

Come interpretare gli indicatori di processo della survey HPV

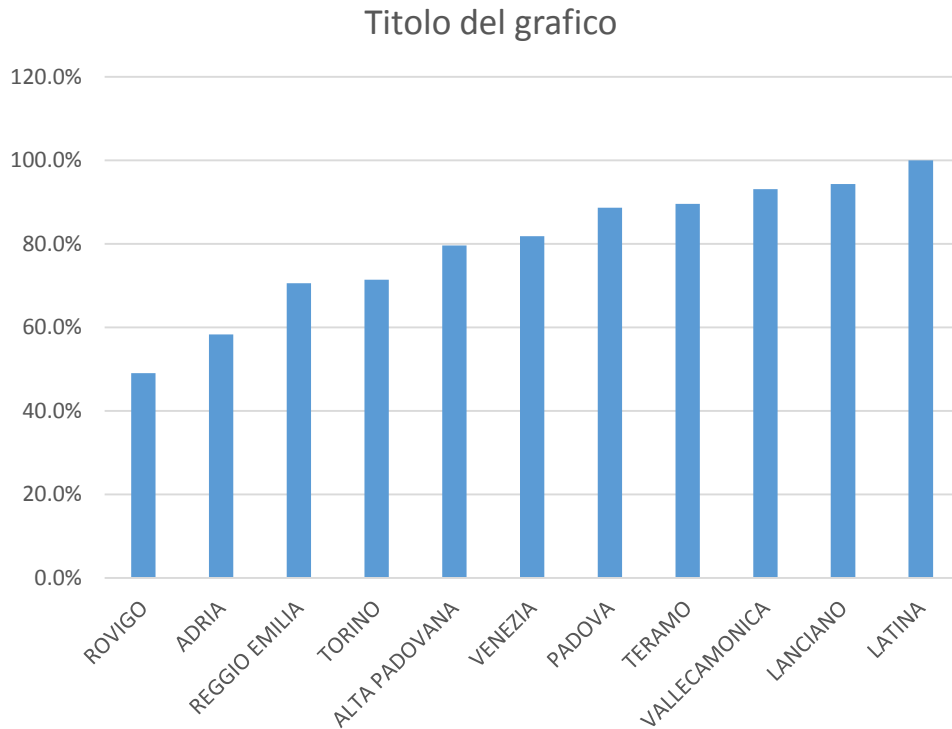
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Peculiarities of process indicators for HPV-based screening

- Detailed description of the process: many indicators and reciprocally correlated
- Protocol in 2 steps (baseline HPV+ cytology and 1-year repeat)
- Intrinsically steps counterbalance reciprocally:
 - Most lesions not detected by cytology are detected by persistent infection (except regression/progression and HPV FNs)
 - If less women referred immediately to colposcopy more invited for 1-year repeat
- Subjective and objective components

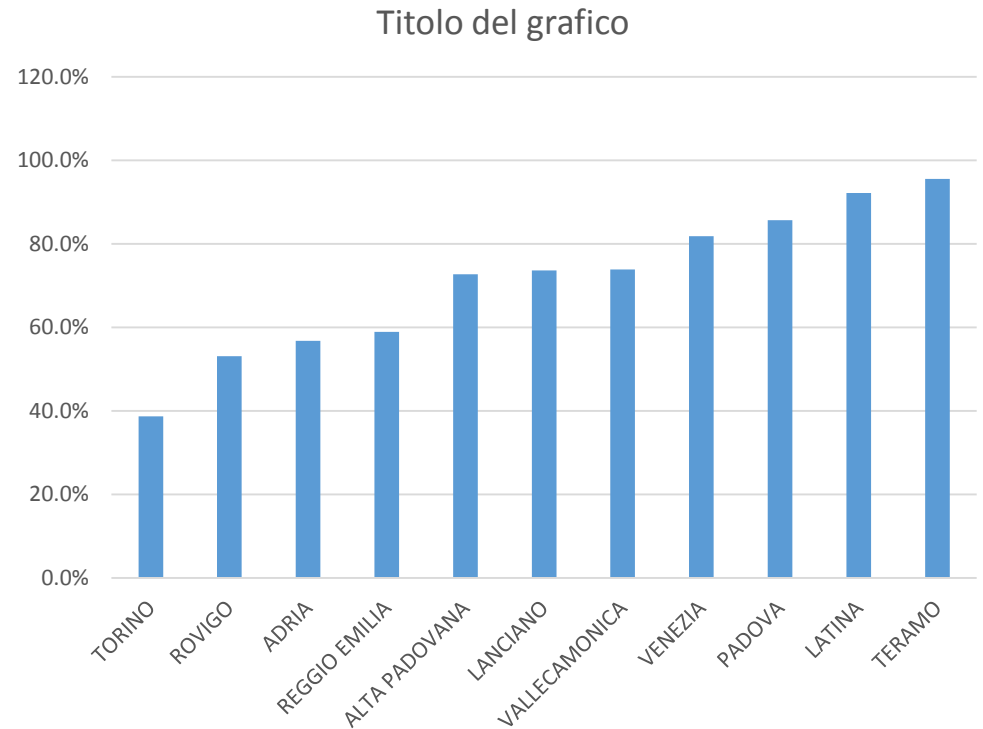
Proportion of CIN2+ detected at baseline (approx sensitivity of cytology) by programme

Overall 80.8%



Proportion of women referred to colposcopy at baseline among all those referred, by programme

Overall 62.1%



In Latina just xx% of women HPV+ cyto- invited for 1-year repeat
Compliance to repeat ranging from 48% in Adria to 93% in Torino

PERFORMANCE INDICATORS (dependant variables)

- Detection rate of CIN2+ and CIN3+ (what is there and is detected)
 - Overall
 - Immediate
 - 1-year
- Positive Predictive Value (efficiency)
 - Overall
 - Immediate
 - 1-year

EXPLANATORY VARIABLES

- % HPV positive in screened women
 - True prevalence
 - Analytical accuracy
- % of HPV+ judged to be ASC-US+
 - Screening history
 - Cytologists' interpretation
- % of HPV+ at 1-year repeat
 - Natural history
 - Behaviour (actual new infections)
 - Analytical accuracy at baseline and repeat

Is there an effect of programmes above studied determinants and age distribution ?

Methods

- 11 programmes included. 4 excluded because of incomplete data or not specified by age (Roma G, Savonese, Trento, Avezzano, Este) one excluded because of small numbers (Florence)
- Restricted to women aged 35-64 years at first screening round with HPV
- Regression (log link, binomial error)
- Adjusted age in 5-year groups and reciprocally
- Effect of programmes adjusted:
 - Age
 - Age and explanatory variables

Correlation coefficients between explanatory variables (p values)

	% HPV positive	% of HPV+ judged to be ASC-US+
% HPV positive	1	
% of HPV+ judged to be ASC-US+	-0.03 (0.83)	1
% HPV+ at 1-year repeat	-0.28 (0.023)	-0.22 (0.08)

Overall detection of CIN2+ per 1000 screened women

	Adjusted age		Adjusted age and reciprocally*	
	RR §	p	RR §	p
% HPV positive	1.59	0.087	2.79	0.0089
% of HPV+ judged to be ASCUS+	1.00	1.00	1.35	0.58
% HPV+ at 1 year repeat	1.02	0.58	1.13	0.0282
Approx. Sensitivity of cytology	1.03	0.41		

§ for an increase of 10 percent points (e.g. from 10% to 20%)

* Padova age 35-39 yrs excluded

Overall Detection of CIN2+ by programme

	Adjusted age		Adjusted age, %HPV+, %ASCUS in HPV+, % HPV+ at 1-year repeat	
	RR vs. mean	p	RR vs. mean	p
ADRIA	0.40	0.026	0.48	0.08
ALTA PADOVANA	1.00	0.99	1.47	0.13
LANCIANO	1.37	0.026	0.67	0.37
LATINA	0.81	0.44	0.73	0.28
PADOVA	1.71	<0.0001	1.96	0.02
REGGIO EMILIA	1.25	0.33	1.24	0.36
ROVIGO	1.13	0.52	1.26	0.30
TERAMO	0.90	0.60	0.68	0.24
TORINO	1.34	0.033	1.27	0.25
VALLECAMONICA	-	-	-	-
VENEZIA	0.84	0.333	1.05	0.87

	Adjusted age		Adjusted age and reciprocally	
	RR §	p	RR §	p
Detection rate of CIN2+ at baseline (HPV+ and Cyto+)				
% HPV positive	2.24	0.0055	3.03	0.0012
% of HPV+ judged to be ASCUS+	1.37	0.46	1.80	0.29
Detection rate of CIN2+ at 1 year (persistently HPV+)				
% HPV positive	0.23	0.056	0.30	0.23
% of HPV+ judged to be ASCUS+	0.20	0.11	0.17	0.15
% HPV+ at 1 year repeat	1.55	0.0006	1.37	0.04

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Negative association between %HPV+ at baseline and 1-year persistence due to false positive HPV results (which of course don't persist)?

Strong interaction ($p < 0.0001$) with age. The % of HC2 false positives increases with increasing age (Gillio-Tos et al J Clin Microbiol 2013). Behaviour?

Age group	Relative 1-year HPV persistence for a 10 percent points increase of HPV positivity at baseline
35-39	0.54
40-44	0.83
45-49	0.49
50-54	0.34
55-59	0.35
60-64	0.05

% HPV+ at 1-year repeat by program

	Adjusted age		Adjusted age, %HPV+ at baseline	
	RR vs. mean	p	RR vs. mean	p
ADRIA	1.08	0.69	1.08	0.45
ALTA PADOVANA	1.04	0.56	1.13	0.20
LANCIANO	0.74	<0.0001	0.64	0.0005
LATINA	1.09	0.31	1.06	0.49
PADOVA	1.08	0.31	1.13	0.14
REGGIO EMILIA	1.06	0.48	1.04	0.61
ROVIGO	1.26	<0.0001	1.31	<0.0001
TERAMO	0.55	<0.0001	0.50	<0.0001
TORINO	1.27	<0.0001	1.27	<0.0001
VALLECAMONICA	-	-	-	-
VENEZIA	1.12	0.12	1.17	0.046

Overall Positive Predictive Value for CIN2+

	Adjusted age		Adjusted age and reciprocally	
	RR §	p	RR §	p
% HPV positive	0.75	0.30	1.26	0.53
% of HPV+ judged to be ASCUS+	0.93	0.85	1.12	0.80
% HPV+ at 1 year repeat	1.02	0.68	1.03	0.53

§ for an increase of 10 percent points (e.g. from 10% to 20%)

	Adjusted age		Adjusted age and reciprocally	
	RR §	p	RR §	p
PPV for CIN2+ at baseline (HPV+ and Cyto+)				
% HPV positive	1.54	0.11	0.89	0.71
% of HPV+ judged to be ASCUS+	0.27	0.0015	0.14	0.0002
PPV for CIN2+ at 1 year (persistently HPV+)				
% HPV positive	0.14	0.0133	0.18	0.08
% of HPV+ judged to be ASCUS+	4.33	0.12	1.82	0.61
% HPV+ at 1 year repeat	1.14	0.27	1.03	0.82

§ for an increase of 10 percent points (e.g. from 10% to 20%)

Overall PPV for CIN2+ by programme

	Adjusted age		Adjusted age, %HPV+, %ASCUS in HPV+, % HPV+ at 1-year repeat	
	RR vs. mean	p	RR vs. mean	p
ADRIA	0.43	0.013	0.44	0.04
ALTA PADOVANA	3.19	<0.0001	1.45	0.12
LANCIANO	1.07	0.58	0.75	0.48
LATINA	-	-	-	-
PADOVA	1.43	0.0046	2.09	0.0063
REGGIO EMILIA	1.00	0.99	1.06	0.80
ROVIGO	0.98	0.89	1.09	0.68
TERAMO	0.81	0.24	0.73	0.32
TORINO	1.08	0.57	1.03	0.88
VALLECAMONICA	0.79	0.34	0.98	0.93
VENEZIA	0.73	0.06	1.07	0.81

Conclusions

- % HPV positive in screened women negatively correlated with % HPV+ at repeat (false negative HPVs in some areas?)
- % HPV positive and % HPV+ at repeat determinants of overall detection rate
- No effect of which proportion of HPV+ is judged to be ASC-US+
- No significant effect of % HPV+ in screened women on overall PPV (cfr Giorgi Rossi et al Int J Cancer 20xx).
- %ASC-US+ among HPV+ negative determinant of PPV at baseline but spurious positive association with 1-year PPV, resulting in no effect on overall PPV

Differences between programmes only partly explained by model. Screening history (immigrants Padua) ? Other?

Our protocol entails counterbalance of referral to colposcopy, and CIN detection, immediately and at 1 year.

This limits the effect of subjectivity in cytology interpretation on the overall process.

- Data suggest high sensitivity of cytology.
- Reduced risk of cancer before repeat HPV test
- Intervals for re-testing could be longer , with lower overall referral to colposcopy

