

HPV and its subtypes: Risk factors for cervical cancer

Hennie Botha
Stellenbosch University
2026



Stellenbosch
UNIVERSITY
IYUNIVESITHI
UNIVERSITEIT

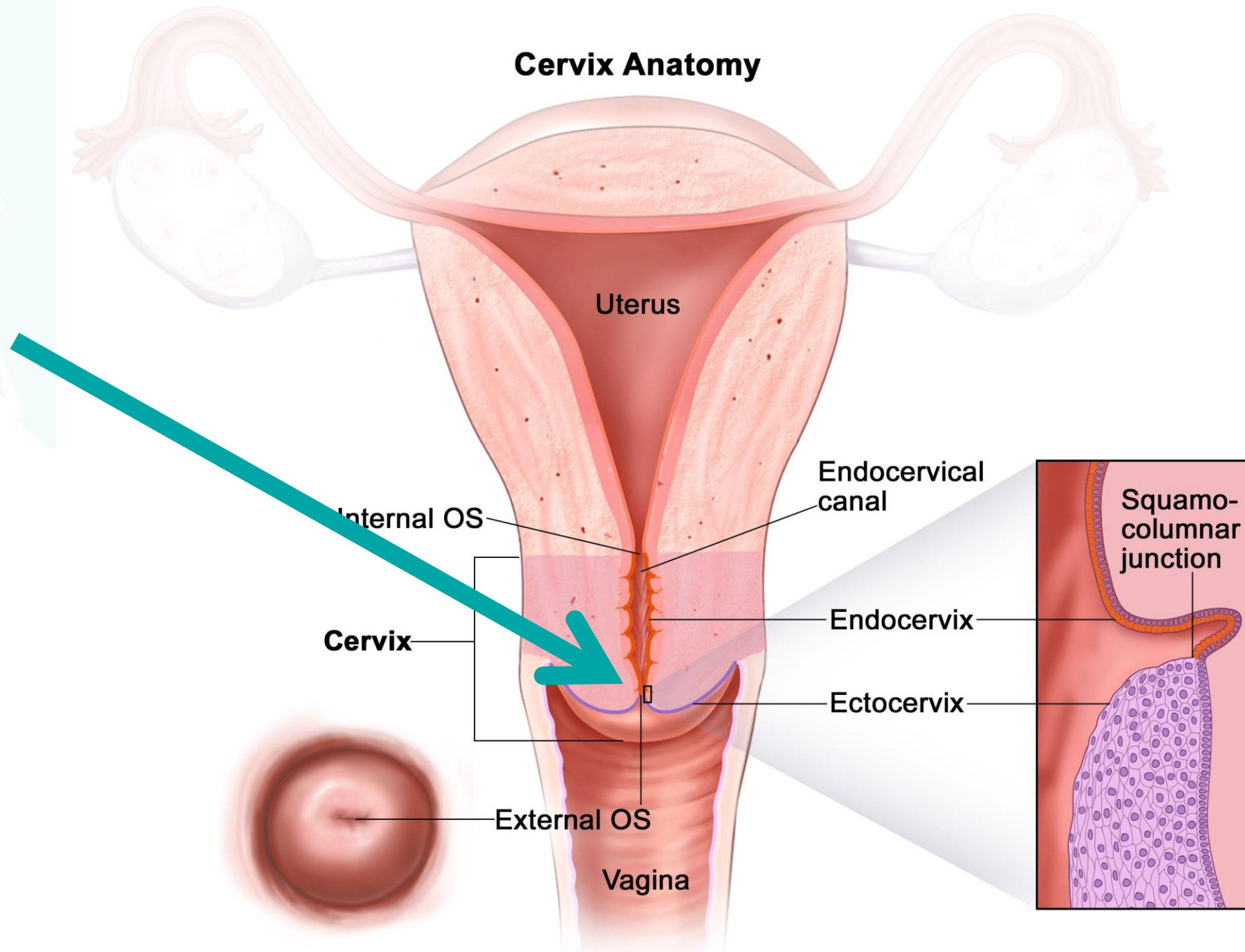
Ca Cx Incidence and Mortality RSA

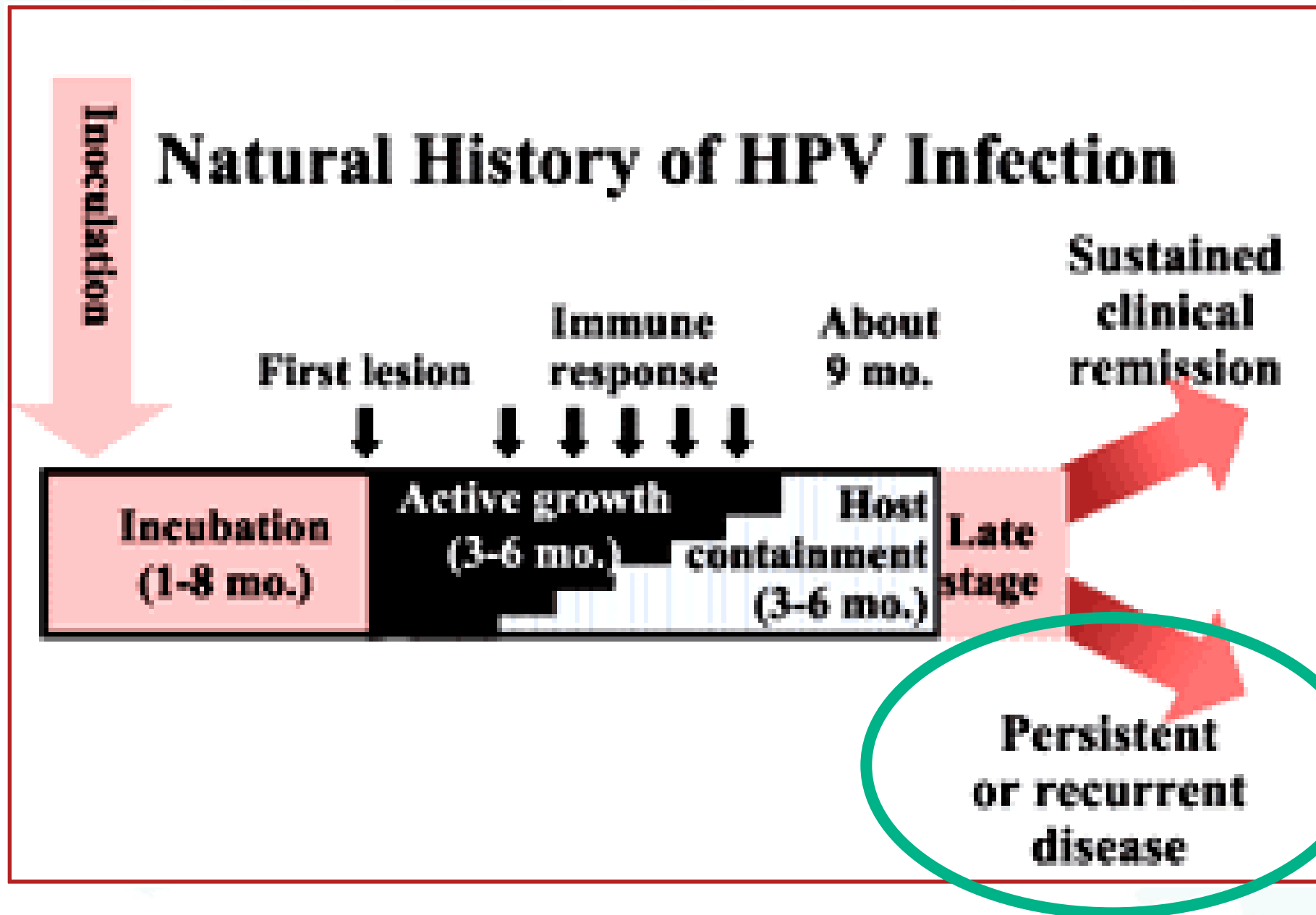
Burden of cervical cancer.*

	INCIDENCE	MORTALITY
Annual number of new cases/deaths	10702	5870
Crude rate*	35.6	19.5
Age-standardized rate*	35.3	19.6
Cumulative risk 0-74 years (%)	3.58	2.10
Ranking of cervical cancer (all years)	2nd	1st
Ranking of cervical cancer (15-44 years)	1st	1st

* Crude and age-standardized rates per 100,000 women and year

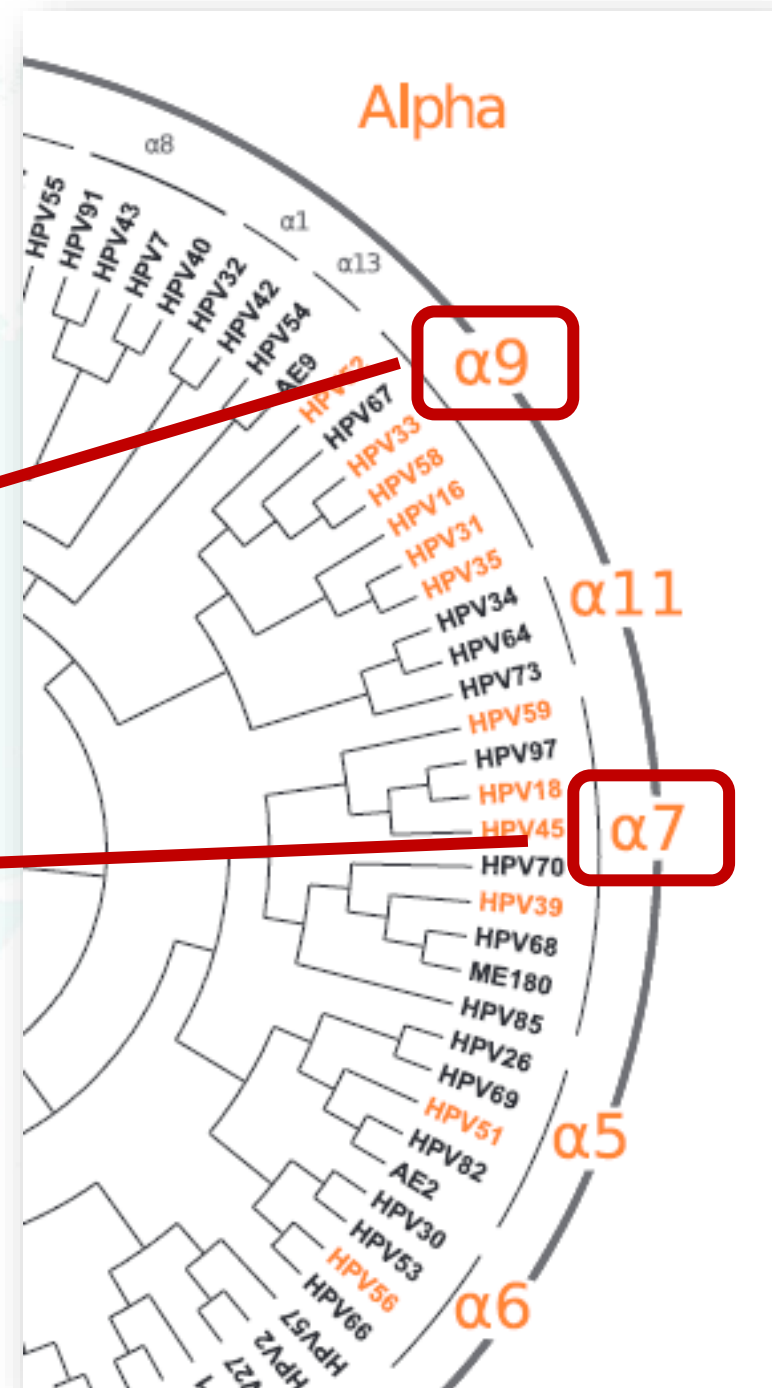
Cervix Anatomy





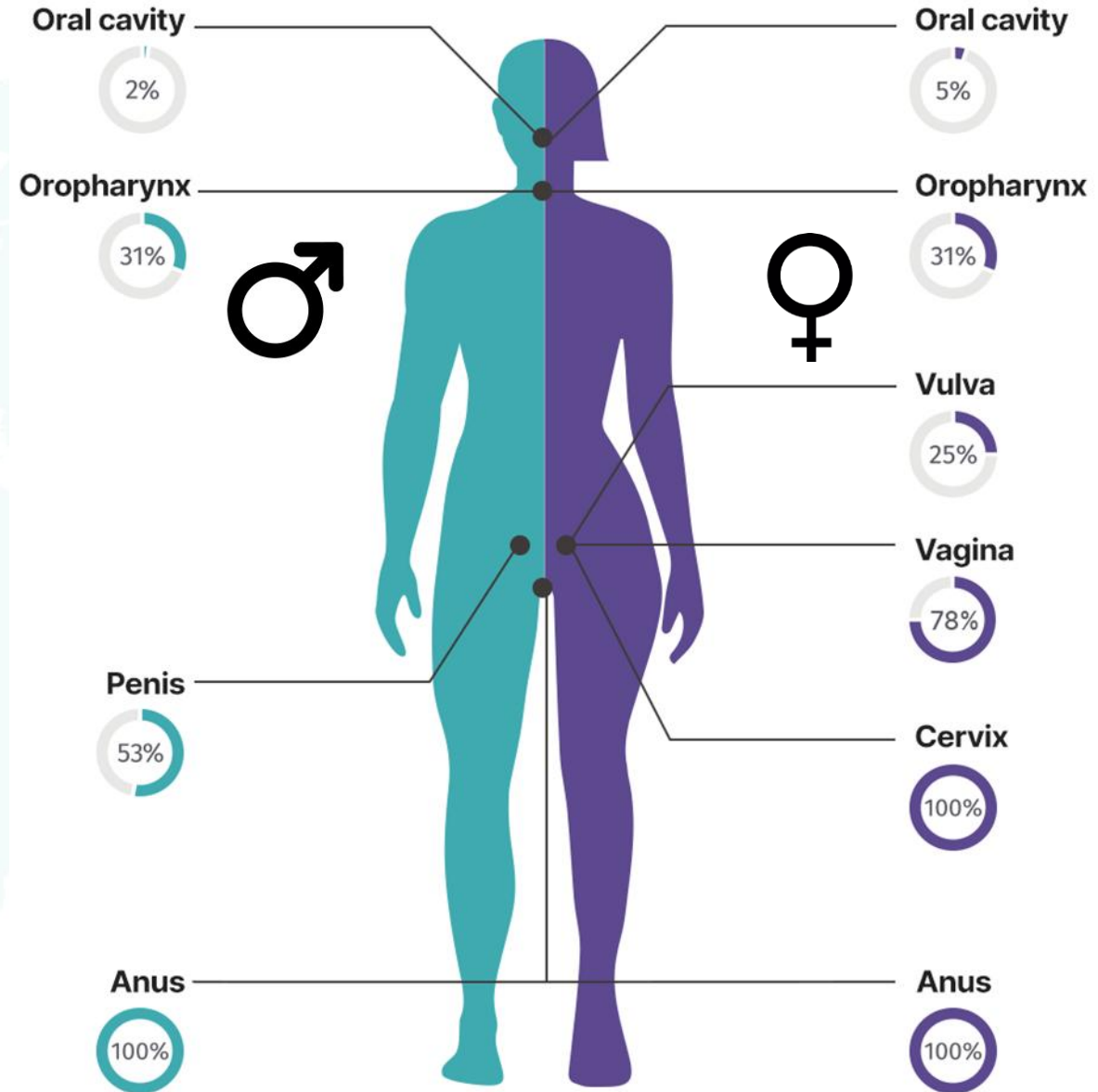
IARC Monographs – 100B [2012]

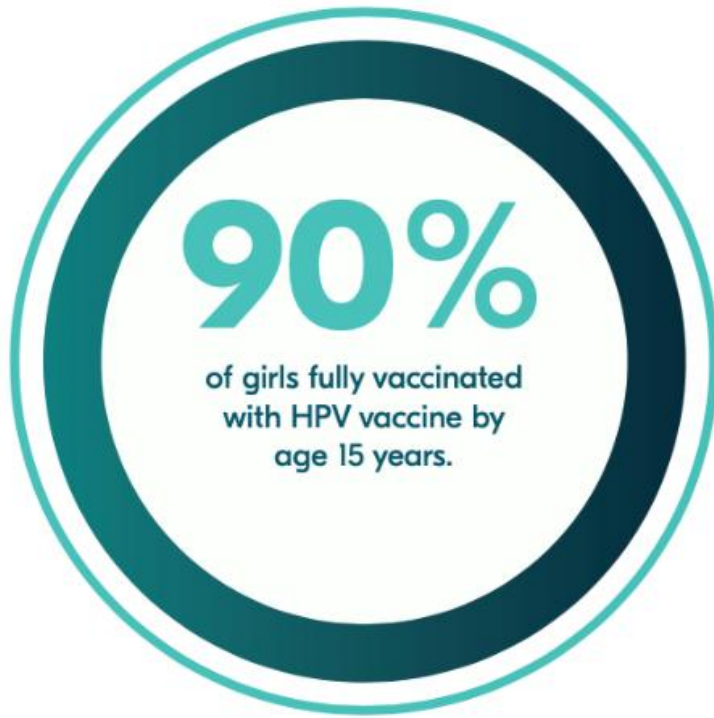
A circular phylogenetic tree showing the relationships between various HPV strains. The tree is divided into three main sections: Alpha (top right, orange text), Beta (bottom left, grey text), and Gamma (top left, grey text). The Alpha section is further subdivided into lineages $\alpha 1$ through $\alpha 15$. A red arrow points to lineage $\alpha 9$. The Beta section is subdivided into lineages $\beta 1$ through $\beta 5$. The Gamma section is subdivided into lineages $\gamma 1$ through $\gamma 5$. Numerous HPV strains are listed along the branches, including HPV6, HPV11, HPV13, HPV74, HPV44, HPV55, HPV91, HPV43, HPV17, HPV40, HPV32, HPV42, HPV54, AE9, HPV52, HPV67, HPV33, HPV58, HPV16, HPV31, HPV35, HPV34, HPV64, HPV73, HPV59, HPV97, HPV18, HPV45, HPV70, HPV39, HPV68, ME180, HPV85, HPV26, HPV69, HPV51, HPV82, AE2, HPV30, HPV53, HPV56, HPV66, ZSAH, HPV2, HPV12, HPV11, HPV100, HPV90, HPV16, HPV17, HPV18, HPV19, HPV20, HPV21, HPV22, HPV23, HPV24, HPV25, HPV26, HPV27, HPV28, HPV29, HPV30, HPV31, HPV32, HPV33, HPV34, HPV35, HPV36, HPV37, HPV38, HPV39, HPV40, HPV41, HPV42, HPV43, HPV44, HPV45, HPV46, HPV47, HPV48, HPV49, HPV50, HPV51, HPV52, HPV53, HPV54, HPV55, HPV56, HPV57, HPV58, HPV59, HPV60, HPV61, HPV62, HPV63, HPV64, HPV65, HPV66, HPV67, HPV68, HPV69, HPV70, HPV71, HPV72, HPV73, HPV74, HPV75, HPV76, HPV77, HPV78, HPV79, HPV80, HPV81, HPV82, HPV83, HPV84, HPV85, HPV86, HPV87, HPV88, HPV89, HPV90, HPV91, HPV92, HPV93, HPV94, HPV95, HPV96, HPV97, HPV98, HPV99, HPV100, HPV101, HPV102, HPV103, HPV104, HPV105, HPV106, HPV107, HPV108, HPV109, HPV110, HPV111, HPV112, HPV113, HPV114, HPV115, HPV116, HPV117, HPV118, HPV119, HPV120, HPV121, HPV122, HPV123, HPV124, HPV125, HPV126, HPV127, HPV128, HPV129, HPV130, HPV131, HPV132, HPV133, HPV134, HPV135, HPV136, HPV137, HPV138, HPV139, HPV140, HPV141, HPV142, HPV143, HPV144, HPV145, HPV146, HPV147, HPV148, HPV149, HPV150, HPV151, HPV152, HPV153, HPV154, HPV155, HPV156, HPV157, HPV158, HPV159, HPV160, HPV161, HPV162, HPV163, HPV164, HPV165, HPV166, HPV167, HPV168, HPV169, HPV170, HPV171, HPV172, HPV173, HPV174, HPV175, HPV176, HPV177, HPV178, HPV179, HPV180, HPV181, HPV182, HPV183, HPV184, HPV185, HPV186, HPV187, HPV188, HPV189, HPV190, HPV191, HPV192, HPV193, HPV194, HPV195, HPV196, HPV197, HPV198, HPV199, HPV200, HPV201, HPV202, HPV203, HPV204, HPV205, HPV206, HPV207, HPV208, HPV209, HPV210, HPV211, HPV212, HPV213, HPV214, HPV215, HPV216, HPV217, HPV218, HPV219, HPV220, HPV221, HPV222, HPV223, HPV224, HPV225, HPV226, HPV227, HPV228, HPV229, HPV230, HPV231, HPV232, HPV233, HPV234, HPV235, HPV236, HPV237, HPV238, HPV239, HPV240, HPV241, HPV242, HPV243, HPV244, HPV245, HPV246, HPV247, HPV248, HPV249, HPV250, HPV251, HPV252, HPV253, HPV254, HPV255, HPV256, HPV257, HPV258, HPV259, HPV260, HPV261, HPV262, HPV263, HPV264, HPV265, HPV266, HPV267, HPV268, HPV269, HPV270, HPV271, HPV272, HPV273, HPV274, HPV275, HPV276, HPV277, HPV278, HPV279, HPV280, HPV281, HPV282, HPV283, HPV284, HPV285, HPV286, HPV287, HPV288, HPV289, HPV290, HPV291, HPV292, HPV293, HPV294, HPV295, HPV296, HPV297, HPV298, HPV299, HPV300, HPV301, HPV302, HPV303, HPV304, HPV305, HPV306, HPV307, HPV308, HPV309, HPV310, HPV311, HPV312, HPV313, HPV314, HPV315, HPV316, HPV317, HPV318, HPV319, HPV320, HPV321, HPV322, HPV323, HPV324, HPV325, HPV326, HPV327, HPV328, HPV329, HPV330, HPV331, HPV332, HPV333, HPV334, HPV335, HPV336, HPV337, HPV338, HPV339, HPV340, HPV341, HPV342, HPV343, HPV344, HPV345, HPV346, HPV347, HPV348, HPV349, HPV350, HPV351, HPV352, HPV353, HPV354, HPV355, HPV356, HPV357, HPV358, HPV359, HPV360, HPV361, HPV362, HPV363, HPV364, HPV365, HPV366, HPV367, HPV368, HPV369, HPV370, HPV371, HPV372, HPV373, HPV374, HPV375, HPV376, HPV377, HPV378, HPV379, HPV380, HPV381, HPV382, HPV383, HPV384, HPV385, HPV386, HPV387, HPV388, HPV389, HPV390, HPV391, HPV392, HPV393, HPV394, HPV395, HPV396, HPV397, HPV398, HPV399, HPV400, HPV401, HPV402, HPV403, HPV404, HPV405, HPV406, HPV407, HPV408, HPV409, HPV410, HPV411, HPV412, HPV413, HPV414, HPV415, HPV416, HPV417, HPV418, HPV419, HPV420, HPV421, HPV422, HPV423, HPV424, HPV425, HPV426, HPV427, HPV428, HPV429, HPV430, HPV431, HPV432, HPV433, HPV434, HPV435, HPV436, HPV437, HPV438, HPV439, HPV440, HPV441, HPV442, HPV443, HPV444, HPV445, HPV446, HPV447, HPV448, HPV449, HPV450, HPV451, HPV452, HPV453, HPV454, HPV455, HPV456, HPV457, HPV458, HPV459, HPV460, HPV461, HPV462, HPV463, HPV464, HPV465, HPV466, HPV467, HPV468, HPV469, HPV470, HPV471, HPV472, HPV473, HPV474, HPV475, HPV476, HPV477, HPV478, HPV479, HPV480, HPV481, HPV482, HPV483, HPV484, HPV485, HPV486, HPV487, HPV488, HPV489, HPV490, HPV491, HPV492, HPV493, HPV494, HPV495, HPV496, HPV497, HPV498, HPV499, HPV500, HPV501, HPV502, HPV503, HPV504, HPV505, HPV506, HPV507, HPV508, HPV509, HPV510, HPV511, HPV512, HPV513, HPV514, HPV515, HPV516, HPV517, HPV518, HPV519, HPV520, HPV521, HPV522, HPV523, HPV524, HPV525, HPV526, HPV527, HPV528, HPV529, HPV530, HPV531, HPV532, HPV533, HPV534, HPV535, HPV536, HPV537, HPV538, HPV539, HPV540, HPV541, HPV542, HPV543, HPV544, HPV545, HPV546, HPV547, HPV548, HPV549, HPV550, HPV551, HPV552, HPV553, HPV554, HPV555, HPV556, HPV557, HPV558, HPV559, HPV560, HPV561, HPV562, HPV563, HPV564, HPV565, HPV566, HPV567, HPV568, HPV569, HPV570, HPV571, HPV572, HPV573, HPV574, HPV575, HPV576, HPV577, HPV578, HPV579, HPV580, HPV581, HPV582, HPV583, HPV584, HPV585, HPV586, HPV587, HPV588, HPV589, HPV590, HPV591, HPV592, HPV593, HPV594, HPV595, HPV596, HPV597, HPV598, HPV599, HPV600, HPV601, HPV602, HPV603, HPV604, HPV605, HPV606, HPV607, HPV608, HPV609, HPV610, HPV611, HPV612, HPV613, HPV614, HPV615, HPV616, HPV617, HPV618, HPV619, HPV620, HPV621, HPV622, HPV623, HPV624, HPV625, HPV626, HPV627, HPV628, HPV629, HPV630, HPV631, HPV632, HPV633, HPV634, HPV635, HPV636, HPV637, HPV638, HPV639, HPV640, HPV641, HPV642, HPV643, HPV644, HPV645, HPV646, HPV647, HPV648, HPV649, HPV650, HPV651, HPV652, HPV653, HPV654, HPV655, HPV656, HPV657, HPV658, HPV659, HPV660, HPV661, HPV662, HPV663, HPV664, HPV665, HPV666, HPV667, HPV668, HPV669, HPV670, HPV671, HPV672, HPV673, HPV674, HPV675, HPV676, HPV677, HPV678, HPV679, HPV680, HPV681, HPV682, HPV683, HPV684, HPV685, HPV686, HPV687, HPV688, HPV689, HPV690, HPV691, HPV692, HPV693, HPV694, HPV695, HPV696, HPV697, HPV698, HPV699, HPV700, HPV701, HPV702, HPV703, HPV704, HPV705, HPV706, HPV707, HPV708, HPV709, HPV710, HPV711, HPV712, HPV713, HPV714, HPV715, HPV716, HPV717, HPV718, HPV719, HPV720, HPV721, HPV722, HPV723, HPV724, HPV725, HPV726, HPV727, HPV728, HPV729, HPV730, HPV731, HPV732, HPV733, HPV734, HPV735, HPV736, HPV737, HPV738, HPV739, HPV740, HPV741, HPV742, HPV743, HPV744, HPV745, HPV746, HPV747, HPV748, HPV749, HPV750, HPV751, HPV752, HPV753, HPV754, HPV755, HPV756, HPV757, HPV758, HPV759, HPV760, HPV761, HPV762, HPV763, HPV764, HPV765, HPV766, HPV767, HPV768, HPV769, HPV770, HPV771, HPV772, HPV773, HPV774, HPV775, HPV776, HPV7



HPV attribution (other than cervix)

- 100% of anal squamous cell carcinoma cases associated with HPV
- 25% of vulvar cancer
- 78% of vaginal cancer
- 53% of penile cancer
- 31% of oropharyngeal cancer
- $\leq 5\%$ of oral cavity cancer

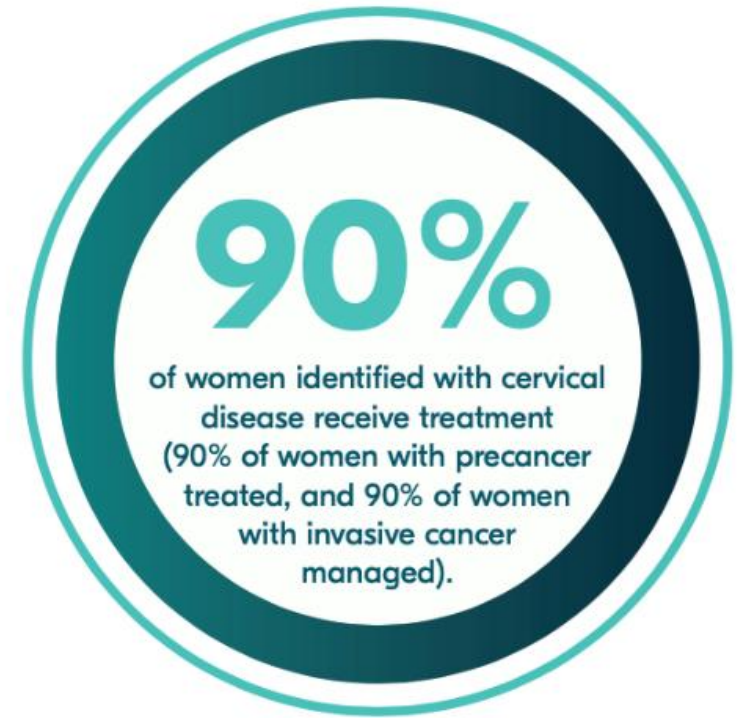




Primary prevention



Secondary prevention



Tertiary prevention

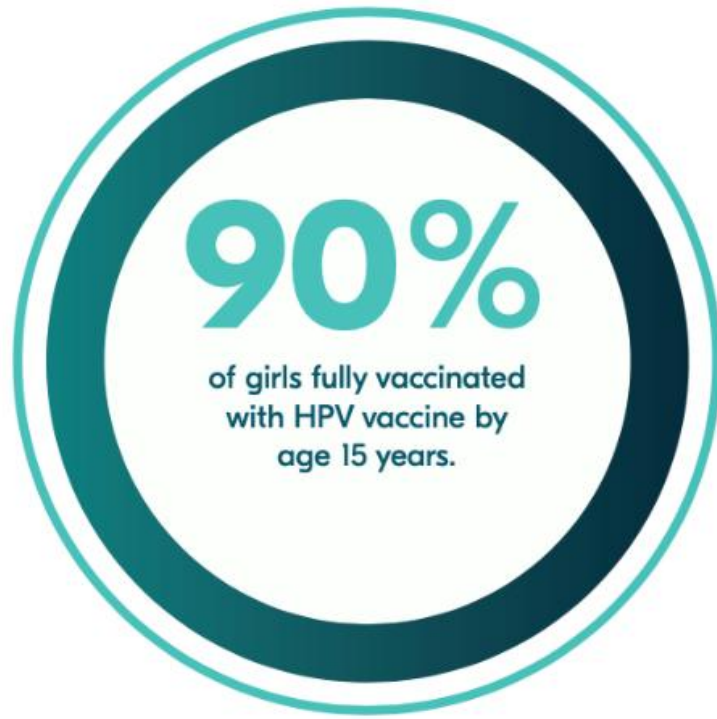


World Health Organization

ELIMINATION TARGETS 2030



World Health Organization



Primary
prevention



World Health
Organization

ELIMINATION TARGETS 2030



World Health
Organization

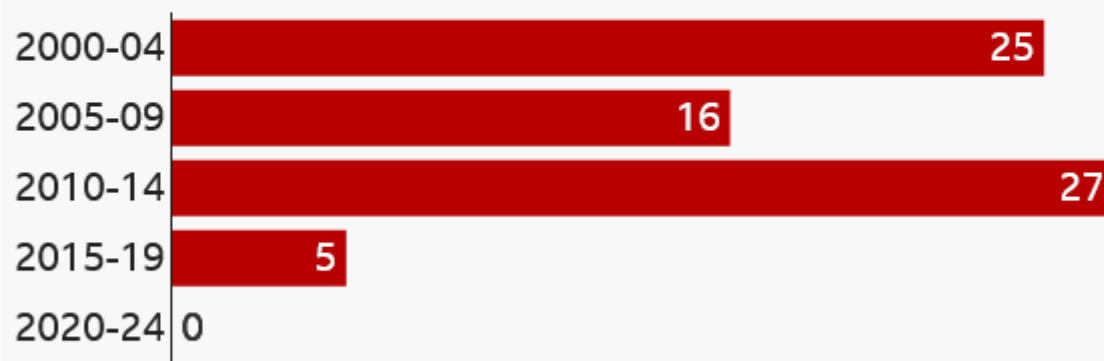
Universal HPV Vaccination

- Targeting **all individuals** within a recommended age group
- Key Advantages:
 - **Best clinical outcomes** preventing HPV infections and disease
 - **Herd protection**
 - **Equitable** access to vaccine
 - **School-based programs** are efficient and cost-effective

Young women now have 'close to zero' risk of cervical cancer death after HPV jab

Deaths from cervical cancer

Deaths of women aged 20 to 24 in England in each five year period



Source: Peter Sasieni, Milena Falcaro, The Lancet



70%

of women are screened
with a high-performance
test by 35 years of age and
again by 45 years of age.

Secondary
Prevention



World Health
Organization

ELIMINATION TARGETS 2030



World Health
Organization

Transition from Cytology to HPV

- WHO recommends **HPV DNA detection** as screening test rather than VIA or cytology
- Excellent **sensitivity**
- **Self-sampling** possible
- If test is negative – **very low risk** for cancer in the next 5-10 years
- **Quick results** – reduce “loss to follow-up”



Target product profiles
for human papillomavirus
screening tests to detect
cervical pre-cancer and cancer



Table 3.1 New stratification of carcinogenic HPV types (IARC Group 1)

Subgroup	Carcinogenic HPV types included
Group 1a	HPV16
Group 1b	HPV18, HPV45
Group 1c	HPV31, HPV33, HPV35, HPV52 and HPV58
Group 1d	HPV39, HPV51, HPV56 and HPV59

Source: adapted from IARC, 2022 (11). See also Table 1.2.

Fig. 1.10 Relative importance of the carcinogenic human papillomavirus (HPV) types

HPV type	HPV species	IARC Group ^a		% HPV type prevalence in cancer	% HPV type prevalence in normal	Odds ratio	% Attributable (etiological) fraction
HPV16	α-9	Group 1	a	55.8	2.6	47.6	62.4
HPV18	α-7	Group 1	b	14.3	1	15.7	15.3
HPV45	α-7	Group 1	b	4.8	0.6	8.3	4.8
HPV33	α-9	Group 1	c	4	0.6	7.1	3.9
HPV58	α-9	Group 1	c	4	0.8	5.1	3.7
HPV31	α-9	Group 1	c	3.5	1	3.7	2.9
HPV52	α-9	Group 1	c	3.2	1	3.3	2.6
HPV35	α-9	Group 1	c	1.6	0.4	3.9	1.4
HPV59	α-7	Group 1	d	1.2	0.4	2.9	0.9
HPV39	α-7	Group 1	d	1.3	0.6	2.0	0.8
HPV68	α-7	Group 2A		0.6	0.4	1.5	0.2
HPV51	α-5	Group 1	d	1	0.9	1.2	0.2
HPV56	α-6	Group 1	d	0.8	0.6	1.3	0.2
HPV73	α-11	Group 2B		0.5	0.3	1.8	0.2
HPV26	α-5	Group 2B		0.2	0.1	4.1	0.2
HPV30	α-6	Group 2B		0.2	0.1	2.6	0.1
HPV69	α-5	Group 2B		0.2	0.1	1.4	0.1
HPV67	α-9	Group 2B		0.3	0.2	1.2	< 0.1
HPV82	α-5	Group 2B		0.2	0.1	1.2	< 0.1
HPV34	α-11	Group 2B		0.1	0.1	1.0	Not attributable
HPV66	α-6	Group 2B		0.3	0.6	0.4	Not attributable
HPV70	α-7	Group 2B		0.2	0.8	0.3	Not attributable
HPV53	α-6	Group 2B		0.5	1.1	0.4	Not attributable

Fig. 1.10 Relative importance of the carcinogenic human papillomavirus (HPV) types

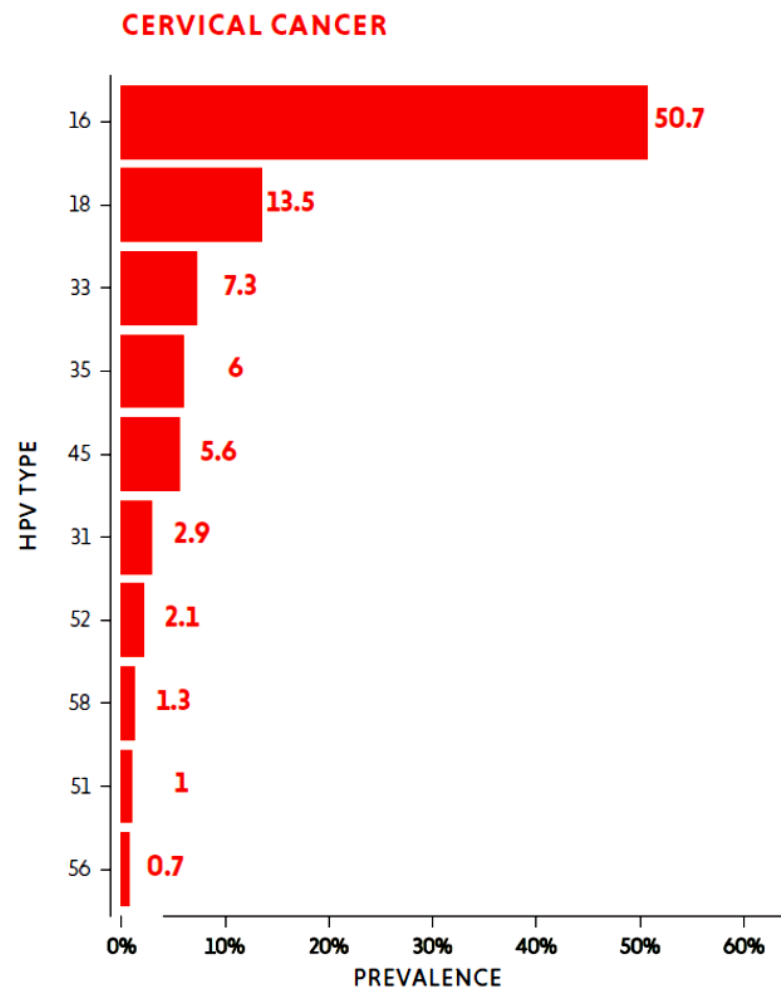
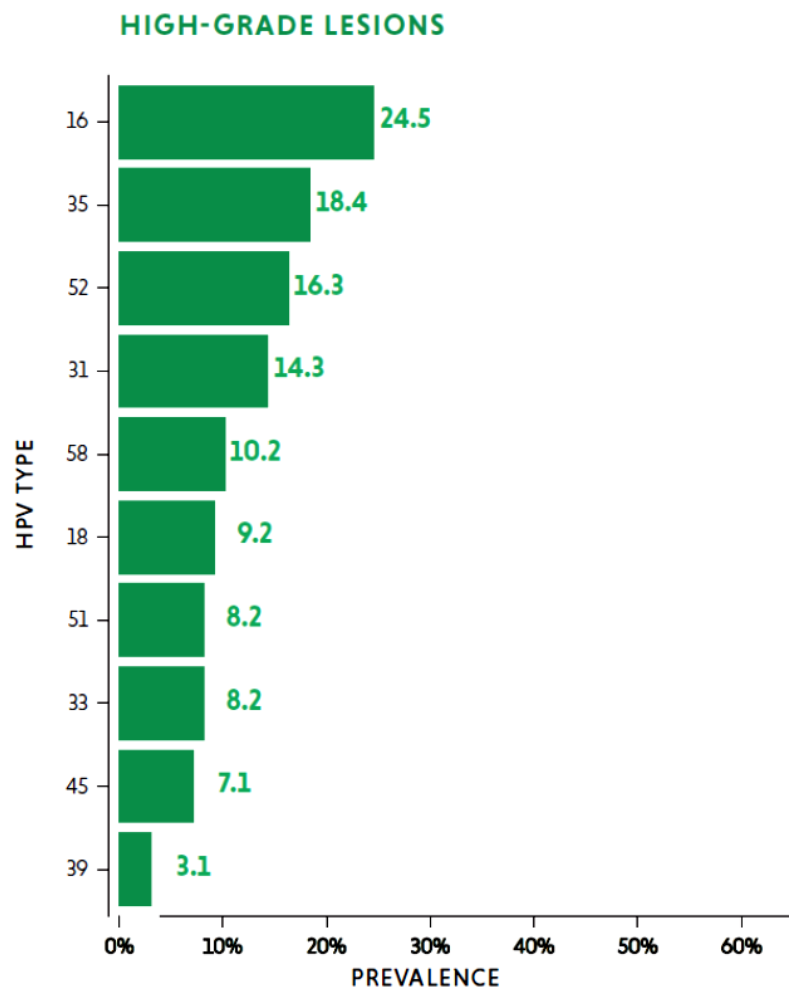
HPV type	HPV species	IARC Group ^a		% HPV type prevalence in cancer	% HPV type prevalence in normal	Odds ratio	% Attributable (etiological) fraction
HPV16	α-9	Group 1	a	55.8	2.6	47.6	62.4
HPV18	α-7	Group 1	b	14.3	1	15.7	15.3
HPV45	α-7	Group 1	b	4.8	0.6	8.3	4.8
HPV33	α-9	Group 1	c	4	0.6	7.1	3.9
HPV58	α-9	Group 1	c	4	0.8	5.1	3.7
HPV31	α-9	Group 1	c	3.5	1	3.7	2.9
HPV52	α-9	Group 1	c	3.2	1	3.3	2.6
HPV35	α-9	Group 1	c	1.6	0.4	3.9	1.4
HPV59	α-7	Group 1	d	1.2	0.4	2.9	0.9
HPV39	α-7	Group 1	d	1.3	0.6	2.0	0.8
HPV68	α-7	Group 2A		0.6	0.4	1.5	0.2
HPV51	α-5	Group 1	d	1	0.9	1.2	0.2
HPV56	α-6	Group 1	d	0.8	0.6	1.3	0.2
HPV73	α-11	Group 2B		0.5	0.3	1.8	0.2
HPV26	α-5	Group 2B		0.2	0.1	4.1	0.2
HPV30	α-6	Group 2B		0.2	0.1	2.6	0.1
HPV69	α-5	Group 2B		0.2	0.1	1.4	0.1
HPV67	α-9	Group 2B		0.3	0.2	1.2	< 0.1
HPV82	α-5	Group 2B		0.2	0.1	1.2	< 0.1
HPV34	α-11	Group 2B		0.1	0.1	1.0	Not attributable
HPV66	α-6	Group 2B		0.3	0.6	0.4	Not attributable
HPV70	α-7	Group 2B		0.2	0.8	0.3	Not attributable
HPV53	α-6	Group 2B		0.5	1.1	0.4	Not attributable

Fig. 1.10 Relative importance of the carcinogenic human papillomavirus (HPV) types

HPV type	HPV species	IARC Group ^a		% HPV type prevalence in cancer	% HPV type prevalence in normal	Odds ratio	% Attributable (etiological) fraction
HPV16	α-9	Group 1	a	55.8	2.6	47.6	62.4
HPV18	α-7	Group 1	b	14.3	1	15.7	15.3
HPV45	α-7	Group 1	b	4.8	0.6	8.3	4.8
HPV33	α-9	Group 1	c	4	0.6	7.1	3.9
HPV58	α-9	Group 1	c	4	0.8	5.1	3.7
HPV31	α-9	Group 1	c	3.5	1	3.7	2.9
HPV52	α-9	Group 1	c	3.2	1	3.3	2.6
HPV35	α-9	Group 1	c	1.6	0.4	3.9	1.4
HPV59	α-7	Group 1	d	1.2	0.4	2.9	0.9
HPV39	α-7	Group 1	d	1.3	0.6	2.0	0.8
HPV68	α-7	Group 2A		0.6	0.4	1.5	0.2
HPV51	α-5	Group 1	d	1	0.9	1.2	0.2
HPV56	α-6	Group 1	d	0.8	0.6	1.3	0.2
HPV73	α-11	Group 2B		0.5	0.3	1.8	0.2
HPV26	α-5	Group 2B		0.2	0.1	4.1	0.2
HPV30	α-6	Group 2B		0.2	0.1	2.6	0.1
HPV69	α-5	Group 2B		0.2	0.1	1.4	0.1
HPV67	α-9	Group 2B		0.3	0.2	1.2	< 0.1
HPV82	α-5	Group 2B		0.2	0.1	1.2	< 0.1
HPV34	α-11	Group 2B		0.1	0.1	1.0	Not attributable
HPV66	α-6	Group 2B		0.3	0.6	0.4	Not attributable
HPV70	α-7	Group 2B		0.2	0.8	0.3	Not attributable
HPV53	α-6	Group 2B		0.5	1.1	0.4	Not attributable

91%

Top 10 oncogenic HPV prevalence in SA



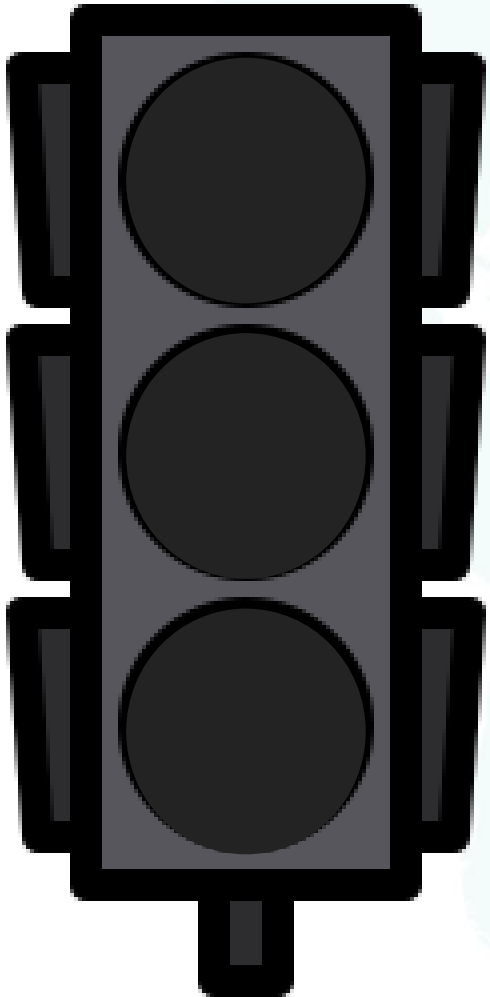
Interpreting Risk Using Genotype Information

- Internal control β -globin gene (test can be invalid)

- **High risk: HPV 16, 18, 45**

- **Moderate risk: 5 HPV types (33, 35, 58, 31, 52)**

- **Negative: Extremely low risk for cancer**



HPV primary screening all women 25yrs and older
(consider self sampling to increase coverage)

HPV
negative

HIV
negative

Rescreen in 10
years

HIV positive

Rescreen in 5
years

HPV
positive

HPV pos
(16, 18 &
45)

Gynaecological
assessment under
VIA

HPV pos
(other high
risk)

Reflex
Cytology

Conclusion

- **HPV vaccination a major win** for public health
- Screening - **HPV testing** identify those at **highest risk for cancer**
- “Loss to follow-up” a major problem
- **Effective treatment** will prevent cancers (not only doing a screening test)
- We have the tools – **Let’s get it done!**