Efficacia dello screening con HPV nella prevenzione dell'adenocarcinoma

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Argomenti trattati

- Proporzione di adenocarcinomi positivi all'HPV
- Distribuzione dei tipi di HPV negli adenocarcinomi
- Prove di efficacia dello screening con HPV
- Impatto della vaccinazione

Conflitti d'interesse:

Come ex-PI di uno studio indipendente (finanziato dal Ministero della salute) ho condotto trattative con Hologic, Roche, Beckton Dickinson per ottenere reagenti a prezzi ridotti o gratis.

Proporzione di adenocarcinomi positivi all'HPV

	Cases of invasive cervical cancer analysed for HPV	HPV-positive cases*	Single HPV types†	Multiple HPV types†	Undetermined HPV types†
Histological type					
Squamous cell carcinoma	9486	8252 (87%)	7678 (93%)	530 (6%)	44 (<1%)
Adenocarcinoma	760	470 (62%)	426 (91%)	39 (8%)	5 (1%)
Adenosquamous cell carcinoma	191	155 (81%)	142 (92%)	10 (6%)	3 (2%)
Other diagnosis‡	138	100 (72%)	92 (92%)	8 (8%)	0
Total	10 575	8977 (85%)	8338 (93%)	587 (7%)	52 (<1%)

Data are number or number (%). *Denominators are number of cases analysed for HPV. †Denominators are number of HPV-positive cases. ‡Includes undifferentiated, neuroendocrine, not otherwise specified, basal adenoid, and cystic adenoid carcinomas.

ADC HPV-negativi = 179
Squamosi HPV-negativi = 1073

De Sanjosé et al. Lancet Oncol 2010

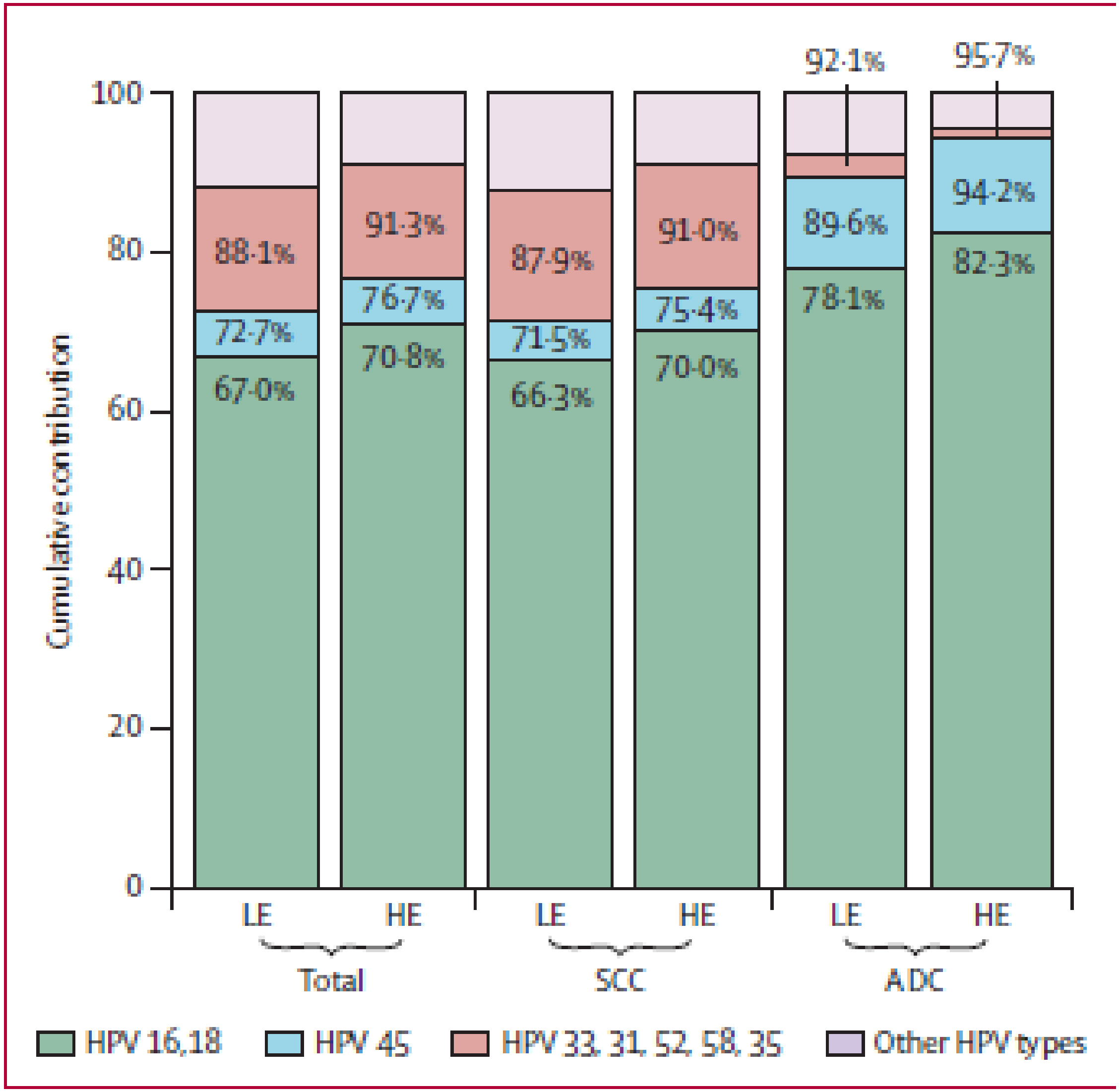
Tipi della famiglia alpha 7 sono più correlati ad adenocarcinoma

TABLE I – TYPE-SPECIFIC PREVALENCE OF 19 HPV TYPES IN ADENO/ADENOSQUAMOUS CARCINOMA (ADC) AND SQUAMOUS CELL CARCINOMA (SCC) OF THE CERVIX, AND CORRESPONDING ADC:SCC PREVALENCE RATIOS

HPV type/species	SCC		ADC		ADC:SCC prevalence ratio (95% CI)
	N	%	*N*	%	
Any HPV	11,693	90.1	2,373	80.3	0.90 (0.89–0.92)
Any multiple	7,253	9.1	1,408	8.5	0.98 (0.75–1.28)
Alpha 7					
18	11,786	12.2	2,512	37.9	3.16 (2.91–3.43)
39	7,058	1.5	1,289	0.8	0.64 (0.33–1.23)
45	7,849	3.8	1,616	5.6	1.65 (1.29–2.12)
59	6,882	1.0	1,430	1.1	1.64 (0.92–2.92)
68	6,704	0.5	1,209	0.6	1.60 (0.62–4.09)
70	6,384	0.4	989	0.3	0.82 (0.25–2.71)
Alpha 9					
16	11,878	56.6	2,521	35.3	0.57 (0.54–0.60)
31	9,071	3.6	1,639	2.0	0.49 (0.34–0.72)
33	10,309	5.2	2,005	2.1	0.39 (0.28–0.53)
35	8,340	1.5	1,530	0.7	0.69 (0.36–1.33)
52	8,737	3.5	1,573	1.3	0.52 (0.33–0.80)
58	9,088	5.9	1,613	1.9	0.39 (0.27–0.56)
Other					
6	9,049	0.4	1,497	0.1	0.09 (0.01–0.74)
11	8,400	0.2	1,308	0.1	0.55 (0.07–4.32)
51	7,281	1.0	1,286	0.2	0.26 (0.06–1.04)
56	7,232	1.0	1,445	0.2	0.23 (0.07–0.76)
66	6,969	0.3	1,131	0.3	0.98 (0.28–3.38)
73	5,929	0.3	774	0.0	–
82	6,135	0.2	828	0.0	–

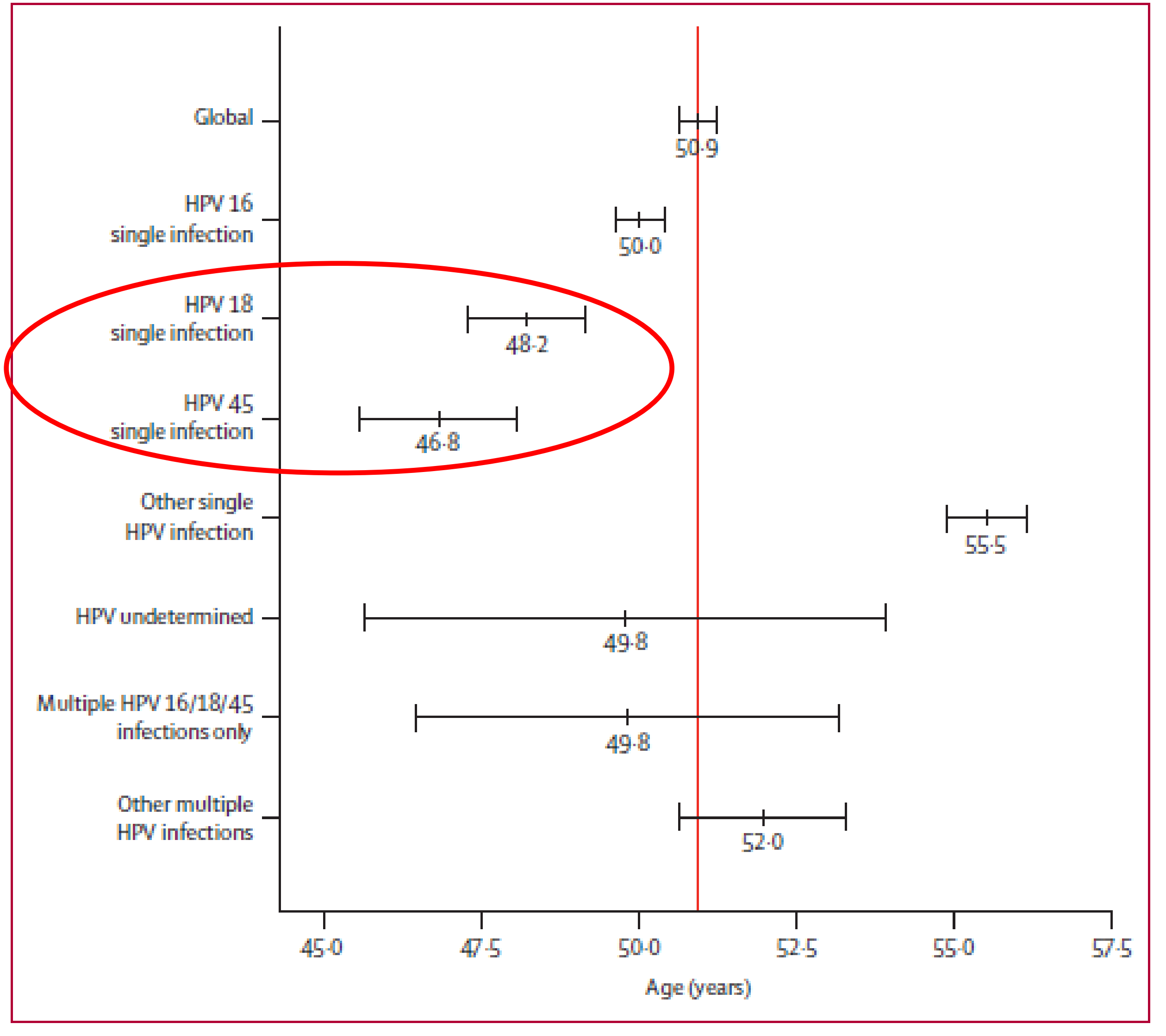
Clifford et al Int J Cancer 2008

Tipi HPV correlati



De Sanjosè et al Lancet Oncol 2010

Tipi HPV ed età



De Sanjosè et al Lancet Oncol 2010

Considerazioni

- ADC hanno una maggiore proporzione di HPV-negativi
- Gli HPV positivi si concentrano in Alpha 7 (18, 45) e HPV 16
- Per ogni ADC HPV-negativo ci sono 10 SCC HPV-negativi
- Età all'insorgenza più bassa, età all'infezione simile, fase pre-clinica più breve.

Proporzione di HPV-positivi, casistica Europea

Table 2. Histology and human papillomavirus (HPV) status by country

	HG-CIN	AIS		ICC	ASC		ADC		Usual-type	
Country	*N*	% of HG-CIN (95% CI)[1]	% HPV +	*N*	% of ICC (95% CI)[1]	% HPV+	% of ICC (95% CI)[1]	% HPV+	% of ADC (95% CI)[1]	% HPV+
Denmark	276	3.6 (1.8-6.6)	100.0	261	3.4 (1.6-6.4)	100.0	16.1 (11.9-21.1)	95.2	90.5 (77.4-97.3)	97.4
Greece	259	1.2 (0.2-3.3)	100.0	291	2.1 (0.8-4.4)	66.7	16.2 (12.1-20.9)	63.8	76.6 (62.0-87.7)	80.6
Portugal	253	2.8 (1.1-5.6)	100.0	321	2.8 (1.3-5.3)	88.9	19.9 (15.7-24.7)	75.0	76.6 (64.3-86.2)	87.8
Norway	259	1.9 (0.6-4.4)	100.0	338	4.7 (2.7-7.6)	81.3	18.0 (14.1-22.6)	83.6	86.9 (75.8-94.2)	92.5
Hungary	230	3.0 (1.2-6.2)	85.7	226	0.9 (0.1-3.2)	100.0	8.8 (5.5-13.3)	70.0	70.0 (45.7-88.1)	92.9
Germany	NC	–	–	177	7.3 (4.0-12.2)	100	15.3 (10.3-21.4)	74.1	77.8 (57.7-91.4)	90.5
Scotland	NC	–	–	260	3.5 (1.6-6.5)	77.8	13.1 (9.2-17.8)	79.4	85.3 (68.9-95.0)	89.7
Wales	NC	–	–	332	2.4 (1.0-4.7)	75.0	16.9(13.0-21.3)	76.8	76.8 (63.6-87.0)	95.3
Poland	205	1.0 (0.1-3.5)	100.0	193	6.2 (3.3-10.6)	75.0	7.8 (4.4-12.5)	73.3	66.7 (38.4-88.2)	100.0
Czech Republic	272	1.5 (0.4-3.7)	75.0	254	3.5 (1.6-6.6)	100.0	18.1 (13.6-23.4)	84.8	84.8 (71.1-93.7)	94.9
Romania	169	0.0 (0.0-2.2)	–	254	2.0 (0.6-4.5)	80.0	6.3 (3.6-10.0)	43.8	43.8 (19.8-70.1)	57.1
Belgium	NC	–	–	255	2.4 (0.9-5.1)	83.3	12.9 (9.1-17.7)	63.6	75.8 (57.7-88.9)	84.0
Austria	209	2.4 (0.8-5.5)	100.0	NC	–	–	–	–	–	–
Estonia	250	0.0 (0.0-1.5)	–	NC	–	–	–	–	–	–
Spain	265	0.8 (0.0-2.7)	100.0	NC	–	–	–	–	–	–
Ireland	241	1.7 (0.5-4.2)	75.0	NC	–	–	–	–	–	–
Russia	215	0.0 (0.0-1.7)	–	NC	–	–	–	–	–	–
Overall	3,103	1.6 (1.2-2.1)	93.9	3,162	3.3 (2.7-4.0)	85.6	14.6 (13.4-15.9)	76.1	79.0 (74.9-82.6)	90.4

2,5% degli ICC

[1]95%CI calculations are *post hoc* analyses.
Abbreviations: HG-CIN: any high-grade cervical intraepithelial neoplasia (includes any adenocarcinoma *in situ* (AIS)); AIS: adenocarcinoma *in situ* (includes AIS and AIS+ any high-grade cervical intraepithelial neoplasia (HG-CIN)); ICC: invasive cervical cancer including squamous cell carcinoma (SCC), cervical adenocarcinoma (ADC), cervical adenosquamous carcinoma (ASC), and other; usual-type: Usual-type ADC; HPV: human papillomavirus; NC: Not collected in the country; 95% CI: lower bound of 95%CI - upper bound 95%CI.

Holl et al. Int J Cancer 2015

Cosa sono gli ADC HPV-negativi?

Table 3. Number of cases of cervical adenocarcinoma (ADC) and its subtypes, and human papillomavirus status (HPV) by country

	ADC	Usual-type	Clear-cell			Serous			Gastric			Endo			NOS		
Country	*N*	*N*	*N*	% of ADC	% HPV+	*N*	% of ADC	% HPV+	*N*	% of ADC	% HPV+	*N*	% of ADC	% HPV+	*N*	% of ADC	% HPV+
Denmark	42	38	0	0.0	–	1	2.4	0.0	0	0.0	–	2	4.8	100.0	1	2.4	100.0
Greece	47	36	0	0.0	–	5	10.6	20.0	0	0.0	–	6	12.8	0.0	0	0.0	–
Portugal	64	49	8	12.5	50.0	3	4.7	33.3	2	3.1	0.0	1	1.6	0.0	1	1.6	–
Norway	61	53	5	8.2	20.0	2	3.3	50.0	0	0.0	–	1	1.6	0.0	0	0.0	–
Hungary	20	14	1	5.0	0.0	3	15.0	33.3	0	0.0	–	2	10.0	0.0	0	0.0	–
Germany	27	21	2	7.4	50.0	0	0.0	–	2	7.4	0.0	2	7.4	0.0	0	0.0	–
Scotland	34	29	1	2.9	0.0	1	2.9	0.0	1	2.9	0.0	2	5.9	50.0	0	0.0	–
Wales	56	43	4	7.1	0.0	4	7.1	25.0	0	0.0	–	3	5.4	33.3	2	3.6	–
Poland	15	10	1	6.7	0.0	0	0.0	–	1	6.7	0.0	2	13.3	0.0	1	6.7	100.0
Czech Republic	46	39	2	4.3	50.0	1	2.2	100.0	0	0.0	–	4	8.7	0.0	0	0.0	–
Romania	16	7	3	18.8	33.3	3	18.8	33.3	0	0.0	–	2	12.5	0.0	1	6.3	100.0
Belgium	33	25	2	6.1	0.0	0	0.0	–	1	3.0	0.0	4	12.1	0.0	1	3.0	–
Overall	461	364	29	6.3	27.6	23	5.0	30.4	7	1.5	0.0	31	6.7	12.9	7	1.5	42.9

Abbreviations: ADC: any cervical adenocarcinoma; usual-type: usual-type ADC; clear-cell: clear-cell ADC; serous: serous ADC; gastric: minimal deviation/gastric ADC; Endo: endometrioid ADC; NOS: ADC not otherwise specified.

90,4%

Holl et al. Int J Cancer 2015

Ancora sugli ADC HPV-negativi

TABLE 4 Summary table of somatic mutations, immunohistochemical staining patterns and final HPV status in 45 analysable cases of different types of CADC

		ADC-CX																				ADC-ENDO								ADC-SER						ADC-CC			ADC-GAS			ADC-NOS					Count positives
	Case ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	
	HPV type	16	45	16	18	18	59	16	16	16	16	45	16	16	16	16	45	18	0	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	18
IHC	p16	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	0	1	1	1	0	0	0	0	0	0	0	1	0	1	1	1	0	1	1	0	0	0	0	0	1	0	0	0	25
	PR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	9
	p53-WT	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	1	1	0	0	0	1	0	1	1	1	1	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	25
	p53-MUT	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	1	1	1	0	0	0	0	0	0	0	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	16
	β-cat [b]																						1	1	1																					1	4
	MSI [a]	0	NI	0	0	0	0	0	0	0	0	0	0	NI	0	0	0	0	0	0	0	0	NI	0	0	1	NI	NI	NI	0	1	0	NI	0	0	0	0	0	0	0	0	NI	NI	NI	1	NI	3
Genes mutated	TP53	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0	1	0	0	1	0	1	1	0	1	1	0	0	1	1	0	1	1	0	1	0	14
	PIK3CA	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0	0	0	1	1	1	1	0	1	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	1	0	0	1	13
	KRAS	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	1	1	0	0	0	0	7
	PTEN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	6
	CTNNB1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	4
	FBXW7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
	CDKN2A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	4
	AKT1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	4
	GNAS	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
	STK11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2
	FOXL2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	APC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
	NRAS	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Count	Mutation positive	0	0	0	0	0	0	0	0	0	1	2	2	2	4	0	1	1	2	2	2	2	3	2	2	0	4	2	1	1	1	2	2	0	2	1	0	1	2	2	3	3	2	1	2	2	

Note: 0 = negative; 1 = positive; IHC empty cell = not tested; NI = Staining noninformative.
[a] MSI, Microsatellite instability based on MLH1, MSH2, MSH6 and PMS2 IHC and PCR analysis.
[b] β-cat staining is done to confirm CTNNB1 mutation.

Brotherton et al. Int J Cancer 2017

Table 2. Human papillomavirus (HPV) Types, among women aged 18–39 years, by final case diagnosis (n = 3,746)

	AIS						CIN3		
	Total AIS		AIS Only		AIS + CIN		CIN3 only		
HPV type characteristics	*n*	%	*n*	%	*n*	%	*n*	%	*p*-value[1]
Total typed	189		79		110		3,557		
HPV positivity									
Positive for any HPV type	188	99	78	99	110	100	3,491	98	0.26
Positive for single type	151	80	65	82	86	78	2,887	81	
Positive for multiple types	37	20	13	16	24	22	604	17	
HPV type groups									
Any 16 and/or 18	174	92	73	92	101	92	2,224	63	<0.01
Any 9-valent HR-HPV[2]	180	95	74	94	106	96	3,085	87	<0.01
Any HR-HPV[3]	184	97	77	97	107	97	3,387	95	0.22
Alpha-7[4]	81	43	36	46	45	41	438	12	<0.01
Alpha-9[4]	116	61	43	54	73	66	3,007	85	<0.01
HPV types targeted by 9-valent vaccine[5]									
16	108	57	42	53	66	60	2,080	58	0.72
18	72	38	33	42	39	36	172	5	<0.01
31	4	2	1	1	3	3	392	11	<0.01
33	2	1	0	0	2	2	143	4	0.03
45	4	2	1	1	3	3	80	2	1.00
52	6	3	0	0	6	6	286	8	0.01
58	3	2	1	1	2	2	165	5	0.05
Other high-risk types[5]									
35	3	2	0	0	3	3	138	4	0.12
39	2	1	1	1	1	1	98	3	0.24
51	3	2	1	1	2	2	156	4	0.06
56	0	0	0	0	0	0	35	1	0.42
59	1	1	1	1	0	0	53	1	0.52
66	3	2	2	3	1	1	63	2	1.00
68	1	1	0	0	1	1	31	1	1.00

[1]*p*-value comparison of total AIS and CIN3 by chi-square or Fisher's exact test.
[2]9-valent HR-HPV types include HPV 16, 18, 31, 33, 45, 52 and 58.
[3]High-risk HPV types include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68.
[4]HPV alpha species: alpha-7 include HPV 18, 39, 45, 59, 68 or 70; alpha-9 include HPV 16, 31, 33, 35, 52, 58, or 67.
[5]Categories are not mutually exclusive due to multiple types detected in individual cases.
Abbreviations: AIS, adenocarcinoma in situ; CIN3, cervical intraepithelial neoplasia grade 3; HR-HPV, high-risk human papillomavirus.

Gli Adeno-carcinomi in situ sono HPV-positivi

50% screening con Pap
50% screening co-testing

Cleveland et al. Int J Cancer 2020

Cosa c’è nelle citologie AGC

Table 3. Pooled disease rate (proportion, 95% CI) among women with a positive (hrHPV+) or negative (hrHPV-) hrHPV test result, by age category

		<40 y		40–50 y		≥50 y	
Outcome	**#[1]**	**hrHPV+ (%)**	**hrHPV− (%)**	**hrHPV+ (%)**	**hrHPV− (%)**	**hrHPV+ (%)**	**hrHPV− (%)**
CIN2+/AIS+	4	42.2 (36.1–48.5)	9.3 (1.2–22.1)	26.5 (8.1–50.1)	1.4 (0.0–5.3)	5.8 (0.0–22.7)	0.4 (0.7–5.9)
AIS+	2	13.0 (4.4–24.7)	8.0 (0.0–27.9)	4.0 (0.0–25.9)	1.9 (0.0–6.4)	0.0 (0.0–5.9)	0.0 (0.0–4.5)
CC	2	4.5 (0.3–11.9)	2.0 (0.0–16.5)	2.6 (0.0–17.4)	0.3 (0.0–3.4)	0.0 (0.0–5.9)	0.0 (0.0–0.0)
nHRC	3	0.4 (0.0–3.0)	1.0 (0.0–6.5)	3.4 (0.1–9.6)	3.5 (1.1–6.8)	3.2 (0.0–16.6)	18.0 (2.6–40.7)

[1]number of studies.
Abbreviations: AIS+, adenocarcinoma *in situ* or worse; CC, cervical cancer; CI, confidence interval; CIN2+, cervical intraepithelial neoplasia grade two or worse; hrHPV, high-risk human papillomavirus; nHRC, non-HPV related cancer.

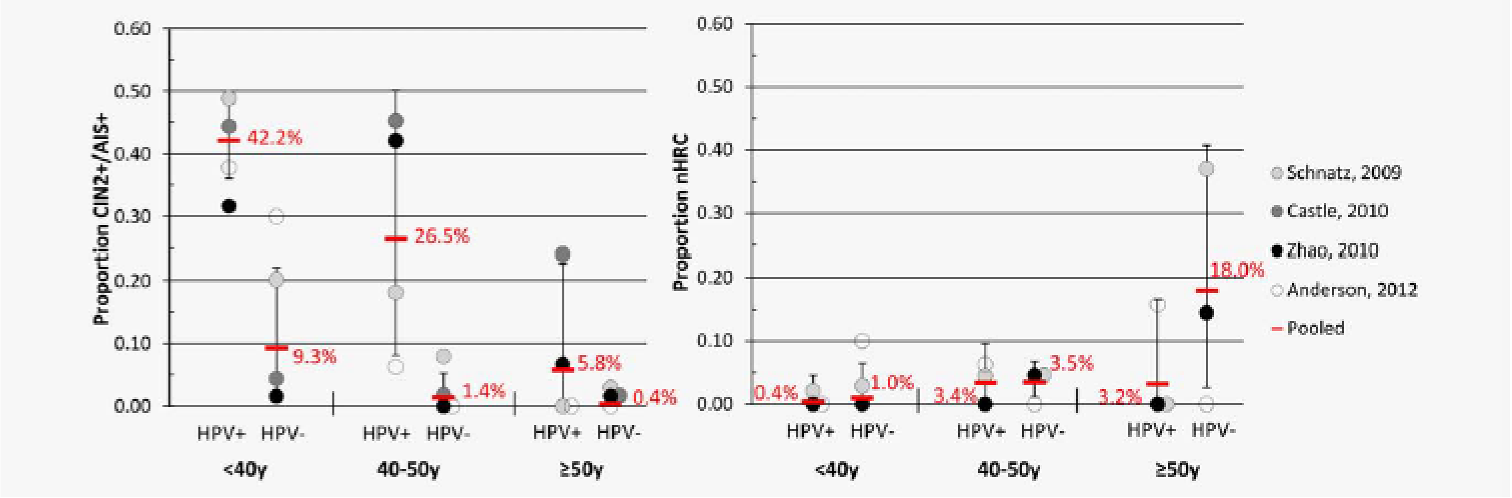


Figure 3. Risk of (a) CIN2+/AIS+ and (b) nHRC for women who have AGC and are hrHPV-positive or hrHPV-negative, by age group. Circles are values from individual studies. Horizontal red bars represent the meta-analytically pooled values. Vertical black bars represent 95% confidence intervals around the pooled value. Abbreviations: AGC, atypical glandular cells; AIS+, adenocarcinoma *in situ* or worse; CIN2+, cervical intraepithelial neoplasia grade two or worse; HC2, Hybrid Capture 2; hrHPV, high-risk HPV; nHRC, non-HPV related cancer. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com]

Verdoodt et al. Int J cancer 2016

Considerazioni

- Gli AIS sono in larga parte HPV-positivi
- Gli ADC usual type sono in gran parte HPV-positivi, mentre clear-cell, sierosi, gastrici e endometriali sono in gran parte HPV-negativi
- Gli HPV-negativi hanno più mutazioni somatiche.
- Nelle AGC in donne >50 anni la probabilità di trovare cancri non HPV-correlati è alta

Perché si trovano cancri in donne screenate?

Table 2
A evaluation of the programmatic correlates leading to cervical cancer diagnoses. Abbreviations: SCC, squamous cell carcinoma, ADC, adenocarcinoma.

Programmatic correlates of cervical cancer diagnoses	All			SCC			ADC			Other cancers			Unknown[d]			p[c]
	n = 623			n = 351			n = 212			n = 19			n = 41			
	n	%col	%col[b]	n	%col	%col[b]	n	%col	%col[b]	n	%col	%col[b]	n	%col	%col[b]	
Prevalent cancers	360	57.8%	–	227	64.7%	–	101	47.6%	–	6	31.6%	–	26	63.4%	–	<0.001
Non-prevalent cancers	263	42.2%	100%	124	35.3%	100%	111	52.4%	100%	13	68.4%	100%	15	36.6%	100%	<0.001
False-negative cotest (screen)	70	11.2%	26.6%	36	10.3%	29.0%	25	11.8%	22.5%	7	36.8%	53.8%	2	4.9%	13.3%	0.07
Algorithm delays	48	7.7%	18.3%	15	4.3%	12.1%	29	13.7%	26.1%	2	10.5%	15.4%	2	4.9%	13.3%	0.04
False-negative diagnoses (colposcopy and biopsy)	56	9.0%	21.3%	20	5.7%	16.1%	28	13.2%	25.2%	3	15.8%	23.1%	5	12.2%	33.3%	0.2
Treatment failure	27	4.3%	10.3%	23	6.6%	18.5%	3	1.4%	2.7%	0	0.0%	0.0%	1	2.4%	6.7%	<0.001
Non-compliance with guidelines (all)	56	9.0%	21.3%	29	8.3%	23.4%	21	9.9%	18.9%	1	5.3%	7.7%	5	12.2%	33.3%	0.9
Non-compliance with screening	9	1.4%	3.4%	4	1.1%	3.2%	4	1.9%	3.6%	1	5.3%	7.7%	0	0.0%	0.0%	0.6
Non-compliance with follow-up[e]	45	7.2%	17.1%	23	6.6%	18.5%	17	8.0%	15.3%	0	0.0%	0.0%	5	12.2%	33.3%	0.1
Non-compliance with screening and follow-up	2	0.3%	0.8%	2	0.6%	1.6%	0	0.0%	0.0%	0	0.0%	0.0%	0	0.0%	0.0%	0.6
Mixed[a]	6	1.0%	2.3%	1	0.3%	0.8%	5	2.4%	4.5%	0	0.0%	0.0%	0	0.0%	0.0%	0.3

[a] Several possible explanations.
[b] Column percentage among non-prevalent cancers.
[c] Fisher's exact test for differences for a correlate by histology category among non-prevalent cancers.
[d] The histology of microinvasive cancers was not available.
[e] Includes failure to come back for follow-up testing, colposcopy, treatment, or post-treatment surveillance according to recommendations.

Castle et al, Gynecol Oncol 2016

Risultati di screening precedenti alla diagnosi di cancro

Table 3
The relationship of last cotesting results with histology and cancer stage. Abbreviations: SCC, squamous cell carcinoma; ADC, adenocarcinoma; HPV, human papillomavirus; Cyto, cytology.

	HPV+ (n = 532)		HPV− (n = 91)		Cyto+ (n = 514)		Cyto− (n = 108)		HPV−/Cyto− (n = 51)		HPV−/Cyto+ (n = 40)		HPV+/Cyto− (n = 58)		HPV+/Cyto+ (n = 474)	
	n	%col	n	%col	n	%col	n	%col	n	%col	n	%col	n	%col	n	%col
Histology																
SCC	298	56.0%	53	58.2%	309	60.1%	42	38.9%	27	52.9%	26	65.0%	15	25.9%	283	59.7%
ADC	185	34.8%	27	29.7%	158	30.7%	54	50.0%	17	33.3%	10	25.0%	37	63.8%	148	31.2%
Other	9	1.7%	10	11.0%	8	1.6%	11	10.2%	7	13.7%	3	7.5%	4	6.9%	5	1.1%
Unknown[a]	40	7.5%	1	1.1%	39	7.6%	2	1.9%	0	0.0%	1	2.5%	2	3.5%	38	8.0%
Stage																
Localized	302	56.8%	31	34.1%	285	55.4%	48	44.4%	14	27.5%	17	42.5%	34	58.6%	268	56.5%
Regional (all)	67	12.6%	26	28.6%	72	14.0%	21	19.4%	15	29.4%	11	27.5%	6	10.3%	61	12.9%
Distant	15	2.8%	14	15.4%	20	3.9%	9	8.3%	9	17.7%	5	12.5%	0	0.0%	15	3.2%
Unknown/missing	148	27.8%	20	22.0%	137	26.7%	31	28.7%	13	25.5%	7	17.5%	18	31.0%	130	27.4%

[a] The histology of microinvasive cancers was not available.

Considerazioni

- Gli ADC nelle donne screenate sono più frequenti dell’atteso (rispetto agli squamosi)
- Più spesso sono cancri incidenti
- Spesso sfuggono al secondo livello o per mancata compliance al follow up
- Sono più spesso HPV-positivi

Efficacia dello screening con HPV

	Pooled rate ratio* (95% CI)	I^2 (p for heterogeneity between studies)
Morphology		
Squamous-cell carcinoma	0·78 (0·49–1·25)	0·0% (0·84)
Adenocarcinoma	0·31 (0·14–0·69)	0·0% (0·59)
Adenocarcinoma vs squamous-cell carcinoma	0·34 (0·12–0·90)	..

	Invasive cell carcinomas (n)					Total	Median
Experimental	10	3	3	8	2	136 223	7·5
Control	4	3	1	3	1	45 376	7·5
Pooled							
Experimental§	44	21	19	35	9	653 209	6·6
Control§	63	32	31	38	25	561 206	6·2
All	107	53	50	73	34	1 214 415	6·5

Ronco et al Lancet 2014

Efficacia della vaccinazione vs. AIS

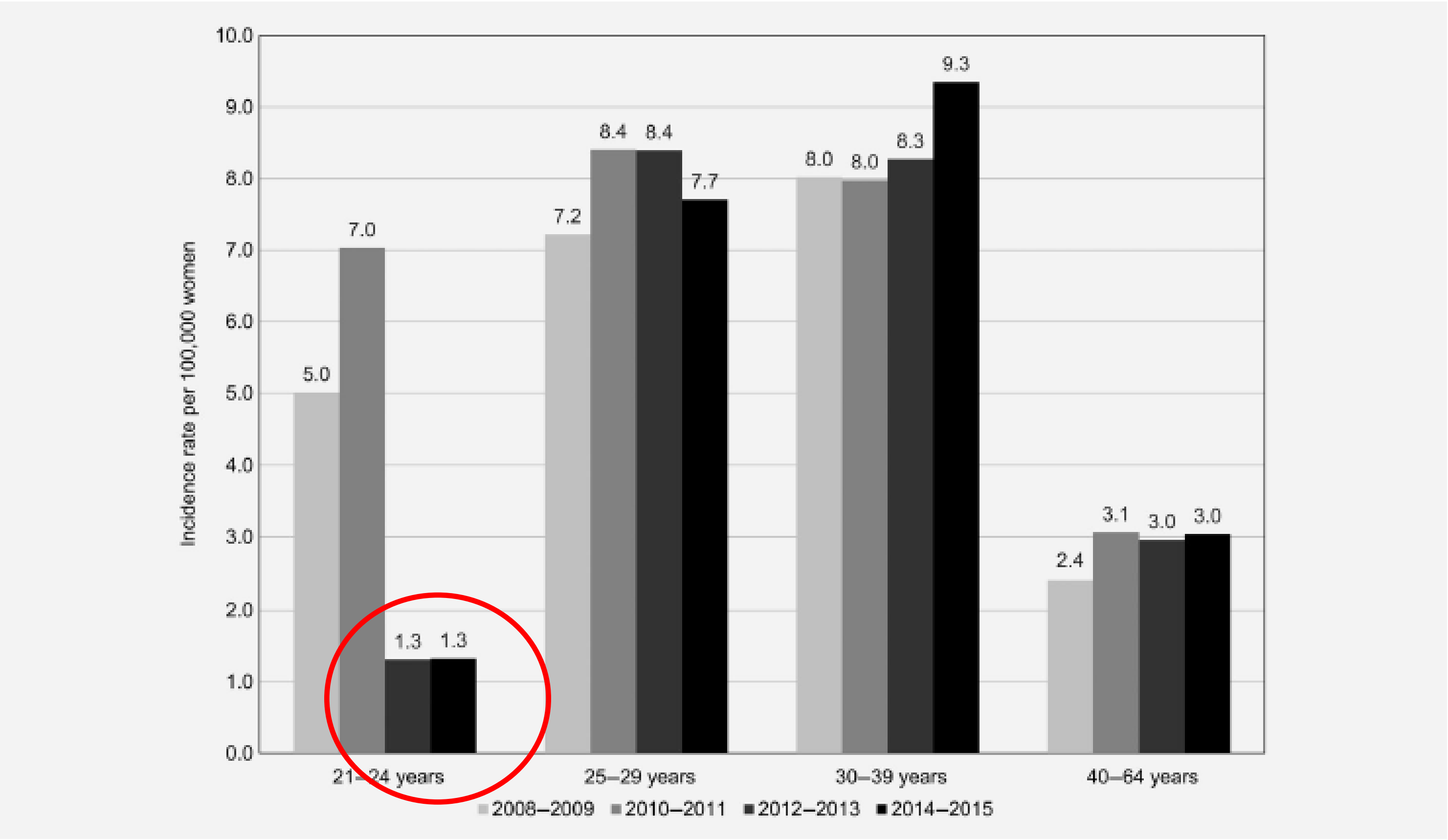


Figure 1. Adenocarcinoma *in situ* average annual 2-year incidence rates per 100,000 women, by age group. For a smoother graphical presentation, average annual incidence rates were calculated for each 2-year interval.

Cleveland et al. Int J Cancer 2020

In conclusione

- Il test HPV è molto più efficace del Pap test nel prevenire l'ADC (3 volte di più)
- L'ADC è meno prevenibile dello squamoso:
  - Fase preclinica più breve
  - Minore campionamento di cellule
  - Minore visibilità in colpo
  - Parte di ADC non HPV correlati
- Gli ADC non HPV correlati non hanno precursori noti…

Grazie per l'attenzione

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