



Etiology of HPV infections and other related cancers

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Disclosure and Disclaimer

Received travel and research grants from

- GSK
- MSD
- Adcock Ingram
- Bayer
- Novo Nordisk
- Sanofi

Drug Research Trials

- Bayer - 2 trials
- Pfizer – 1 trial
- GSK – 1 trial

Advisory Boards

- GSK ,MSD,Adcock Ingram,Bayer,Novo Nordisk
- The content of this presentation at this scientific meeting is the view of the presenter based on clinical expertise, research, and experience

Agenda

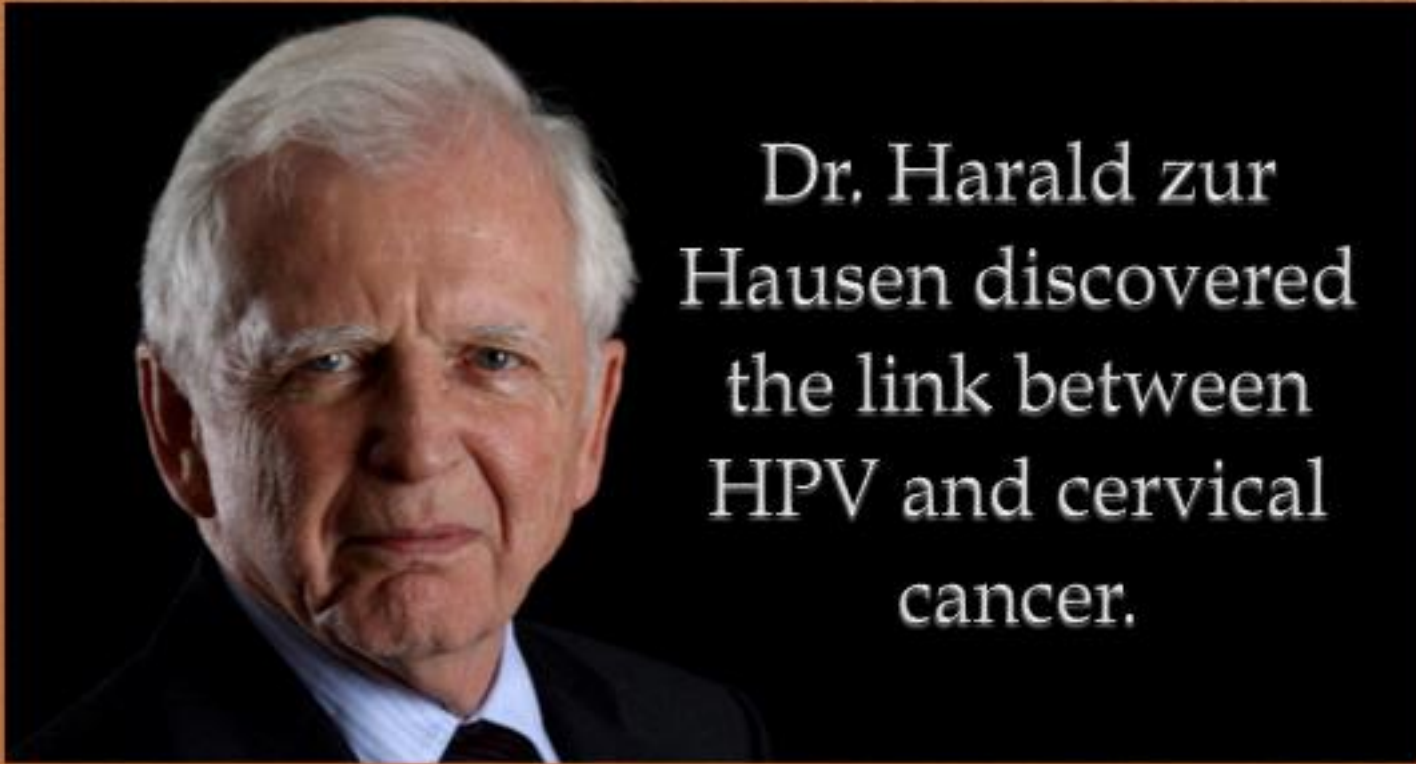
HPV disease,

SA epidemiology,

HPV screening

Prevention

type of vaccines available.



In 1976, he published the hypothesis that [human papillomavirus](#) plays an important role in the cause of [cervical cancer](#).

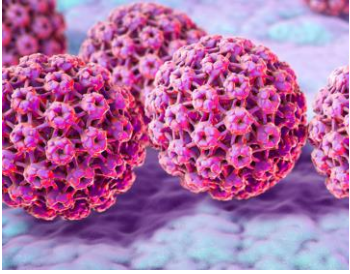
Success story of medicine

Nobel Price for Medicine 2008
to Harald zur Hausen...

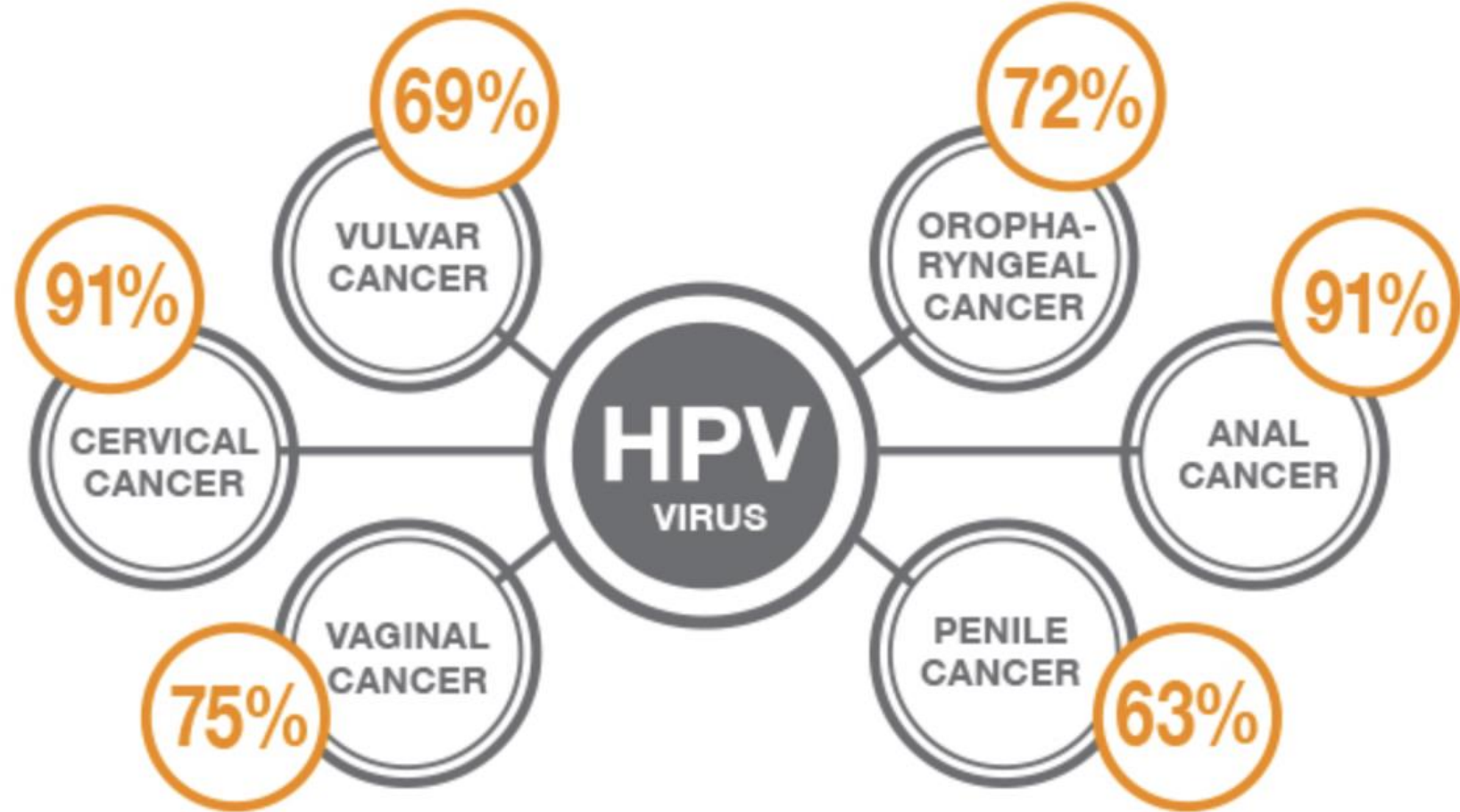
...for the proof that cervical cancer is induced by Human Papillomaviruses (HPV)

1983 he identified
HPV 16 and HPV 18

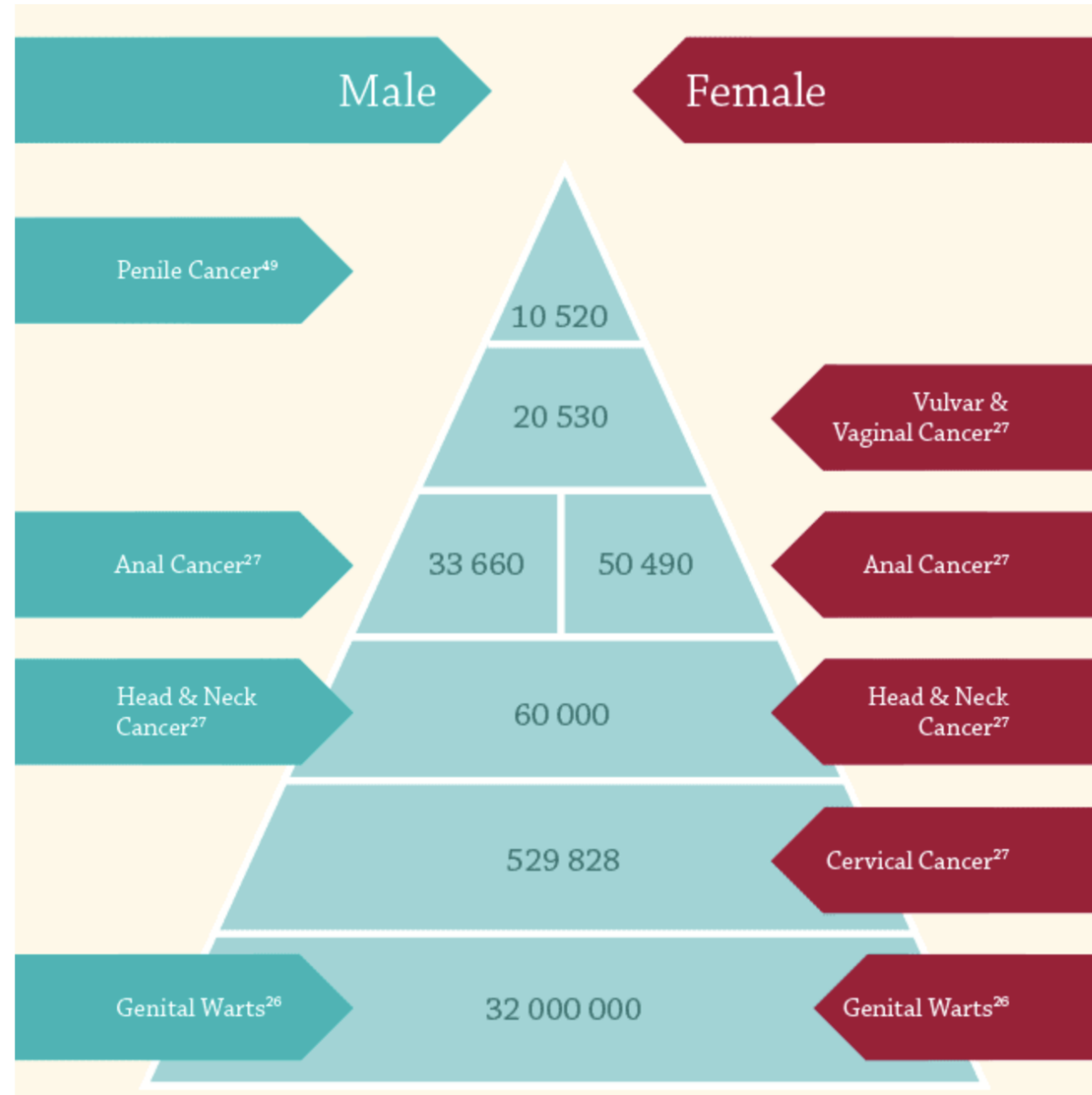




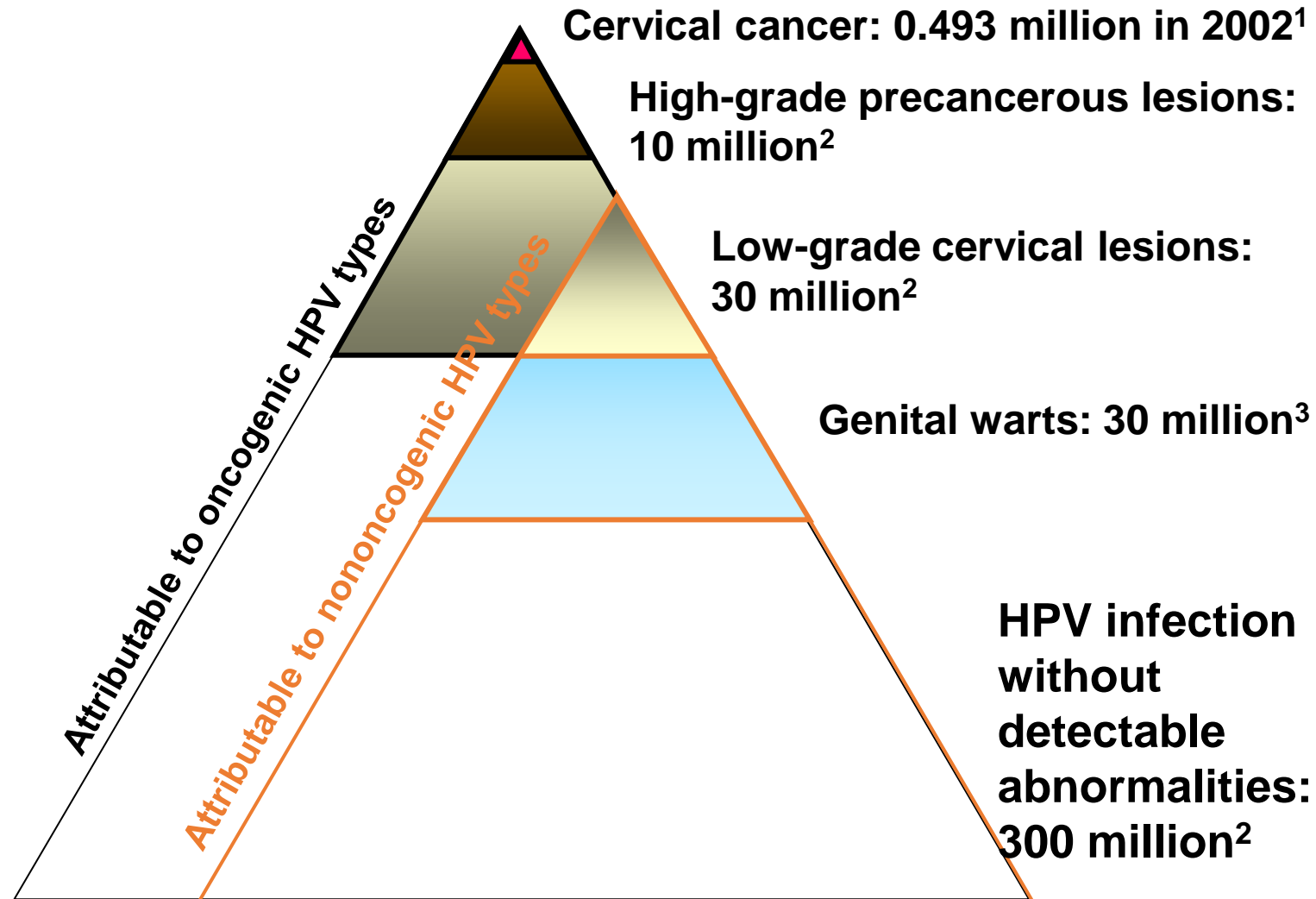
HPV CAUSES SIX TYPES OF CANCER



Estimated annual new HPV-related disease cases among males and females globally ^{14, 16, 27}

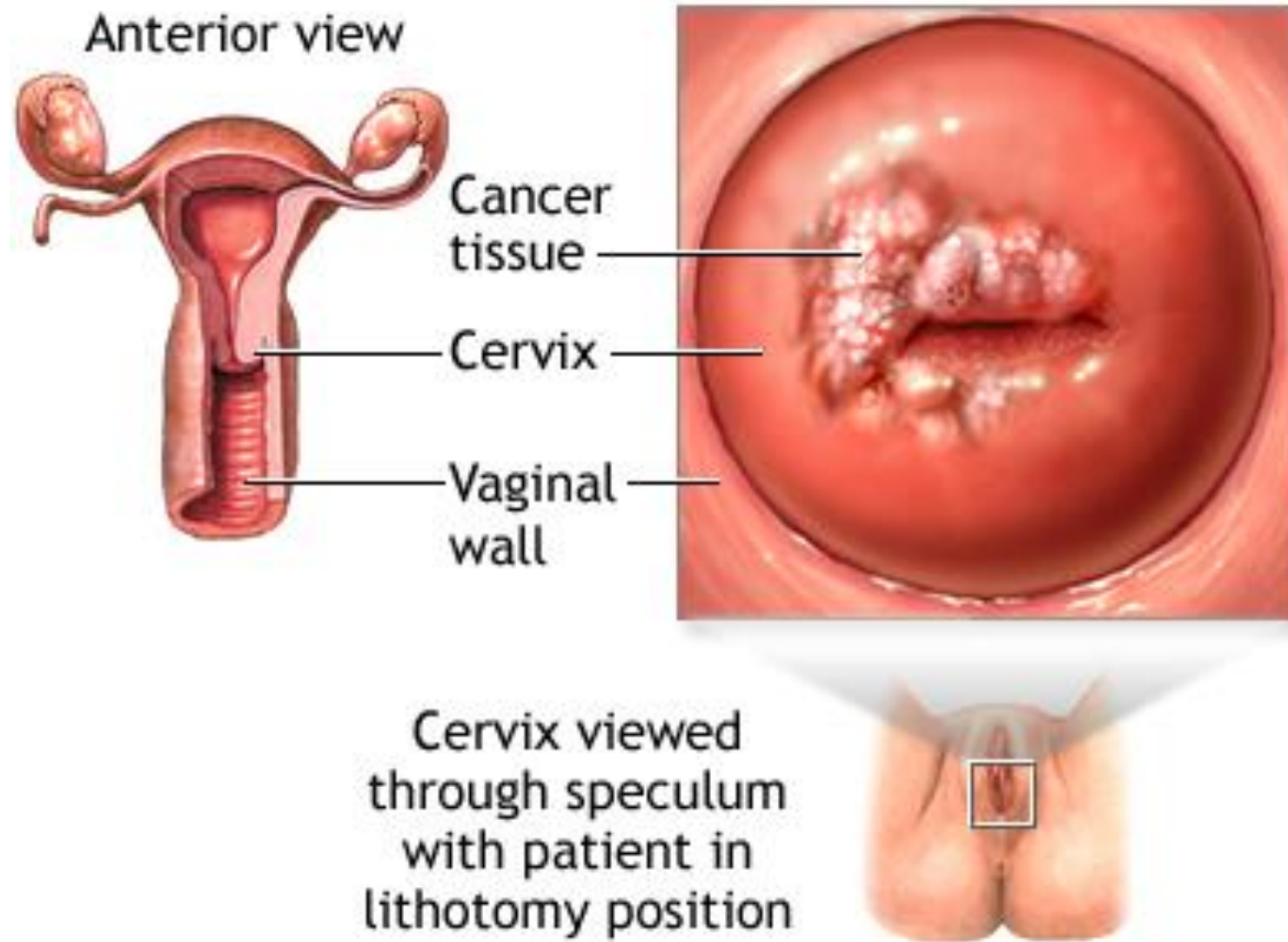


Estimated World Burden of HPV-Related Diagnoses

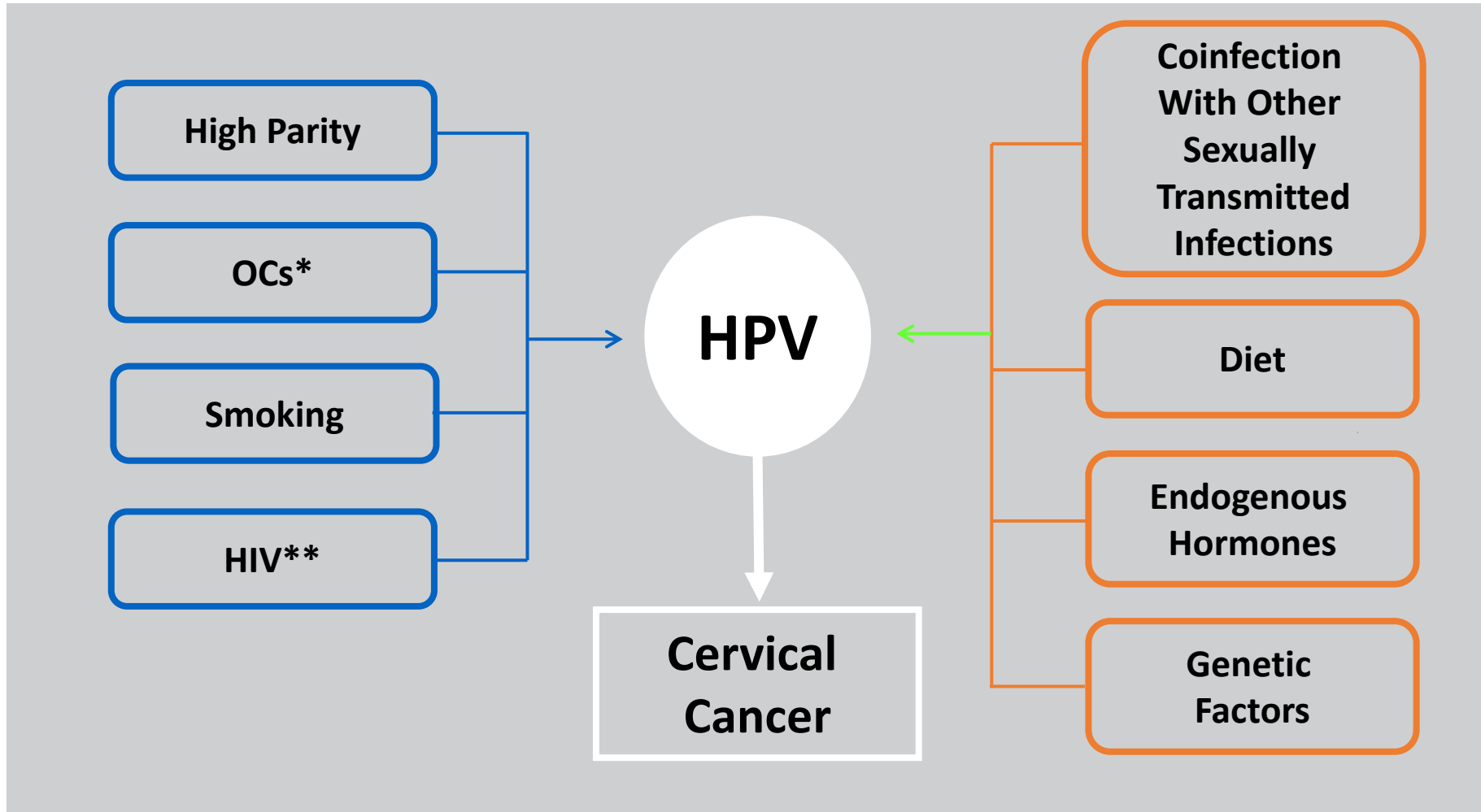


1. Parkin DM, Bray F, Ferlay J, Pisani P. *CA Cancer J Clin.* 2005;55:74–108. 2. World Health Organization. Geneva, Switzerland: World Health Organization; 1999:1–22. 3. World Health Organization. WHO Office of Information. *WHO Features.* 1990;152:1–6.

Cervical cancer



Established and **Potential** Cofactors Involved in HPV Carcinogenesis



*OCs = oral contraceptives

**HIV = human immunodeficiency virus

HPV AND CERVICAL CANCER

Putting risk into perspective

- Risk of cervical cancer if HPV 16 (+) positive compared to HPV 16 (-) is **434**
- Risk of lung cancer in U.S. white male smoker compared to non-smoker is only **8**
- **Risk of breast cancer with HRT in Women's Health Initiative only 1.3**

Risk of HPV infection

- HPV infections are very common
- The cumulative risk of acquiring cervical HPV infection in women with only one sexual partner is **46%** (3 years after first sexual encounter)¹
- The risk of oncogenic HPV infection is high even after first intercourse and **continues throughout** a woman's sexually active lifetime²⁻⁴
- Up to 80% of women will acquire an HPV infection in their lifetime⁵⁻⁷
 - While most infections are cleared, women are less likely to clear infections as they get older⁸

1. Collins S, et al. *Br J Obstet Gynaecol* 2002; **109**:96–98; 2. Schiffman M, et al. *J Natl Cancer Inst* 2003; **31**:14–19;
3. Sellors JW, et al. *CMAJ* 2003; **168**:421–425; 4. Dunne EF, et al. *JAMA* 2007; **297**:813–819;
5. Brown DR, et al. *J Infect Dis* 2005; **191**:182–192; 6. Koutsky L, et al. *Am J Med* 1997; **102**:3–8;
7. Bosch FX, et al. *J Natl Cancer Inst Monogr* 2003; **31**:3–13; 8. Castle PE, et al. *J Infect Dis* 2005; **19**:1808–1816.

HPV Transmission and Acquisition

Sexual contact

- Through sexual intercourse
- Genital–genital, manual–genital, oral–genital
- Proper condom use may help reduce the risk, but is not fully protective against infection.

Nonsexual routes

- Mother to newborn



ICO/IARC Information Centre on HPV and Cancer

South Africa

Human Papillomavirus and Related Cancers, Fact Sheet 2021 (2021-10-22)



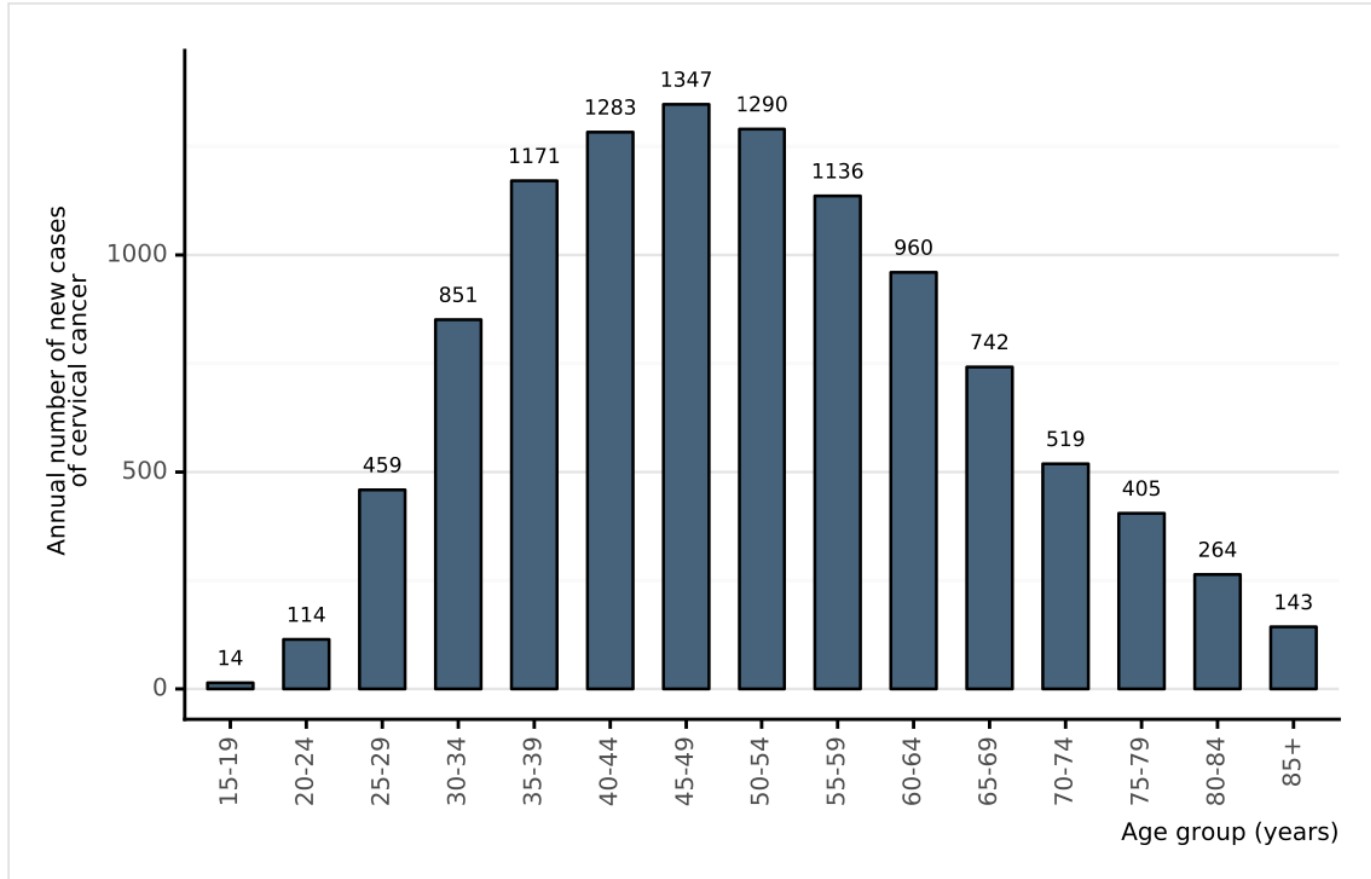
Key Stats.

About **5,870 cervical cancer deaths** occur annually in **South Africa** are diagnosed **annually** (estimations for 2020).

Cervical cancer **ranks*** as the **1st leading cause of cancer deaths** of female cancer deaths in **South Africa**.

Cervical cancer is the **1st leading cause of cancer deaths** in **women aged 15 to 44 years** in **South Africa**.

Figure 9: Annual number of new cases of cervical cancer in South Africa (estimates for 2020)



Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

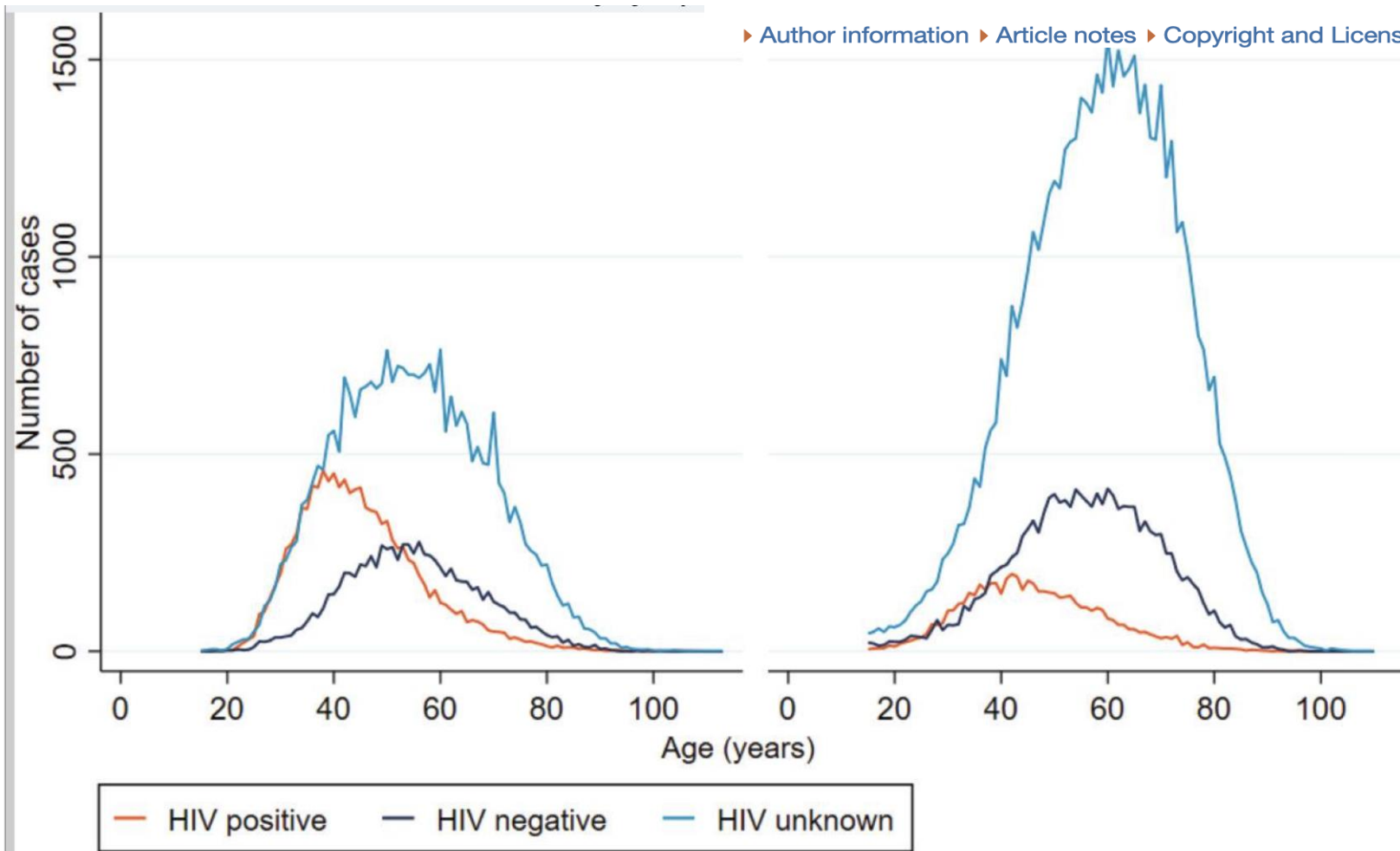
Data Sources:

Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Cervical cancer in women living in South Africa: a record linkage study of the National Health Laboratory Service and the National Cancer Registry

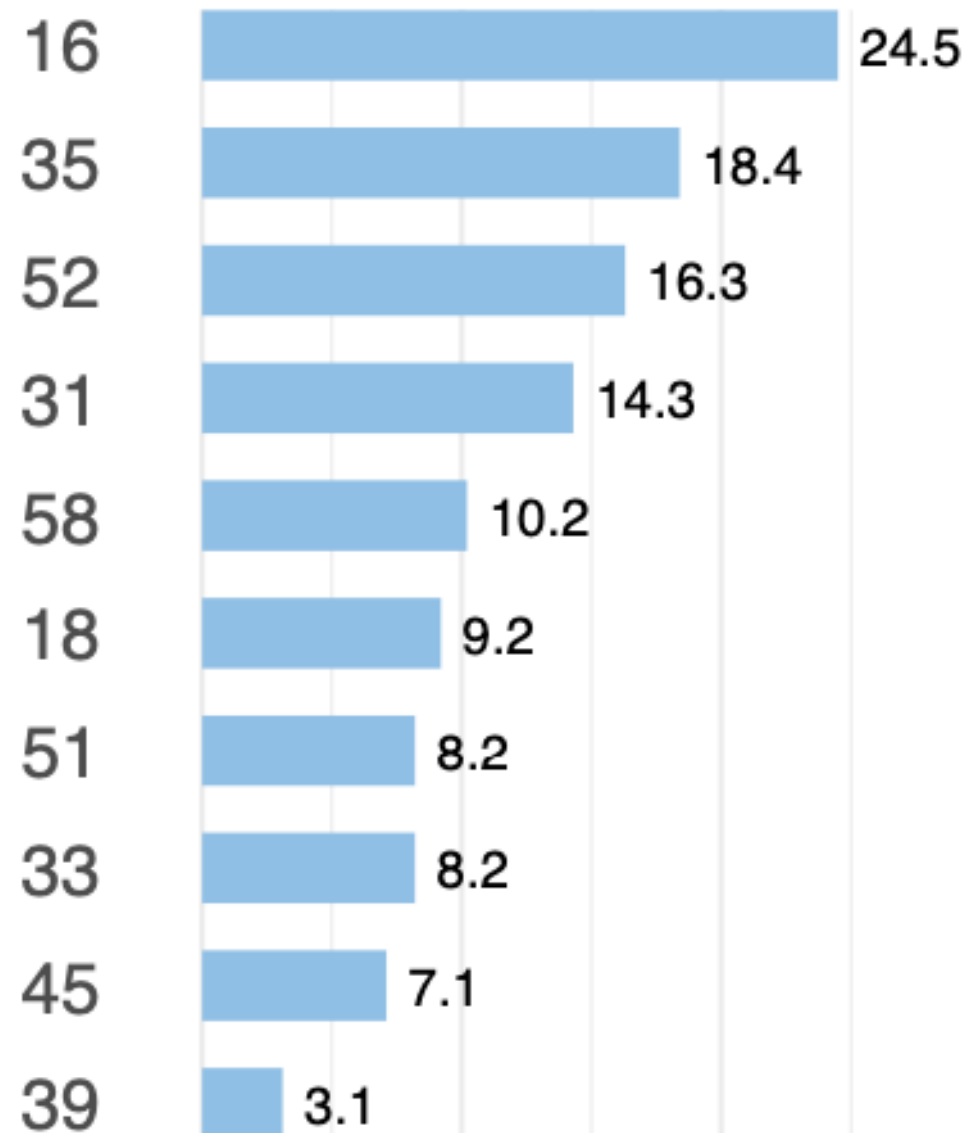
[Tafadzwa Dhokotera](#),^{1,2,3} [Serra Asangbeh](#),^{2,3} [Julia Bohlius](#),^{3,4,5} [Elvira Singh](#),^{1,6} [Matthias Egger](#),^{5,7,8} [Eliane Rohner](#),⁵ [Jabulani Ncayiyana](#),^{6,9} [Gary M Clifford](#),¹⁰ [Victor Olago](#),^{1,6} and [Mazvita Sengayi-Muchenetzi](#)^{1,6,11}

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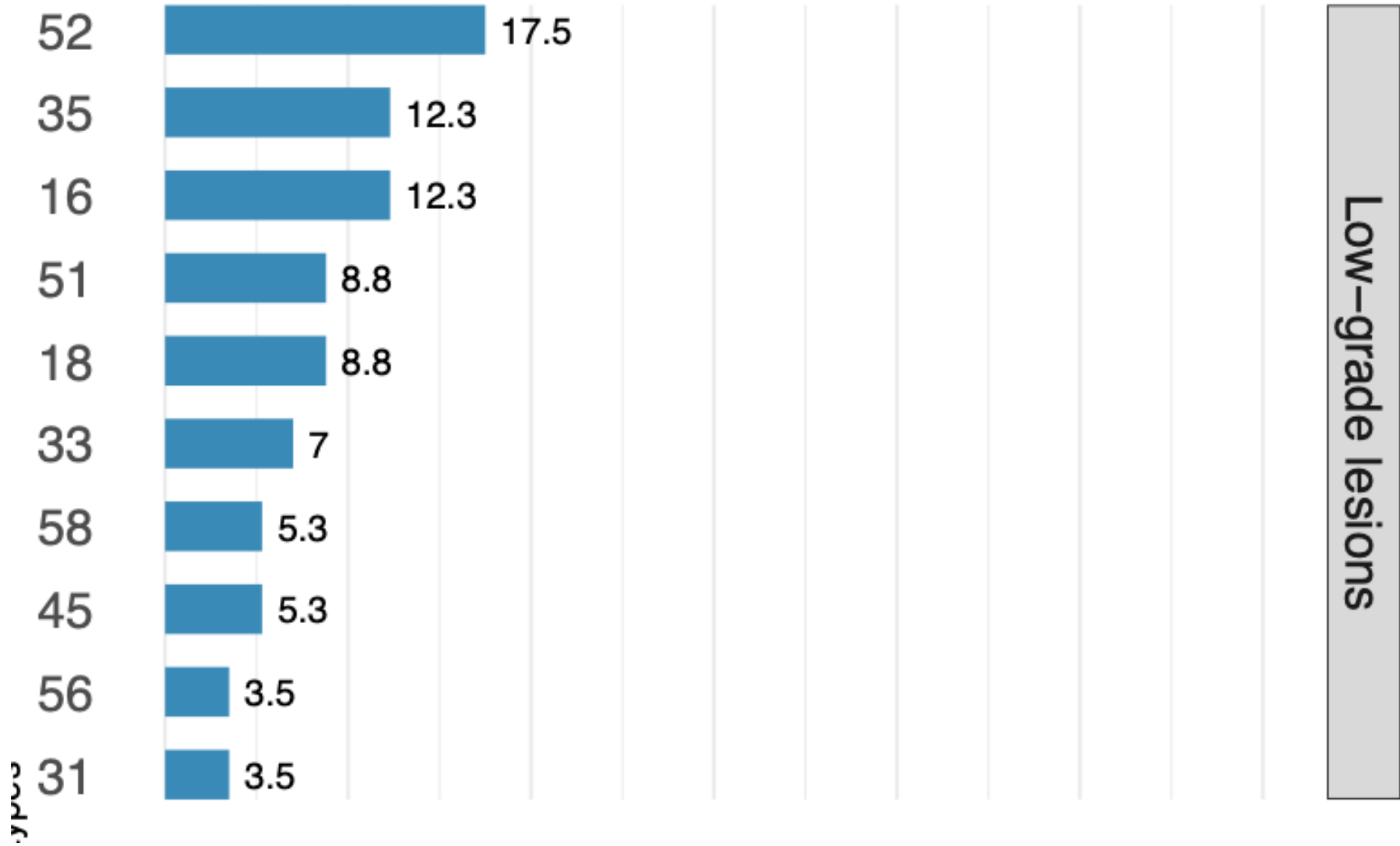


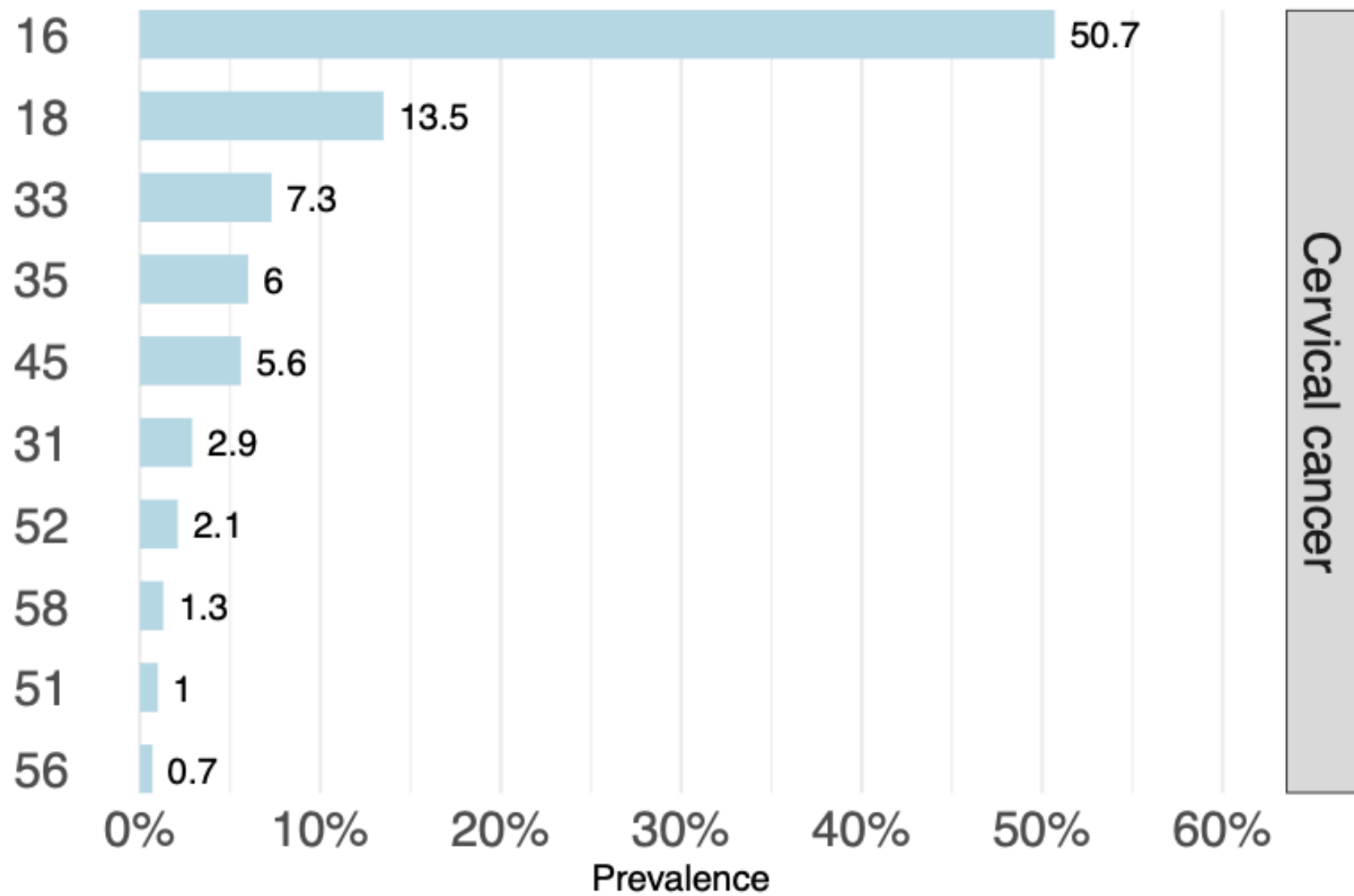
Graphs by Cervix

Distribution of age at CC and non-infection related cancer diagnosis by HIV status.



High-grade lesions





A vibrant pop art illustration. On the left, a woman's face is shown in profile, with her hand raised near her mouth. She has blonde hair and is wearing red lipstick. The background is a bold red color, decorated with white geometric shapes and areas of halftone dot patterns in green and black. The text 'Let's Talk About' is written in a white, rounded, sans-serif font with a black outline, positioned above the word 'SEX'.

Let's Talk About

SEX

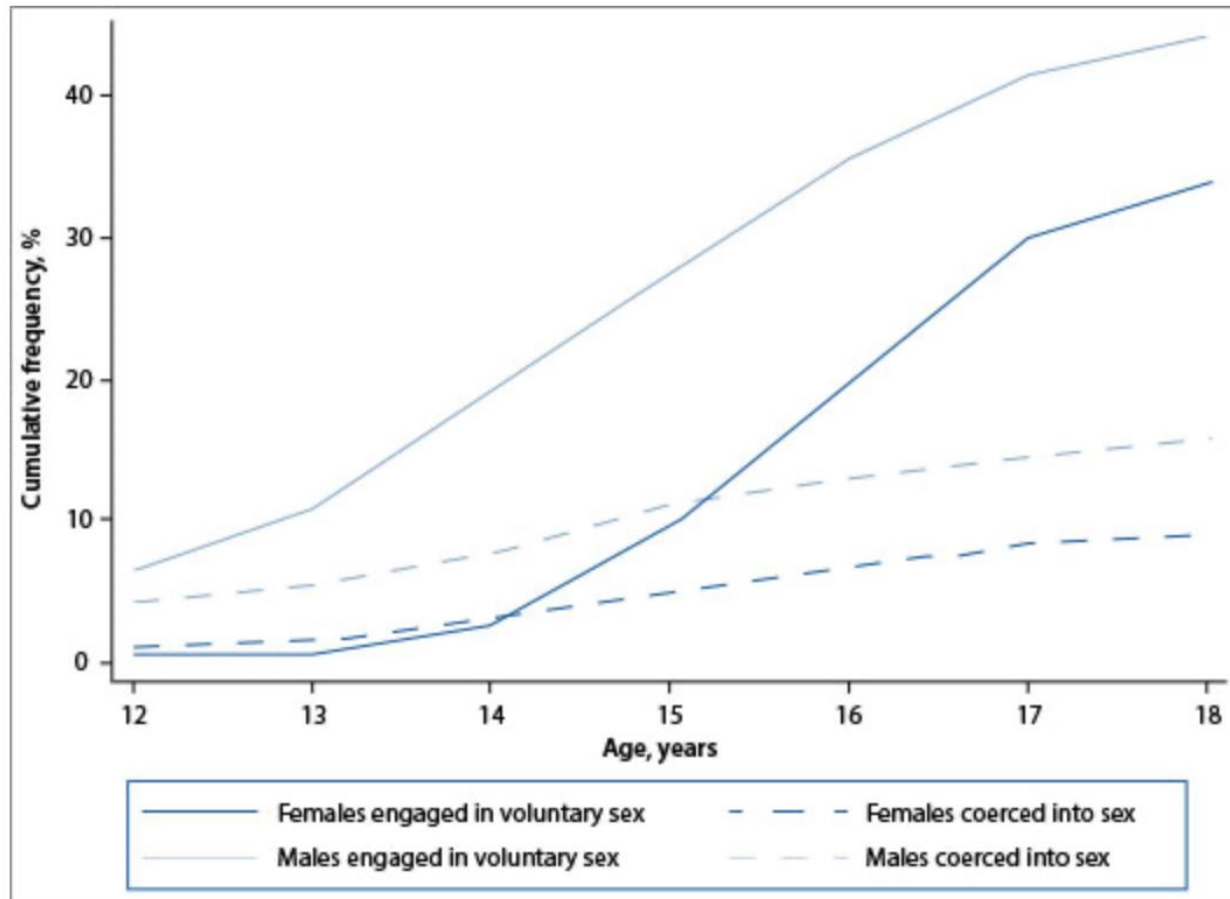


Fig. 1. Sexual debut for males and females by age from the first retrospective report of sexual intercourse, starting before 12 years of age.

SAMJ: South African Medical Journal

On-line version ISSN 2078-5135

Print version ISSN 0256-9574

SAMJ, S. Afr. med. j. vol.105 n.4 Pretoria Apr. 2015

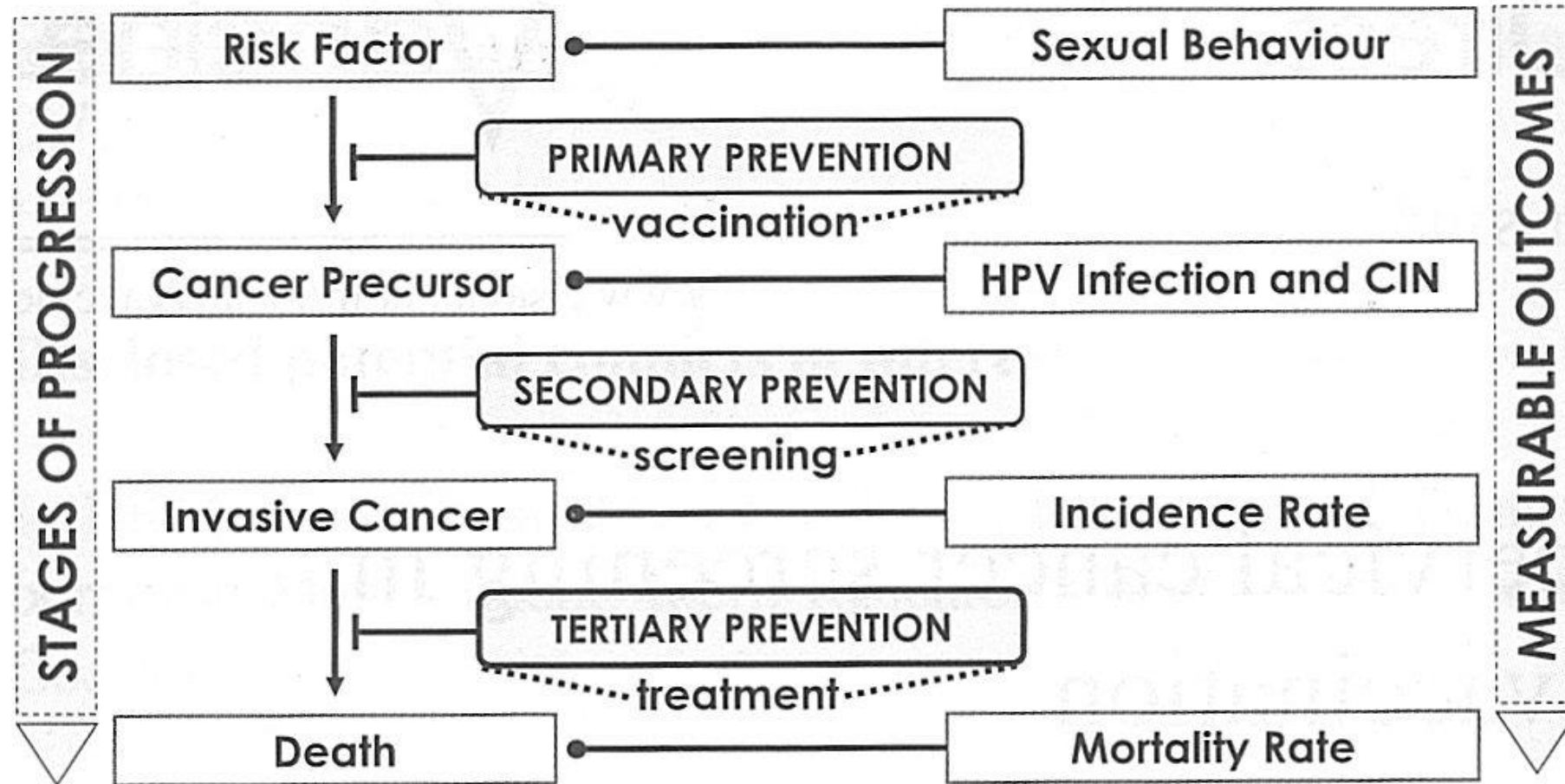
<http://dx.doi.org/10.7196/SAMJ.8925>

Table 3. Partner age differences and sexual experience (voluntary or coerced) at first sexual intercourse by gender

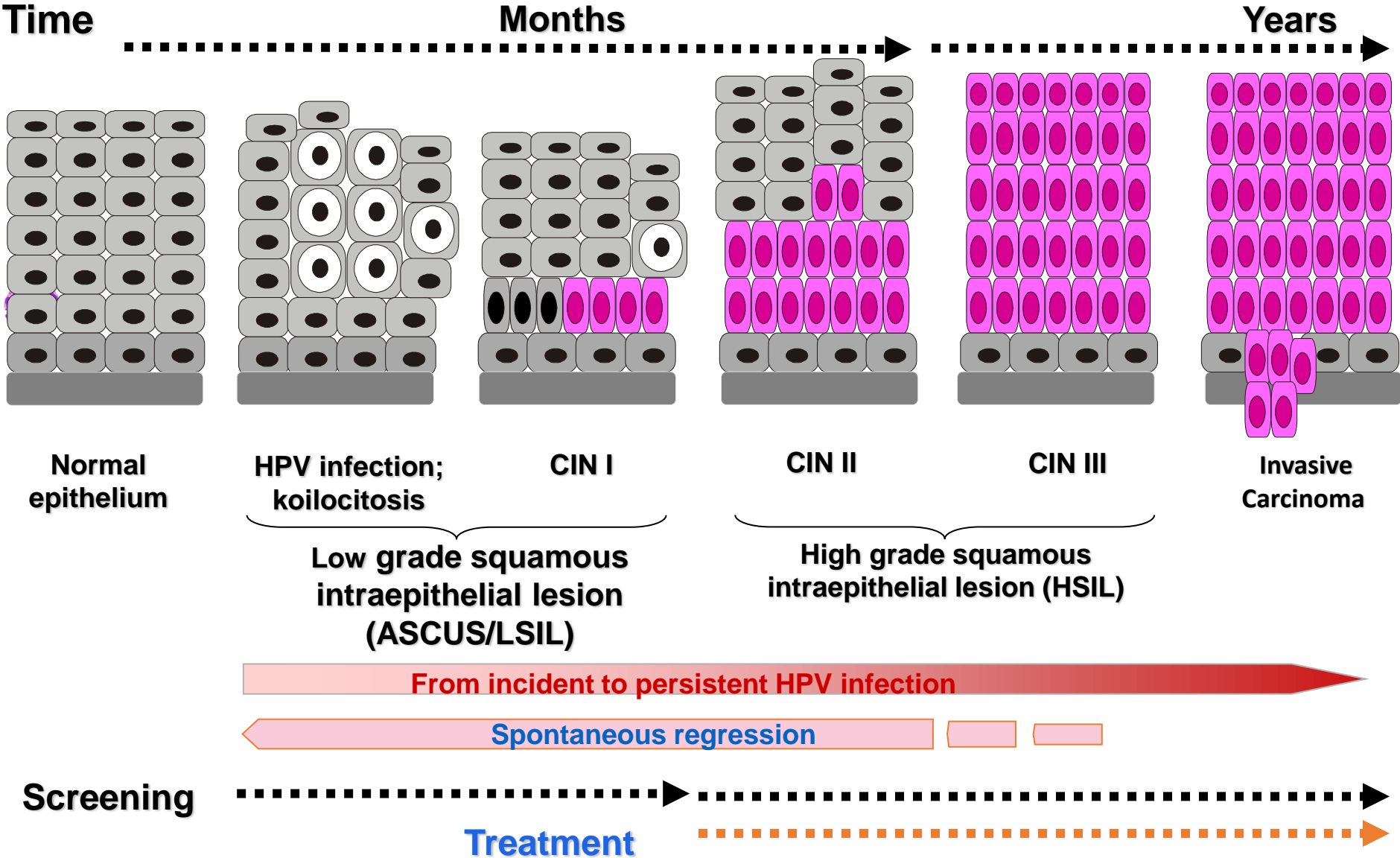
Age difference	Voluntary		Coerced	
	Females (N=348) n (%)	Males (N=419) n (%)	Females (N=91) n (%)	Males (N=149) n (%)
Partner ≥5 years younger	1 (0.3)	2 (0.5)	0 (0%)	0 (%)
Partner 1 - 4 years younger	3 (0.9)	115 (27.4)*	1 (1.1)	45 (30.2)*
Partner same age	42 (12.1)	143 (34.1)*	15 (16.5)	53 (35.6)*
Partner 1 - 4 years older	239 (68.7)*	115 (27.4)	55 (60.4)*	30 (20.1)
Partner ≥5 years older	45 (12.9)*	2 (0.5)	10 (11.0)*	2 (1.3)

*Significant at $p < 0.05$.

CERVICAL CANCER CONTROL INTERVENTIONS



Natural History From Infection to Cervical Cancer



CERVICAL CANCER OCCURS DESPITE ESTABLISHED SCREENING PROGRAMS

	Recommendation				
Country	Age Range (Years)	Interval (Years)	% Regularly Screened	Cervical Cancer mortality/1000,000	Cervical Cancer Incidence/100,000
Finland	30-60	5	93	3.0	6.2
England	25-64	3-5	83	5.1	10.5
Sweden	23-60	3	83	5.6	10.9
Belgium	25-64	3	78	6.2	12.8
The Netherlands	30-60	5	77	3.8	9.4
Denmark	23-59	3	75	8.6	16.3
France	25-65	3	69	5.4	13.6
Italy	25-64	3	53-74	4.0	11.6
Germany	20-85	1	50	7.1	14.7
Spain	25-65	3	27	3.6	10.3

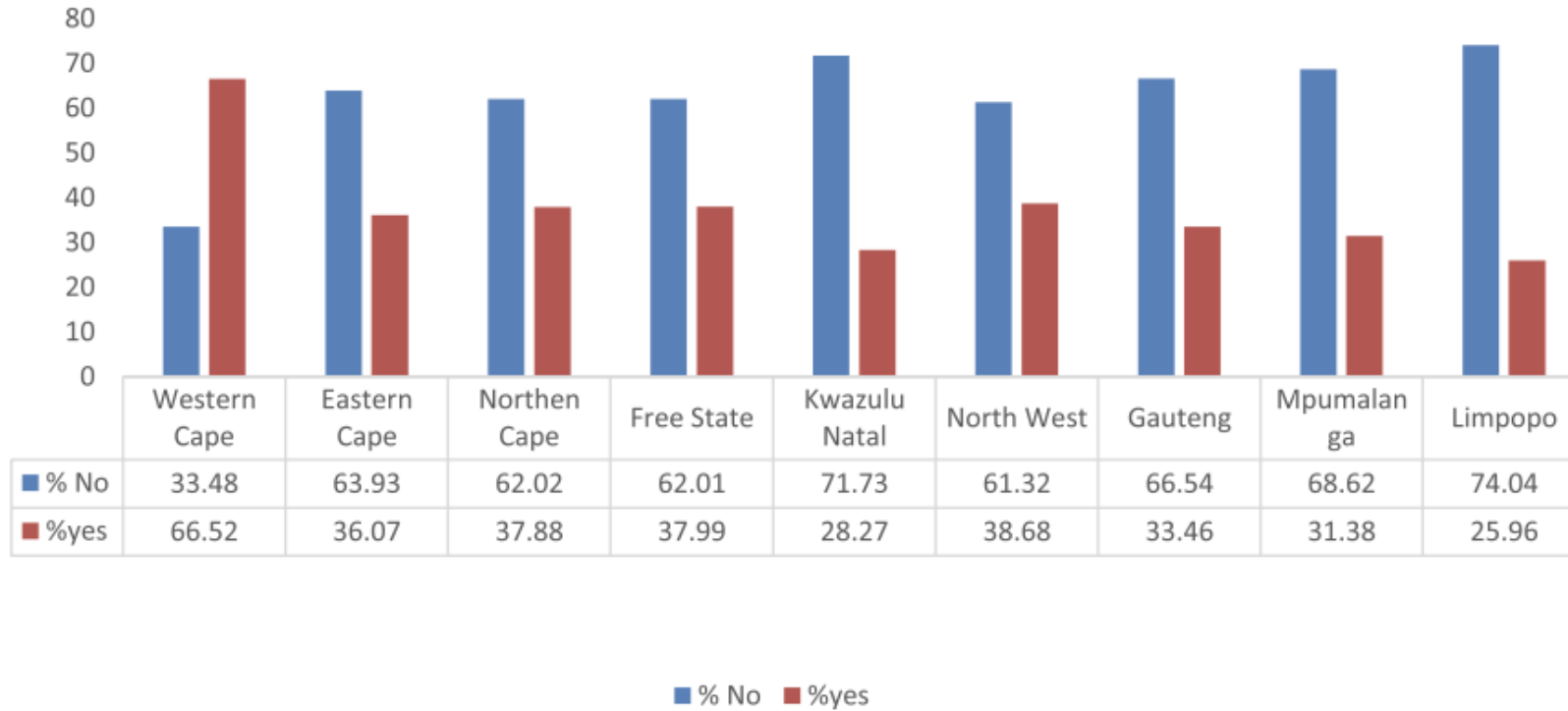
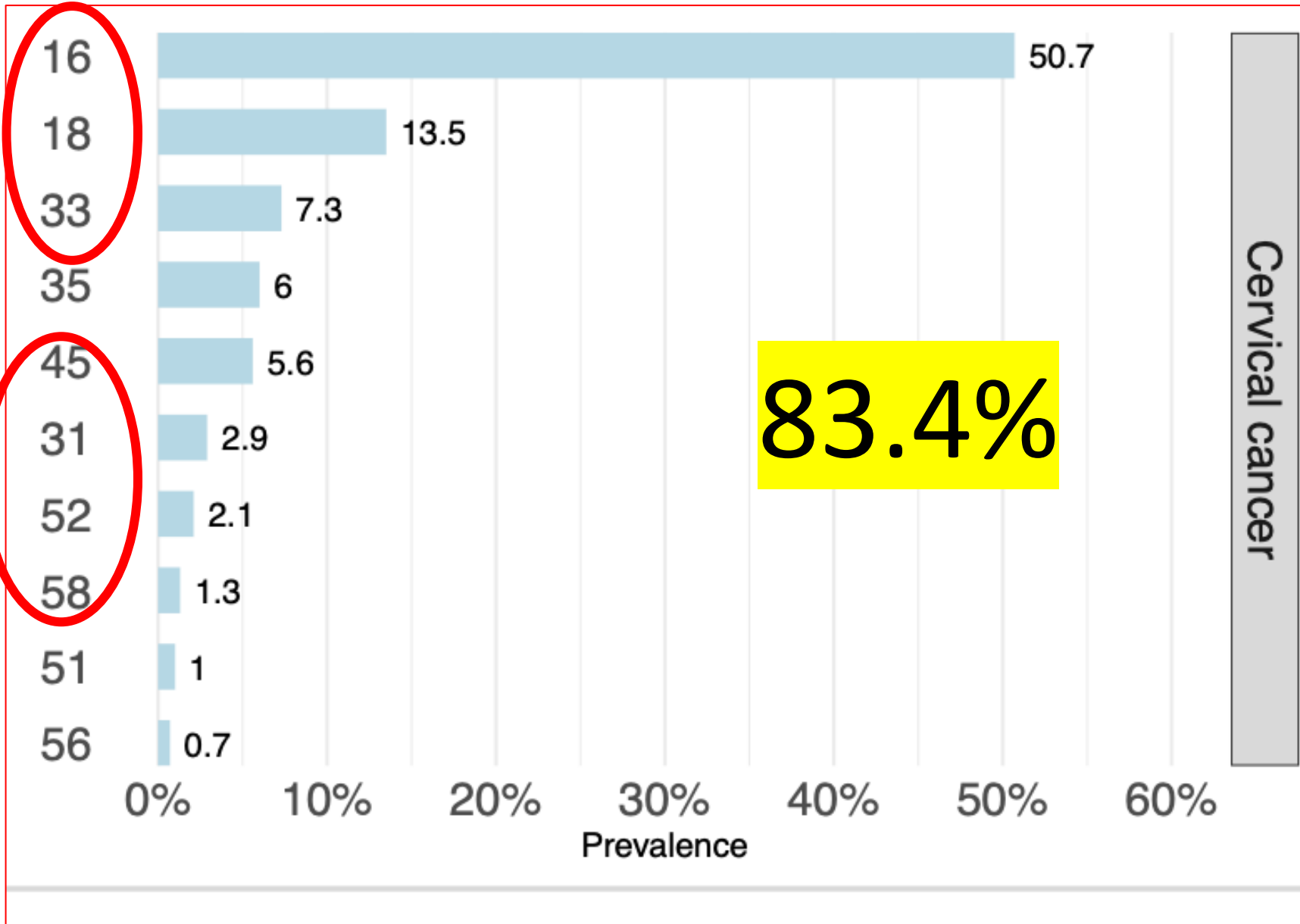


Fig. 1 Graph showing proportion of women of reproductive age who have ever had a Pap smear, by province

Types of vaccines available on the market



Manufacturer	Merck™ (Gardasil®)	GlaxoSmithKline™ (Cervarix®)	Merck™ (Gardasil® 9)
LI VLP types	6, 11, 16, and 18	16 and 18	6, 11, 16, 18, 31, 33, 45, 52, and 58
Dose	20/40/40/20 µg	20/20 µg	30/40/60/40/20/20/20/20/20 µg
Producer cells	<i>Saccharomyces cerevisiae</i> (baker's yeast) expressing LI	<i>Trichoplusia ni</i> (Hi 5) insect cell line infected with LI recombinant baculovirus	<i>Saccharomyces cerevisiae</i> (baker's yeast) expressing LI
Adjuvant	225 µg aluminium hydroxyphosphate sulfate	500 µg aluminium hydroxide, 50 µg 3-O-deacylated-4'-monophosphoryl lipid A	500 µg aluminium hydroxyphosphate sulfate
Vaccination schedule	0, 2, and 6 months	0, 1, and 6 months	0, 2, and 6 months



Universal mass vaccination (UMV) programme in Scotland



UMV programme:^{1,2}

- bHPV-vaccine-based programme initiated in Scotland in 2008^{1,2}
 - Target age group: 12–13 year old girls; catch-up program up to 18 years old
- Vaccine uptake: >90% in target age group and up to 80% in the catch up cohorts²
- Women born in 1990–1993 (catch-up cohort, mixture of non-vaccinated and vaccinated women), entered the Scottish Cervical Screening Programme in 2010–2013 (at age 20–21 years)¹
- Registries allow for linking of vaccination status to screening and histology outcomes to calculate real world vaccine impact^{1,2}

bHPV, bivalent HPV vaccine; UMV, universal mass vaccination

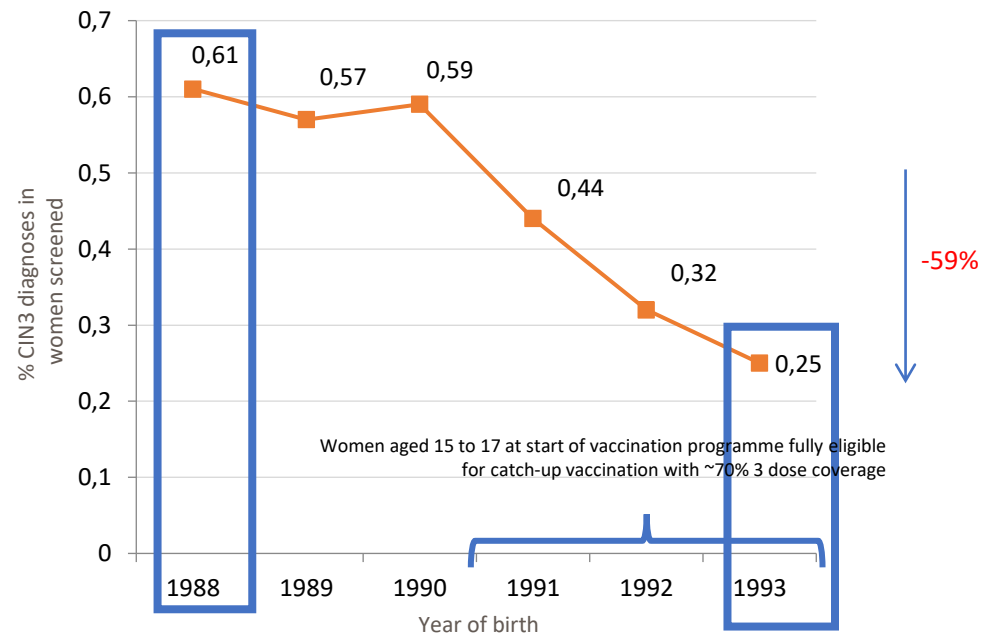
1. Palmer TJ *et al. Br J Cancer* 2016;114:582–9

2. Pollock K *et al. Br J Cancer* 2014;1–7

Screening outcome in women entering the Scottish screening programme at age 20 years



Outcome of first screening visit irrespective of vaccination status:
CIN3 diagnoses (%)



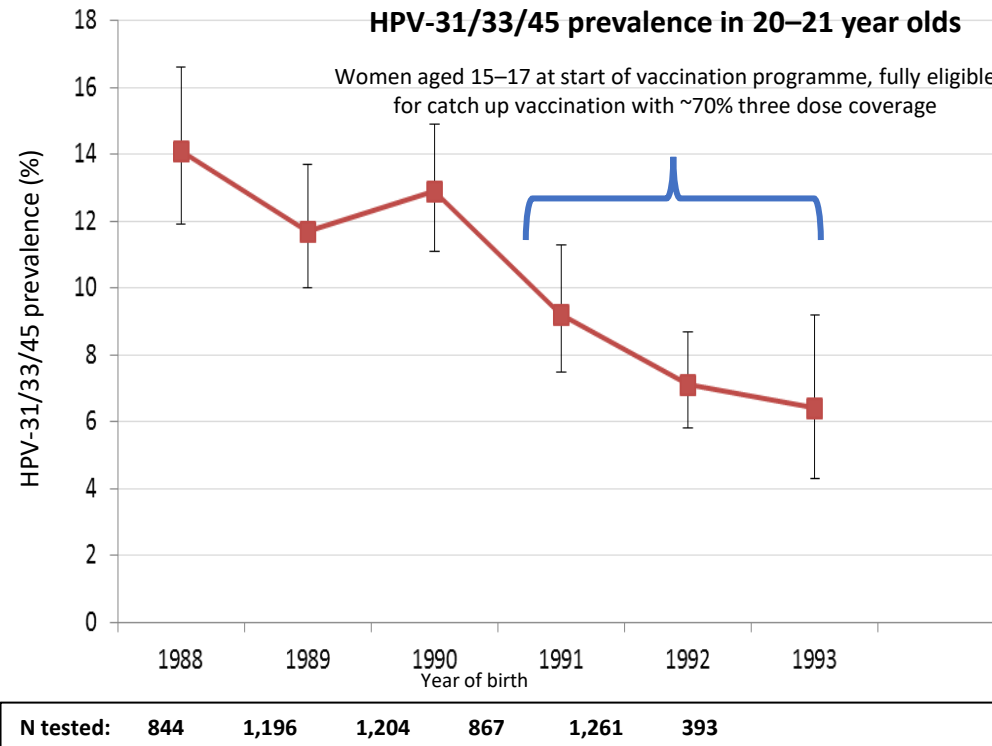
N screened: 17,139 16,451 17,040 17,125 16,382 11,739

Based on data from women born between 1 January 1988 and 30 September 1993 who attended for cervical screening within 1 year of becoming 20 years, by year of birth

HPV-31/33/45 prevalence in bHPV vaccinated individuals up to 5 years after vaccination in Scotland



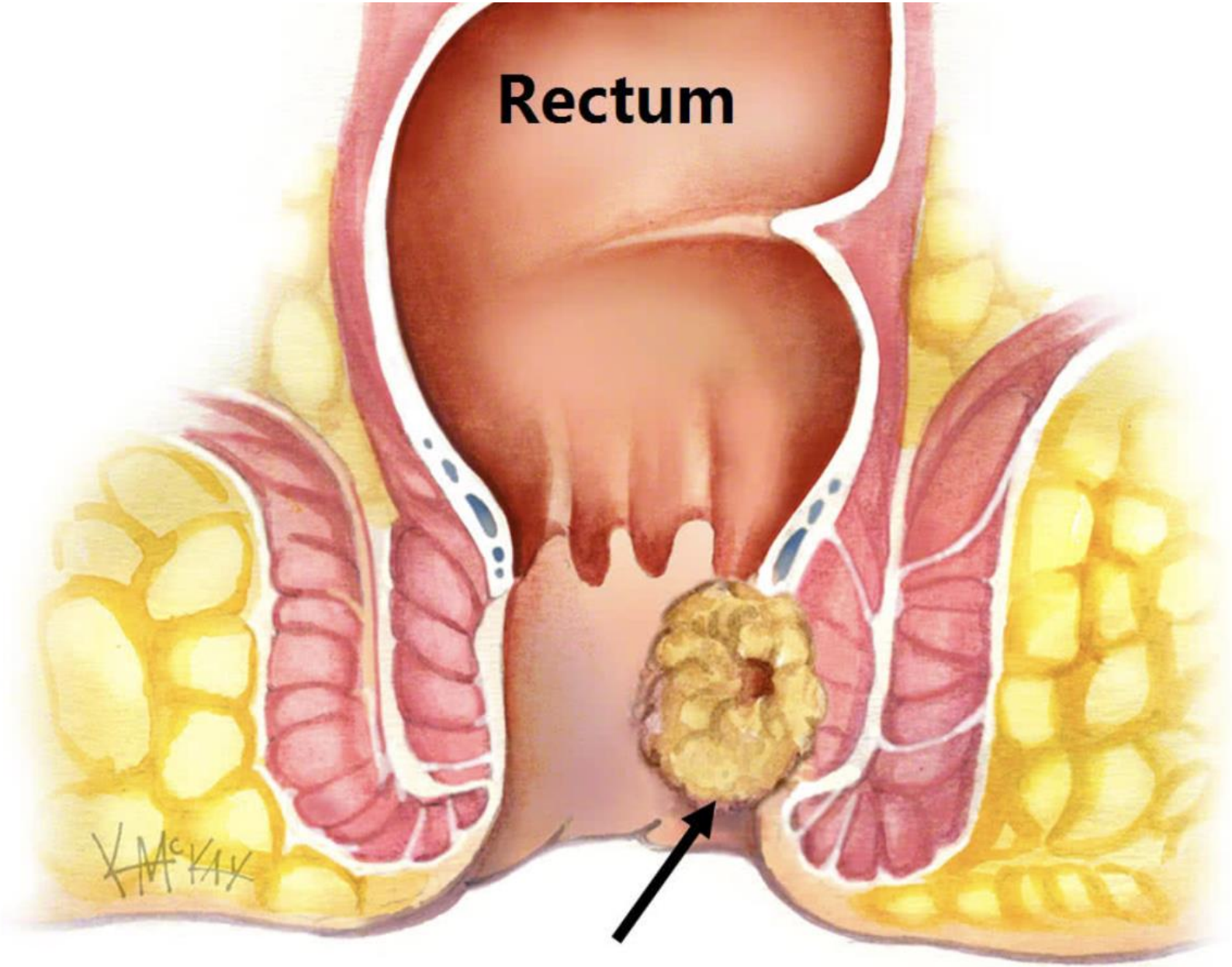
bHPV vaccination programme started in September 2008 with a catch-up programme for women up to 18 years. Women enter national screening programme at age 20 years.



Fully vaccinated vs unvaccinated women	Odds ratio* (95% CI)
HPV 16 or 18	0.27 (0.19–0.37)
HPV 31, 33 or 45	0.45 (0.29–0.68)

*Adjusted for birth cohort year and deprivation score

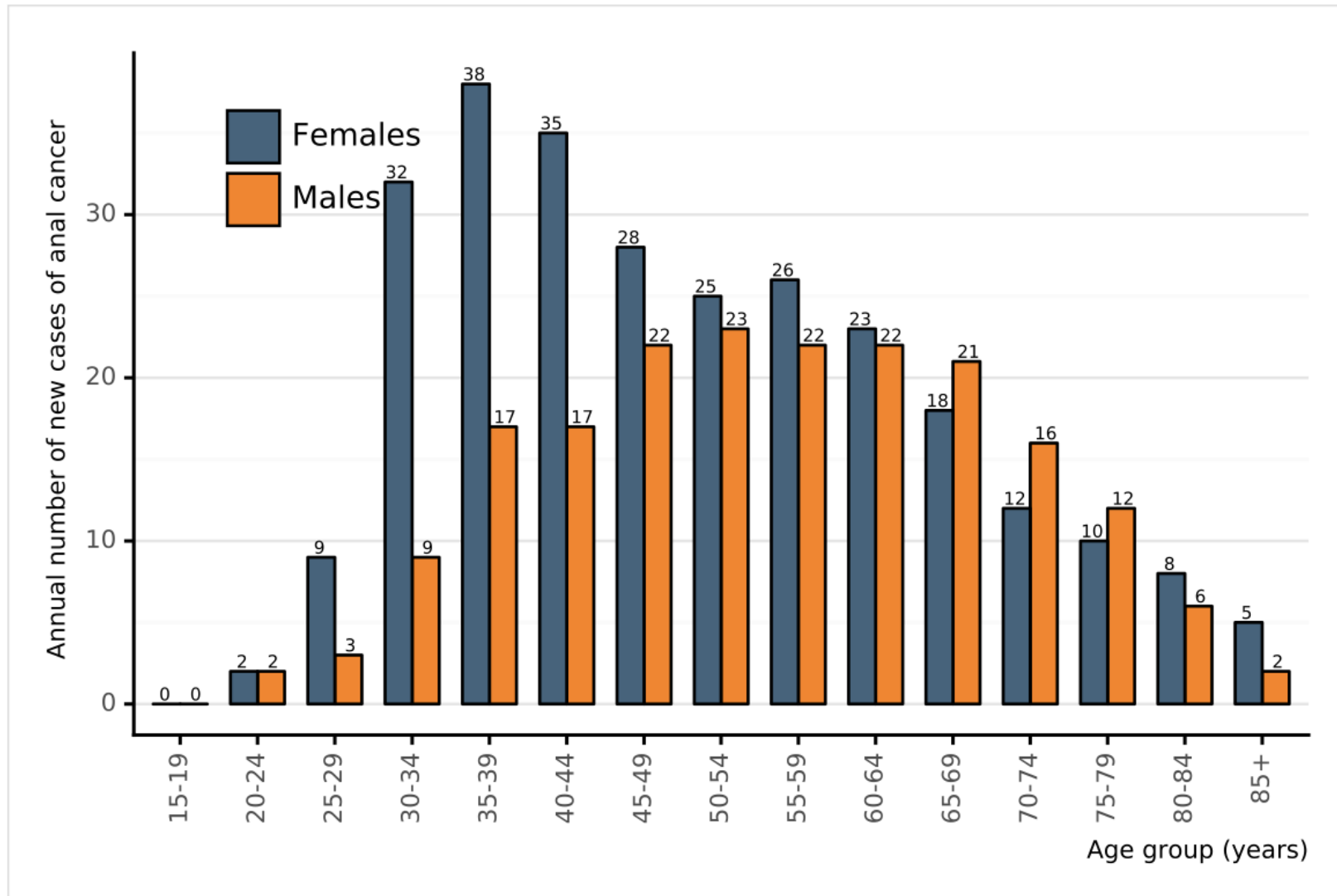
Graph shows typing results of 5,765 liquid-based cytology samples collected from women 20–21 years of age undergoing their first cervical smear collection, in Scotland, in 2009–2013



Rectum

Anal Cancer

Figure 16: Annual number of new cases of anal cancer in South Africa (estimates for 2020)




Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

Data Sources:

Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Human papillomavirus vaccination and anal high-grade precancerous lesions and cancer—a real-world effectiveness study

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JNCI: Journal of the National Cancer Institute, 2024, **116(2)**, 283–287

<https://doi.org/10.1093/jnci/djad189>

Advance Access Publication Date: September 18, 2023

Table 1. Hazard ratios comparing vaccinated with unvaccinated women for histological anal high-grade squamous intraepithelial lesion or worse

Vaccination status	No.	Person-years ^a	Events ^a	Unadjusted HR (95% CI)	Adjusted ^b HR (95% CI)
Unvaccinated	594 392	3 391 782	37	Referent	Referent
Age at vaccination younger than 17 y	374 489	2 325 710	<5	0.30 (0.10 to 0.89)	0.30 (0.10 to 0.87)
Age at vaccination 17-32 y	198 214	1 573 338	26	1.30 (0.78 to 2.15)	1.21 (0.73 to 2.03)

^a Cell counts less than 5 cannot be disclosed because of Danish legislation. CI = confidence interval; HR = hazard ratio.

^b Adjusted for maximum level of own, mother's, or father's education.

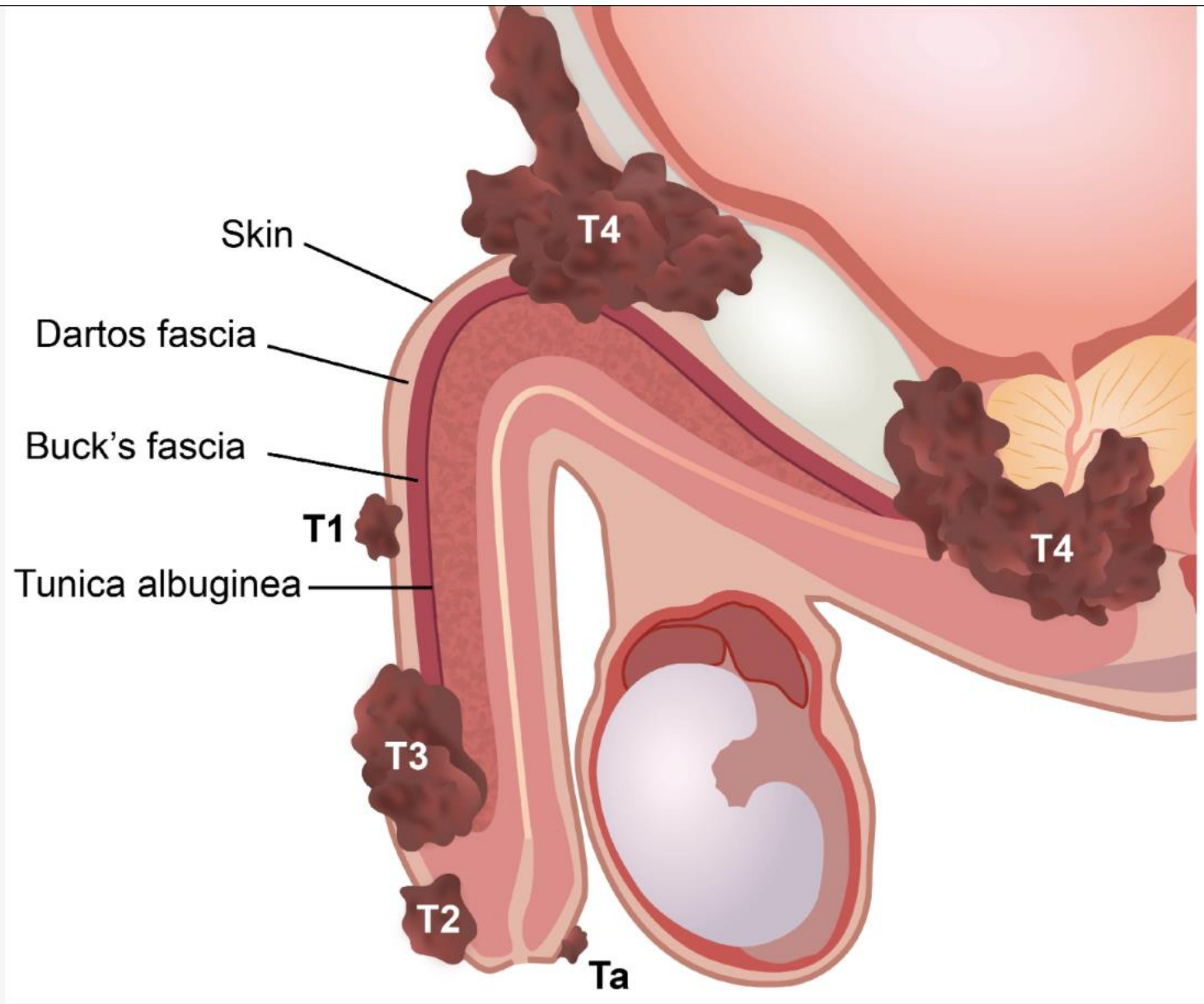
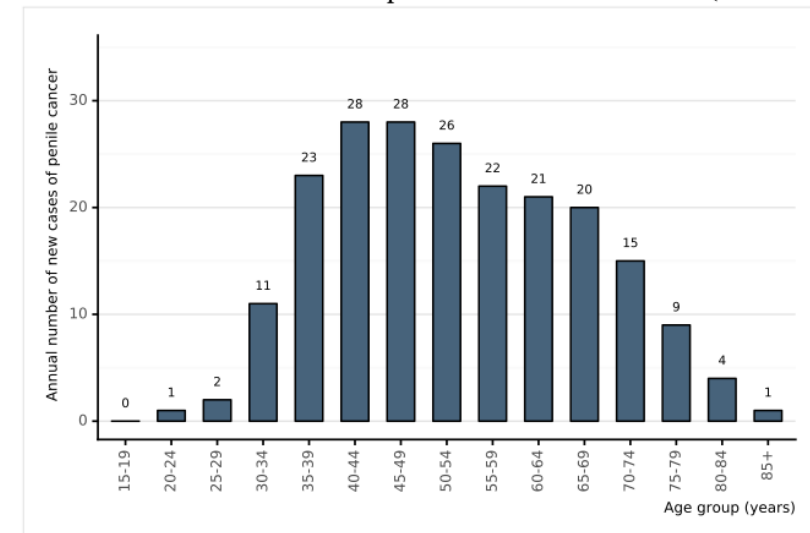


Table 13: Penile cancer incidence in South Africa (estimates for 2020)

Indicator	South Africa	Southern Africa	World
Annual number of new cancer cases	211	311	36,068
Uncertainty intervals [95% UI]	[177-252]	[258-376]	[30,963-42,015]
Crude incidence rate ^b	0.72	0.94	0.92
Age-standardized incidence rate ^b	0.84	1.12	0.80
Cumulative risk (%) at 75 years old ^a	0.10	0.12	0.09

Data accessed on 27 Jan 2021

Figure 32: Annual number of new cases of penile cancer in South Africa (estimates for 2020)

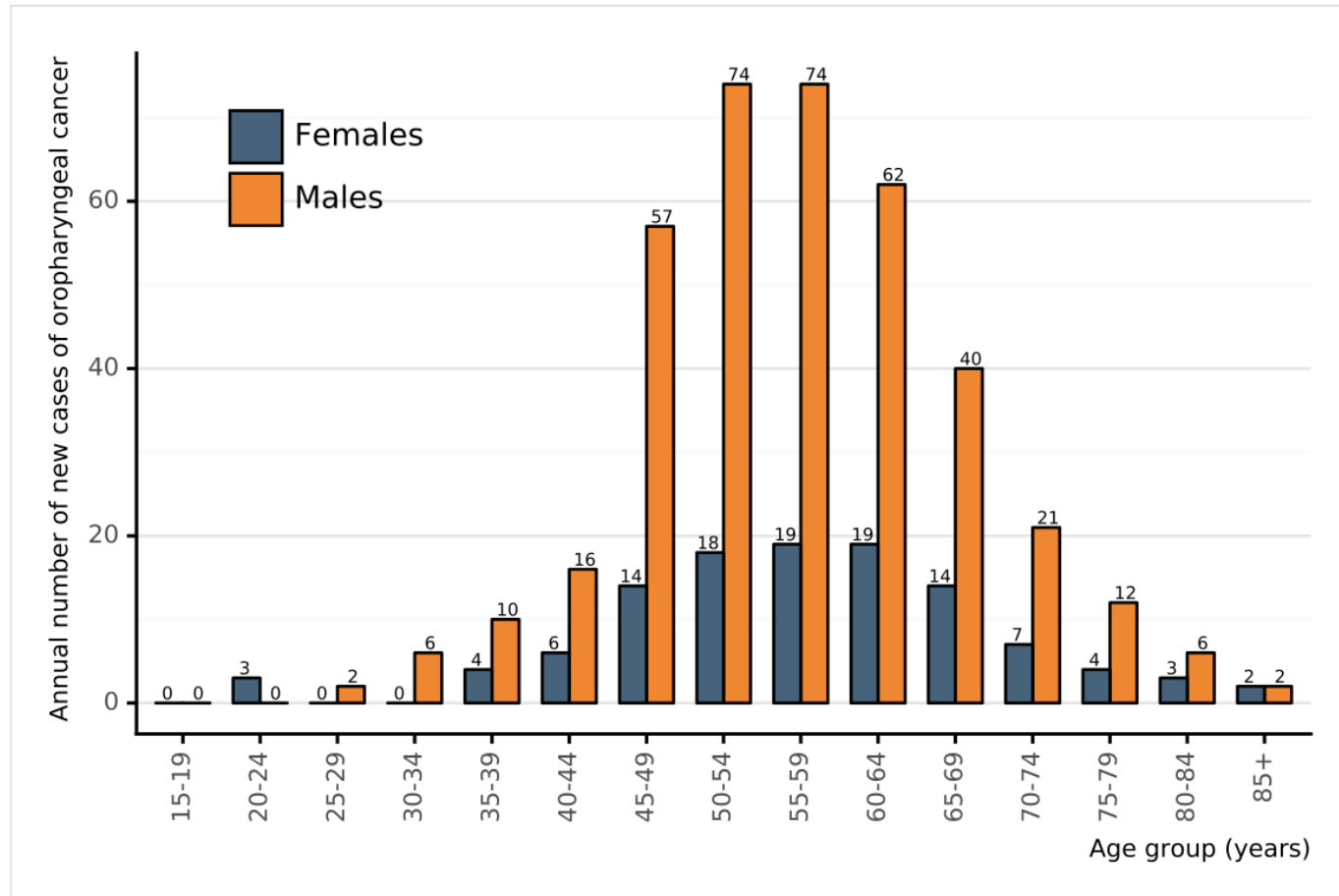


Penile Cancer

- 130 000 new cases annually
- HPV DNA prevalence in penile cancer of 50.8%
- HPV DNA prevalence in penile intraepithelial neoplasia (PeIN) of 79.8%.
- HPV 16 is the most common cause of these lesions with a pooled prevalence of 68.3% and 69.8%, respectively, in penile cancer and PeIN.
- Gender Neutral vaccine



Figure 37: Annual number of new cases of oropharyngeal cancer in South Africa (estimates for 2020)



Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

Data Sources:

Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.fr/today>, accessed [27 January 2021].



Overview

- Human papillomavirus (HPV) is a very common virus; nearly 80 million people are currently infected in the United States.¹
- HPV infection can cause cancer in the back of the throat, including the base of the tongue and tonsils (called oropharyngeal cancer).²
- HPV is thought to cause 70% of oropharyngeal cancers in the United States.²
- HPV vaccination could **prevent more than 90% of cancers caused by HPV** from ever developing.³
- Dental professionals have a vested interest in recommending HPV vaccination to their patients.⁴

Genital warts

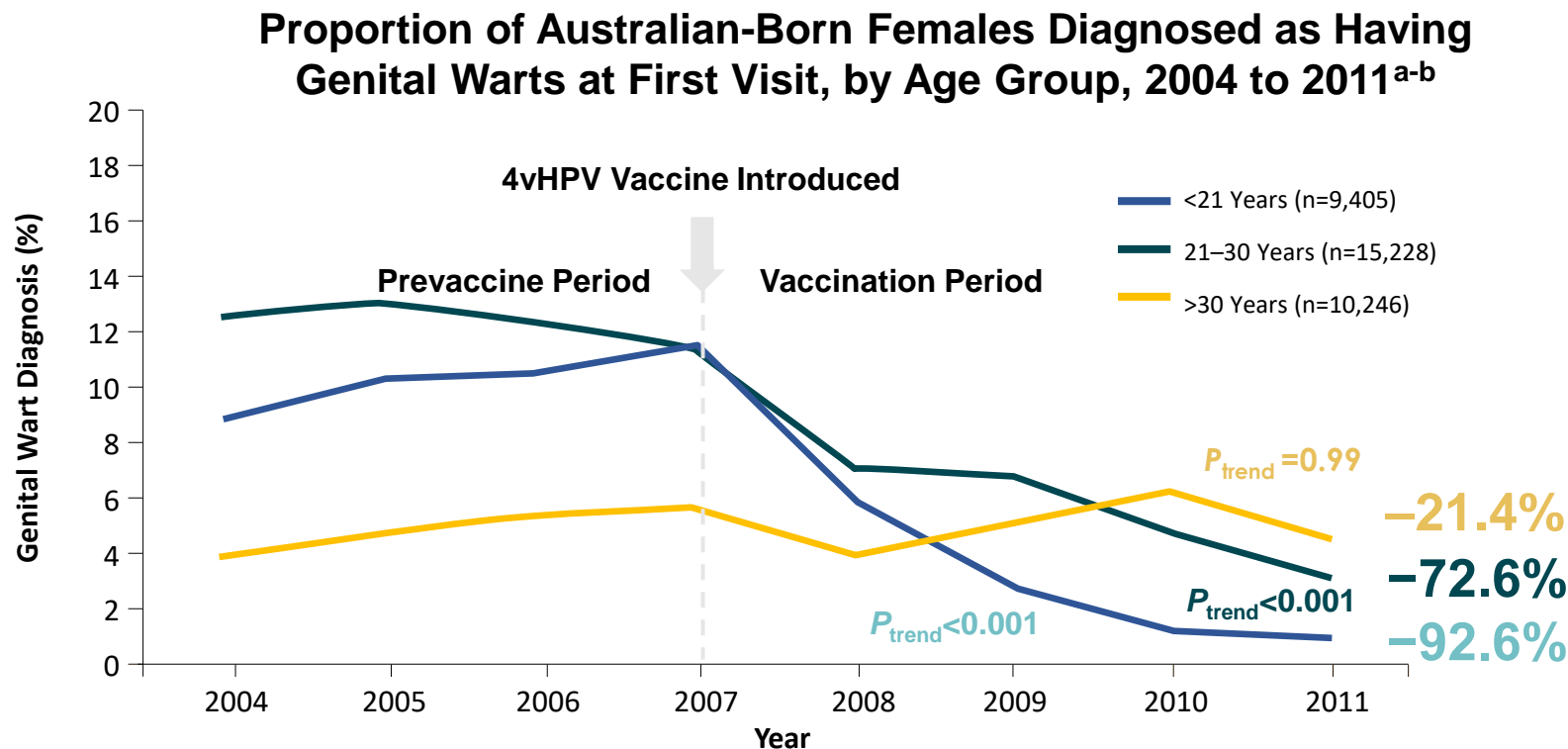


- MASSIVE PROBLEM
- Caused by HPV
- Low risk HPV
- Type 6 and 11
- Not covered by bivalent
- Covered by quadrivalent (4 types of HPV) or Nonavalent (9 types of HPV)



Proportion of Australian-Born Females With Genital Warts, by Age Group (2004–2011)¹

- » A significant decline in the proportion of females <21 to 30 years of age diagnosed with genital warts at first visit was seen during the 4vHPV vaccination period.
 - » No significant declines were seen in the proportion of females >30 years of age during the 4vHPV vaccination period.



^aAnalyses included a total of 34,900 females. ^b4vHPV vaccination was introduced to the Australia National Immunization Program in 2007 for 12- to 13-year-old girls.²

Figure reproduced from *BMJ*, Ali H et al, 346, f2032, 2013, with permission from BMJ Publishing Group Ltd.

1. Ali H et al. *BMJ*. 2013;346:f2032. 2. Immunise Australia Program: Human papillomavirus. Australian Government Department of Health website.

<http://www.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-hpv>. Accessed January 15, 2016.

Conclusion

- Cervical cancer is caused by HPV
- Vaccination is effective
- Vaccination is our answer

Global Health

November 19, 2019

Summit Leaders Urge Greater HPV Vaccination in Africa

Bridget Kuehn, MSJ

JAMA. 2019;322(19):1853. doi:10.1001/jama.2019.17713

