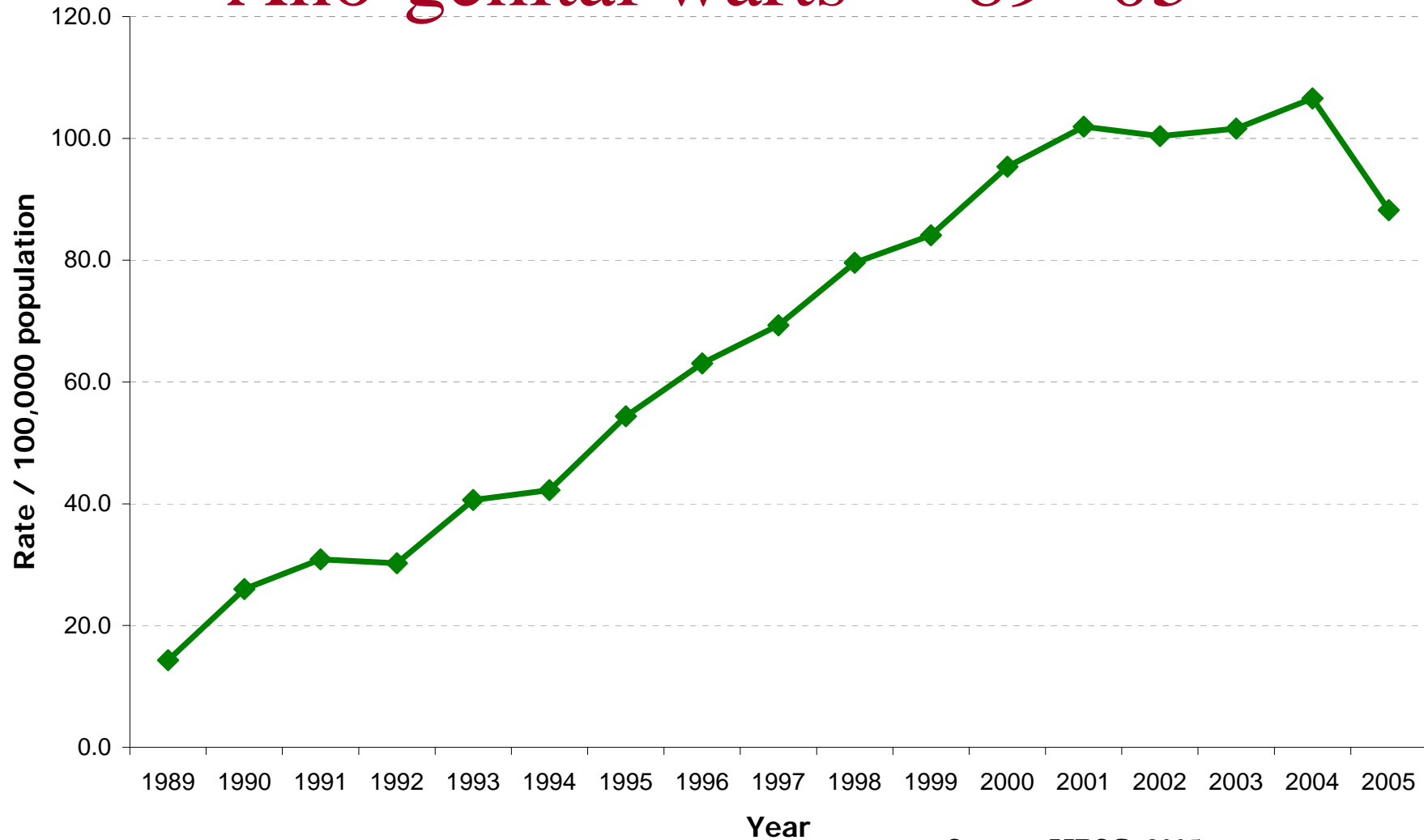
Incidence and mortality for invasive cervical cancer in Ireland. 1994-2005.

2. National Cancer Registry Ireland, 2010: data on file





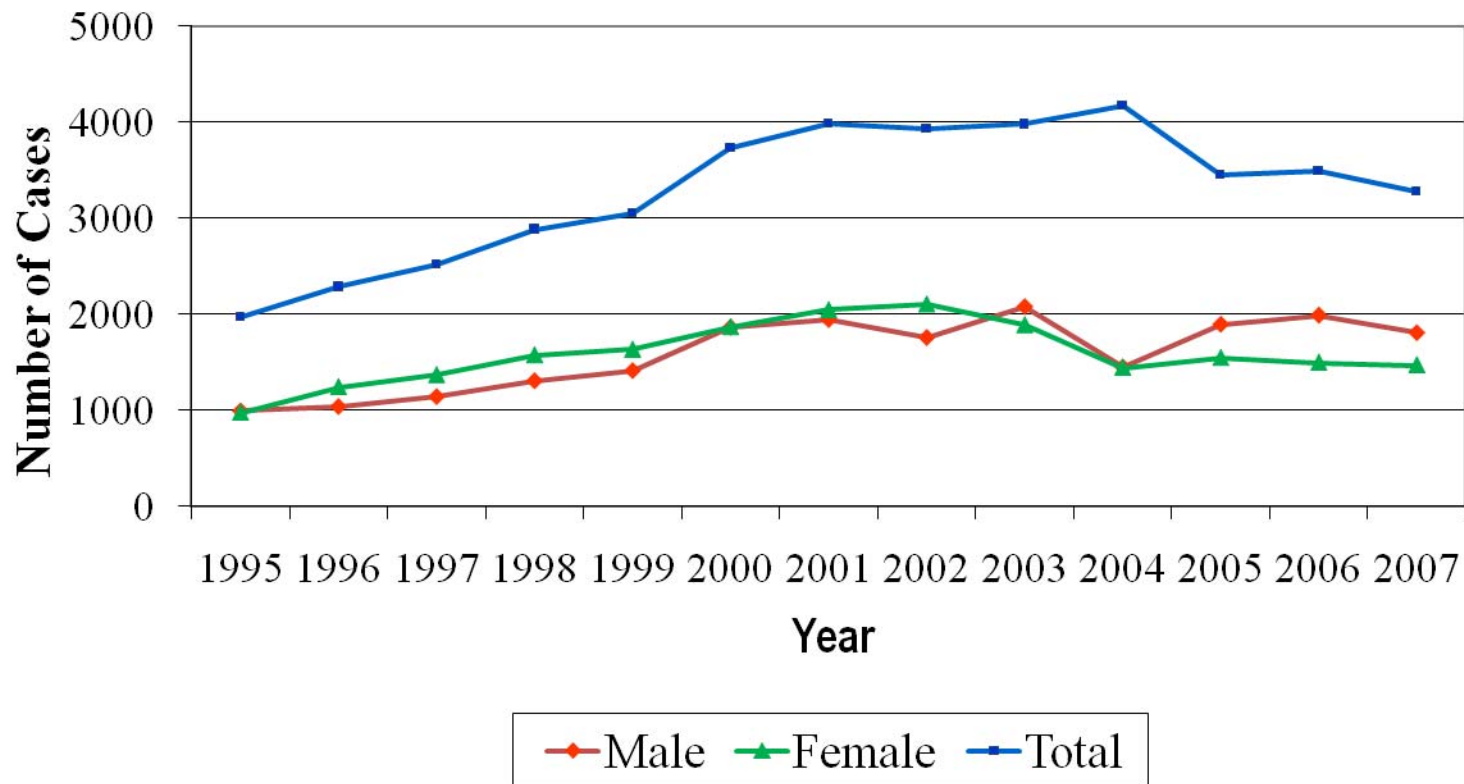
# Ano-genital warts – '89-'05



Source: HPSC, 2005

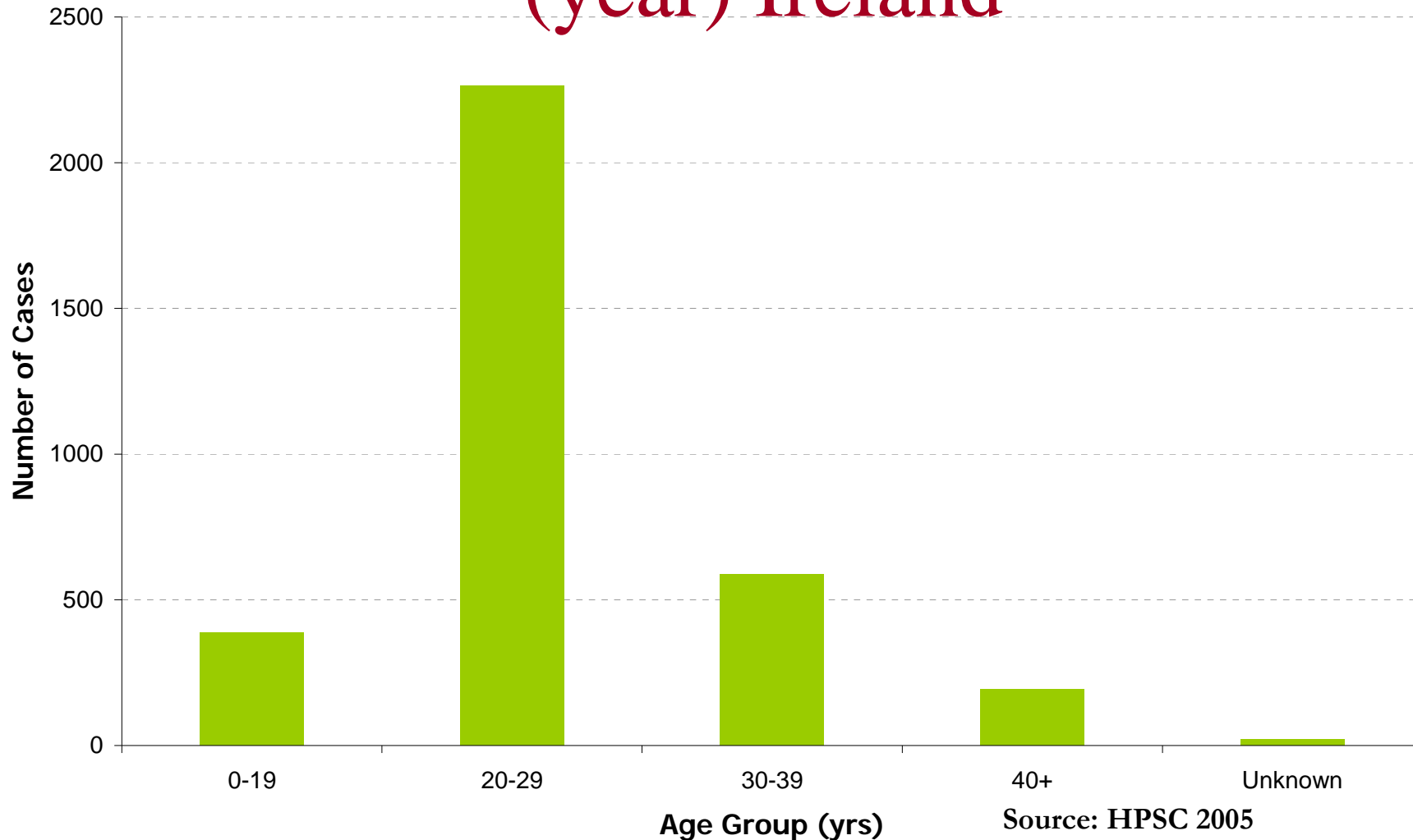


# Anogenital Warts, by gender, 1995-2007, Ireland



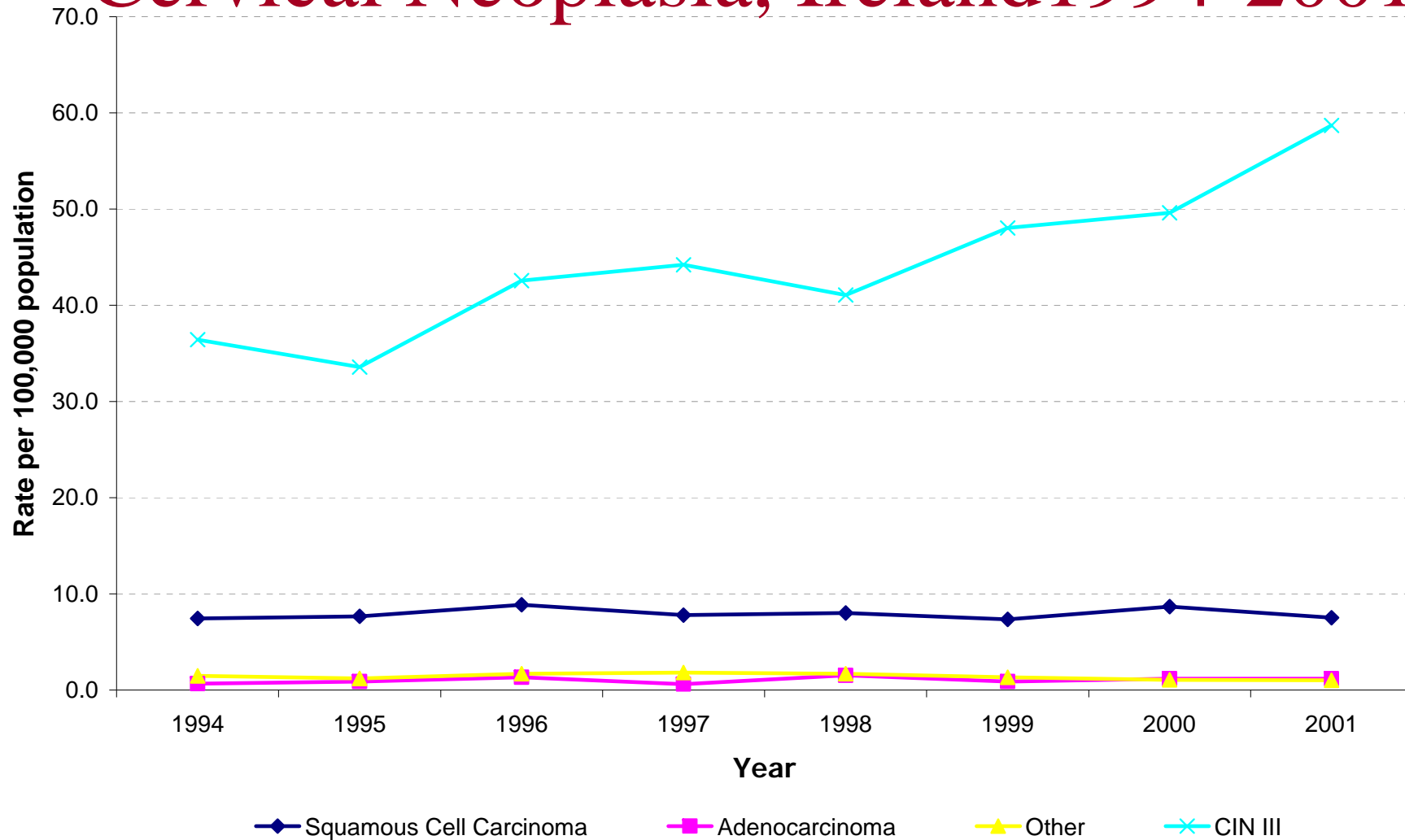


# Ano –genital warts by age group, (year) Ireland





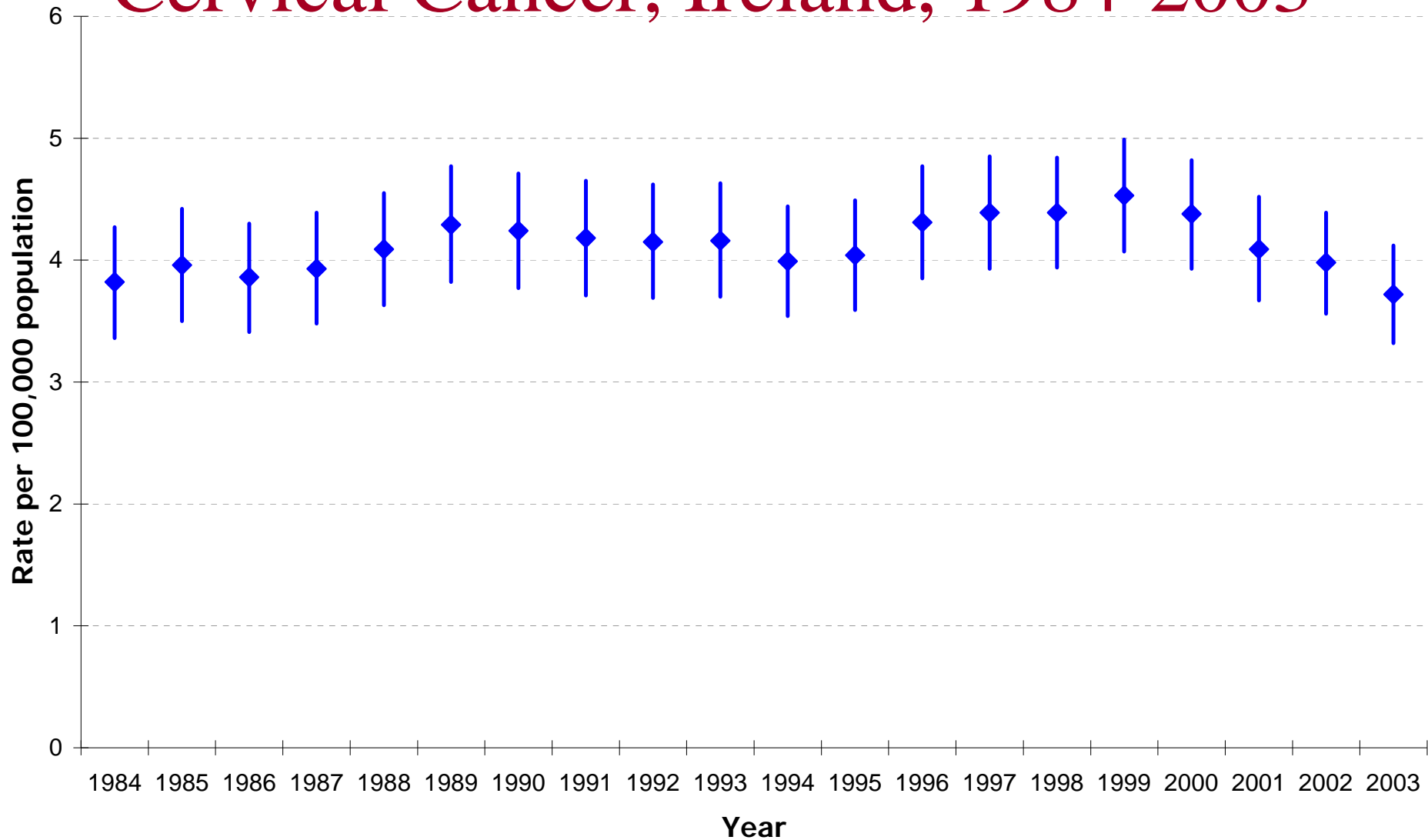
# Cervical Neoplasia, Ireland 1994-2001



Source: Irish Cancer Registry



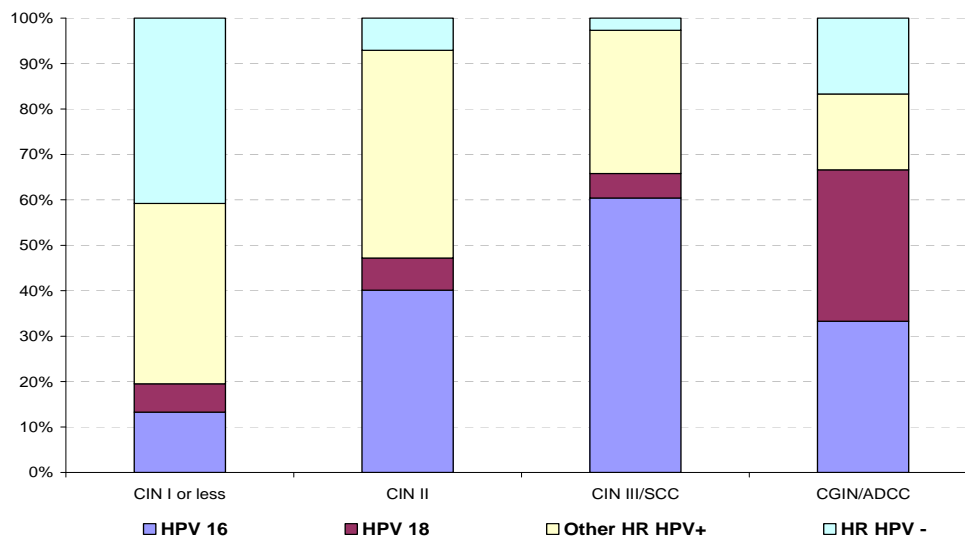
# Cervical Cancer, Ireland, 1984-2003



Source: Irish Cancer Registry

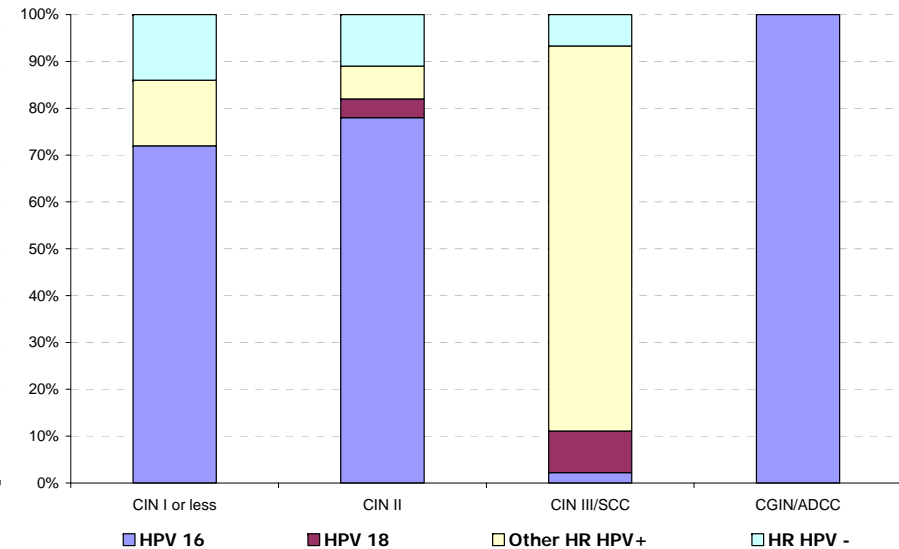


# Prevalence of High Risk HPV by histology



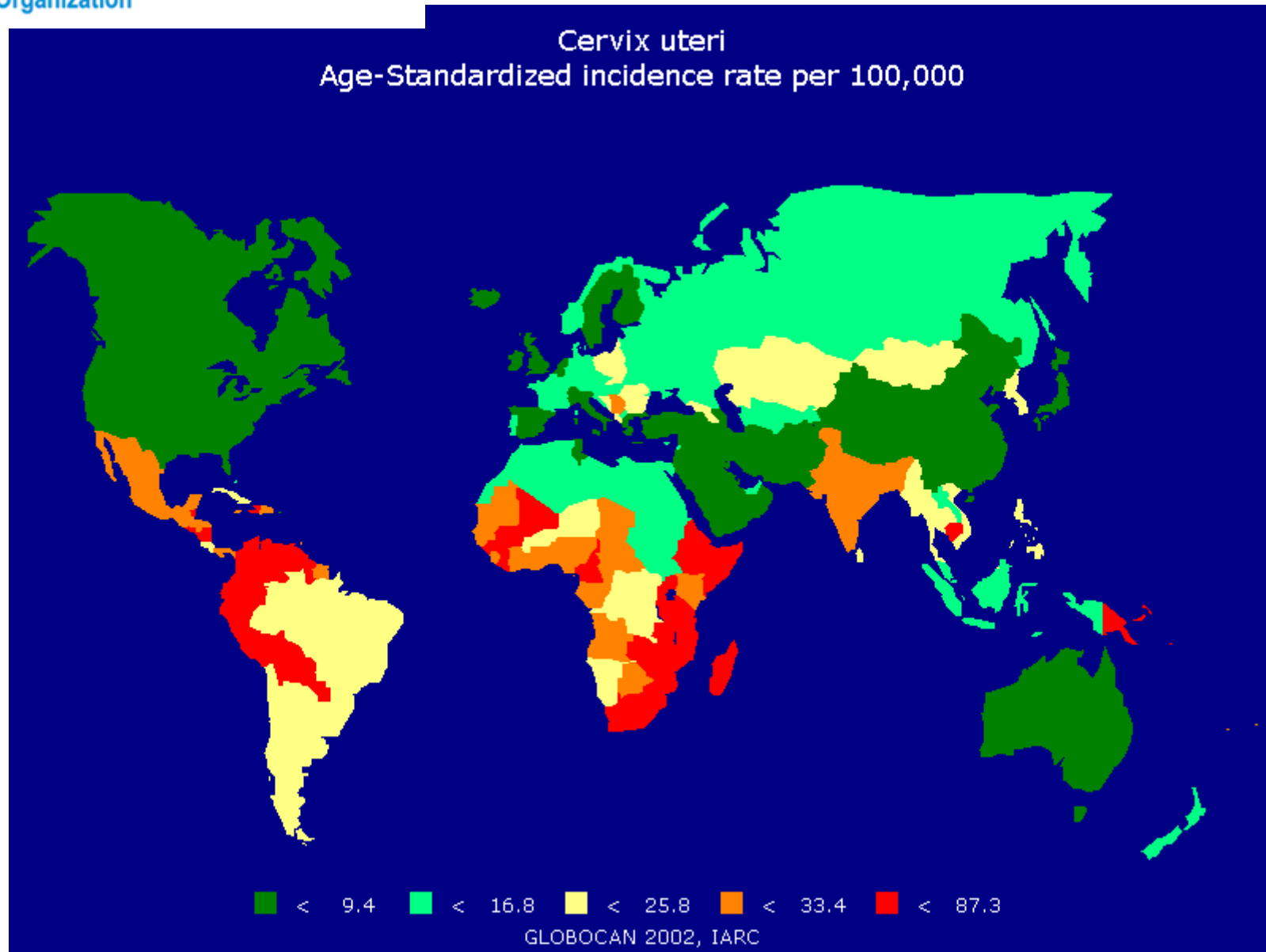
**Kitchener et al**

**n = 24,510**



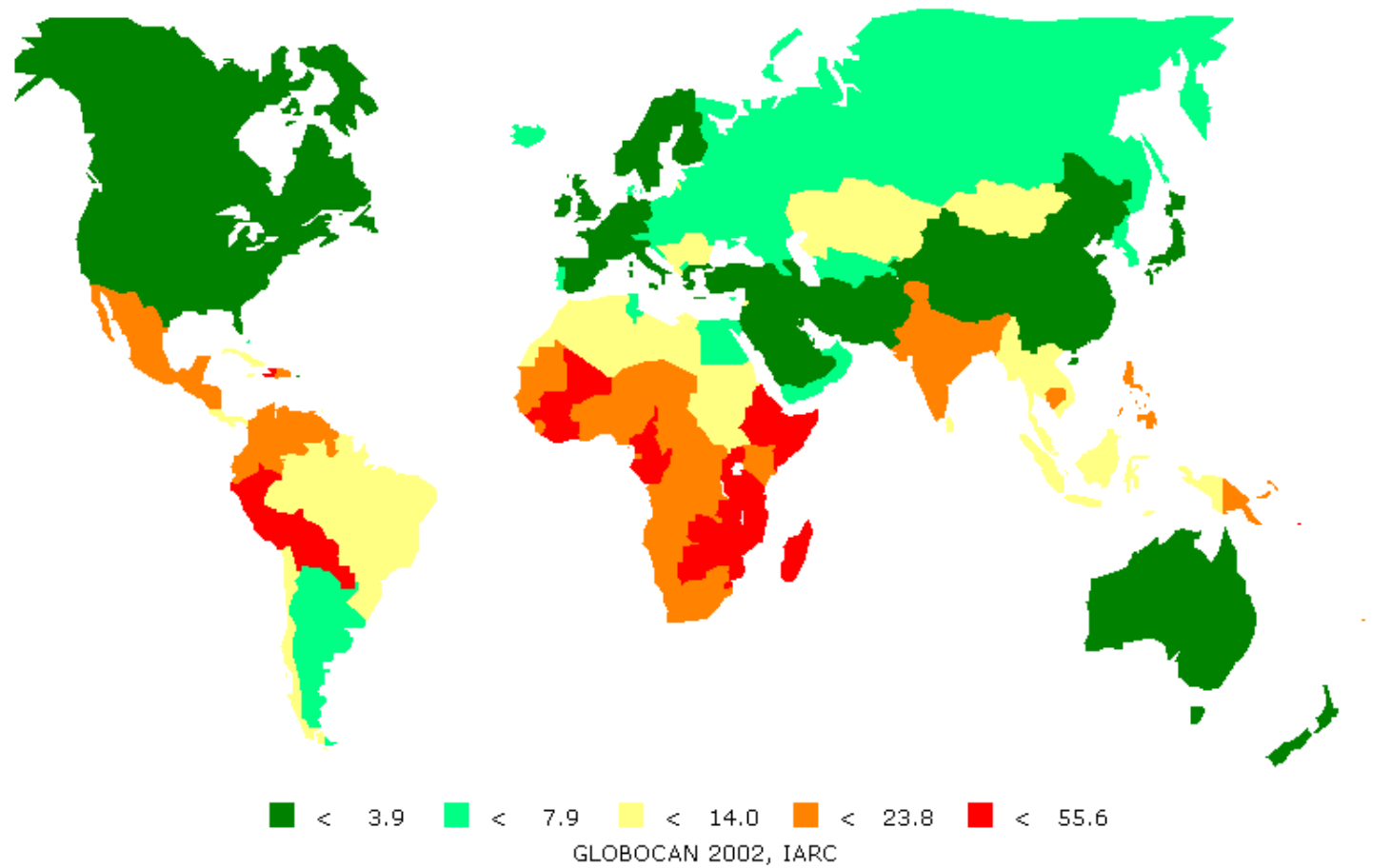
**Murphy et al**

**n = 187**



Source: International Agency for Research on Cancer. Globan 2002

Cervix uteri  
Age-Standardized mortality rate per 100,000



Source: International Agency for Research on Cancer. Globan 2002





## Conclusions

- HPV causes substantial morbidity and mortality
- Early prevention and protection is key to cancer control
- Vaccines provide opportunity to prevent disease
- Future developments?
  - New vaccines with extended coverage or usage (males)