



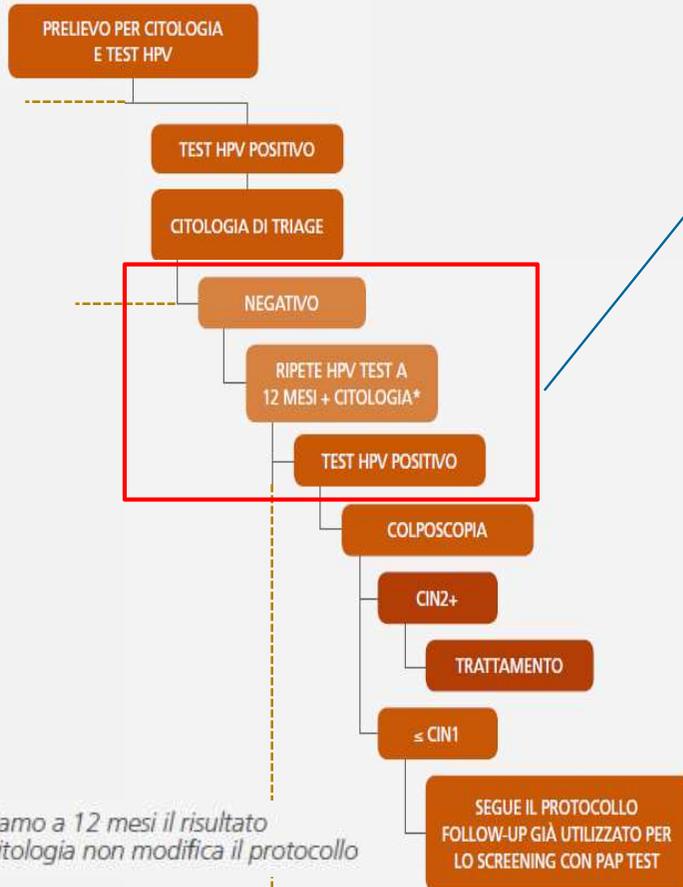
# HPV POSITIVO A 12 MESI: QUALE RISCHIO E QUALE GESTIONE?

***Laura De Marco***

*S.C. Epidemiologia dei Tumori U - CPO  
AOU Città della Salute e della Scienza  
PO Molinette - Torino*

*Centro Unificato Screening Cervico Vaginale  
AOU Città della Salute e della Scienza  
PO S. Giovanni Antica Sede - Torino*

# OBIETTIVO



- *Raccomandazioni HTA - 2012*  
- *Raccomandazioni sul test HR-HPV come test di screening primario – GISCi 2017*

**VERIFICARE LA POSSIBILITA'  
DI RIDUZIONE DELLA QUOTA  
DI INVIO IN COLPO  
GARANTENDO SEMPRE  
EFFICACIA DELLA  
PREVENZIONE**

**TUTELA DELLA SALUTE DELLA DONNA**

# IL CONTESTO

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Review

Triage of HPV positive women in cervical cancer screening 

Nicolas Wentzensen<sup>a,\*</sup>, Mark Schiffman<sup>a</sup>, Timothy Palmer<sup>b</sup>, Marc Arbyn<sup>c</sup>

<sup>a</sup> Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville, MD, USA  
<sup>b</sup> The University of Edinburgh, Edinburgh, UK  
<sup>c</sup> Belgian Cancer Centre/Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium

...For primary HPV screening, all HPV positive results need additional triage, but the management of HPV positive women with negative cytology is particularly challenging, since the risk in this group is too high to return women to regular screening, but too low for colposcopy referral...

# IL CONTESTO

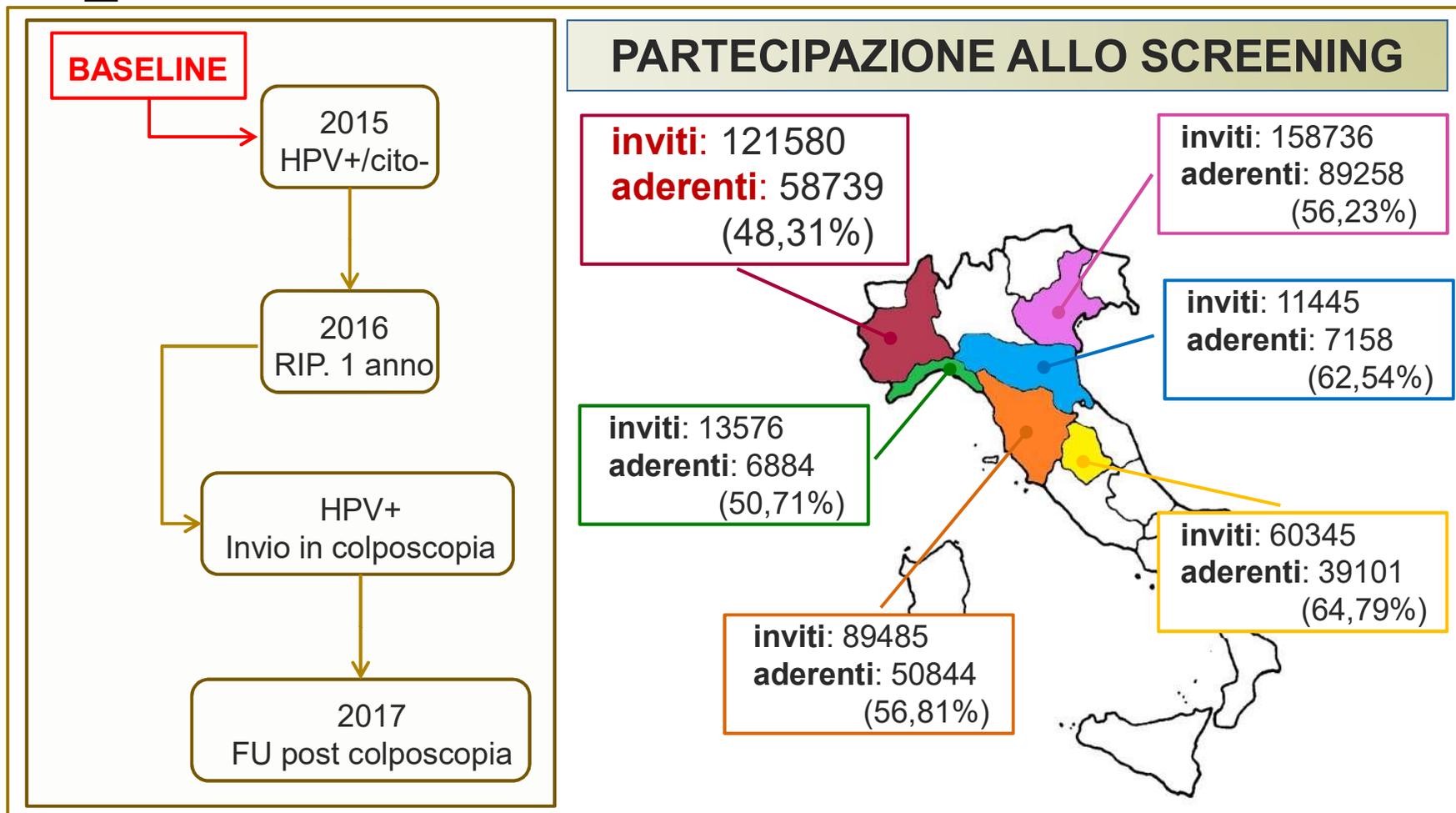
➤ ...A QUALE LIVELLO DELL'ALGORITMO SI POTREBBE INTERVENIRE?

## CONCLUSIONS triage with HPV re-testing

1. Increased sensitivity of the immediate triage test reduces cancer risk just until re-testing (very small gains with 1-year interval). Cancer risk reduction after HPV re-testing negligible (if any)
2. Reducing the referral to colposcopy of the immediate triage test has little effect on overall colposcopy consumption
3. Relevant reductions in colposcopy consumption possible only by increasing the interval to HPV re-testing.
4. For this purpose higher sensitivity of the immediate triage test is needed
5. This is the best (and practically only, see 1) way of exploiting improvements in sensitivity of the immediate triage test

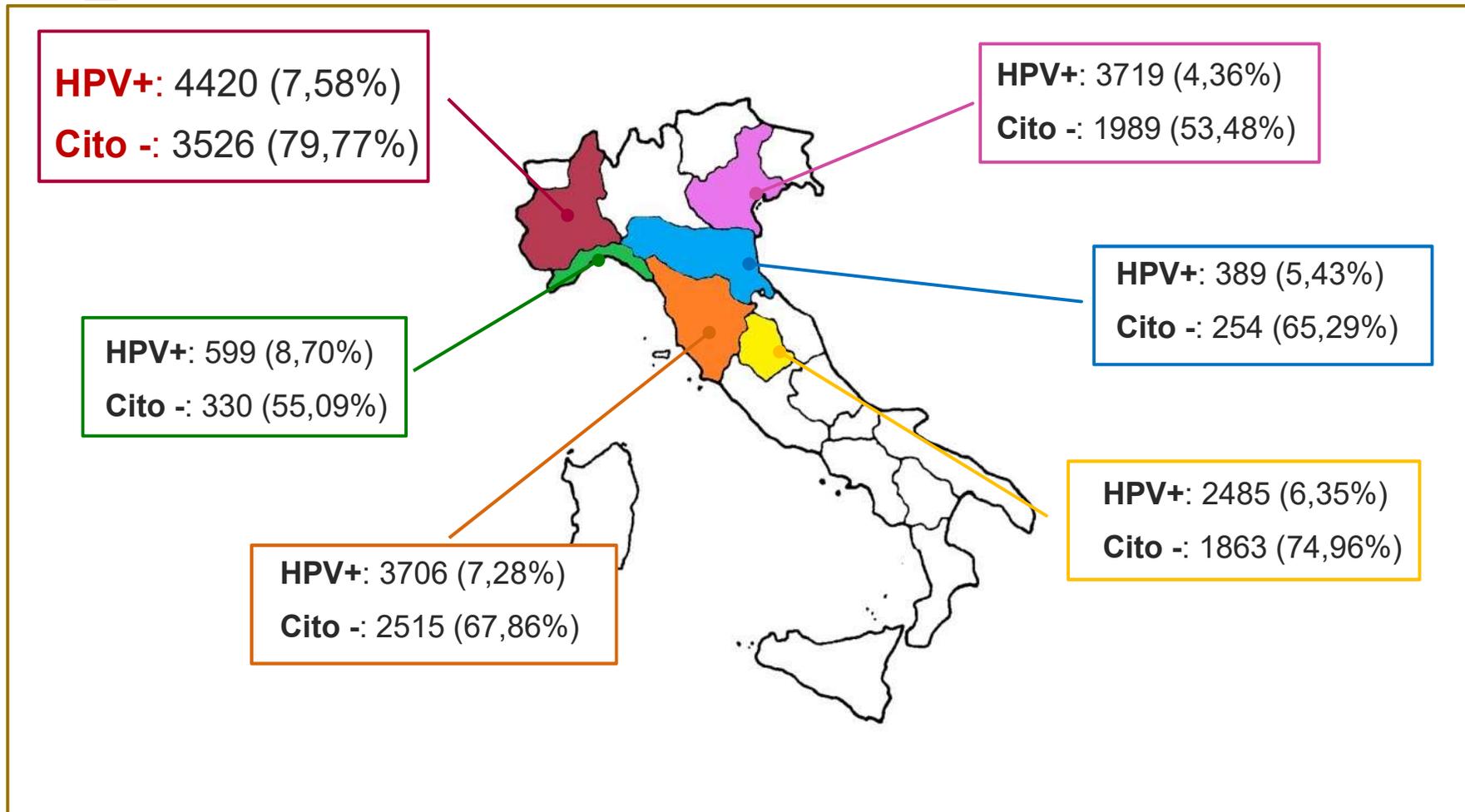
da G. Ronco – EUROGIN 2017 - IMMEDIATE TRIAGE AND RE-TESTING

# COORTI E REGIONI VALUTATE



dati ottenuti dalla survey

# 2015: HPV POSITIVI E CITOLOGIA DI TRIAGE



*dati ottenuti dalla survey*

# 2016: PERSISTENZA A 1 ANNO

REGIONE	RIPETIZIONE 1 AA						COLPOSCOPIA		
	INVITI	ADERENTI	%	HPV-	HPV+	%	ISTOLOGIA		
							CIN 2	CIN3+	VPP CIN2+
<b>PIEMONTE</b>	3547	2930	83,6	1363	1555	53,3	31	53	6,14%
LIGURIA	319	236	99,8	105	147	58,3	3	1	2,90%
EMILIA ROMAGNA	259	241	93,0	106	136	56,2	7	4	9,70%
VENETO	1910	1663	87,0	705	968	57,8	46	12	6,49%
TOSCANA	2050	1749	85,3	824	924	52,3	47	50	11,97%
UMBRIA	1914	1657	86,6	642	948	59,6	50	24	9,20%

DATI PIEMONTESI FOLLOW-UP IN COLPO (A 9 MESI)										
ETA'	N° COLPO	N° ESAMI TEST HPV	HPV+	%	CITOLOGIA			ISTOLOGIA		VPP CIN 2+
					NEG	LSIL	HSIL	CIN 2	CIN3+	
30-64	329	239	134	56,0	181	26	7	10	11	6,38%

VPP CIN2+  
7,68%

dati ottenuti dalla survey



# **QUALI SCENARI IPOTIZZABILI...**

# CONSIDERARE I VALORI DI RLU/CO o cT?

## Strumentazione utilizzata

### Hybrid Capture 2 - Qiagen



- Piemonte (gara regionale 2014)
- Basilicata
- Liguria

Risultati espressi come RLU/CO (pos se >1)

### Cobas® 4800 - Roche



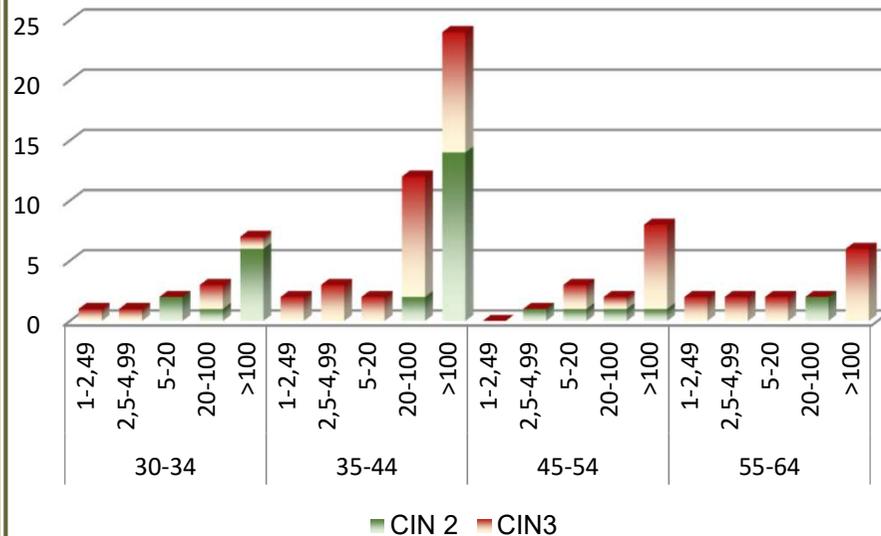
- Veneto
- Emilia Romagna
- Toscana
- Umbria
- Trento

Risultati espressi come cT (pos se <39-40)

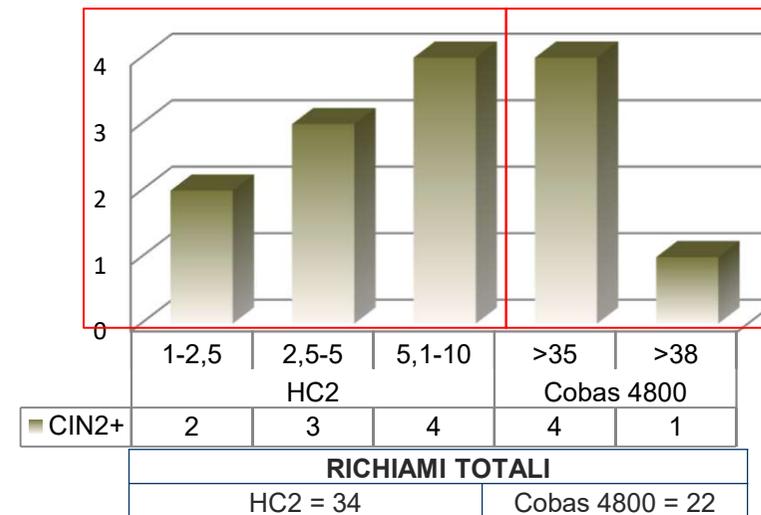
# CONSIDERARE I VALORI DI RLU/CO o cT?

Anno di riferimento 2016

**PIEMONTE: DISTRIBUZIONE CIN2/CIN3 AL RICHIAMO 1 ANNO**



**ISPRO FIRENZE: DISTRIBUZIONE CIN2+ AL RICHIAMO 1 ANNO**



...RLU/CO e CT sembrerebbero non essere discriminanti

# CITOLOGICO + HPV A 1 ANNO?

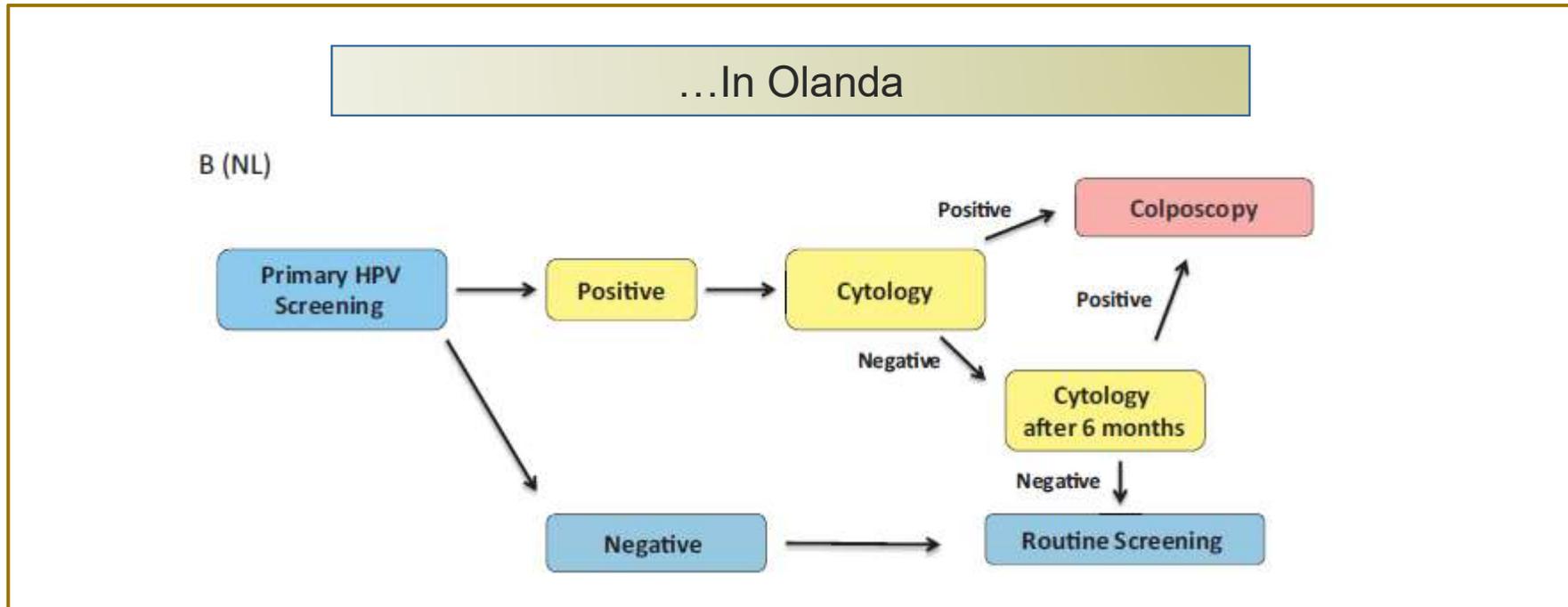


Fig. 2. Two examples of algorithms for primary HPV screening.

(A) In the United States, primary HPV screening using the cobas assay (Roche) was approved by the FDA. Women negative for HPV will go back to routine screening with 3-year intervals. Women with HPV16/18-positive results are referred to colposcopy immediately. Among women positive for other carcinogenic types, cytology is performed and women with ASC-US or higher are referred to colposcopy, while women with normal cytology are re-tested after 12 months (B) **In the Netherlands**, a primary HPV screening approach has been proposed and approved for implementation. All HPV-positive women are triaged with cytology. If cytology is positive, women are referred to colposcopy. **Women with negative cytology will have repeat cytology after 6 months and are referred to colposcopy when cytology is positive**, otherwise they are released back to routine screening. For women with a previous negative HPV screening test, the screening interval is 5 years if <45 years and 10 years for women aged > - 45. **For women 45 years or older with a positive HPV test but with double negative cytology triage, the next invitation will be sent after 5 years instead of after 10 years.**

da Wentzensen N et al. J Clinical Virology 2016 - modificato

# CITOLOGICO + HPV A 1 ANNO?

Anno di riferimento 2016

REGIONE	N° RIP 1 AA	HPV+	%	CITOLOGIA			COLPO	ISTOLOGIA		
				ASC US+	ASC H	HSIL		CIN 2+	CIN2/CIN3	VPP CIN2+
§ LOMBARDIA	780	356	45,6	—	—	—	326	23		7,00%
*EMILIA ROMAGNA	655	309	47,2	167		32	137	12		8,80%
VENETO	352	185	52,0		7	3	185		4/4	3,20%
TOSCANA	828	514	62,0	22		6	514	41		11,00%
UMBRIA	1702	966	57,0		48	25	966		50/24	9,20%

§ fonte Pasquale et.al. GISCi 2017: Screening Valcamonica (2011-2013)

\* dati dell'Emilia Romagna riferiti al FU – dati assimilabili

— dati non disponibili

# CITOLOGICO + HPV A 1 ANNO? ESPERIMENTO TORINESE

Anno di riferimento 2017

## 102 CITOLOGIE A 1 ANNO CONSECUTIVE

	NO CIN	CIN 2	CIN3+	TOT	VPP CIN2+
< ASC US	69	0	0	69	0
ASC US	10	0	0	10	0
LSIL	11	1	0	12	0
ASC H	2	0	3	5	60,00%
HSIL	1	1	4	6	83,30%
<b>TOTALE</b>	<b>93</b>	<b>2</b>	<b>7</b>	<b>102</b>	<b>8,82%</b>
<b>ASC US +</b>	<b>24</b>	<b>2</b>	<b>7</b>	<b>33</b>	<b>27,30%</b>

# HPV A 1 ANNO PIU' BIOMARCATORE?

## GENOTIPIZZAZIONE:

- può predire un rischio aumentato di lesioni pre-cancerose
- HPV 16, 33, 35 ➡ ➡ ↑ rischio di progressione, ma ↓ se in co-infezione con altri tipi  
*(Wentzensen N et al. JCV 2016 ; Del Mistro et al. IJC 2018)*
- HPV 18, 45 ➡ ➡ associazione con adenocarcinoma
- HPV 56,51 ➡ ➡ basso rischio di lesioni pre-cancerose e cancro
- necessità di sistemi che li rilevano come tipi singoli

## MRNA:

- valutato solo come triage di HPV-DNA primario  
*(Benevolo M et al, JCM 2011; Giorgi Rossi P et al JCM 2017)*
- confronto con la ripetizione 1 aa ➡ ➡ studi e analisi ancora in corso (NTCC2\*)  
*\*PI – M. Benevolo*

## P16/Ki-67:

- vs. citologia triage: alta sensibilità e specificità con bassa referral rates in colposcopia  
*(Wentzensen N et al. JCV 2016 )*
- confronto con la ripetizione 1 aa ➡ ➡ studi e analisi ancora in corso (NTCC2\*)

# ALLUNGARE INTERVALLO RETESTING?

## DALLA LETTERATURA:

- quasi 90% clearance HPV entro 1–2 anni dall'infezione (*Schiffman M et al. Lancet 2007;*  
*Gravitt PE et al. Viruses 2017*)
- ... “Sensitivity decreased and specificity increased further when testing intervals were increased from 12 to 24 months”...(*Marks MA et al. JCM 2012*)

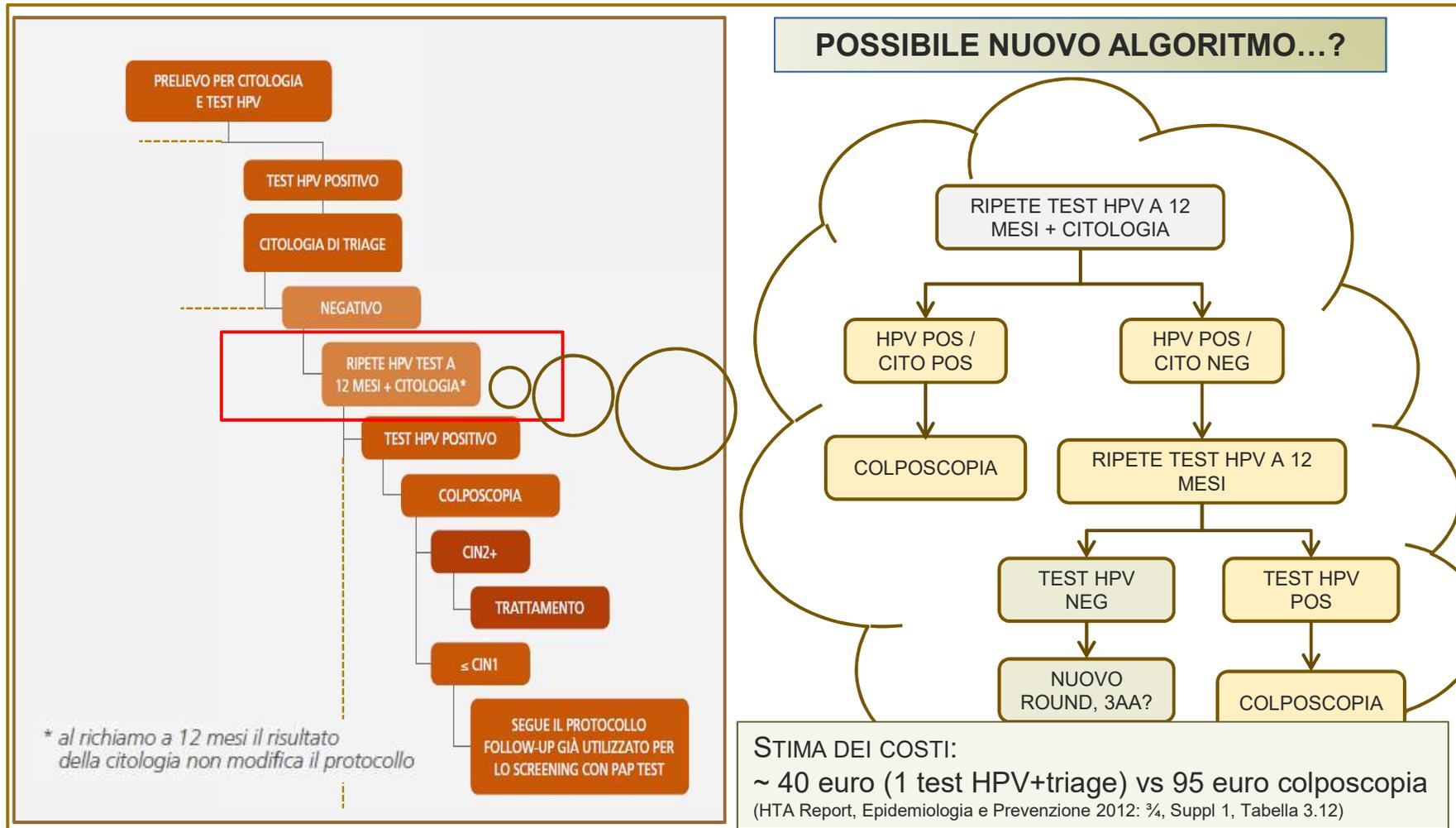


...2 ANNI PERIODO  
TROPPO LUNGO

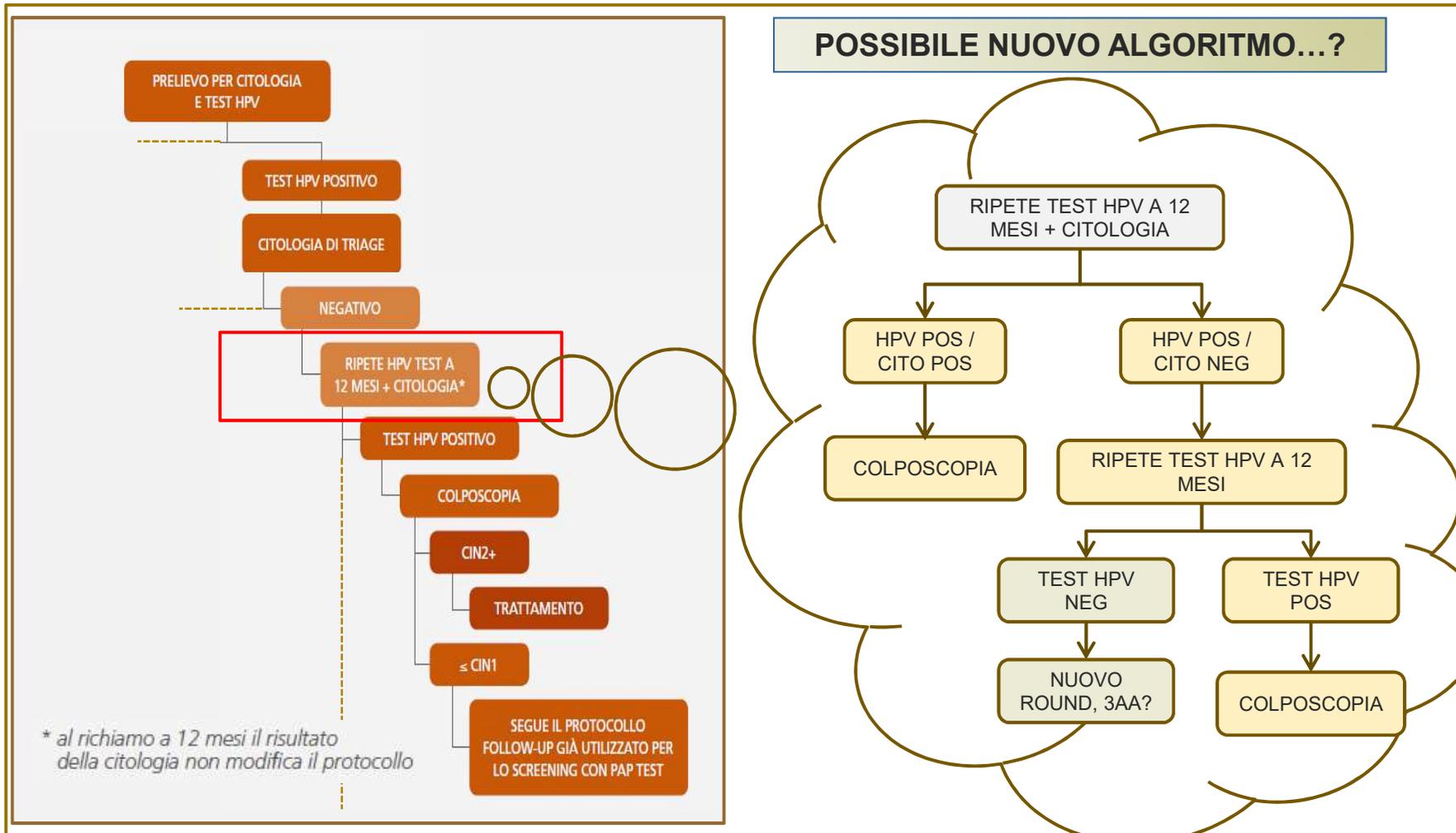


**RISCHIO**  
**DI PERDERE LA DONNA?**

# RIFLESSIONE...PROVOCATORIA?



# RIFLESSIONE...PROVOCATORIA?





**GRAZIE PER L'ATTENZIONE**

*Ringraziamenti...*

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