SCHAP

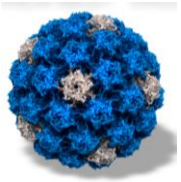
XXIII Congreso Chileno de Anatomía Patológica

Detección y genotipado de HPV Cambios en el cribado de lesiones cervicales

Eva Musulén

Hospital Universitari General de Catalunya
Grupo quirónsalud

Fundación JOSEP CARRERAS contra la leucemia

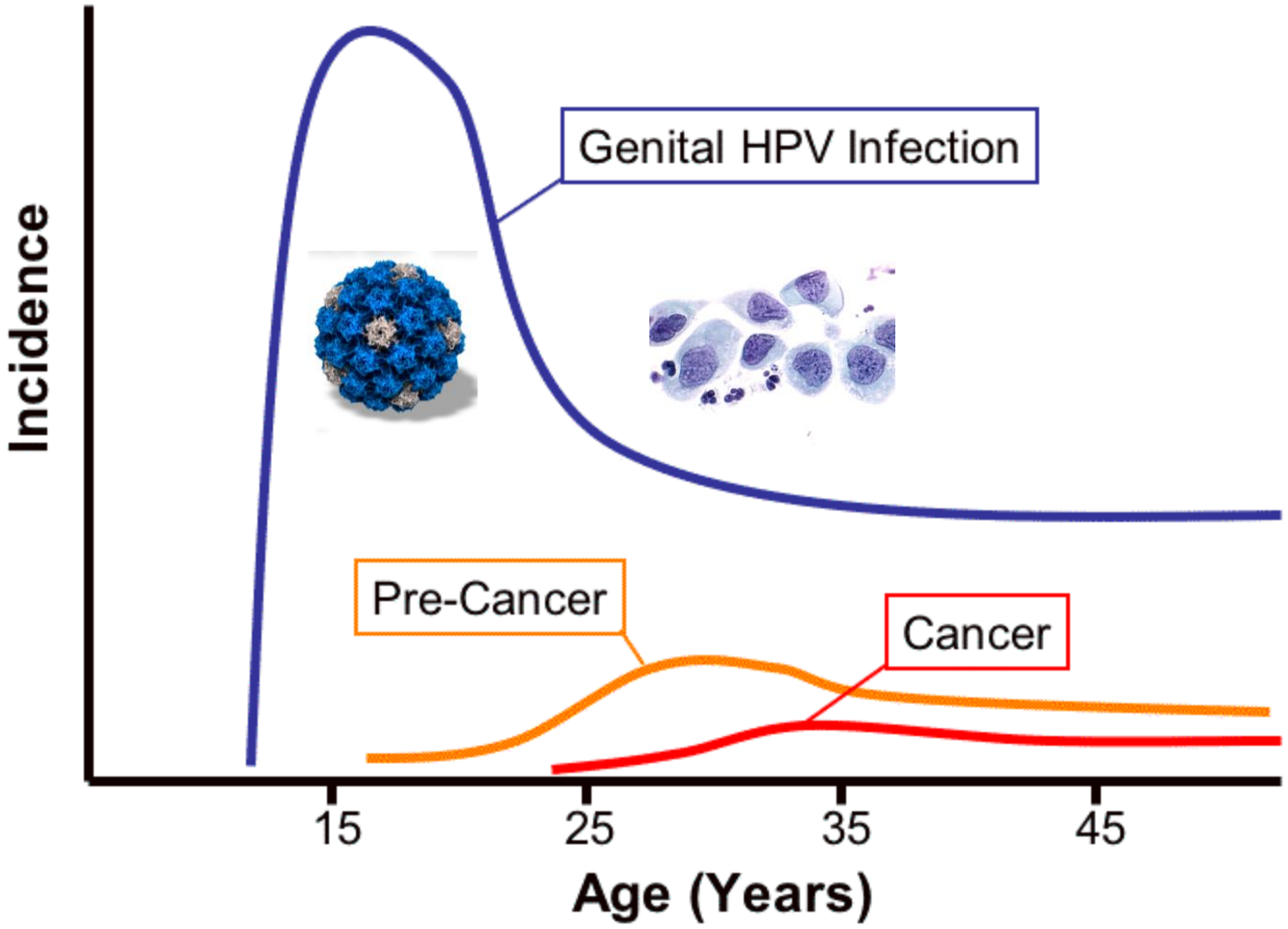


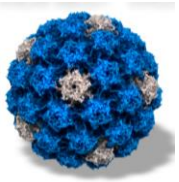
- El virus del papiloma humano (VPH) es la infección de transmisión sexual más frecuente

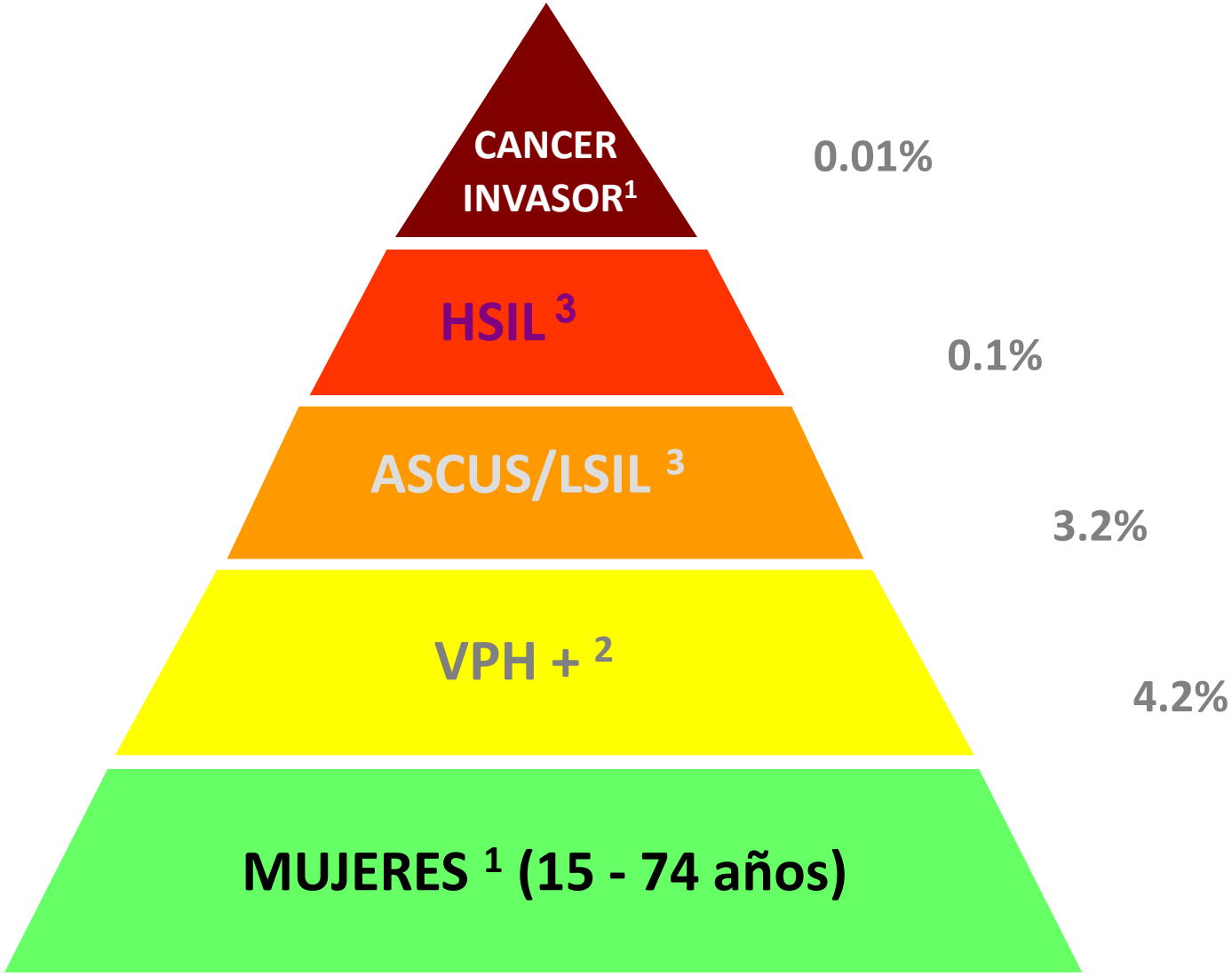
- El VPH es uno de los carcinógenos más potentes

- Aproximadamente 610.000 (5%) nuevos cánceres anuales son atribuibles al VPH:
    - Cáncer de cérvix uterino: 530.000 (275.000 muertes)
    - Cáncer anal: 24.000
    - Pene, vulva, vagina, orofaringe

- El 80% de estos cánceres aparecen en países en vías de desarrollo (95% de mujeres nunca cribadas).


Incidence
Genital HPV Infection
Pre-Cancer
Cancer
15
25
35
45
Age (Years)





1 Globocan 2000.

2 Estimación basada en estudios de prevalencia de HPV de población general en 2 areas urbanas de Cataluña.

3 Estimación de prevalencia de SIL basado en 2.

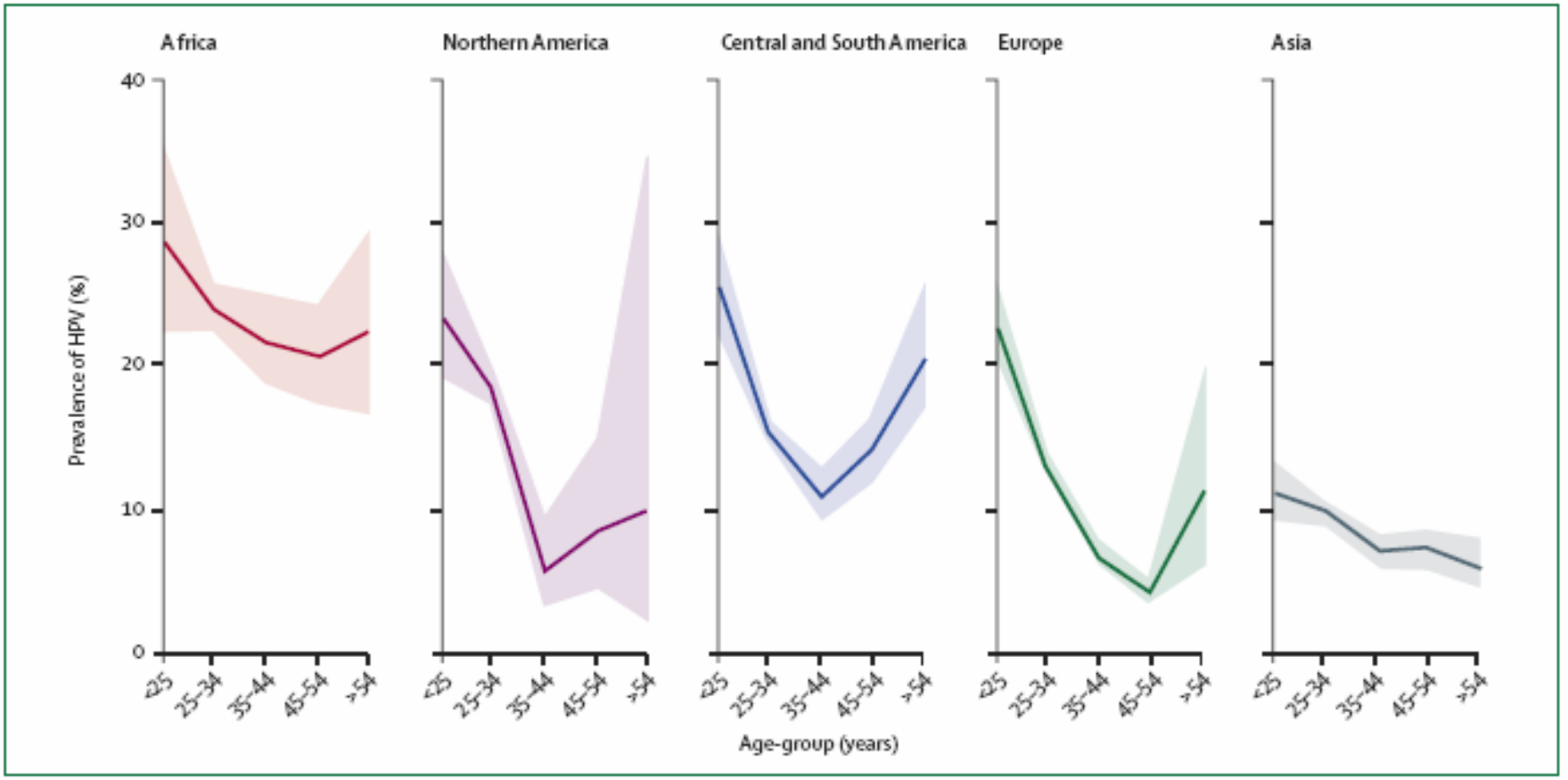
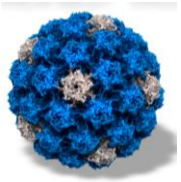


Figure 2: Age-specific HPV prevalence among women with normal cytology, by world region
Shaded areas represent 95% CIs.

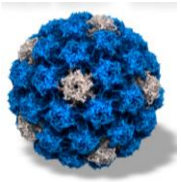
de Sanjose et al. 2007

Progresión de las lesiones intraepiteliales

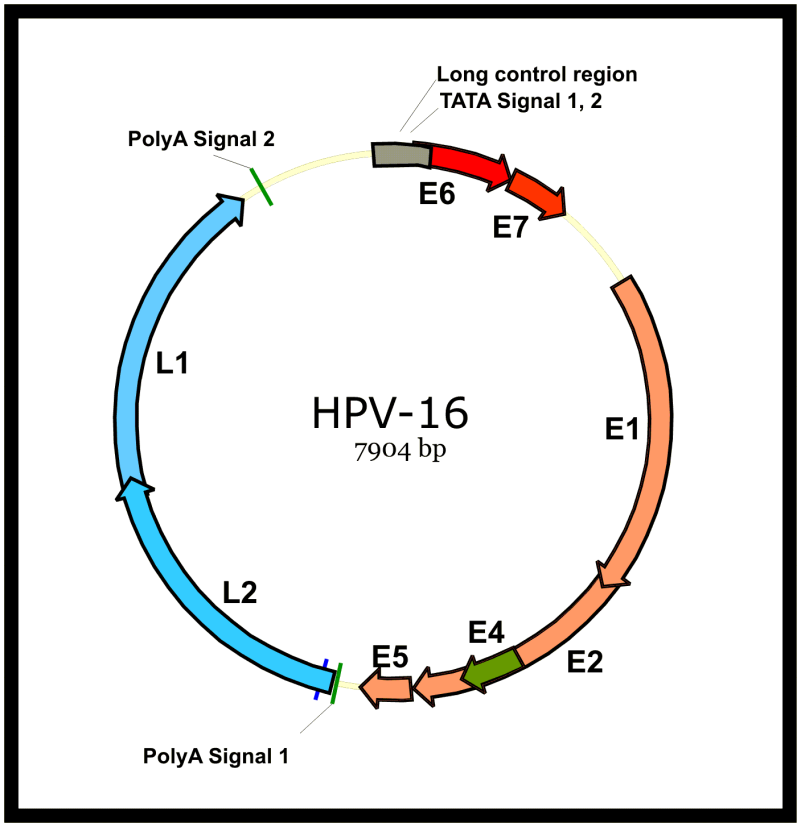


- Aproximadamente el 20% de CIN1 progresa a CIN2
- Aproximadamente el 30 % de CIN 2 progresa a CIN 3 (si no se trata)
- Aproximadamente el 40% de CIN3 puede progresar a cáncer (si no se trata)

Virus del papiloma humano



- Fam Papillomaviridiae (de Villiers et al. 2004)
- Virus DNA de doble cadena sin envoltura
- Genoma circular de aprox. 8 kb

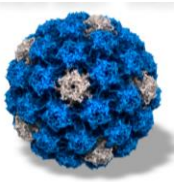


>120 tipos secuenciados

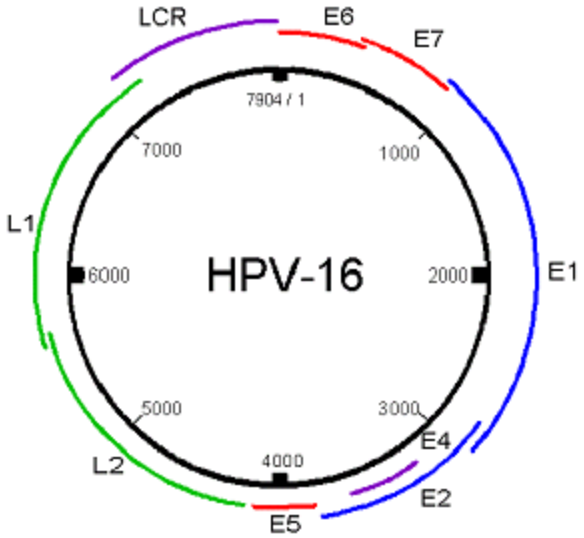
- Mucosas

- Bajo riesgo oncogénico

- Alto riesgo oncogénico



A



Integration

B

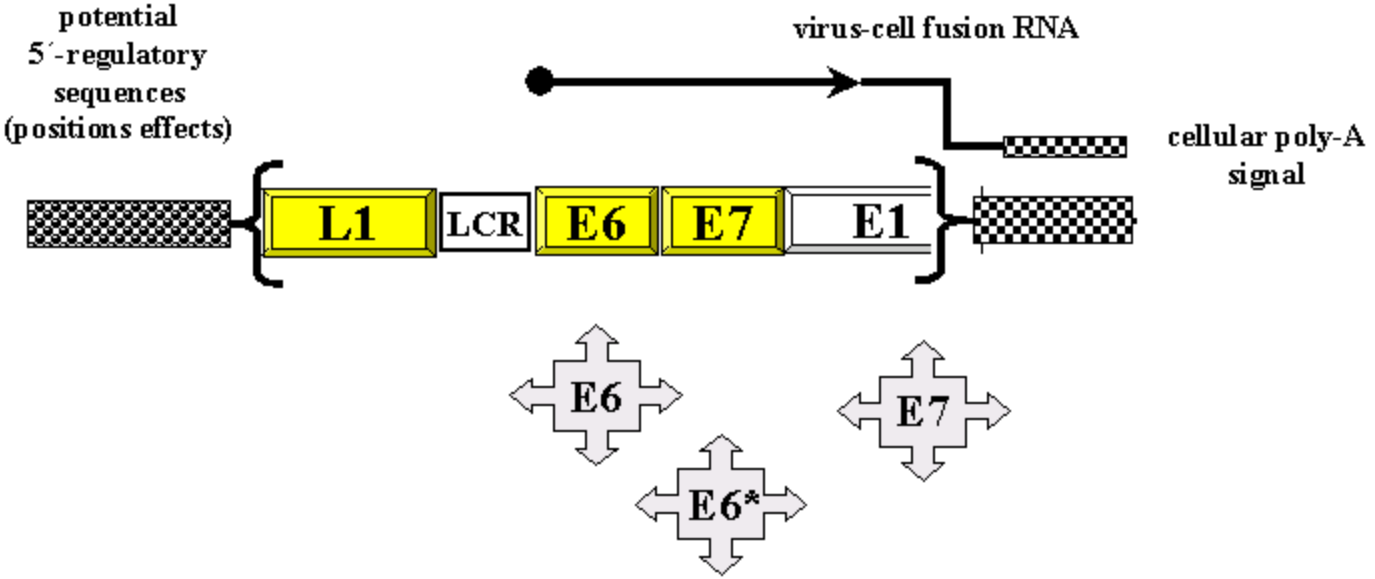
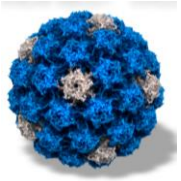


Fig. 1

Métodos diagnósticos de la infección por HPV



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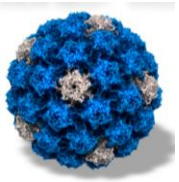
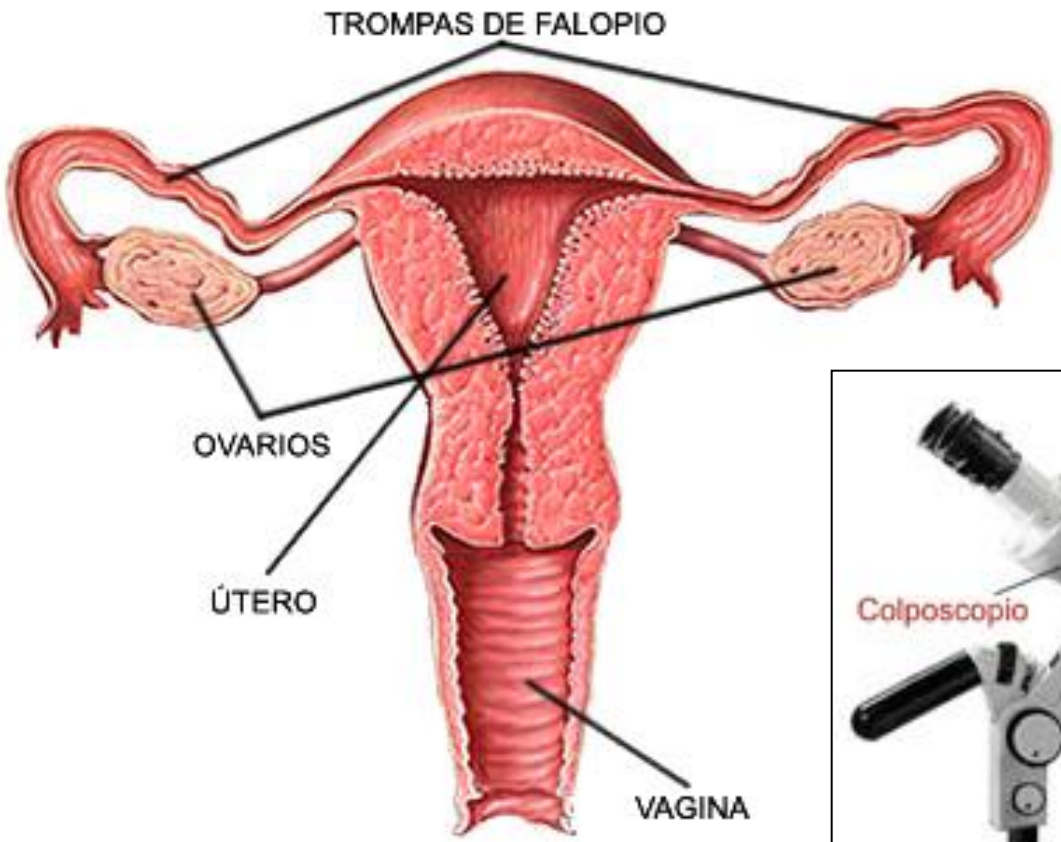
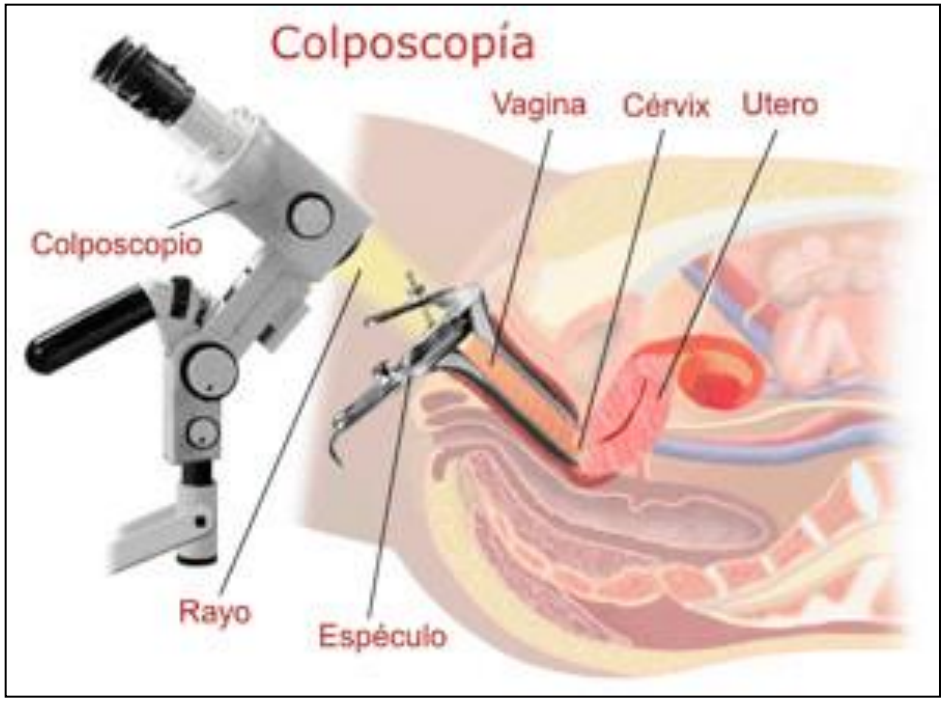
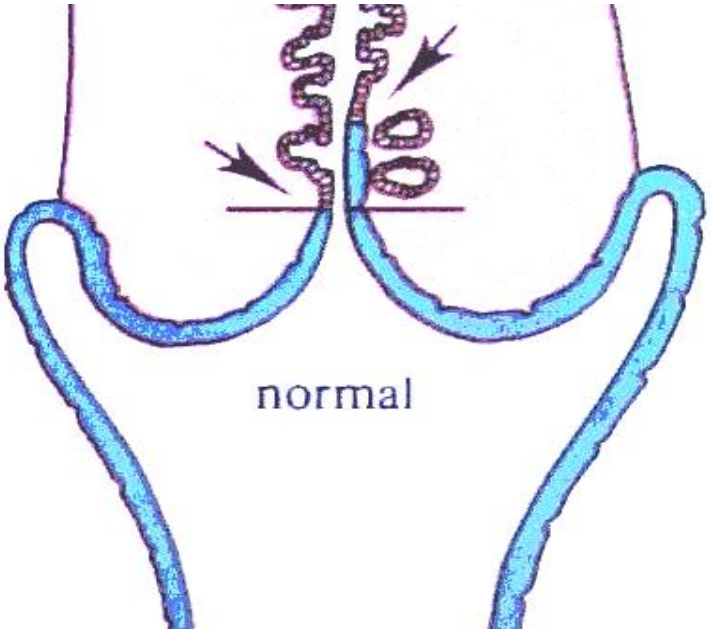
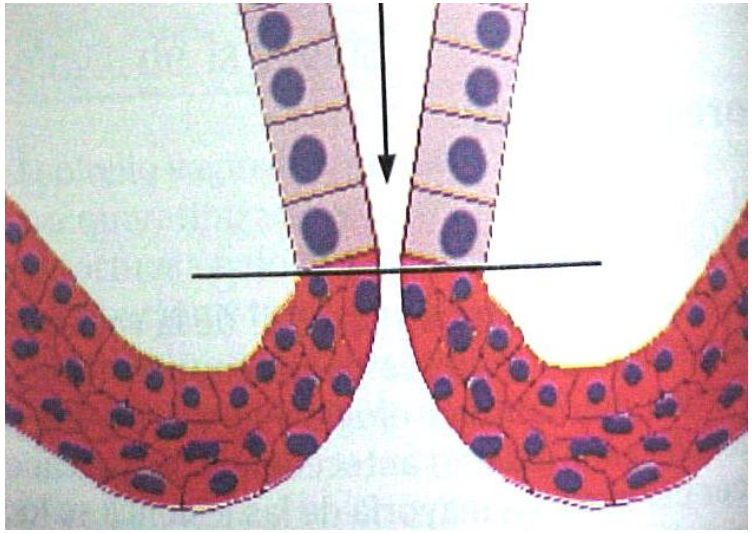
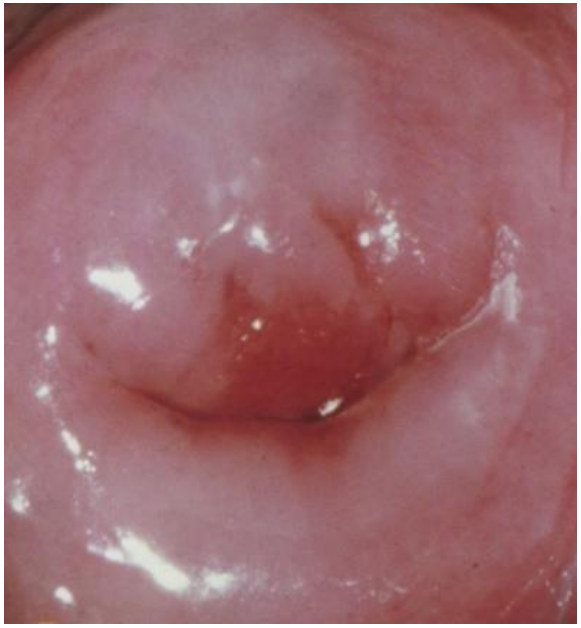




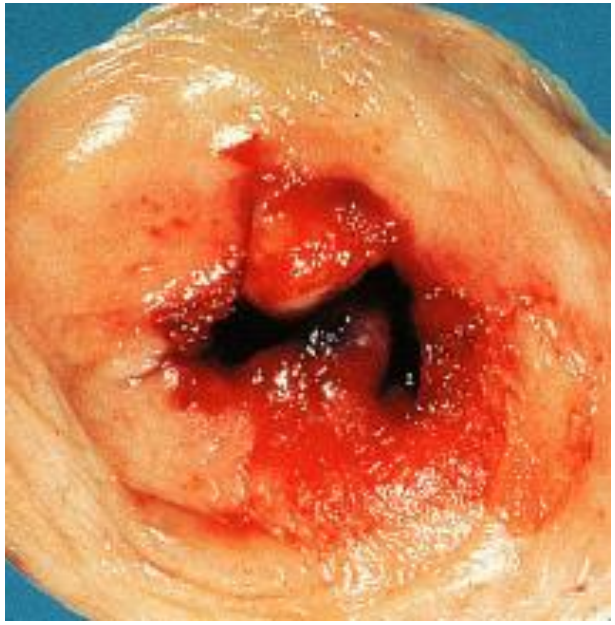




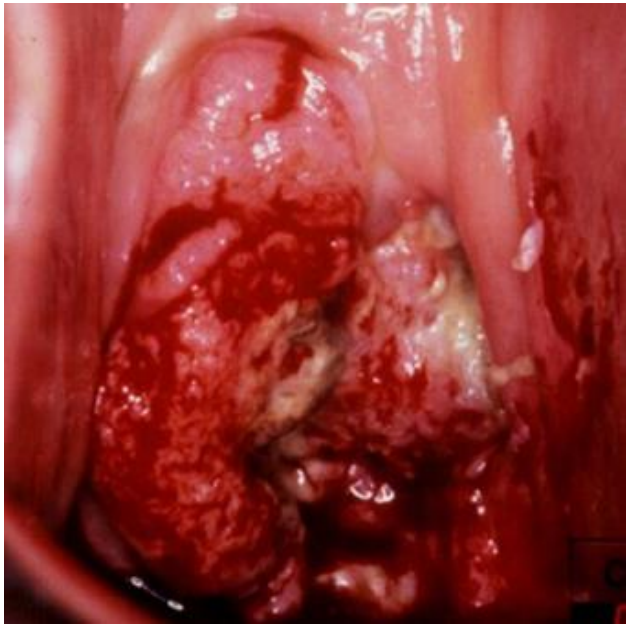




NORMAL

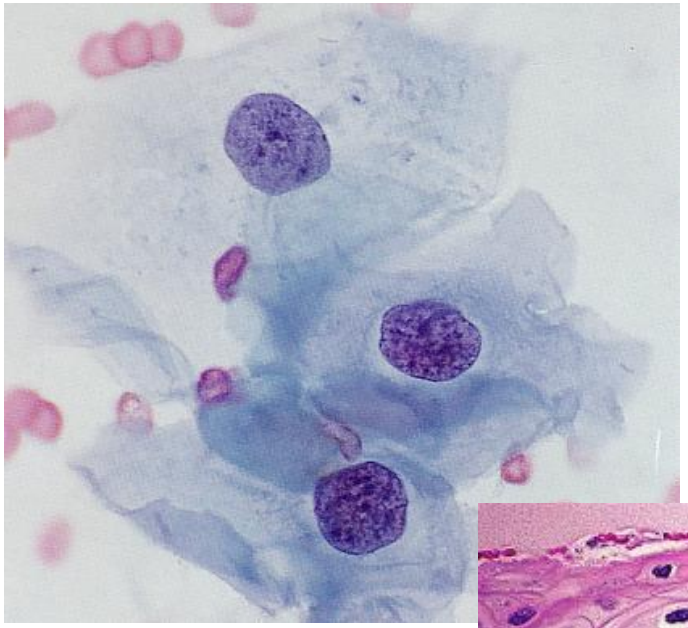


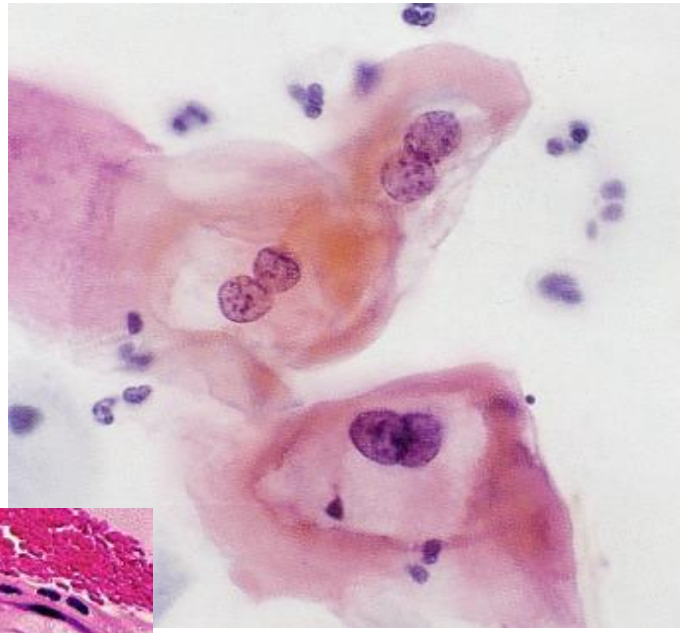
PRENEOPLASIA

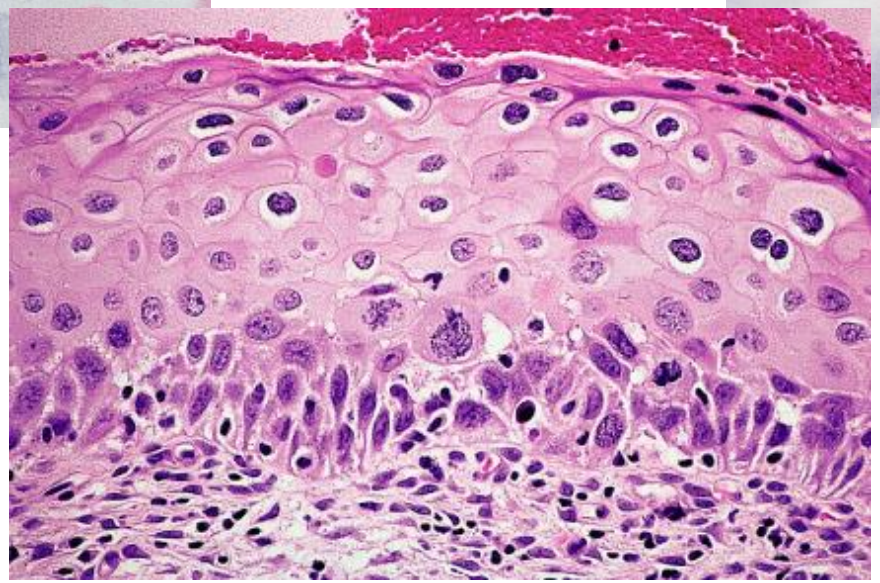


CÁNCER

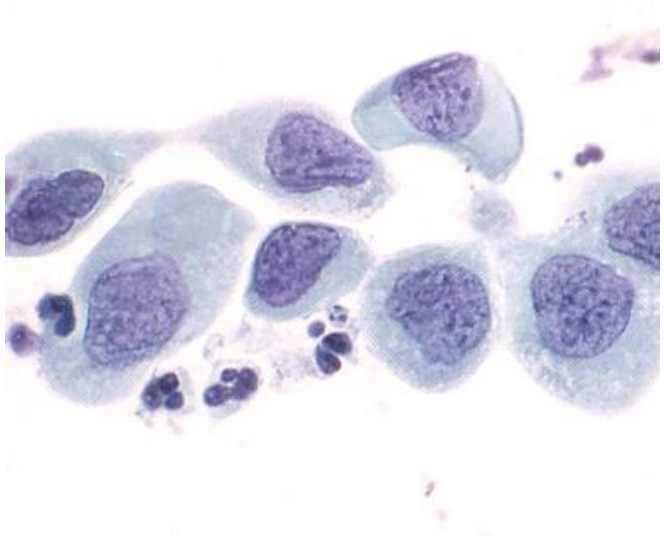
LSIL:
LOW GRADE SQUAMOUS INTRAEPITHELIAL LESION

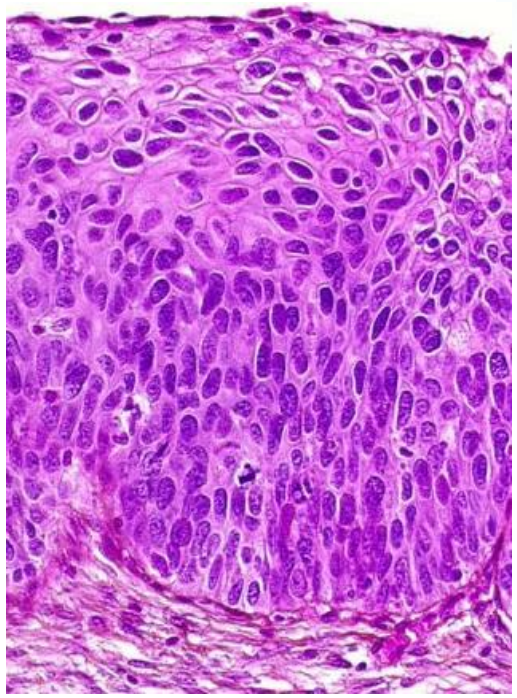


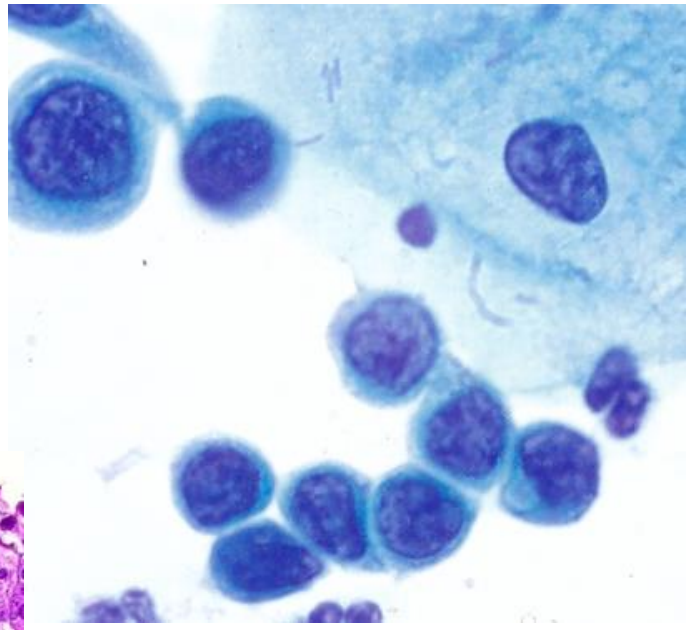




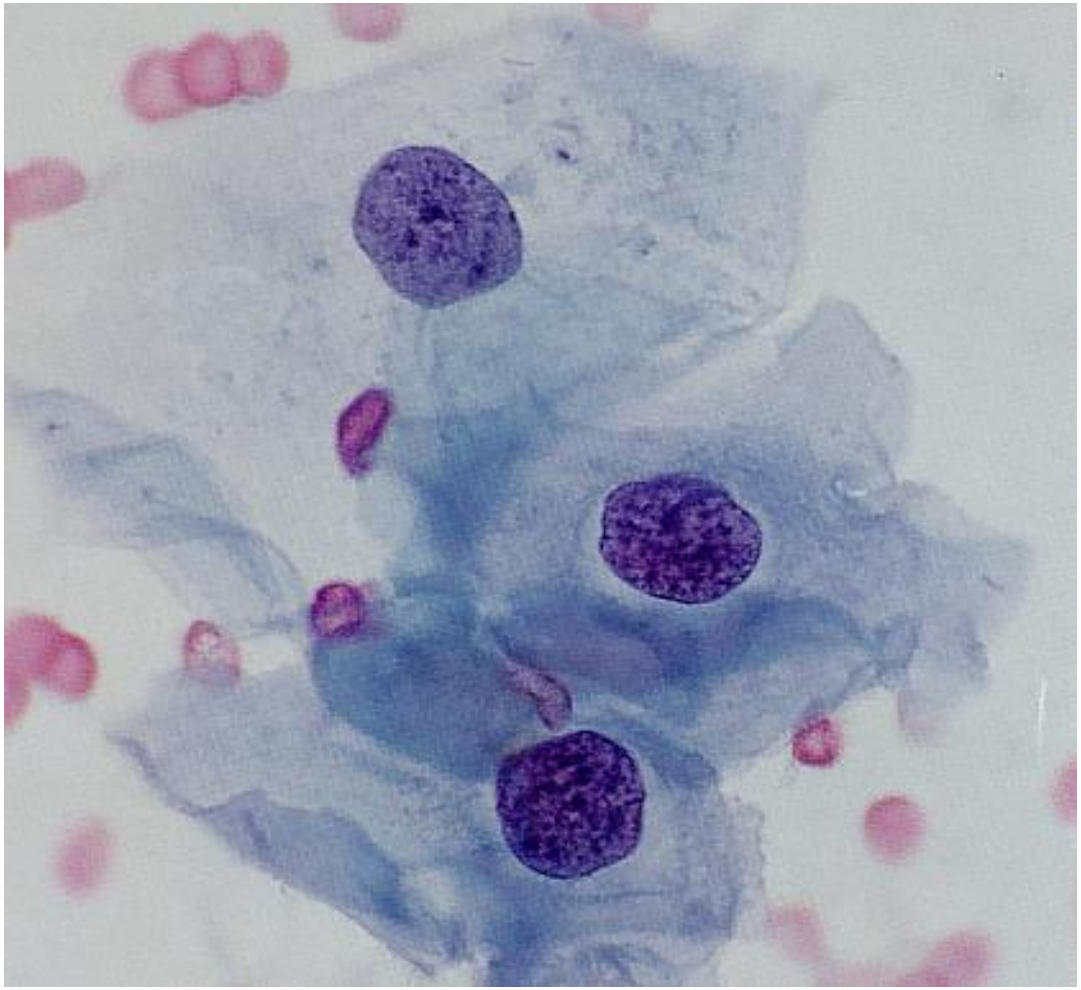
HSIL:
HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION



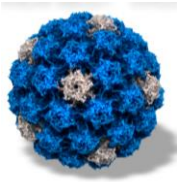




BETHESDA 1991/2001: *ATYPICAL SQUAMOUS CELLS OF UNKNOWN SIGNIFICANCE* (ASC-US)

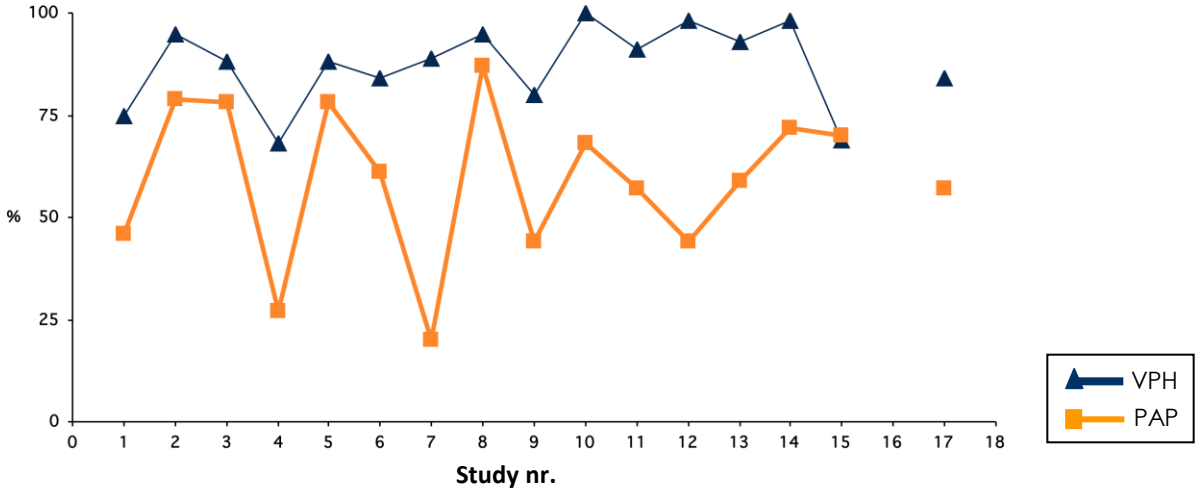


HPV vs Citología en cribado

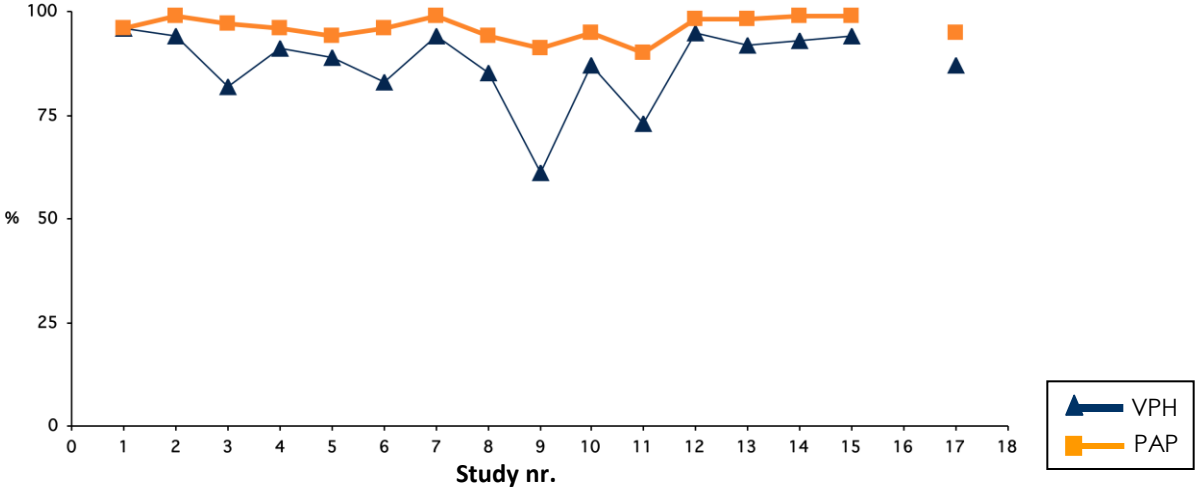


HPV aumenta la sensibilidad 46%
Pap smear aumenta la especificidad 8.9%

SENSITIVITY



SPECIFICITY



Técnicas de detección y tipificación del VPH en el cribado

- **Detección directa:**
  - Hibridación *in situ*
  - Inmunohistoquímica

BAJA SENSIBILIDAD

- **Amplificación de señal:**
  - Captura de híbridos (QIAGEN)
  - Cervista (HOLOGIC)

- **Amplificación ADN/ARN (PCR):**
  - Validados: COBAS, GENPROBE

SENSIBILIDAD ADECUADA

  - No validados

SENSIBILIDAD CLINICA DESCONOCIDA

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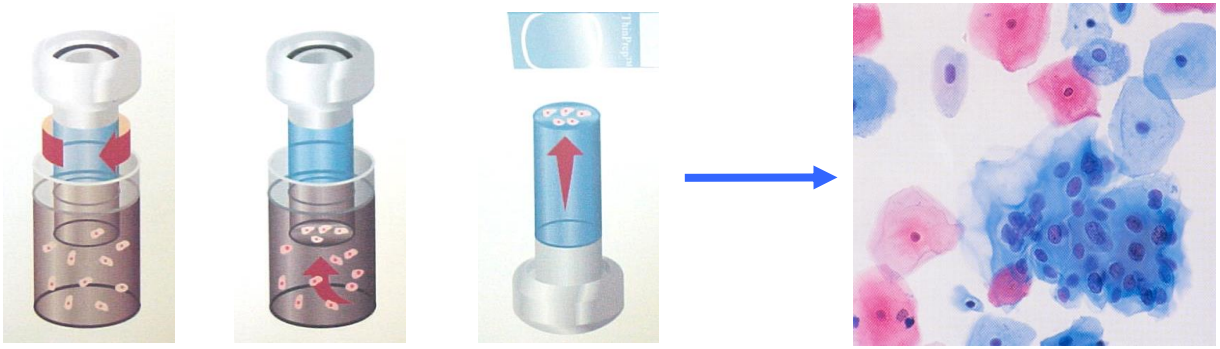
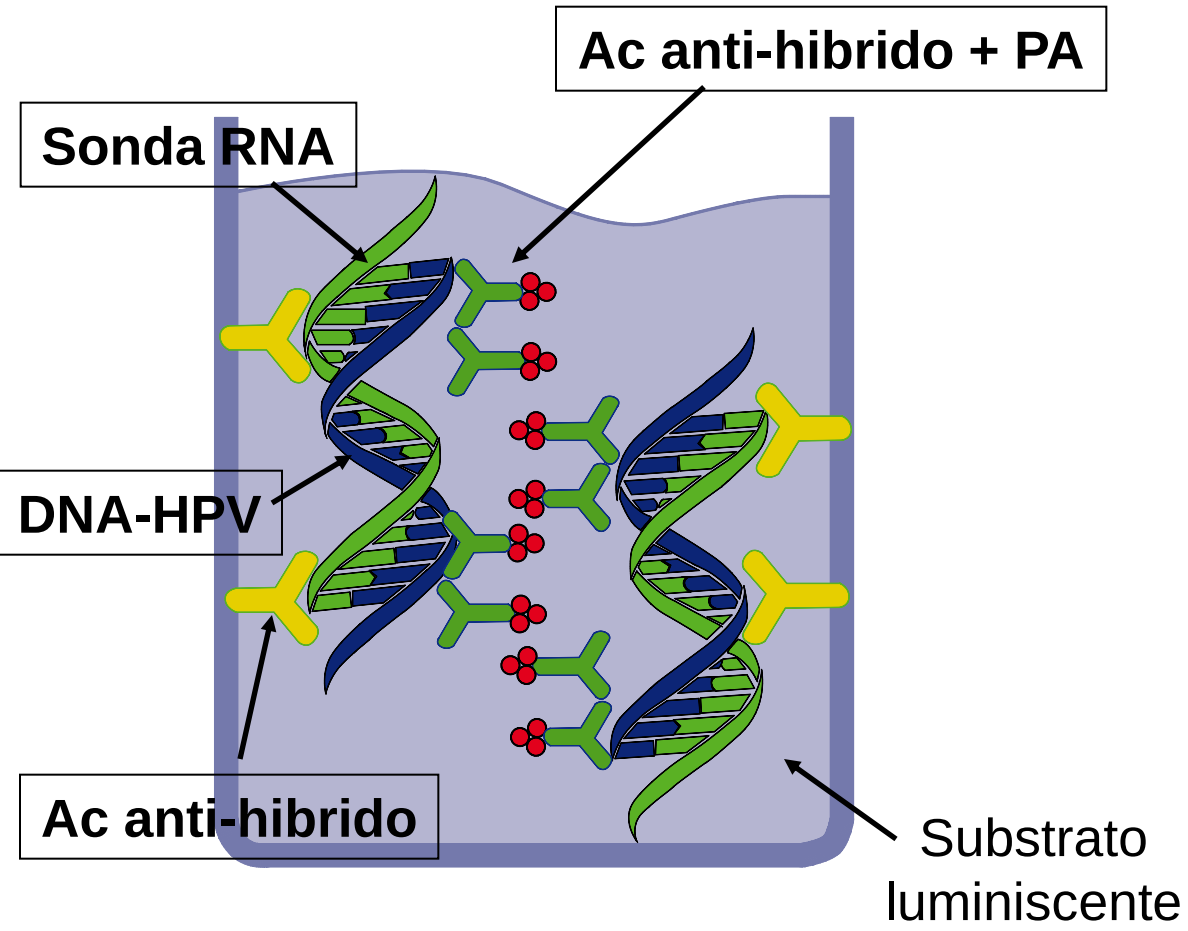
Citología líquida



HPV

CAPTURA DE HIBRIDOS

HC2 (QIAGEN)



Hibridación

↓

Captura

↓

Ac + PA

↓

Substrato

↓

Reacción qluminiscente

RLU/CO > 1 = POSITIVO

SONDAS HPV BAJO RIESGO: 6 / 11 / 42 / 43 /44

SONDAS HPV ALTO RIESGO: 16 / 18 / 31/ 33 / 35 / 39 / 45 / 51 / 52 / 56 / 58 / 59 / 68

Test Name	Area	Operator	Kit Lot #	Valid Run	Validated By	Primary Positive Cutoff	Primary Negative Cutoff	Secondary Positive Cutoff	Secondary Negative Cutoff
High Risk	A1..H12	MONICA	3448	Yes	Digene	65.33	65.33	65.33	65.33

		1	2	3	4	5	6	7	8	9	10	11	12
A	ID	NC	Z10304208	Z10301142	Z10303338	Z10301101	Z10305543	T-979	T-988	T-996	T-1004	RC-2169	RC-2176
	RLU		40	14	14	12	19	15	9660	27	19	24	18
	Ratio		0.81	0.21	0.21	0.18	0.19	0.22	[illegible]	0.41	0.29	0.98	0.24
	Result		–	–	–	–	–	–	High Risk	–	–	–	–
B	ID	Gutter NC	Z10303695	Z10301105	Z10303776	Z10303599	Z10303592	T-981	B156	T-995	T-1005	RC-2170	RC-2177
	RLU		10	8	11	15	15	[illegible]	14	804	19	17	17
	Ratio		0.15	0.12	0.16	0.22	0.22	[illegible]	0.21	[illegible]	0.29	0.28	0.28
	Result		–	–	–	–	–	High Risk	–	High Risk	–	–	–
C	ID	NC	Z10303679	Z10303003	Z10303347	Z10303595	T-974	T-982	T-989	T-998	T-1006	RC-2171	RC-2178
	RLU		12	11	14	928	42	[illegible]	29	928	15	18	15
	Ratio		0.18	0.16	0.21	[illegible]	0.84	[illegible]	0.58	[illegible]	0.22	0.27	0.22
	Result		–	–	–	High Risk	–	High Risk	–	High Risk	–	–	–
D	ID	HRC	RC-2135C	Z10303226	Z10303007	Z10303078	T-975	T-983	T-990	T-1000	T-1007	RC-2172	RC-2179
	RLU		[illegible]	10	10	62	15	18	52	19	15	14	14
	Ratio		[illegible]	0.15	0.15	0.94	0.22	0.24	0.43	0.19	0.22	0.21	0.21
	Result		High Risk	–	–	–	–	–	–	–	–	–	–
E	ID	HRC	RC-2116C	Z10303416	B154	Z10303234	T-976	T-984	T-991	T-999	F-64	B157	RC-2180
	RLU		56	19	3	18	10	18	[illegible]	[illegible]	[illegible]	[illegible]	14
	Ratio		0.25	[illegible]	0.12	0.24	0.15	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0.21
	Result		–	–	–	–	–	–	High Risk	–	–	–	–
F	ID	HRC	T-9638	Z10303019	Z10303004	Z10303961	T-977	T-985	T-992	T-1001	F-65	RC-2173	PA-34
	RLU		[illegible]	1	14	12	15	[illegible]	15	12	17	15	7
	Ratio		[illegible]	0.18	0.21	0.18	0.27	[illegible]	[illegible]	[illegible]	0.28	0.22	0.10
	Result		High Risk	–	–	–	–	High Risk	–	–	–	–	–
G	ID	Z10303388	B153	Z10304129	Z10302102	Z10302438	B155	T-986	T-993	T-1002	RC-2167	RC-2174	DR2-34
	RLU	12	9	14	58	28	10	17	23	308	14	15	1
	Ratio	0.18	0.19	0.21	0.56	0.59	0.15	0.28	[illegible]	[illegible]	0.21	0.22	0.01
	Result	–	–	–	–	–	–	–	–	High Risk	–	–	–
H	ID	Z10303488	Z10301106	Z10303149	Z10301144	Z10302295	T-978	T-987	T-994	T-1003	RC-2168	RC-2175	WB+DR2-34
	RLU	52	19	14	12	19	18	19	5	130	15	15	1
	Ratio	0.43	0.19	0.21	0.18	0.29	0.24	0.19	0.32	[illegible]	0.22	0.22	0.01
	Result	–	–	–	–	–	–	–	–	High Risk	–	–	–

Subreport:PlateColumnReport.rpt

DIGENE Hybrid Capture® II Software v.2.0

Instrument Serial #:

Supervisor: _____ Date: _____

Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women 30 years and older

Chris J.L.M. Meijer[1*], Johannes Berkhof[2], Philip E. Castle[3], Albertus T. Hesselink[1], Eduardo L. Franco[4], Guglielmo Ronco[5], Marc Arbyn[6,7], F. Xavier Bosch[8], Jack Cuzick[9], Joakim Dillner[10], Daniëlle A.M. Heideman[1] and Peter J.F. Snijders[1]

CLINICAL CRITERIA (NO ANALYTICAL)

= CLINICAL VALIDATION

- Gold standard: HC2 or GP5+/6+
  - 90% sensitivity (min 60 cases CIN2+)
  - 98% specificity (min 800 cases no CIN 2+)
  - 87% reproducibility (intra and inter)
- Women > 30 y.o.
- Laboratory procedures
- Quality control

Int. J. Cancer: **124,** 516–520 (2009)

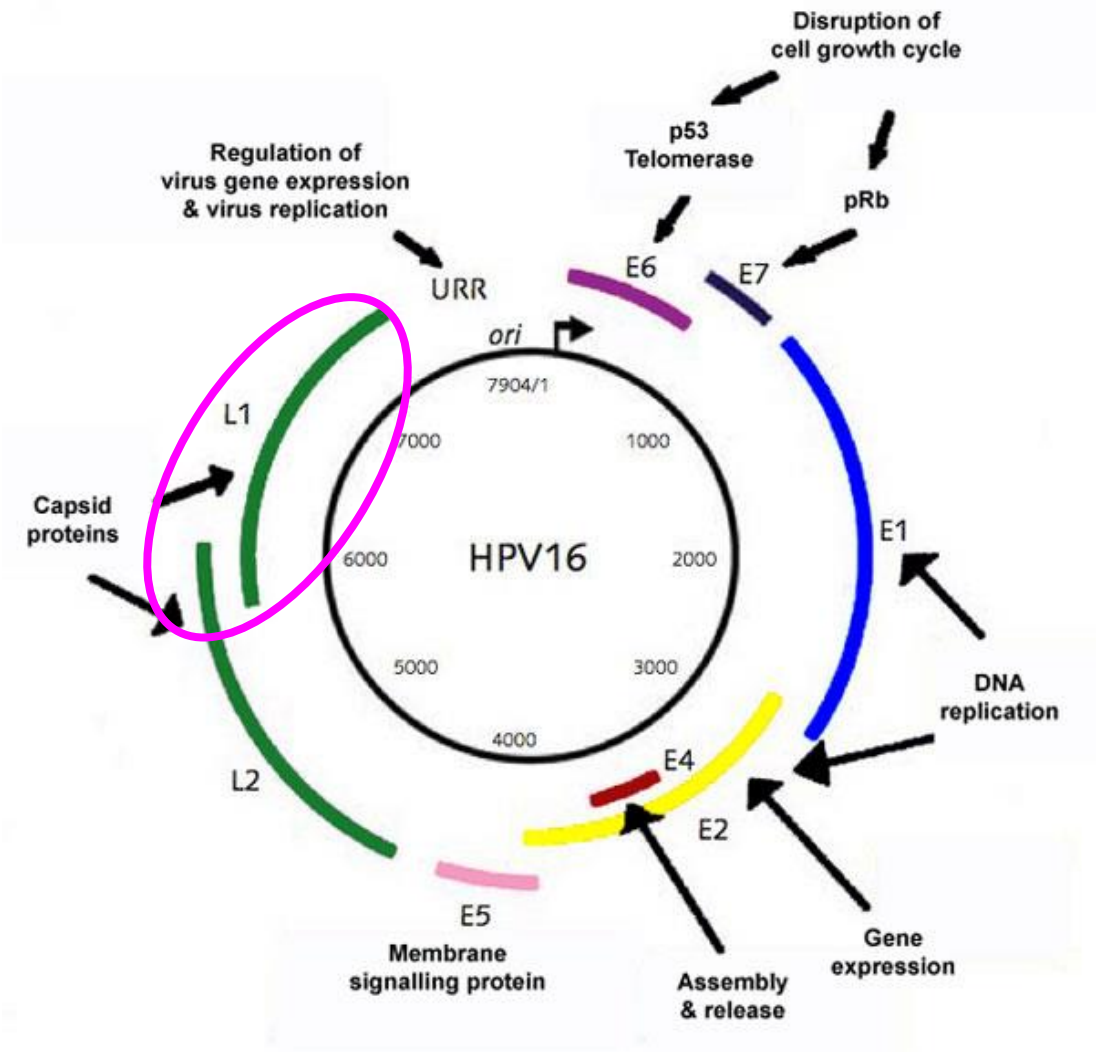
cobas® 4800
HPV test (Roche)

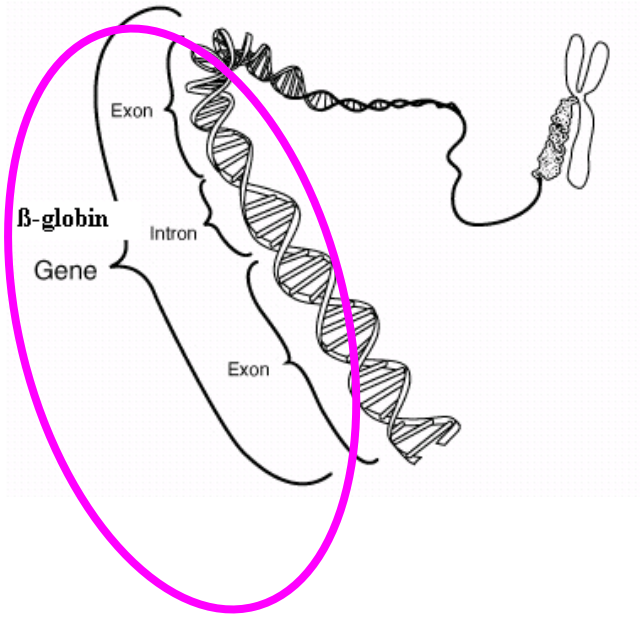
166 cm

57 cm

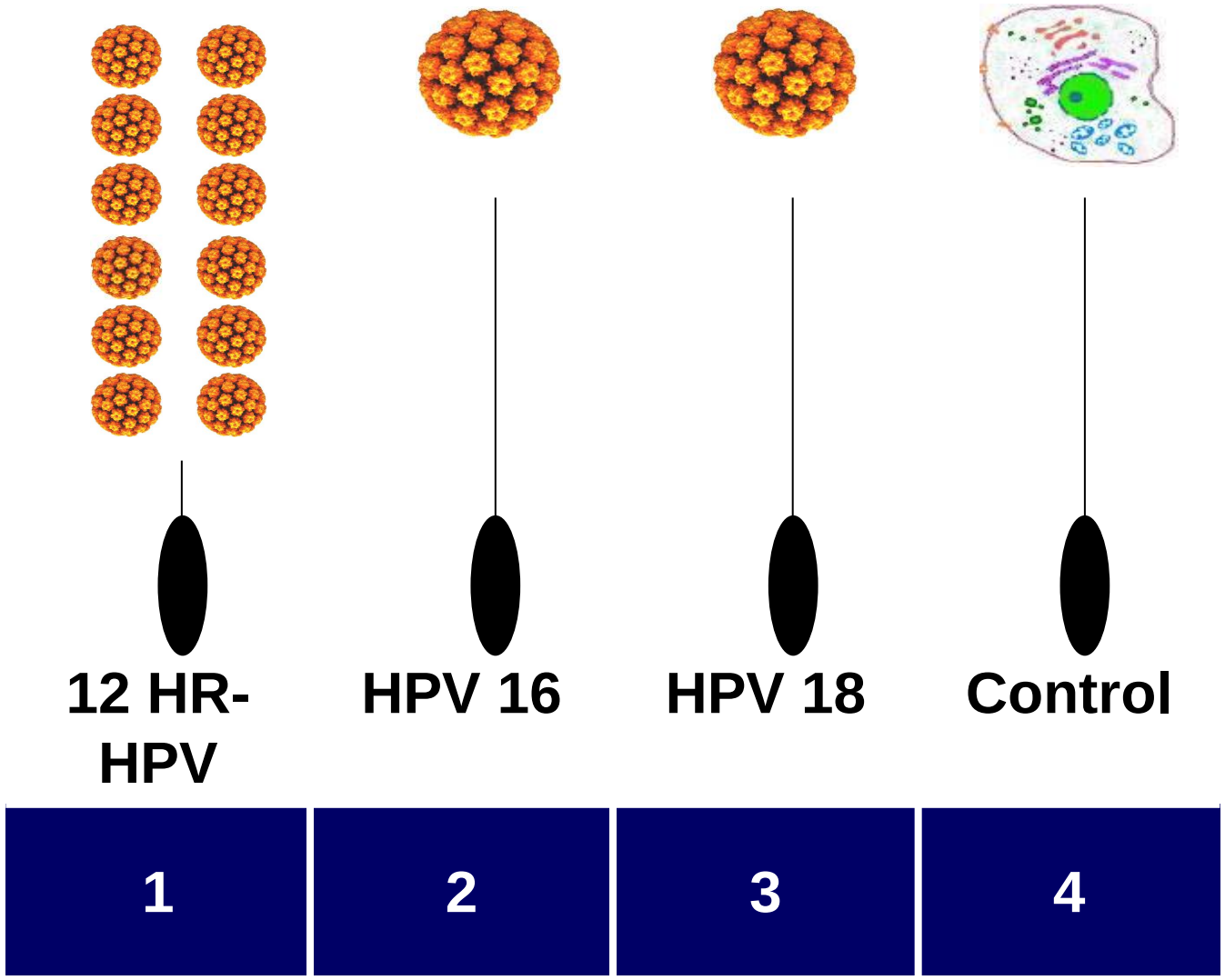
- Automated DNA extraction
- Real time PCR with LightCycler® 480
- High throughput : 282 HPV tests / day

cobas® 4800
HPV test (Roche)





cobas HPV test



Primary cervical cancer screening with human papillomavirus: End of study results from the ATHENA study using HPV as the first-line screening test☆

Thomas C. Wright [a,*], Mark H. Stoler [b], Catherine M. Behrens [c], Abha Sharma [c], Guili Zhang [c], Teresa L. Wright [d]

Gynecologic Oncology 136 (2015) 189–197

A B S T R A C T

Objectives. ATHENA evaluated the cobas HPV Test as the primary screen for cervical cancer in women ≥25 years. This reports the 3-year end-of-study results comparing the performance of HPV primary screening to different screening and triage combinations.

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Primary cervical cancer screening with human papillomavirus: End of study results from the ATHENA study using HPV as the first-line screening test☆

Thomas C. Wright [a,*], Mark H. Stoler [b], Catherine M. Behrens [c], Abha Sharma [c], Guili Zhang [c], Teresa L. Wright [d]

Gynecologic Oncology 136 (2015) 189–197

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Results. 3-year CIR of CIN3+ in cytology-negative women was 0.8% (95% CI; 0.5–1.1%), 0.3% (95% CI 0.1–0.7%) in HPV-negative women, and 0.3% (95% CI; 0.1–0.6%) in cytology and HPV negative women. The sensitivity for CIN3+ of cytology was 47.8% (95% CI; 41.6–54.1%) compared to 61.7% (95% CI; 56.0–67.5%) for the *hybrid strategy* (cytology if 25–29 years and cotesting with cytology and HPV if ≥30 years) and 76.1% (95% CI; 70.3–81.8%) for *HPV primary*.

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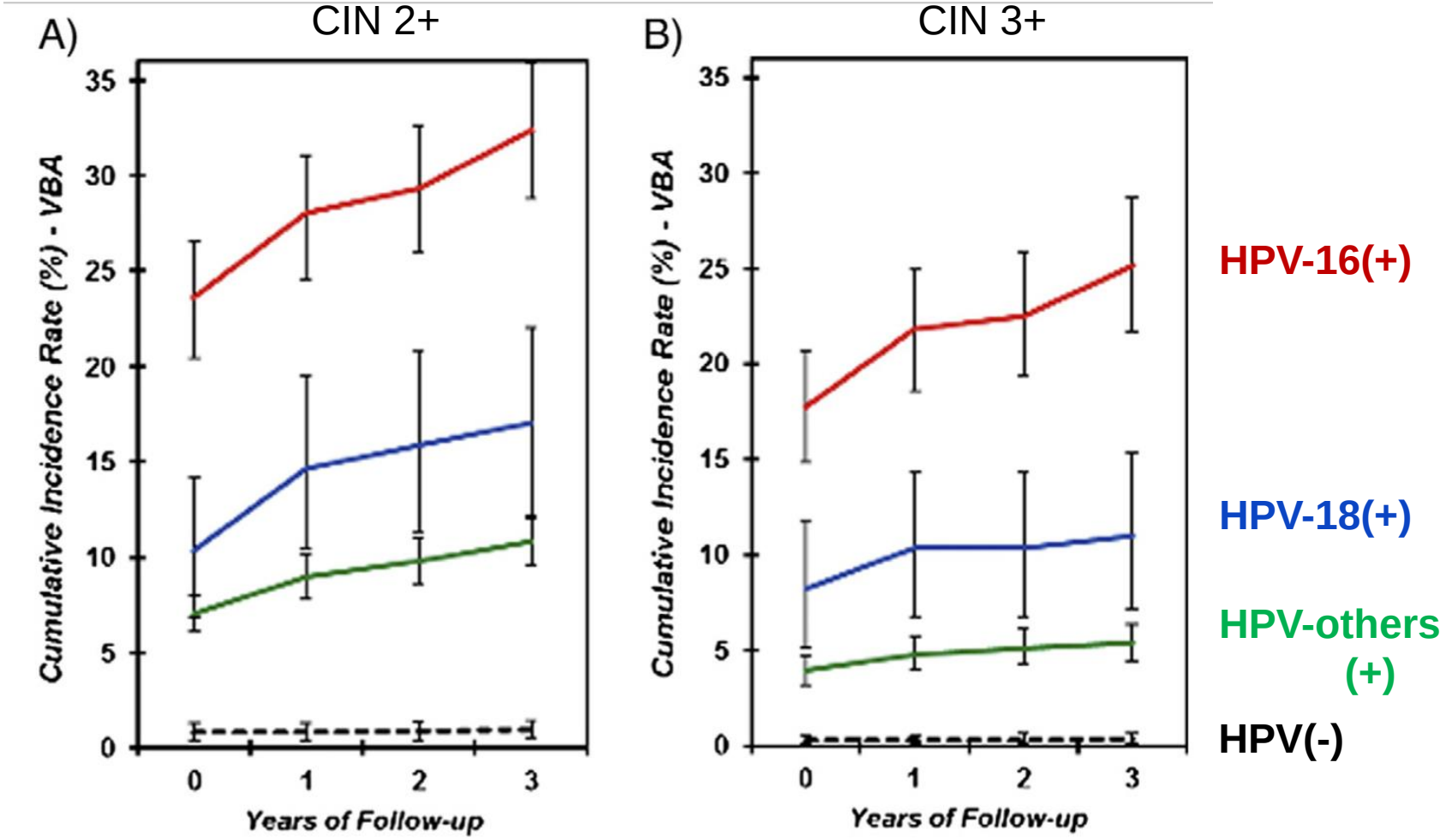

Fig. 2. Verification bias-adjusted (VBA) cumulative incidence of consensus pathology cervical intraepithelial neoplasia 2+ (CIN2+) (A) and CIN3+ (B) during 3 years of follow-up stratified by baseline human papillomavirus (HPV) status. Red solid line, HPV-16 positive; blue solid line, HPV-18 positive; green solid line, 12 other HPV genotypes positive; black dotted line, HPV-negative.

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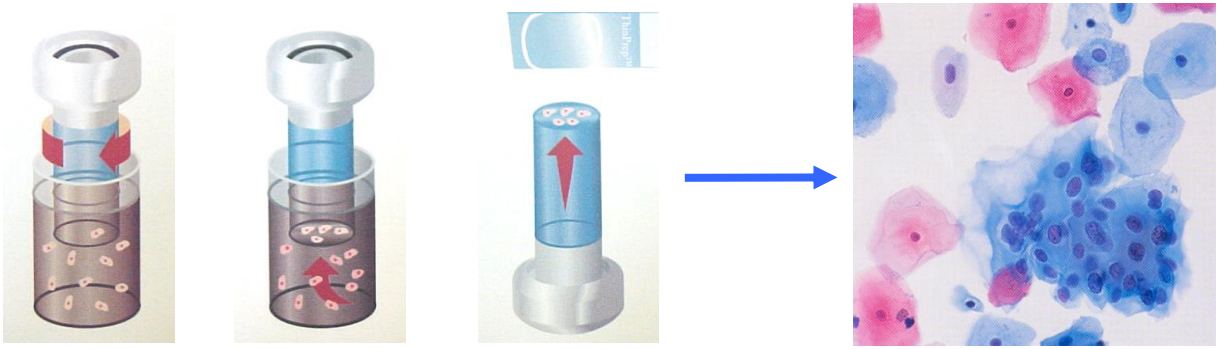
Conclusions. HPV primary screening in women ≥25 years is as effective as a hybrid screening strategy that uses cytology if 25–29 years and cotesting if ≥30 years. However, HPV primary screening requires less screening tests.

Ventajas cobas vs HC2

- No hay necesidad de conversión cuando se usan muestras de citología líquida
- Evita una posible causa de contaminación y disminuye el riesgo de errores de pipeteo
- La información por separado sobre los tipos de VPH 16 y 18 puede tener relevancia clínica con respecto al riesgo de persistencia y progresión
- La amplificación de ADN de la beta-globina celular asegura la buena calidad de la muestra en la prueba de cobas HPV

En realidad, un resultado negativo de una prueba de HC2 podría deberse a la ausencia o baja cantidad de células en una muestra, mientras que una prueba de cobas HPV arrojaría un resultado no válido.

Citología líquida

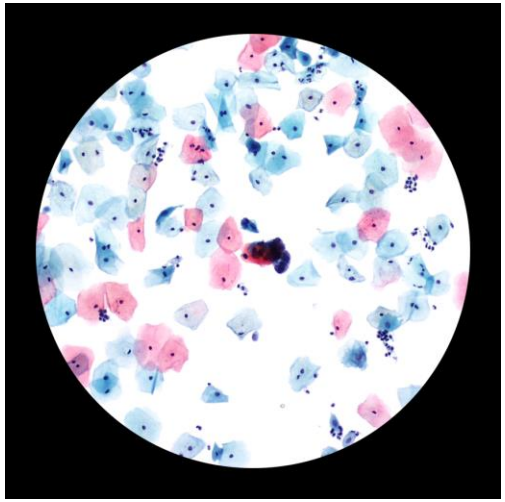


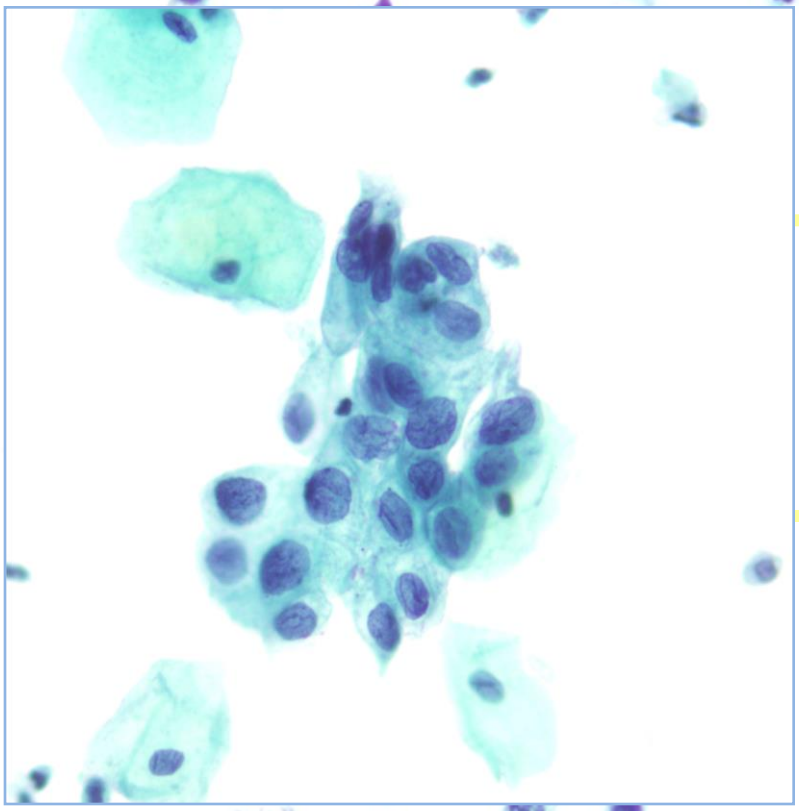
HPV

Citología líquida

+

Automatización del *screening*





Ventajas de la lectura automatizada

- Rápida adaptación
- Facilita la localización de las células atípicas
- Focaliza la interpretación
- Reducción del tiempo de screening

El nº de campos a observar se reduce en un 40% respecto a la lectura convencional

Automated Cervical Screening and Triage, Based on HPV Testing and Computer-Interpreted Cytology

Kai Yu, Noorie Hyun, Barbara Fetterman†, Thomas Lorey, Tina R. Raine-Bennett, Han Zhang, Robin E. Stamps, Nancy E. Poitras, William Wheeler, Brian Befano, Julia C. Gage, Philip E. Castle, Nicolas Wentzensen, Mark Schiffman

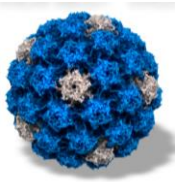
JNCI J Natl Cancer Inst (2018) 110(11): djy044

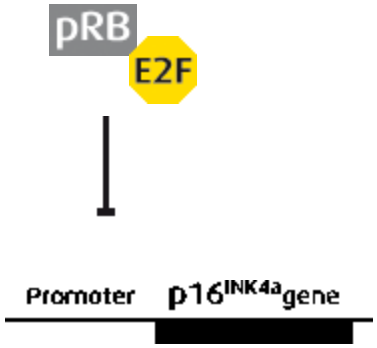
Conclusiones:

Con el enfoque completamente automatizado se puede lograr la detección y clasificación cervical de alta calidad.

La tecnología automatizada podría permitir la extensión de la cobertura de detección / triaje cervical de alta calidad en las regiones actualmente desatendidas.

p16^{INK4a}





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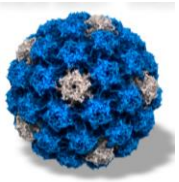
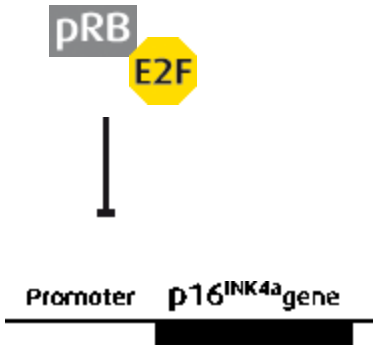


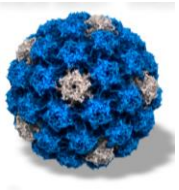


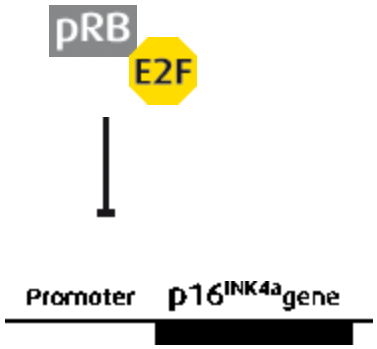
VPH

infección

persistente

p16^{INK4a}





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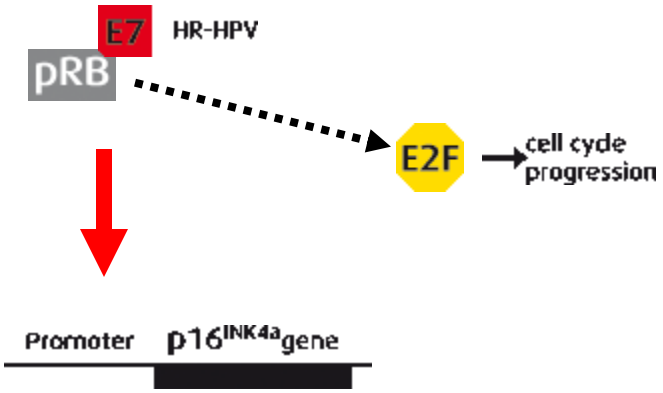

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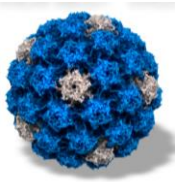
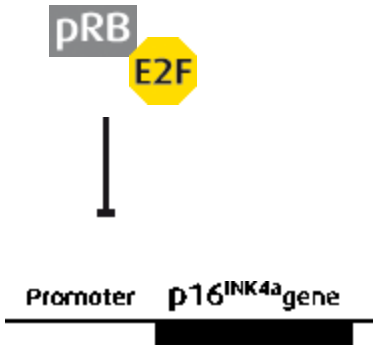
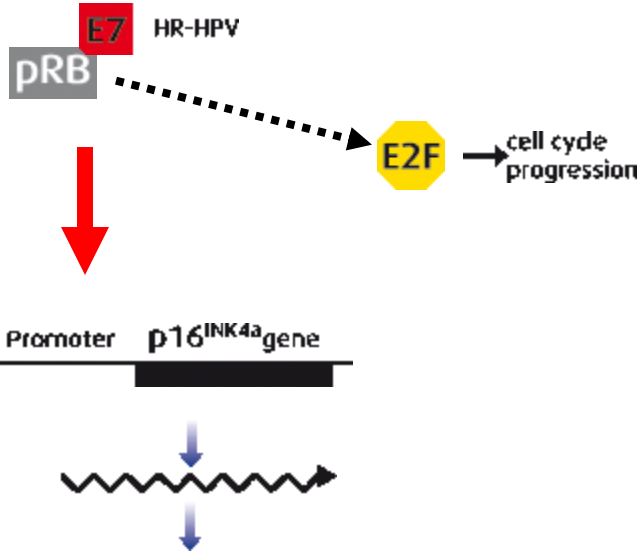




VPH

infección

persistente



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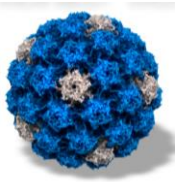

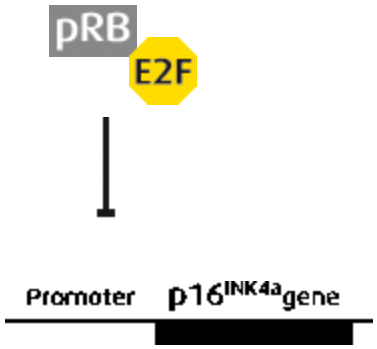

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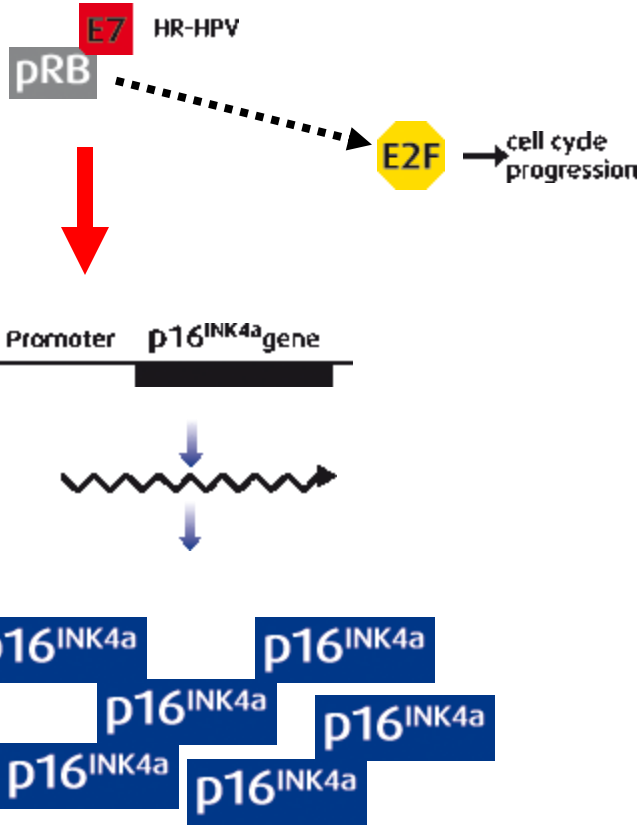

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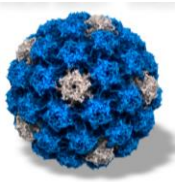

VPH

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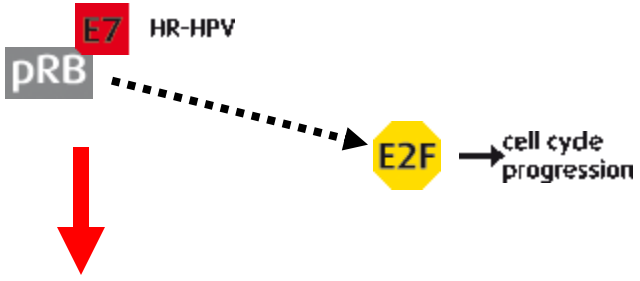
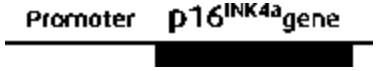
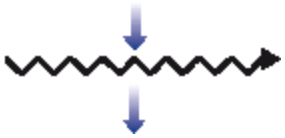
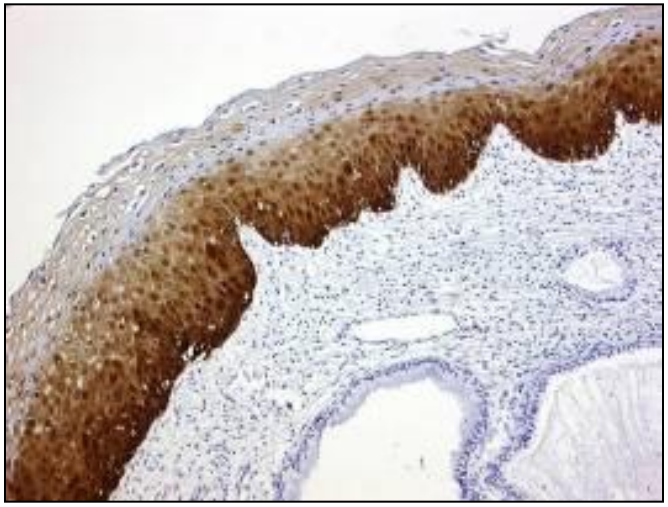
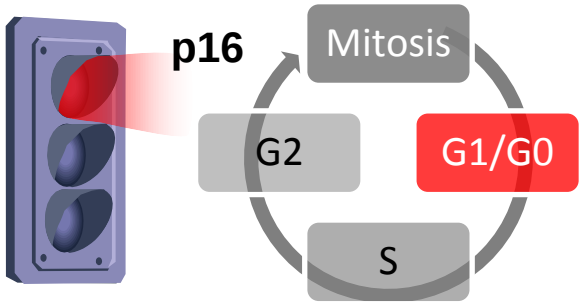






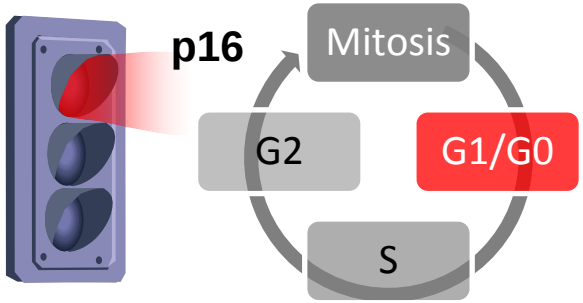


p16/Ki-67 Doble tinción



Arresto del ciclo celular

p16/Ki-67 Doble tinción



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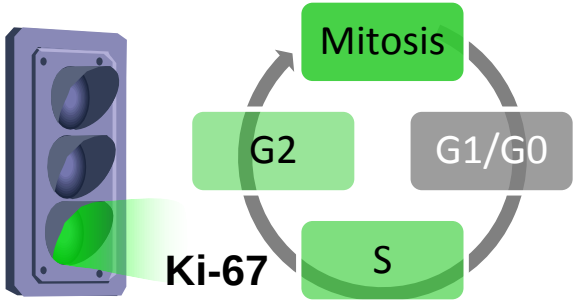

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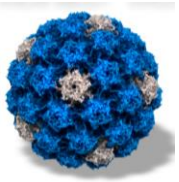
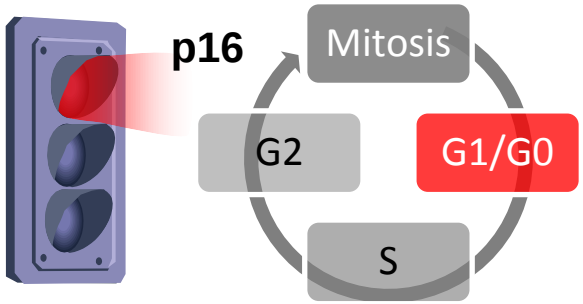


p16/Ki-67 Doble tinción



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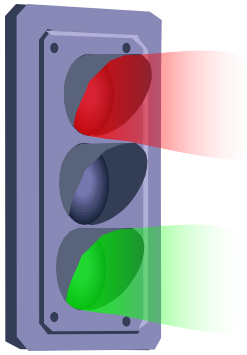

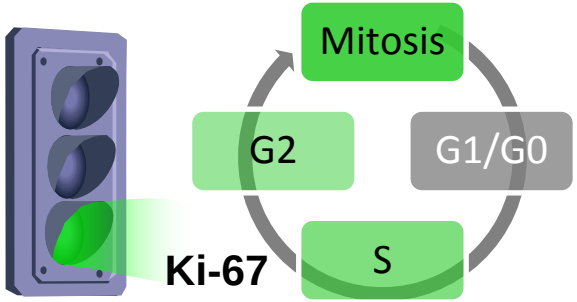

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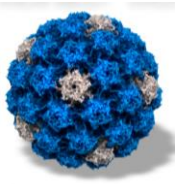
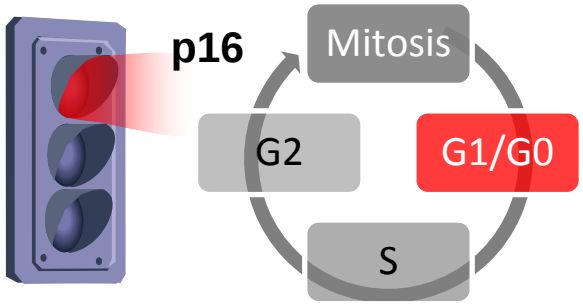


p16/Ki-67 Doble tinción



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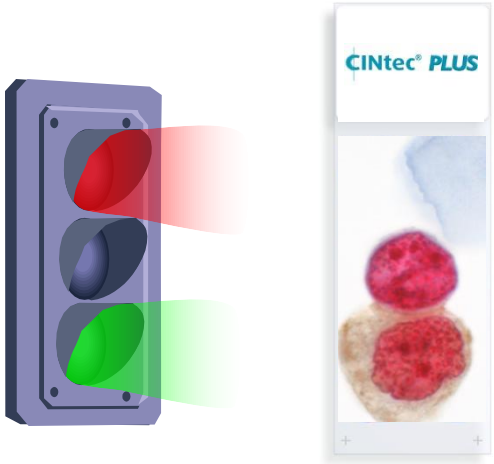
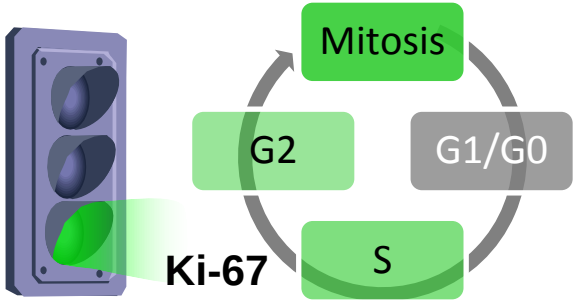




Progresión del ciclo celular

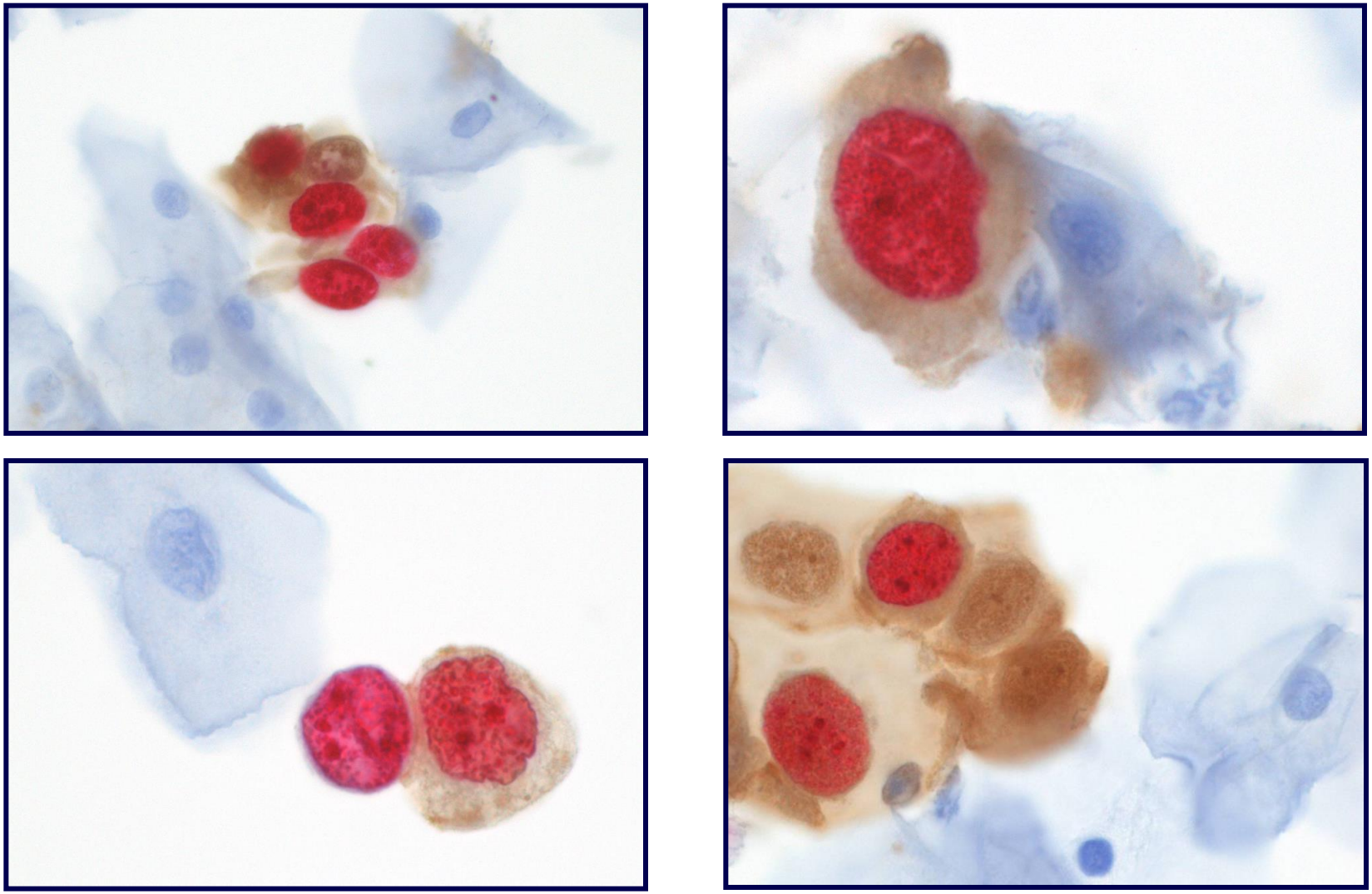
Coexpresión de p16 y Ki-67

- Indica disregulación del ciclo celular

- Marcador de la transformación de la infección por VPH

Dual-Stained Cytology (*CINtec PLUS*)

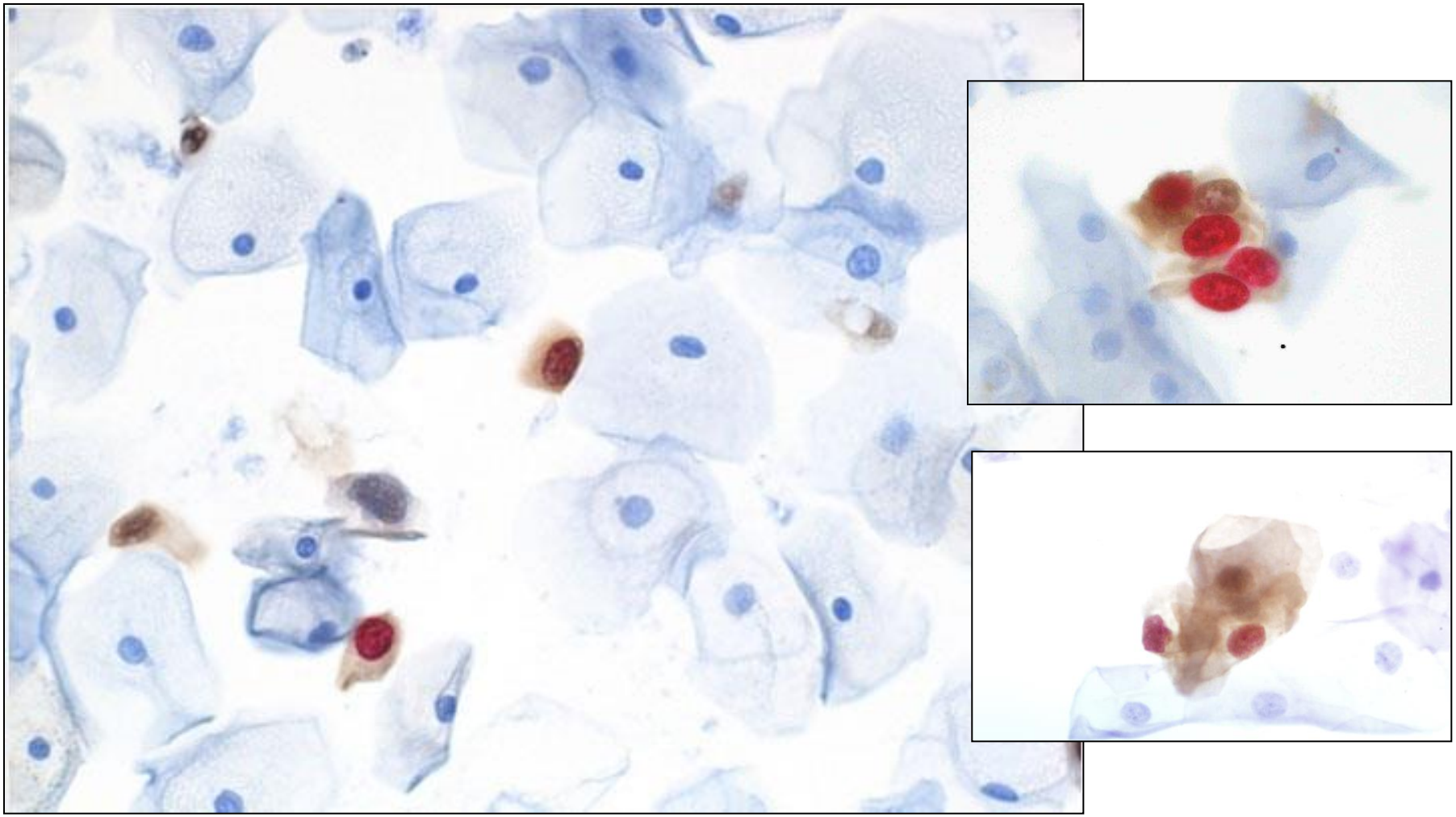
ThinPrep Cytology Specimen



Ventana Medical Systems. http://www.ventana.com/cervical. Accessed 10 August 2015.

Dual-Stained Cytology (*CINtec PLUS*)

ThinPrep Cytology Specimen



Triaging HPV-positive women with p16/Ki-67 dual-stained cytology: Results from a sub-study nested into the ATHENA trial

Thomas C. Wright Jr. [a,*], Catherine M. Behrens [b], James Ranger-Moore [c], Susanne Rehm [c,d], Abha Sharma [b], Mark H. Stoler [e], Ruediger Ridder [c,d]

http://dx.doi.org/10.1016/j.ygyno.2016.10.031

HIGHLIGHTS

- Retrospective study in which residual cytology specimens were dual-stained with p16/Ki-67
- Dual-stained cytology had a higher sensitivity in HPV-positive women than did Pap cytology.
- Positive and negative predictive values were higher for dual-staining than Pap cytology.

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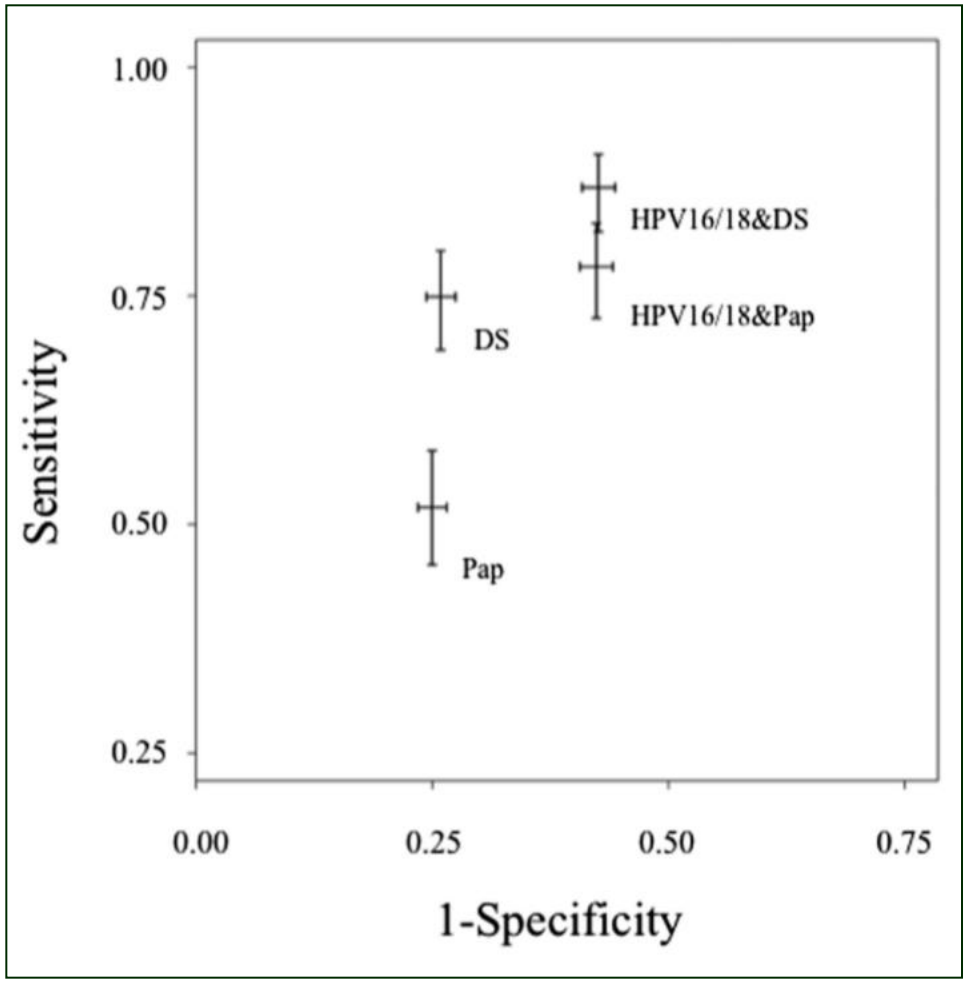
http://dx.doi.org/10.1016/j.ygyno.2016.10.031
0090-8258/



Diagnostic performance for the detection of CIN3+.

Receiver operating characteristic graph for triaging HPV(+) women aged ≥25 years

(i) with dual stained cytology (DS),
(ii) with Pap cytology (Pap),
(iii) by referring HPV16/18 (+) women to colposcopy and triaging 12 other HR-HPV (+) women with dual-stained cytology (HPV16/18&DS),
(iv) by referring HPV16/18 (+) women to colposcopy and triaging 12 other HR-HPV (+) women with Pap cytology (HPV16/18&Pap)

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0090-8258/

A B S T R A C T

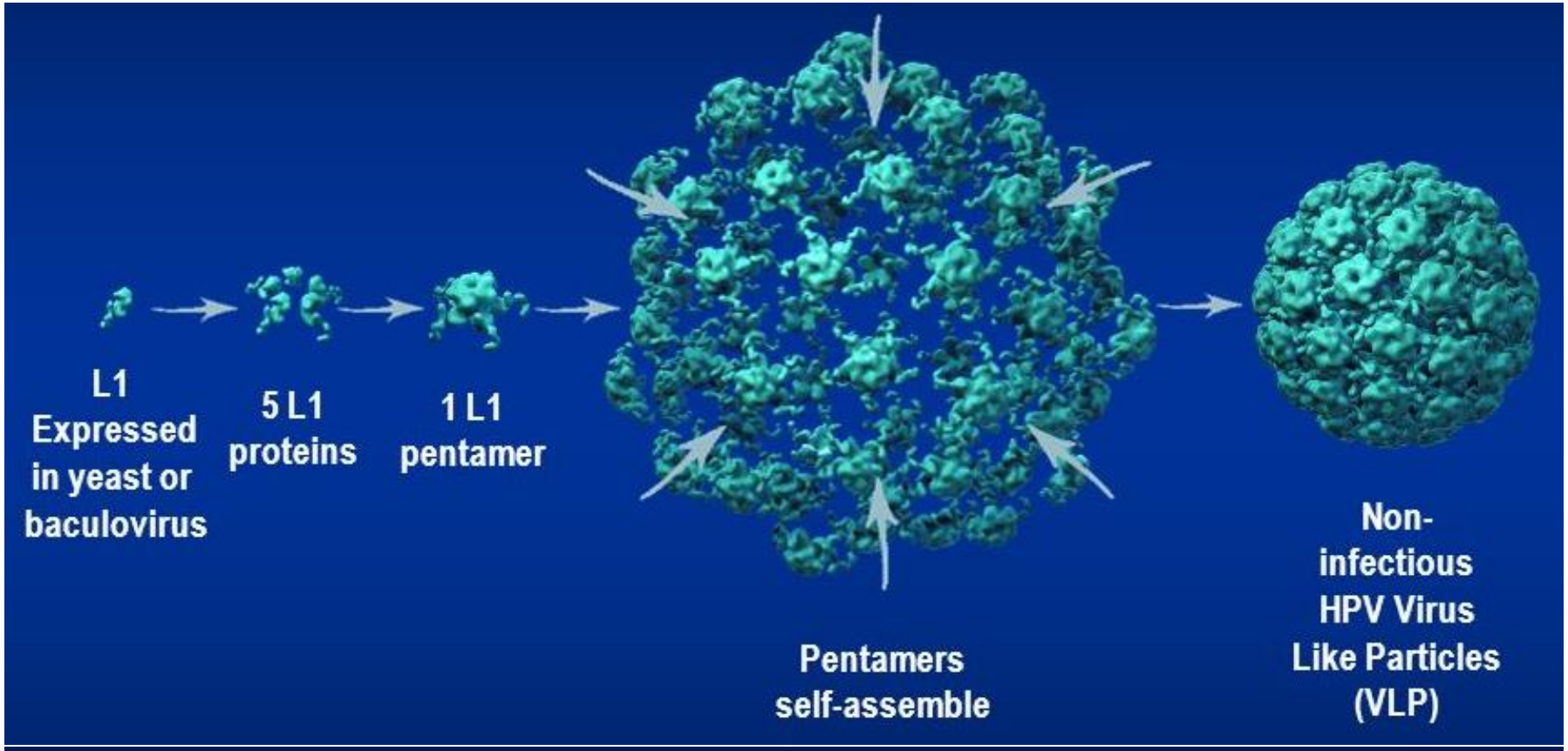
Objectives. In addition to genotyping for HPV16/18, dual-immunostaining for p16/Ki-67 has shown promise as a triage of HPV-positive women. We assessed the performance of p16/Ki-67 dual-stained cytology for triaging HPV-positive women undergoing primary HPV screening.

Methods. All women ≥25 years with valid cervical biopsy and cobas® HPV Test results from the cross-sectional phase of ATHENA who were referred to colposcopy (n = 7727) were eligible for enrolment. p16/Ki-67 dual-stained cytology was retrospectively performed on residual cytologic material collected into a second liquid-based cytology vial during the ATHENA enrolment visit. The diagnostic performance of dual-stained cytology, with or without HPV16/18 genotyping, for the detection of biopsy-confirmed cervical intraepithelial neoplasia grade 3 or worse (CIN3+) was determined and compared to Pap cytology. Furthermore, the number of colposcopies required per CIN3+ detected was determined.

Results. Dual-stained cytology was significantly more sensitive than Pap cytology (74.9% vs. 51.9%; $p < 0.0001$) for triaging HPV-positive women, whereas specificity was comparable (74.1% vs. 75.0%; $p = 0.3198$). Referral of all HPV16/18 positive women combined with dual-stained cytology triage of women positive for 12 "other" HPV genotypes provided the highest sensitivity for CIN3+ (86.8%; 95% CI: 81.9–90.8). A similar strategy but using Pap cytology for the triage of women positive for 12 "other" HPV genotypes was less sensitive (78.2%; 95% CI: 72.5–83.2; $p = 0.0003$), but required a similar number of colposcopies per CIN3+ detected.

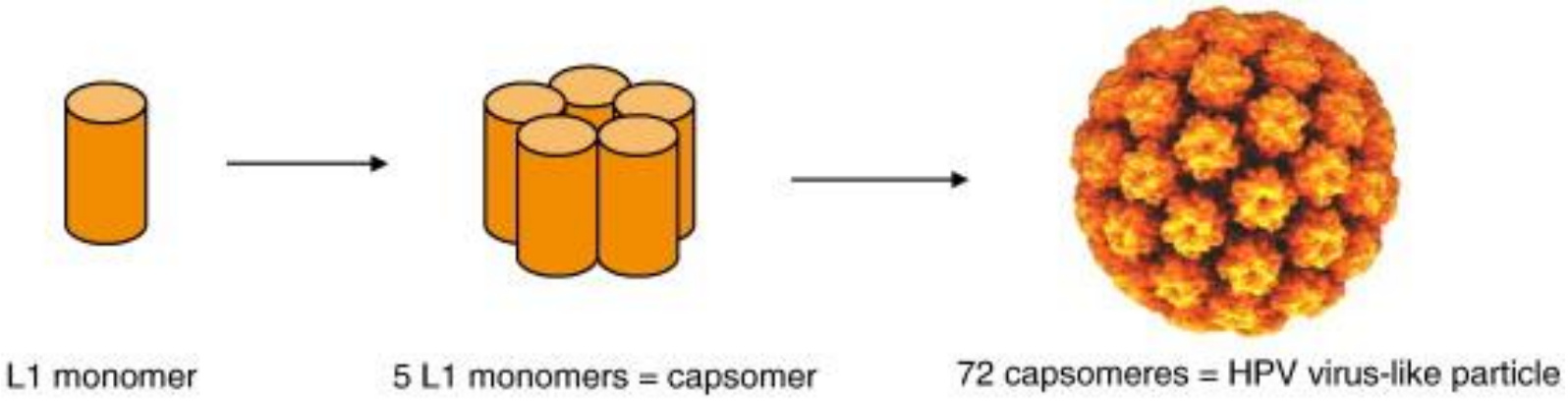
Conclusions. p16/Ki-67 dual-stained cytology, either alone or combined with HPV16/18 genotyping, represents a promising approach as a sensitive and efficient triage for colposcopy of HPV-positive women when primary HPV screening is utilized.

Las vacunas contra el HPV



Gardasil SmPC. EMEA, 2007. - Kirnbauer R, Booy F, Cheng N, et al. Proc Natl Acad Sci USA. 1992;89:12180–12184. - Modis Y, Trus BL, Harrison SC. The EMBO Journal. 2002;21:4754–4762. - Stanley M, Lowy DR, Frazer I. Vaccine 2006; 24 suppl 3 : S106–13

Virus Like Particles (VLPs)

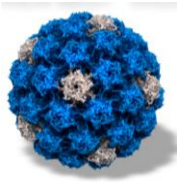


- VLPs de L1 sin ADN con adyuvante para aumentar la inmunogenicidad
- 3 dosis aumentan x 100 la respuesta natural de niveles de anticuerpos
- La respuesta a los VLPs depende de la edad siendo mayor antes de los 15 años

VACUNAS VPH

	Gardasil®	Cervarix®
Fabricante	Merck & Co., Inc.	GlaxoSmithKline
Tipos de VLP	6/11/16/18	16/18
Dosis de proteína L1	20/40/40/20 µg	20/20 µg
Células productoras	*Saccharomyces cerevisiae* (levadura del pan) que expresa L1	Línea celular del insecto *Trichoplusia ni* (Hi-5) infectada con baculovirus recombinante que expresa L1
Adyuvante	225 µg de hidroxifosfato sulfato de aluminio	AS04 (500µg de hidróxido de aluminio, 50µg de 3-O-desacil-4'-monofosforil lípido A)
Pauta de administración	0, 2, 6 meses Intramuscular en deltoides	0, 1, 6 meses Intramuscular en deltoides

VLP: partícula similar a virus.
Gardasil® (Merck & Co., Inc., Whitehouse Station, NJ, Estados Unidos); Cervarix™ (GlaxoSmithKline Biologicals, Rixensart, Bélgica) [4]

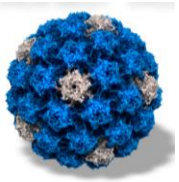


Original Research

Human papillomavirus vaccination: The ESGO–EFC position paper of the European society of Gynaecologic Oncology and the European Federation for colposcopy

Elmar A. Joura [a,b], Maria Kyrgiou [c,d,*], Francisco X. Bosch [e,f,g], Vesna Kesic [h], Pekka Niemenen [i], Charles WE. Redman [j], Murat Gultekin [k]

European Journal of Cancer 116 (2019) 21–26



- Las vacunas contra el virus del papiloma humano (VPH) están disponibles en Europa desde 2006.
- Han sido muy eficaces en la prevención de infecciones y enfermedades causadas por los tipos de las vacunas.
- Los datos de eficacia clínica están disponibles para el precáncer cervical, vulvovaginal y anal y el cáncer cervical invasivo.
- **La reducción de la enfermedad es mejor con la vacunación temprana y una cobertura de más del 70%.**
- **La vacunación de género neutral proporciona protección directa para todos los hombres y mejora la cobertura.**
- A una buena cobertura le sigue la protección del resto de los hombres y mujeres no vacunados.

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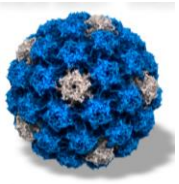

- Los programas basados en la escuela parecen ser más efectivos
- **En menores de 15 años, dos dosis con un intervalo de 6-12 meses son suficientes.**
- A partir de los 15 años, se recomienda el régimen estándar con tres dosis.
- Un amplio programa de captación para mujeres adultas jóvenes y los hombres adultos mejoran la efectividad.
- **Las vacunas también son efectivas en mujeres y hombres sexualmente activos con infecciones previas pero eliminadas.**
- La vacunación además del tratamiento local de la enfermedad relacionada con el VPH parece reducir la enfermedad recurrente o posterior relacionada con el VPH.

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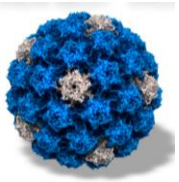

- **La combinación de la vacuna contra el VPH y la detección con la prueba del VPH es el enfoque más efectivo para la prevención del cáncer cervical.**
- Los intervalos de detección pueden aumentar en las cohortes vacunadas.
- El límite superior de edad para la vacunación aún no se ha evaluado, es específico del país y depende de la rentabilidad.
- **La Sociedad Europea de Oncología Ginecológica y la Federación Europea de Colposcopia apoyan firmemente los programas de vacunación de género neutro para niños y adolescentes jóvenes, con un programa de captación para adultos jóvenes.**

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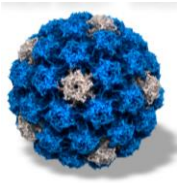
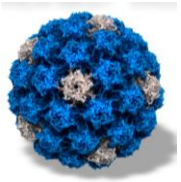
Impacto de las vacunas sobre las lesiones preneoplásicas



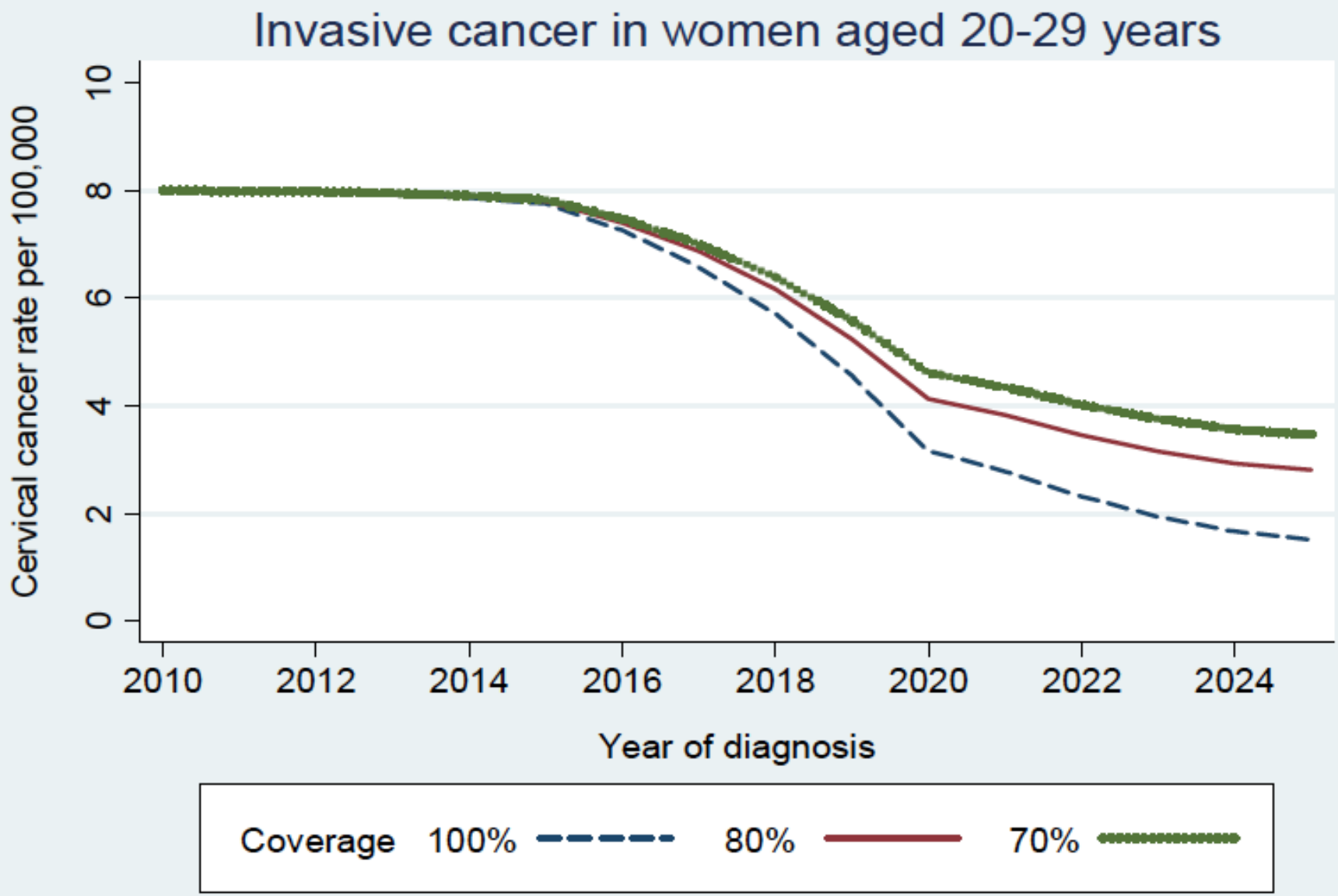
- ↓ 35% DE LSIL (CIN I)
- ↓ 60% DE HSIL (CIN II-III)
- ↓ 90% DE AIS

Impacto de las vacunas sobre el cáncer



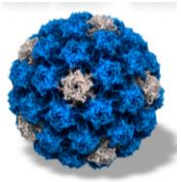
- ↓ 70% de los carcinomas escamosos
- ↓ 80% de los adenocarcinomas

Effect of vaccine on cancer over time



Cuzick et al. 2010

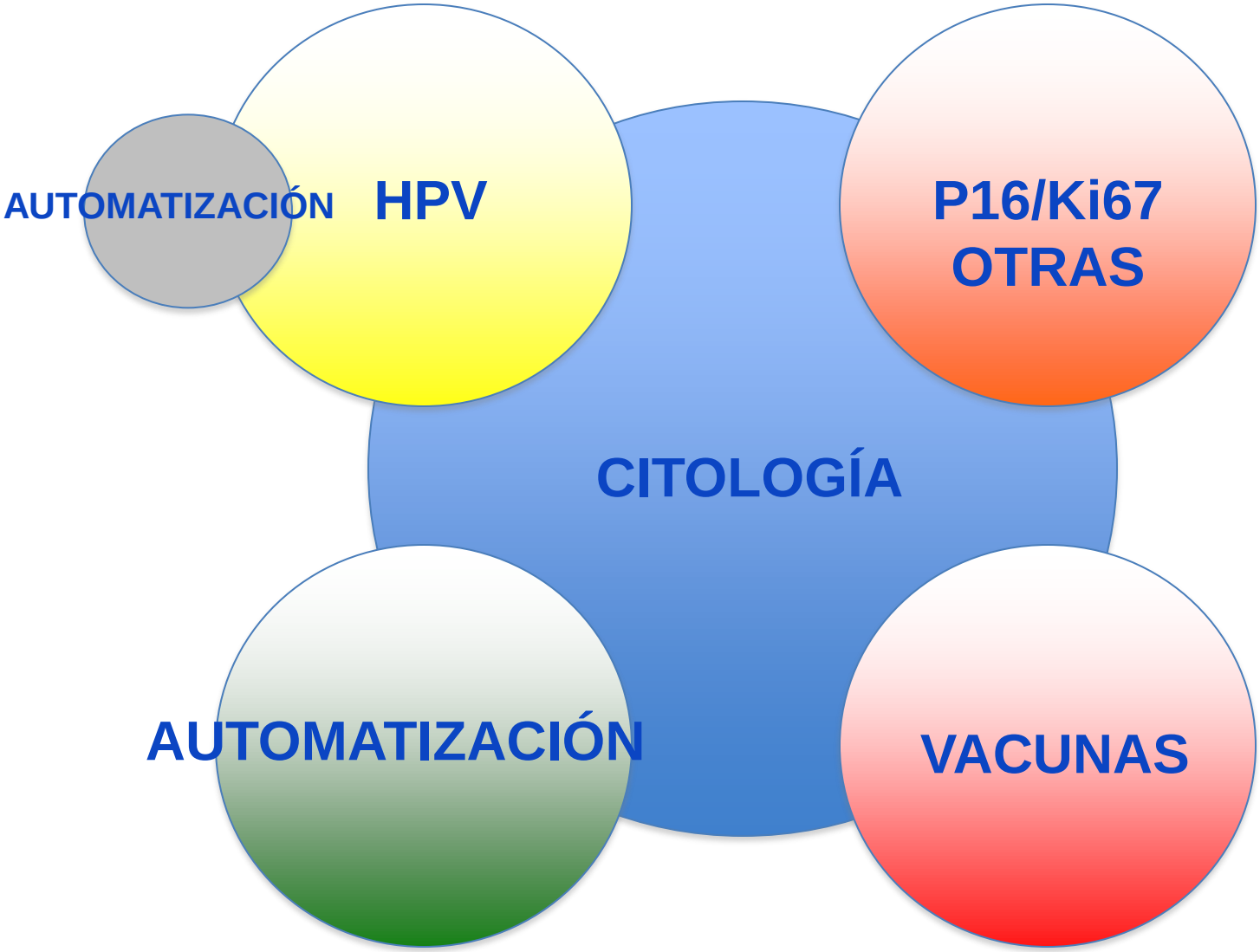
Impacto de las vacunas

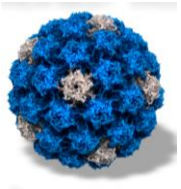


- SOBRE LAS LESIONES PRECURSORAS
- SOBRE EL CÁNCER

- SOBRE EL CRIBADO

CRIBADO DEL CÁNCER DE CÉRVIX EN EL SIGLO XXI





Cribado post vacunas

- Población diana:
  - Vacunadas
  - No vacunadas

- Edad
- Intervalos
- Técnicas

EL PAÍS

SOCIEDAD

ORIOL GÜELL

Barcelona - 26 ABR 2019 - 17:25 CEST

CARTERA DE SERVICIOS ›

La sanidad pública universaliza el cribado para detectar el cáncer de cérvix

Se introduce en la sanidad pública un programa de cribado poblacional frente al cáncer de cérvix o cuello uterino.
A las mujeres de entre 25 y 34 años les será realizada una citología cada tres años.
A las mujeres de 35 a 65 se determinará primero si son portadoras del virus del papiloma humano.
Si el resultado es negativo, la prueba se repetirá cada cinco años.
Si el resultado es positivo, las pacientes pasarán a ser sometidas a citologías regularmente.

ESCENARIO POSIBLE

CITOLOGIA LIQUIDA AUTOMATIZADA

EDAD > 30
ANTEC SIL

VACUNAS

EDAD < 30
NO ANTEC

HPV

\+ -

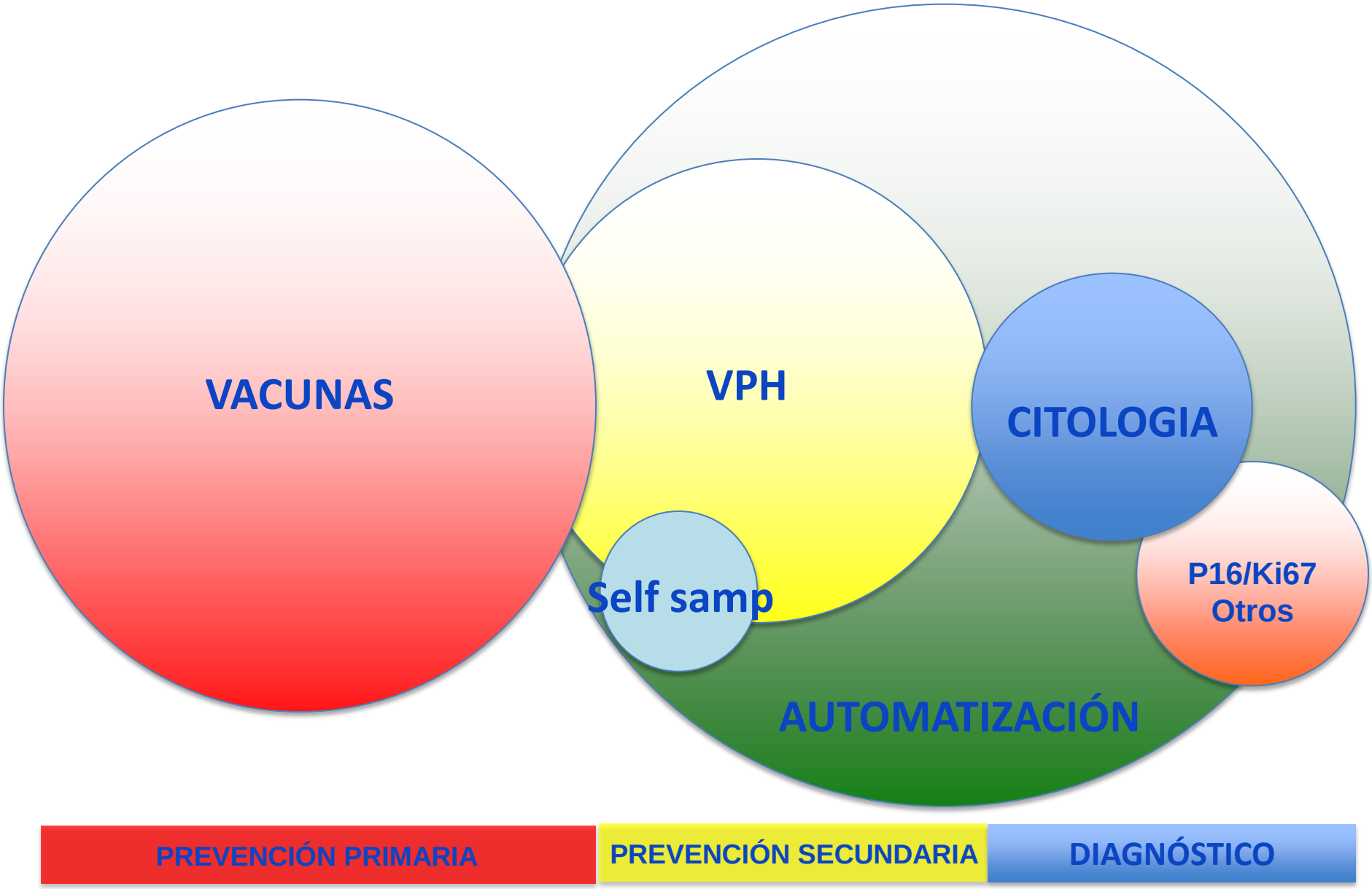
CITO/P16 SCREENING 5 A.

CITOLOGIA

\+ -

P16 / HPV SCREENING 3 A.

SCREENING DEL CÁNCER CERVICAL EN LA ERA DEL VPH



CRIBADO ORGANIZADO + VACUNAS

0% CÁNCER CERVICAL

Casa Batlló

Passeig de Gràcia, 43
Barcelona

Casa Batlló

Sant Jordi
23 de abril