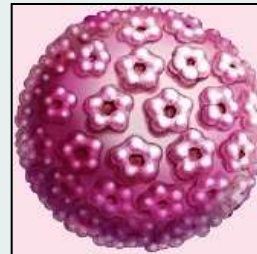
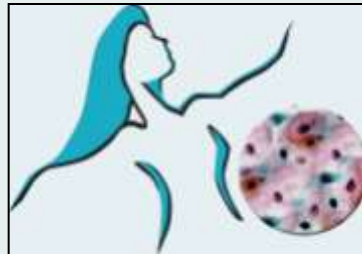
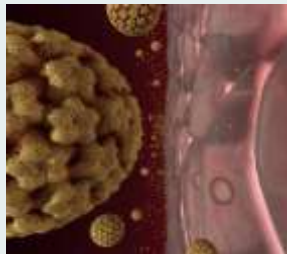
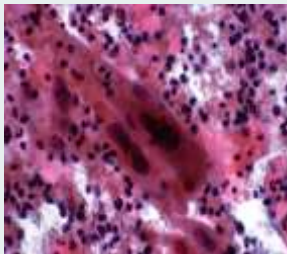


Hospital de São Bernardo

10 de Dezembro de 2012



Infeção por HPV e Cancro do Colo do Útero

Angela Pista

**Instituto Nacional de Saúde Doutor Ricardo Jorge
Departamento de Doenças Infecciosas**

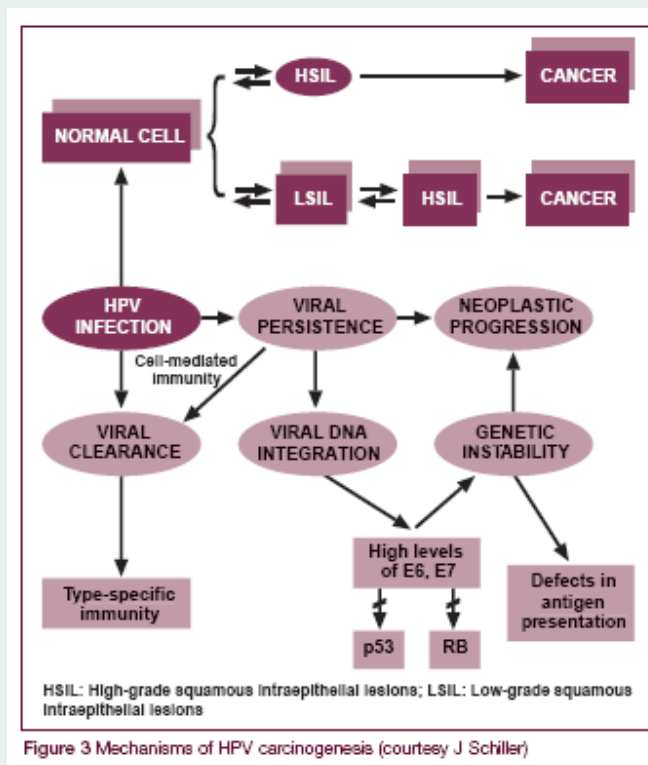
Classificação do HPV

- Cerca de 45 tipos infetam a região anogenital (HR-HPV, LR-HPV)

Potencial oncogénico	Tipo de HPV
Alto Risco (Grupo 1)	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59
Provável Alto Risco (2A) Possível Alto Risco (2B)	68* 26, 53, 66*, 67*, 70*, 73, 82
Baixo risco	6, 11, 40, 42, 43, 44, 54, 61, 72, 81, 89
Risco indeterminado	30, 34, 55, 57, 62, 69, 71, 74, 77, 83, 84, 85, 86, 87, 90, 91, 97

HPV e Cancro

- Infecção
- Persistência
- Progressão
- Invasão



Co-fatores:

- Virais (tipo HPV, infecções mistas, carga viral, integração)
- Hospedeiro
- Externos

Epidemiologia do HPV em Portugal (Estudos CLEOPATRE)

Prevalência do HPV por Região

Region	Countries (no. of studies)	Women, no.		HPV prevalence, % (95% CI)	
		Total tested	HPV positive	Crude	Adjusted ^a
World		1,016,719	73,018	7.2 (7.1–7.2)	11.7 (11.6–11.7)
Less developed regions ^b		120,008	17,207	14.3 (14.1–14.5)	11.8 (11.6–12.0)
More developed regions ^c		895,862	55,747	6.2 (6.2–6.3)	11.3 (11.2–11.3)
Africa		8568	1829	21.3 (20.5–22.2)	21.1 (20.2–22.0)
Northern Africa	Tunisia (1), Morocco (2), Egypt (1), Algeria (1)	863	94	10.9 (8.9–13.2)	9.2 (7.3–11.3)
Sub-Saharan Africa		7705	1735	22.5 (21.6–23.5)	24.0 (23.1–25.0)
Eastern Africa	Zimbabwe (1), Mozambique (1), Kenya (1)	751	252	33.6 (30.2–37.1)	33.6 (30.2–37.1)
Southern Africa	South Africa (3)	2485	521	21.0 (19.4–22.6)	17.4 (15.9–18.9)
Western Africa	Senegal (2), Nigeria (2), Guinea (1), Gambia (1), Cote d'Ivoire (2)	4469	962	21.5 (20.3–22.8)	19.6 (18.5–20.8)
America		692,964	39,522	5.7 (5.6–5.8)	11.5 (11.4–11.6)
Latin America and Caribbean		48,171	8279	17.2 (16.9–17.5)	16.1 (15.8–16.4)
Caribbean	Trinidad and Tobago (1)	212	75	35.4 (29.0–42.2)	35.4 (29.0–42.2)
Central America	Mexico (8), Honduras (2), Guatemala (1), Costa Rica (2), Belize (1)	24,783	5110	20.6 (20.1–21.1)	13.0 (12.6–13.5)
South America	Peru (3), Paraguay (2), Colombia (3), Chile (1), Brazil (6), Argentina (3)	17,500	2302	13.2 (12.7–13.7)	15.3 (14.7–15.8)
Northern America	United States (19), Greenland (1), Canada (6)	644,793	31,243	4.8 (4.8–4.9)	4.7 (4.6–4.7)
Asia		84,710	9235	10.9 (10.7–11.1)	9.4 (9.2–9.6)
Eastern Asia	Mongolia (1), South Korea (6), Japan (12), China (14)	55,365	6983	12.6 (12.3–12.9)	10.7 (10.4–10.9)
Southern Asia	India (12)	23,061	1816	7.9 (7.5–8.2)	7.1 (6.7–7.4)
Southeastern Asia	Vietnam (2), Thailand (7), Philippines (1), Indonesia (1)	4849	405	8.4 (7.6–9.2)	14.0 (13.0–15.0)
Western Asia	Turkey (1), Bahrain (1)	1435	31	2.2 (1.5–3.1)	1.7 (1.1–2.5)
Europe		229,628	22,368	9.7 (9.6–9.9)	14.2 (14.1–14.4)
Eastern Europe	Russian Federation (2), Poland (1), Hungary (1), Belarus (1), Latvia (1)	4053	904	22.3 (21.0–23.6)	21.4 (20.1–22.7)
Northern Europe	United Kingdom (8), Sweden (3), Norway (3), Lithuania (1), Ireland (1), Finland (1), Denmark (4)	97,242	10,531	10.8 (10.6–11.0)	10.0 (9.8–10.2)
Southern Europe	Spain (5), Italy (12), Greece (3), Croatia (1)	41,726	3820	9.2 (8.9–9.4)	8.8 (8.5–9.0)
Western Europe	Switzerland (1), Netherlands (4), Germany (2), France (7), Belgium (4)	77,445	5652	7.3 (7.1–7.5)	9.0 (8.8–9.2)

NOTE. CI, confidence interval.

^a Adjusted HPV prevalence standardized by the world's geographical structure. Model adjusted by geographical subregion, mean age of women, ending year of the study, HPV testing method, proportion of high-risk HPV types tested, proportion of low-risk HPV types tested, and cluster analysis of mixtures).

^b Africa, the Americas (excluding Northern America), Caribbean, Central America, South America, Asia (excluding Japan), and Oceania (excluding Australia and New Zealand) [12].

^c Northern America, Europe, Japan, Australia, and New Zealand [12].



Resultados Citológicos - CLEO I

99,5% das citologias foram satisfatórias.

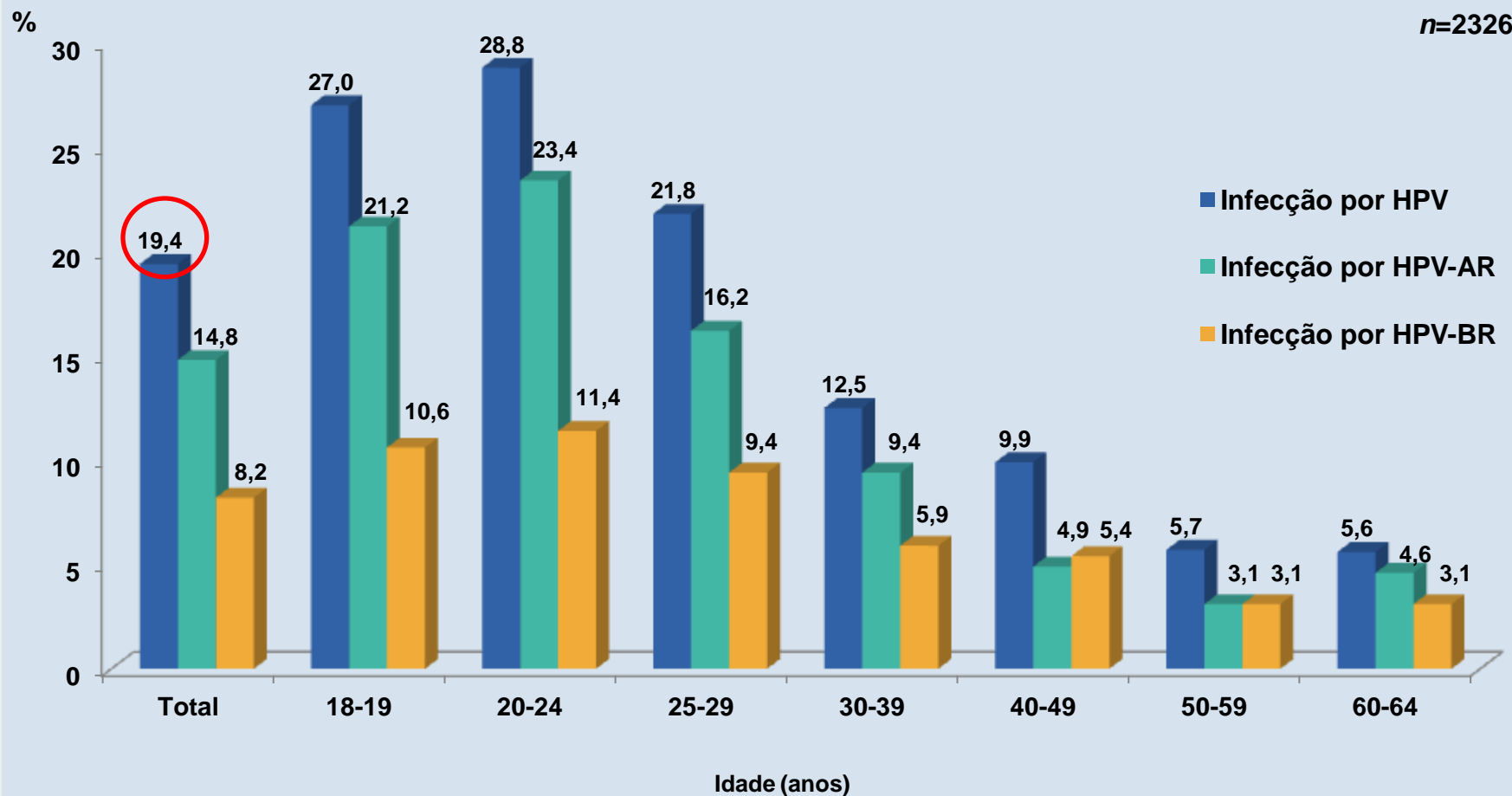
Citologia	População	
	N	%
Normal	2172	93,8
ASC-US	57	2,5
LSIL	74	3,2
ASC-H	2	0,1
HSIL	4	0,2
AGC	6	0,3
Total	2315	

Prevalência global do HPV no estudo: 19,4%.

Prevalência do HPV nas citologias normais: 16,5% (Europa: 9,7%).

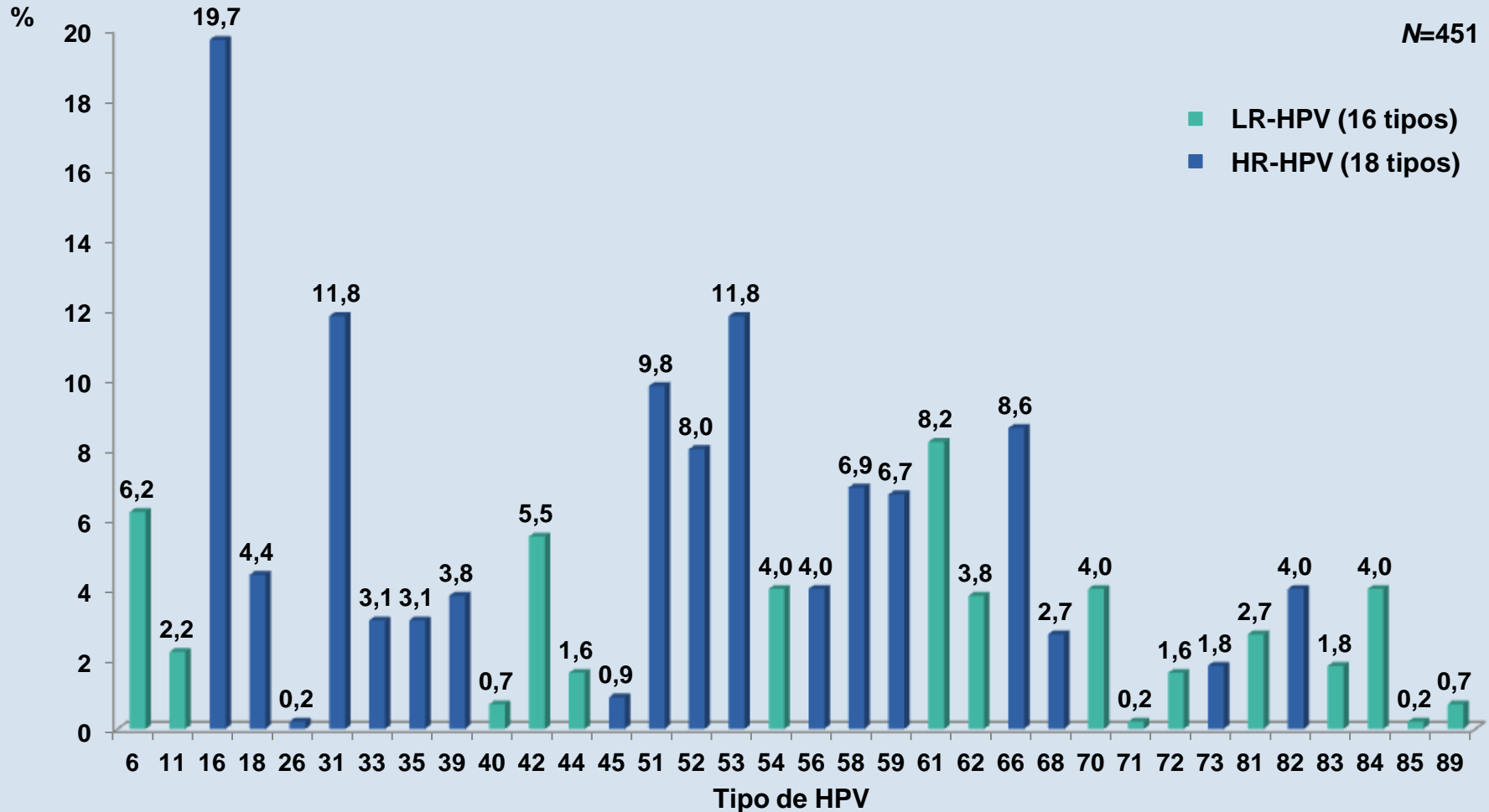


Prevalência HR E LR-HPV / Idade - CLEO I





Prevalência dos Tipos de HPV - CLEO I



HPV 6, 11, 16, 18 - 1 HPV: 32,6%; 2 HPV: 2,0%; 3 ou 4 HPV: 0,0%.

Prevalência do HPV por Histologia - CLEO II

Histologia	Casos	HPV +vos (%)	Inf. Simples (%)	Inf. Mistas (%)
CIN2	177	169 (95,5)	144 (85,2)	25 (14,8)
CIN3	341	339 (99,4)	305 (90,0)	34 (10,0)
SCC	57	56 (98,2)	51 (91,1)	5 (8,9)
ADC	7	6 (85,7)	6 (100)	0 (0,0)
CC	64	62 (96,9)	57 (89,1)	5 (7,8)
Total	582	570 (97,9)	506 (88,8)	64 (11,2)

Importância Clínica dos Diferentes Tipos de HR-HPV

Potencial Oncogénico dos HR-HPV

HPV 16

- 50-65% dos CCU
- risco de persistência e progressão
- > capacidade de evasão ao SI
OR = 434

HPV 18

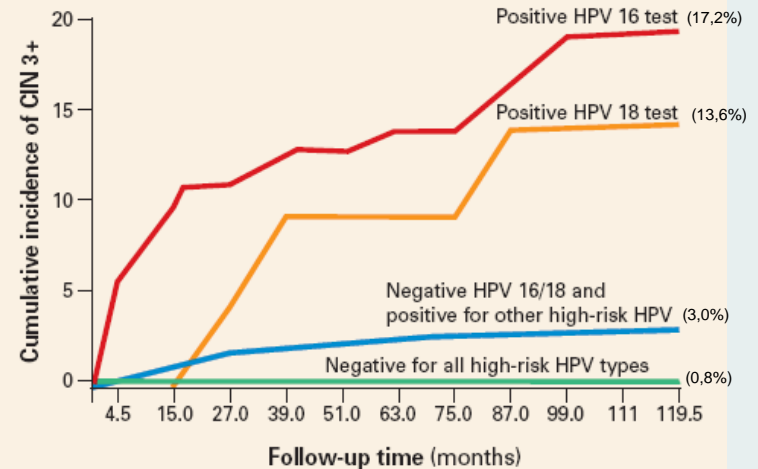
- 7-20% dos CCU
- potencial oncogénico, adenocarcinoma
- > taxa de mortalidade
OR = 248

HPV 31

HPV 45

HPV 33, 52, 58, 35, 59, 56, 51, 39 ...

**Positive HPV 16 or 18
linked to 14% to 17% incidence of CIN3+**



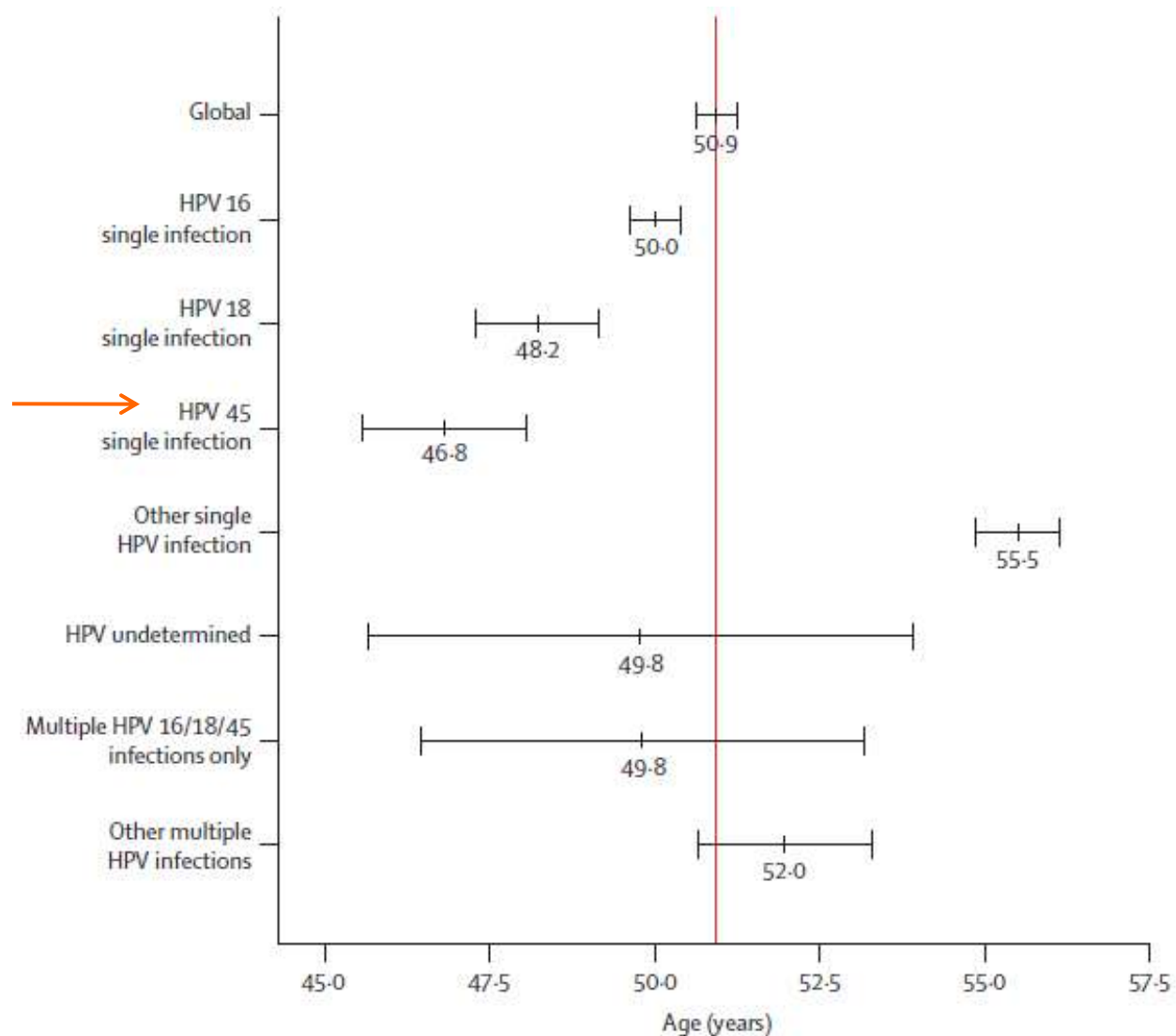


Figure 2: Mean age (95% CIs) at diagnosis of invasive cervical cancer

Data were adjusted for histological type of cancer, year of diagnosis, and geographical region. HPV=human papillomavirus.

Importância do Teste HPV

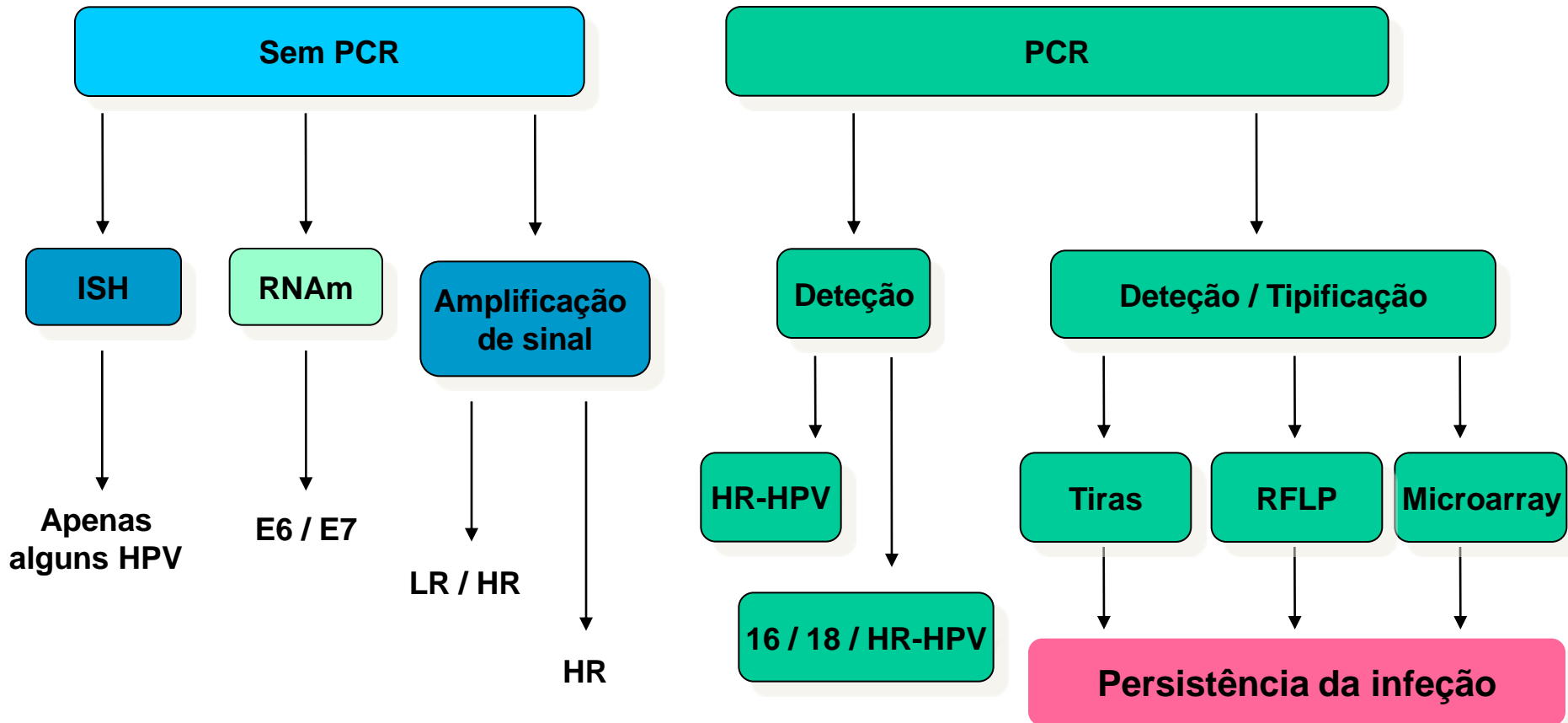
DNA *vs.* RNA

Utilidade Clínica do Teste HPV

➤ **Quando, Porquê, Para Quê?**

Testes HPV

BIOLOGIA MOLECULAR



Utilidade Clínica do Teste HPV

✓ Rastreio

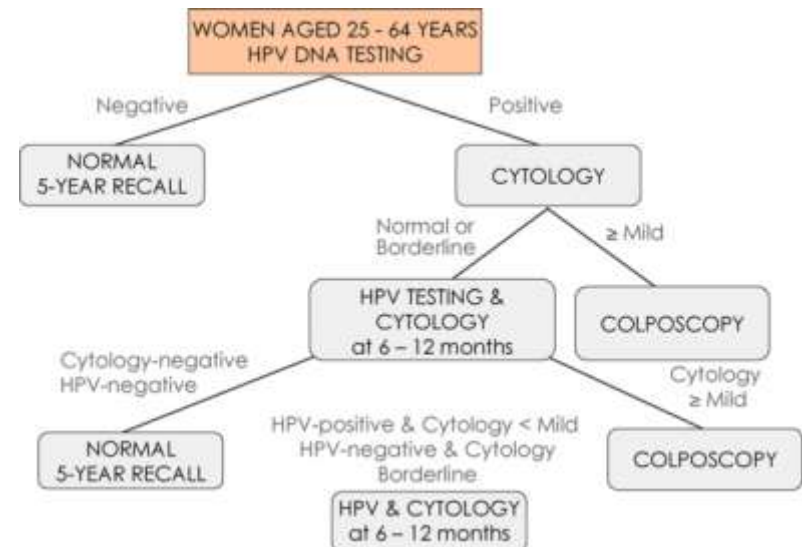
Citologia vs Teste HPV

Aumento médio da sensibilidade: 28%

Perda média da especificidade: 7%

	Sensib.	Especif.
HPV	96%	92%
Citologia	51%	95%

✓ Aumento do intervalo entre testes de rastreio (VPN \Rightarrow 5-8 anos)



Utilidade Clínica do Teste HPV

- ✓ **Redução custo/benefício**
- ✓ **ASC-US**
- ✓ **Citologias normais com HR-HPV (risco de CIN3 em 4 anos)**
- ✓ **LSIL (pós-menopausa)**
- ✓ **Orientação pós-colposcópica dos casos de AGC e ASC-H**
- ✓ **Avaliação pós-tratamento**
- ✓ **Auxiliar de diagnóstico (casos discrepantes, adenocarcinomas)**
- ✓ **Monitorização das mulheres vacinadas**

Utilidade Clínica do Teste HPV

Deteção HR-HPV / Tipificação

ou

Tipificação

✓ **Tipificação:**

- **Persistência da infecção**
- **Avaliação pós-tratamento**
- **Deteção de infecções mistas**
- **Diferente patogenicidade dos HR-HPV**
- **Era pós-vacina (↑ espec. e VPP para ASC-US e LSIL)**

Diagnóstico Especializado - DNA vs RNA

BIOLOGIA MOLECULAR

1º Teste

Detecção / Tipificação

> Sensibilidade e VPN

2º Teste

RNAm do E6/E7

> Especificidade e VPP

Table II: Clinical performance for \geq CIN2 based on Pap smear and biopsy diagnosis

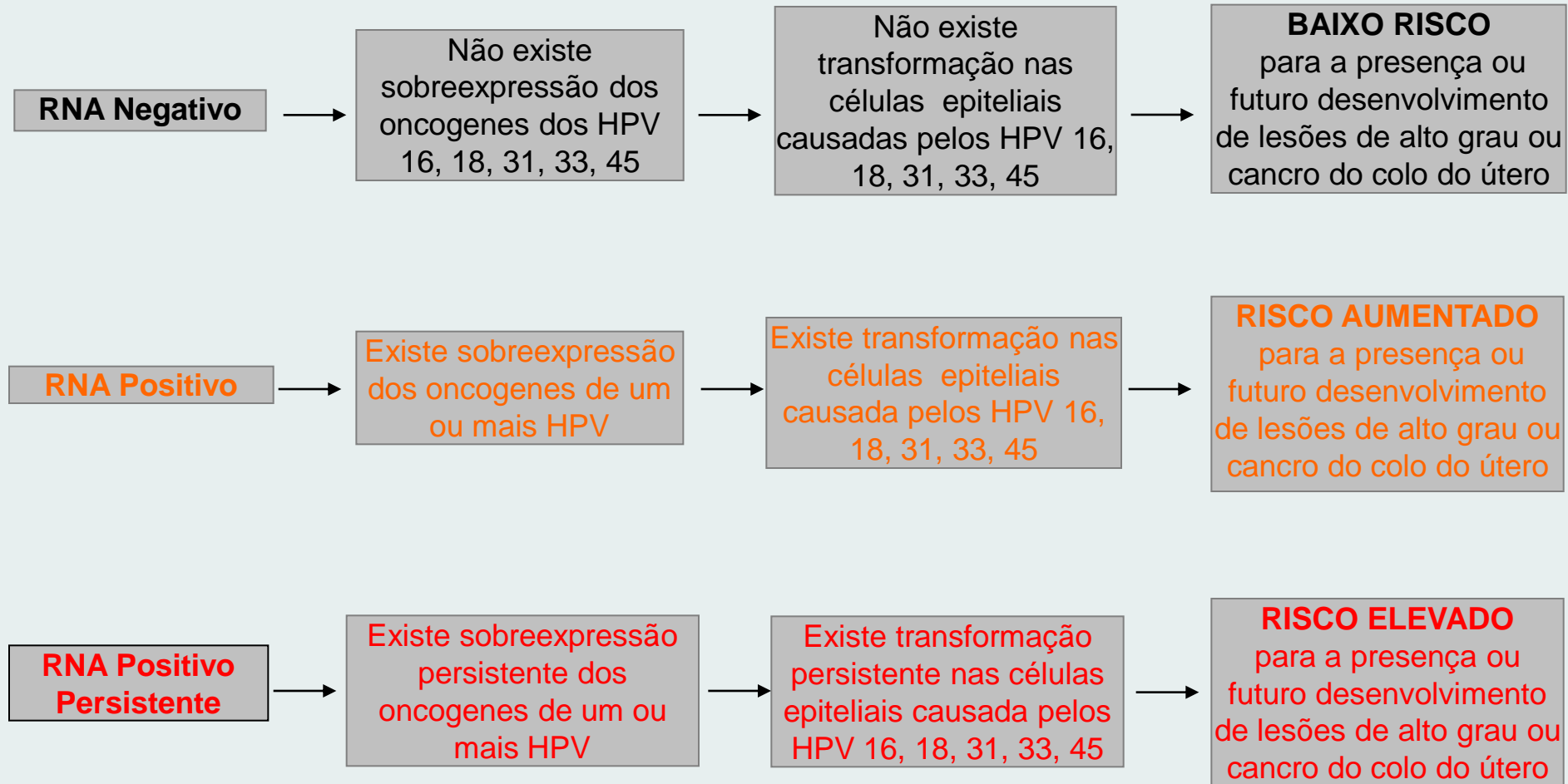
	Clinical Diagnosis		Sensitivity %	Specificity %	PPV %	NPV %
	\leq CIN1	\geq CIN2	(95% CI)	(95% CI)	(95% CI)	(95% CI)
All women						
NucliSENS EasyQ HPV [®]						
Negative	188	61	79.3	72.6	76.7	75.5
Positive	71	234	(75.7-82.6)	(68.4-76.8)	(73.2-79.9)	(71.2-79.4)
CLART-13 HR-HPV ^a						
Negative	110	12	95.9	42.5	65.5	90.2
Positive	149	283	(93.3-97.7)	(39.1-45.9)	(61.7-66.7)	(83.7-94.5)
CLART-5 HR-HPV ^a						
Negative	127	16	94.6	49.0	67.9	88.8
Positive	132	279	(91.7-96.7)	(45.8-51.4)	(65.8-69.4)	(82.9-93.1)

Níveis de E6/E7

Início da replicação

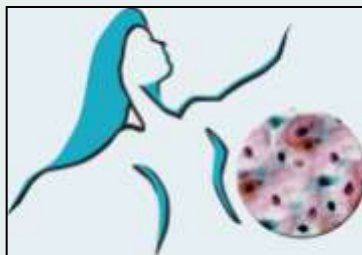
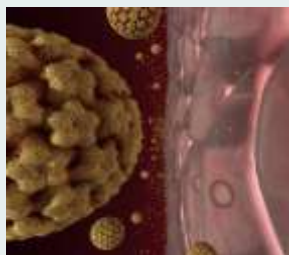
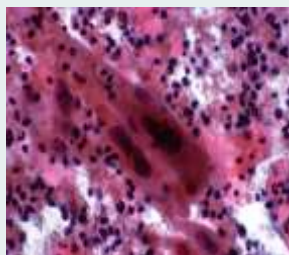
Sobreexpressão de E6/E7

RNA_m – Sobreexpressão dos Oncogenes E6/E7



Hospital de São Bernardo

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Muito obrigada.

