

CONVEGNO NAZIONALE GISCI 2017

Lo screening HPV come modello: tra innovazione tecnologica
e nuovi modelli organizzativi in Sanità pubblica

Giovedì 15 e Venerdì 16 Giugno 2017

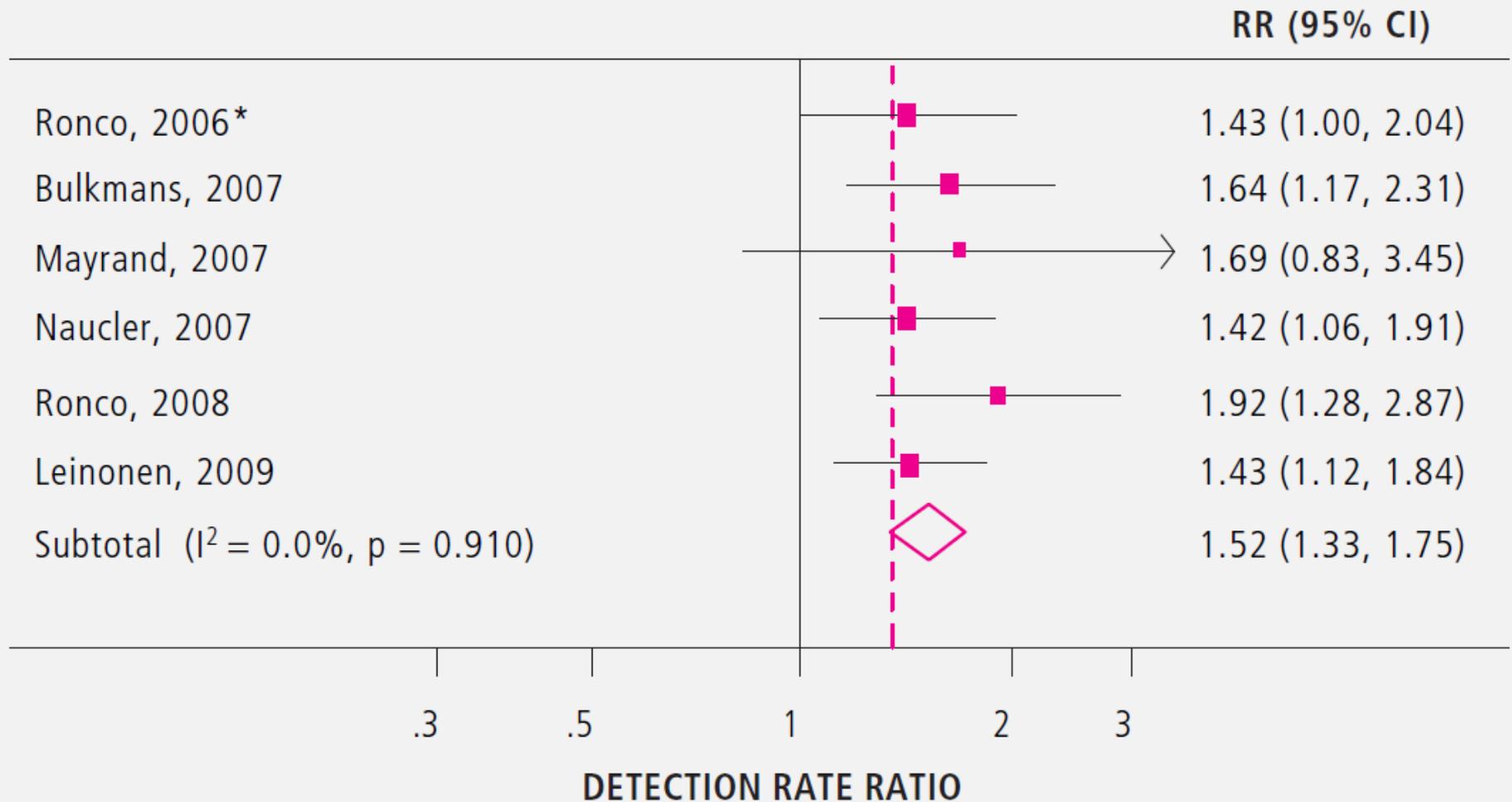
I risultati del secondo round di screening con HPV



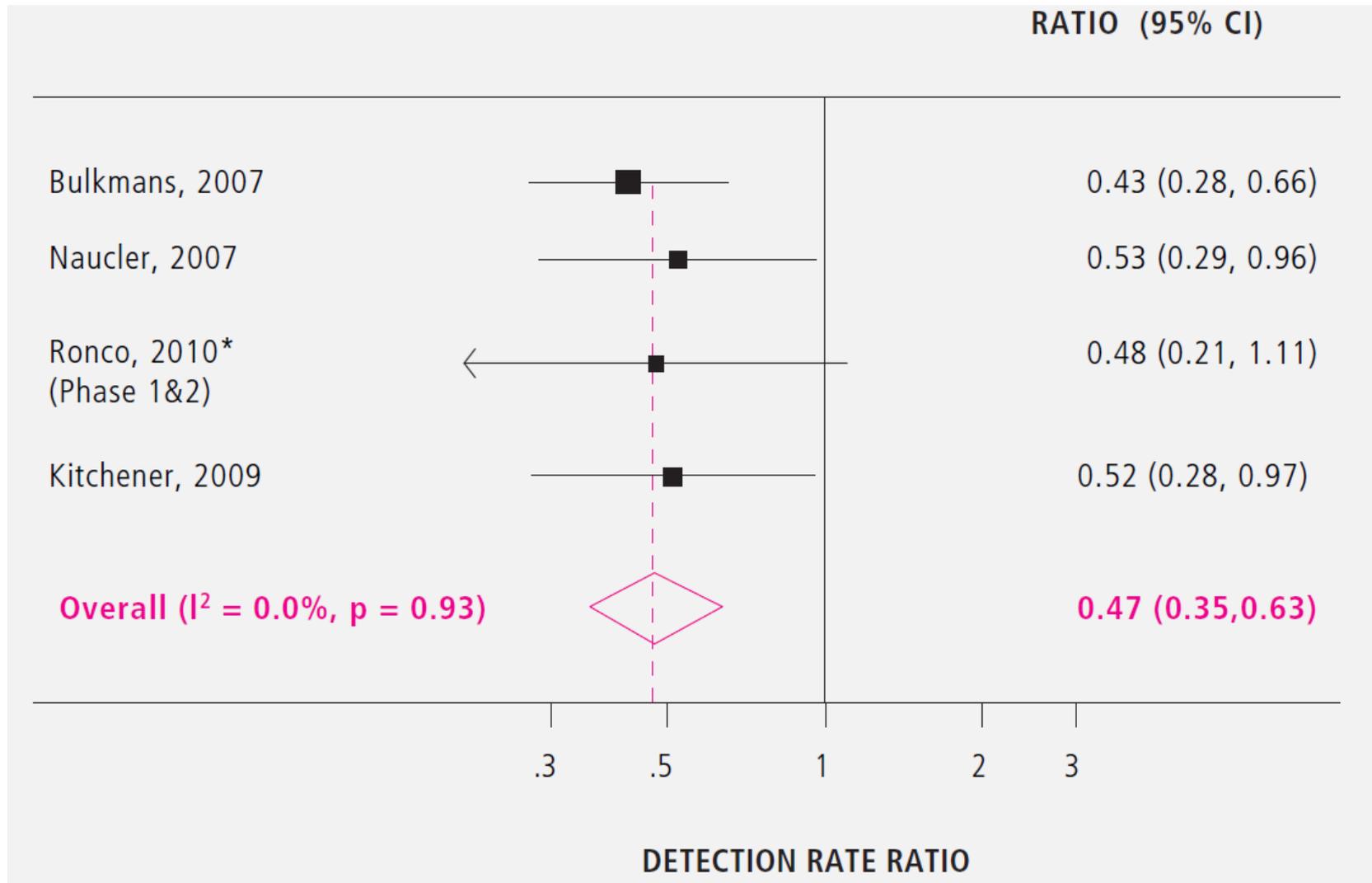
Manuel Zorzi

Registro Tumori del Veneto

Metanalisi del rapporto dei tassi di identificazione di CIN2+ di HPV vs. citologia al primo round di screening



Donne negative al primo round: rapporto dei tassi di identificazione di CIN3+ di HPV vs. citologia



*restricted to women age ≥ 35 years

Human papillomavirus DNA testing for the detection of cervical intraepithelial neoplasia grade 3 and cancer: 5-year follow-up of a randomised controlled implementation trial

N W J Bulkman, J Berkhof, L Rozendaal, F J van Kemenade, A J P Boeke, S Bulk, F J Voorhorst, R H M Verheijen, K van Groningen, M E Boon, W Ruitinga, M van Ballegooijen, P J F Snijders, C J L M Meijer

www.thelancet.com Published online October 4, 2007 DOI:10.1016/S0140-6736(07)61450-0

| | Referral | |
|----------------------------|----------|-------------------------|
| | Number | Rate per woman screened |
| Intervention group | | |
| Baseline round (n=8575) | 201 | 2.3% (2.0–2.7) |
| Subsequent round (n=6887)* | 87 | 1.3% (1.0–1.6) |

European guidelines for quality assurance in cervical cancer screening

*Second Edition
Supplements*

1.2.2.2 Positive test results, repeat tests, and colposcopy referrals

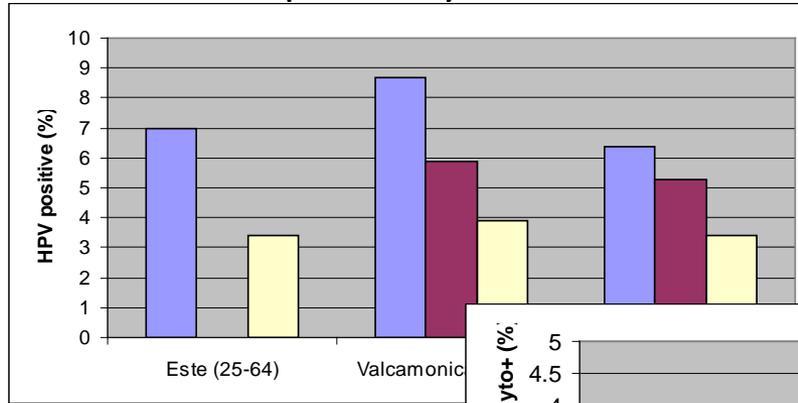
As Swedescreen and NTCC used HPV testing just at the first screening round, they did not provide data on referral to colposcopy with HPV primary screening at subsequent rounds. In POBASCAM (Bulkmans et al. 2007) the referral rate in the intervention arm at round two (1.0%) was much lower than that at round 1 in the intervention (2.3%) and also in the control arm (1.3% at round 1 and 1.5% at round 2). In ARTISTIC referral to colposcopy also strongly decreased in the HPV arm at round 2. This however happened also in the cytology arm, so that the ratio between arms was unchanged (Kitchener et al. 2009a).

Diagnosi di CIN3+ per round di screening e cumulativa

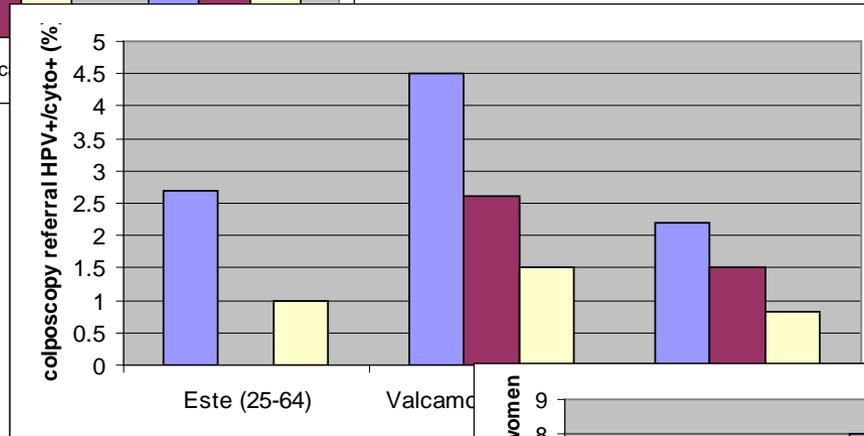
| | | N | Primo round | | Secondo round | | Cumulativa | |
|------------------|-----------|-------|-------------|-------------|---------------|-------------|------------|-------------|
| | | | CIN3+ | DR relativa | CIN3+ | DR relativa | CIN3+ | DR relativa |
| Naucler 2007 | HPV | 6257 | 72 | 1,3 | 16 | 0,5 | 88 | 1,04 |
| | citologia | 6270 | 55 | | 30 | | 85 | |
| Bulkmans 2007 | HPV | 8575 | 68 | 1,7 | 24 | 0,5 | 92 | 1,02 |
| | citologia | 8580 | 40 | | 54 | | 94 | |
| Ronco 2010 | HPV | 34430 | 105 | 1,9 | 8 | 0,2 | 113 | 1,23 |
| | citologia | 34405 | 56 | | 36 | | 92 | |

Second round baseline indicators for three programs: Este (N 5571), Valcamonica (N5106), Perugia (6509)

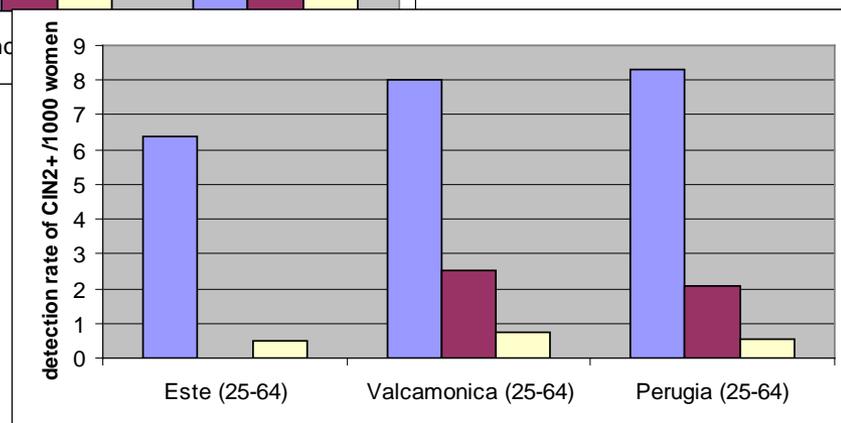
HPV positivity rate



Colposcopy referral

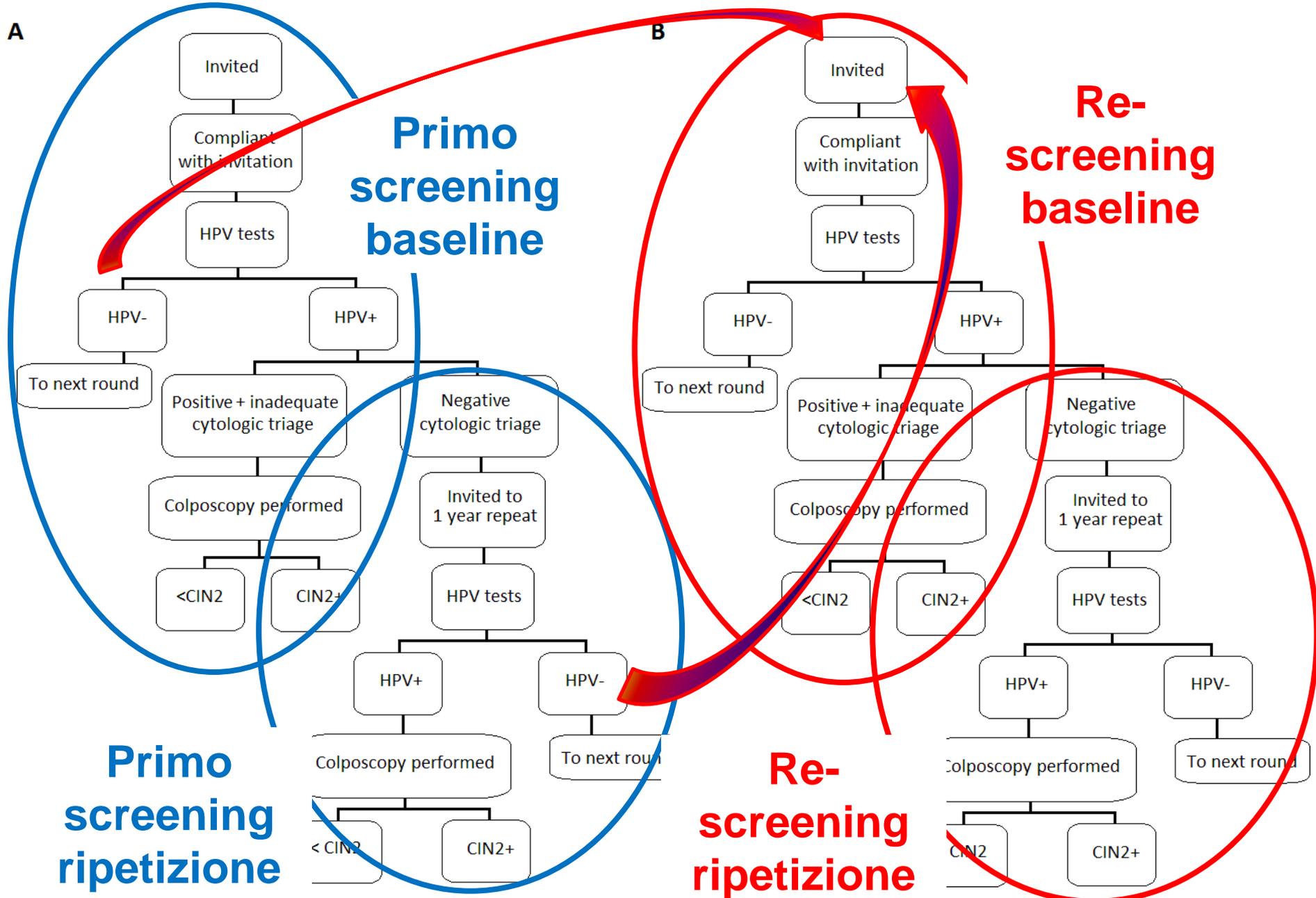


Detection rate



- I Round
- II Round all women
- II Round women previously HPVneg

Terminologia



Re-screening con test HPV

Calcolo dei principali indicatori e confronto con:

- primo screening con test HPV
 - baseline: positività al test HPV, positività al triage
 - ripetizione a 1 anno: positività al test HPV
 - cumulativi: invio a colposcopia, tassi di identificazione di CIN2+
- screening con pap test
 - cumulativi (2 round consecutivi): invio a colposcopia, tassi di identificazione di CIN2+, VPP per CIN2+

Interpretazione degli indicatori

Re-
screening
HPV

Primo
screening
HPV

Screening
pap test

baseline

positività al test HPV
positività al triage

ripetizione a 1 anno

positività al test HPV

cumulativi

invio a colposcopia
tassi di identificazione di CIN2+
VPP per CIN2+

Interpretazione degli indicatori

Re-
screening
HPV

Primo
screening
HPV

Screening
pap test

Interpretazione degli indicatori

Primo
screening
HPV

Re-
screening
HPV

Primo
screening
pap test

Re-
screening
pap test

cumulativi

invio a colposcopia

tassi di identificazione di CIN2+

VPP per CIN2+

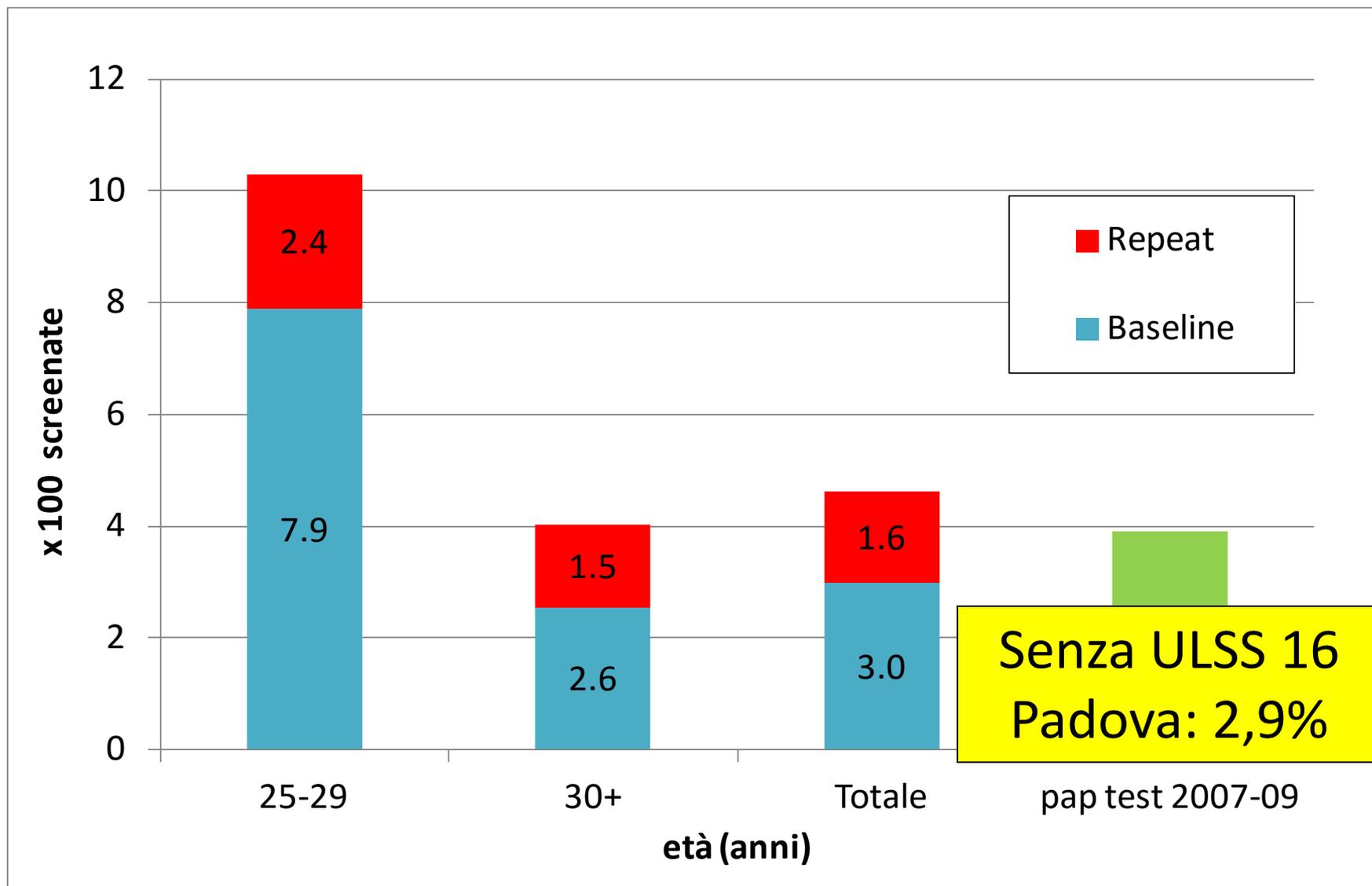
Dati disponibili

| Programma | Primo screening HPV | Re-screening HPV |
|---------------|---------------------|------------------|
| Reggio Emilia | | X |
| Torino | | X |
| Valcamonica | | X |

Survey ONS 2016

PRIMO ROUND CON HPV: invio a colposcopia, per età

Programmi pilota ULSS delle province di Padova e Rovigo



Dati di riferimento

| Programma | Data inizio pilota HPV | Screenate primo round con HPV | Data inizio re-screening | Re-screenate al 15/10/2015 |
|----------------|------------------------|-------------------------------|--------------------------|----------------------------|
| Alta padovana | lug-10 | 29.783 | ago-13 | 11.330 |
| Este Monselice | apr-09 | 18.968 | mag-12 | 10.670 |

Età target: 25-64 anni

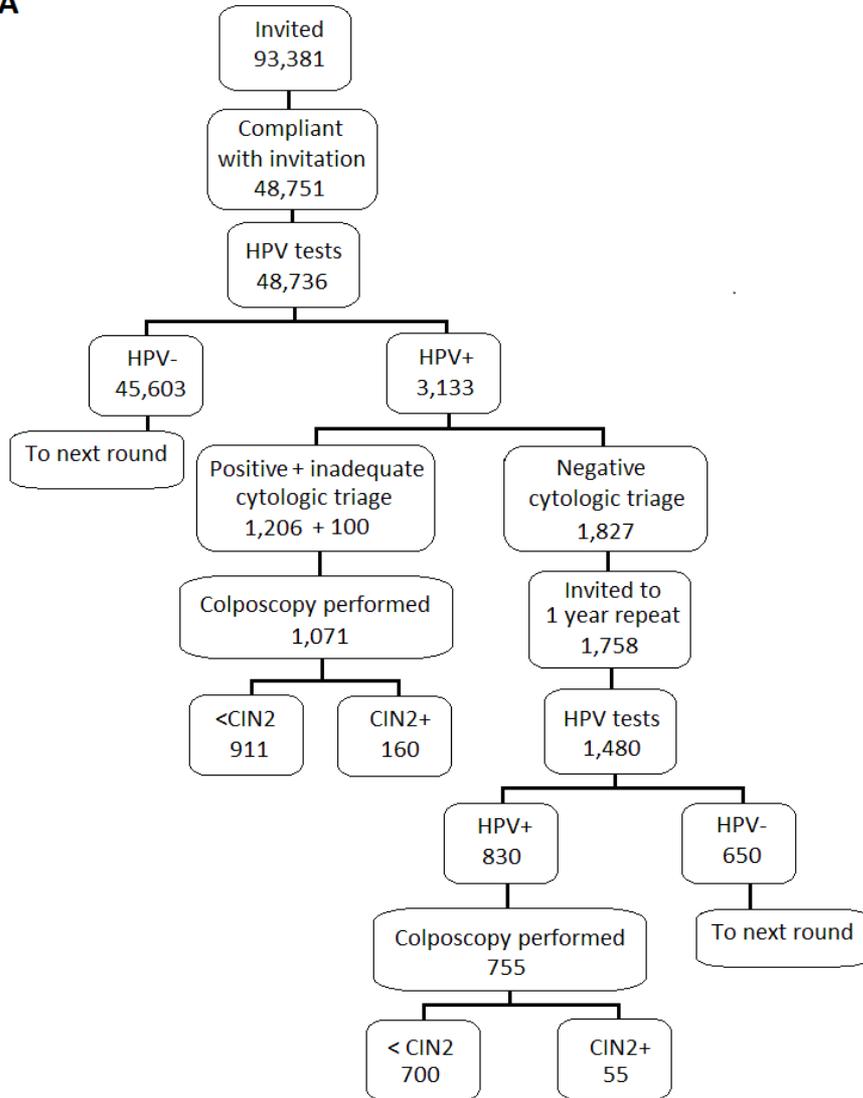
Intervallo di screening: 3 anni

Veneto: dati principali al primo screening HPV e al re-screening con HPV

| | Primo screening HPV | Re-screening HPV |
|-----------------------|----------------------------|-------------------------|
| Screenate | 48736 | 22000 |
| HPV+ | 3133 | 777 |
| CIN2+ | 160 | 17 |
| HPV ripetuti a 1 anno | 1480 | 384 |
| HPV+ | 830 | 200 |
| CIN2+ a 1 anno | 55 | 6 |

Dati principali al primo screening (a) e al re-screening (b)

A



B

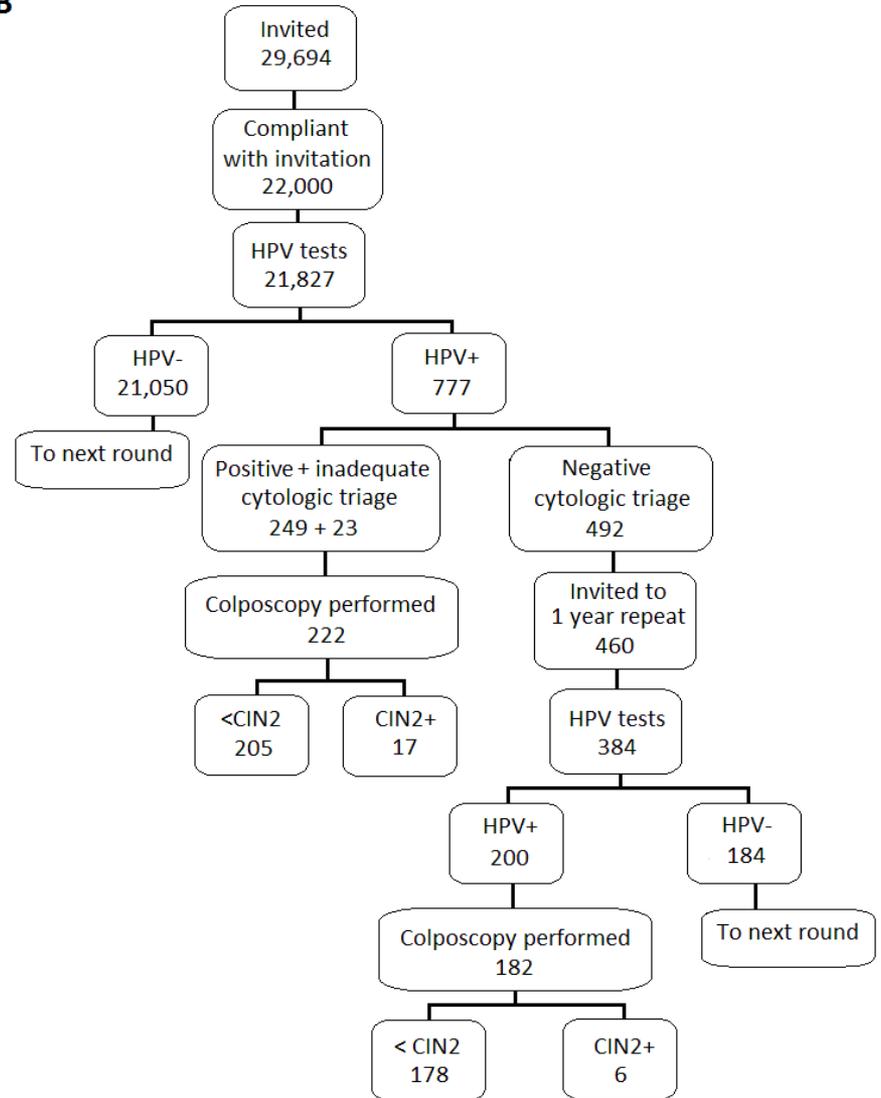


Table 1. Main results of the HPV test-based screening programme at baseline and at the 1-year repeat at the first screening and at 3-year re-screening

| | First screening | | | | Re-screening | | | | Relative frequencies (95% CI)* | |
|---|-----------------|--------------------------------|---------------|-------------|--------------|---------------|---------------|-----------|--------------------------------|------------------|
| | Baseline | | 1 year repeat | | Baseline | | 1 year repeat | | Baseline | 1-year repeat |
| Compliance % | 52.8 72.1** | 48751 / 93381 30145/41800** | 84.8 | 1480 / 1758 | 74.5 | 22000 / 29694 | 85.4 | 393 / 460 | - 1.11 (1.07-1.14)** | 1.01 (0.87-1.18) |
| HPV positive % | | | | | | | | | | |
| 25-64 | 6.4 | 3133 / 48736 | 55.9 | 830 / 1480 | 3.5 | 777 / 21827 | 52.1 | 200 / 384 | 0.55 (0.51-0.60) | 0.93 (0.76-1.13) |
| 25-29 | 14.8 | 754 / 5103 | 58.2 | 203 / 348 | 8.1 | 140 / 1723 | 53.2 | 25 / 47 | 0.55 (0.45-0.67) | 0.91 (0.52-1.57) |
| 30-64 | 5.5 | 2379 / 43647 | 55.2 | 627 / 1132 | 3.1 | 637 / 20104 | 51.9 | 175 / 337 | 0.58 (0.53-0.64) | 0.94 (0.75-1.16) |
| Cytology positive % | 38.5 | 1206 / 3133 | - | | 32.6 | 349 / 764 | - | | 0.85 (0.72-0.99) | |
| Referral rate to colposcopy % | 2.7 | 1306 / 48736 | 55.9 | 830 / 1480 | 1.2 | 272 / 21827 | 52.1 | 200 / 384 | 0.47 (0.41-0.53) | 0.93 (0.76-1.13) |
| Compliance with colposcopy % | 82.0 | 1071 / 1306 | 91.0 | 755 / 830 | 81.6 | 222 / 272 | 91.0 | 182 / 200 | 1.00 (0.82-1.22) | 1.00 (0.79-1.26) |
| Detection rate for CIN2+ % | | | | | | | | | | |
| 25-64 | 3.3 | 160 / 48736 | 37.2 § | 55 / 1480 | 0.8 | 17 / 21827 | 15.6 § | 6 / 384 | 0.24 (0.13-0.39) | 0.42 (0.15-0.99) |
| 25-29 | 8.0 | 41 / 5103 | 34.5 § | 12 / 348 | 2.9 | 5 / 1723 | 42.6 § | 2 / 47 | 0.36 (0.11-0.91) | 1.23 (0.13-5.81) |
| 30-64 | 2.7 | 119 / 43647 | 38.0 § | 43 / 1132 | 0.6 | 12 / 20104 | 11.9 § | 4 / 337 | 0.22 (0.11-0.40) | 0.31 (0.08-0.87) |
| Positive Predictive Value for CIN2+ at colposcopy % | 14.9 | 160 / 1071 | 7.3 | 55 / 755 | 7.7 | 17 / 222 | 3.4 | 6 / 182 | 0.51 (0.29-0.87) | 0.45 (0.16-1.07) |

* Ratio of percentages: re-screening compared with first screening

** Women who had complied with the previous cytology-based round

§ x 1,000 women who repeated after 1 year

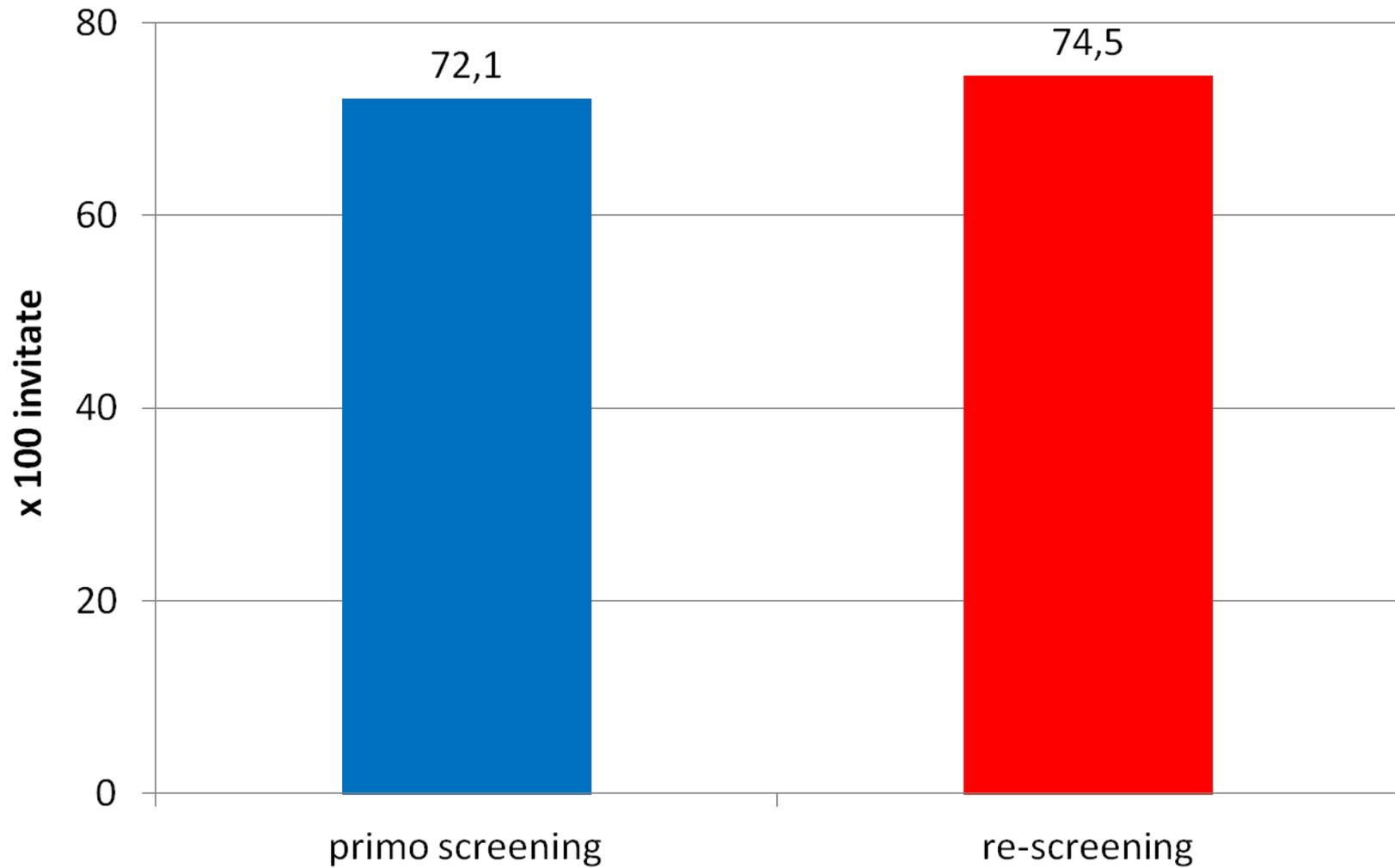
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| | Relative frequencies (95% CI)* | |
|---|--------------------------------|------------------|
| | Baseline | 1-year repeat |
| Compliance % | - 1.11 (1.07-1.14)** | 1.01 (0.87-1.18) |
| HPV positive % | | |
| 25-64 | 0.55 (0.51-0.60) | 0.93 (0.76-1.13) |
| 25-29 | 0.55 (0.45-0.67) | 0.91 (0.52-1.57) |
| 30-64 | 0.58 (0.53-0.64) | 0.94 (0.75-1.16) |
| Cytology positive % | 0.85 (0.72-0.99) | |
| Referral rate to colposcopy % | 0.47 (0.41-0.53) | 0.93 (0.76-1.13) |
| Compliance with colposcopy % | 1.00 (0.82-1.22) | 1.00 (0.79-1.26) |
| Detection rate for CIN2+ ‰ | | |
| 25-64 | 0.24 (0.13-0.39) | 0.42 (0.15-0.99) |
| 25-29 | 0.36 (0.11-0.91) | 1.23 (0.13-5.81) |
| 30-64 | 0.22 (0.11-0.40) | 0.31 (0.08-0.87) |
| Positive Predictive Value for CIN2+ at colposcopy % | 0.51 (0.29-0.87) | 0.45 (0.16-1.07) |

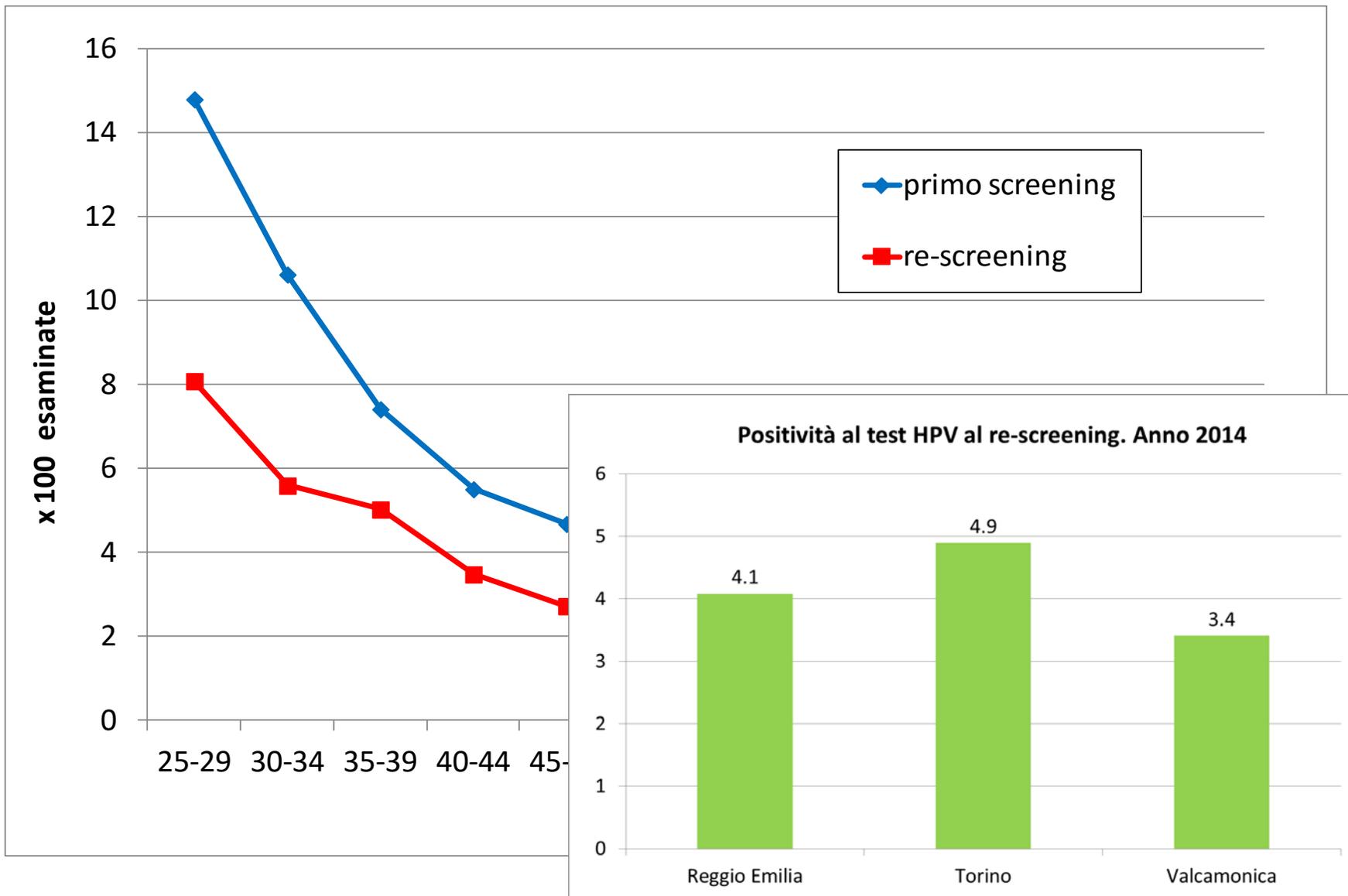
* Ratio of percentages: re-screening compared with first screening

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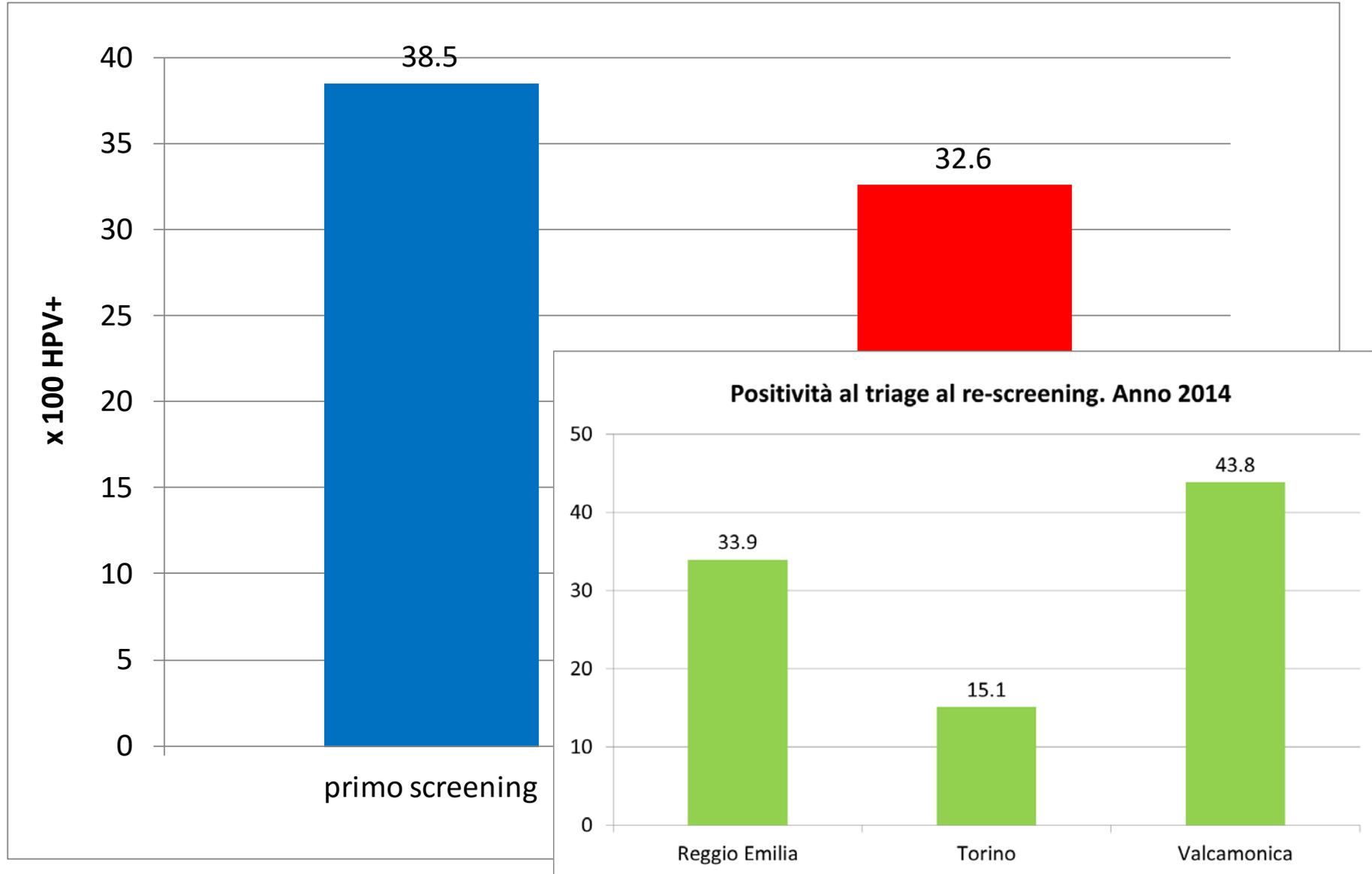
Adesione corretta



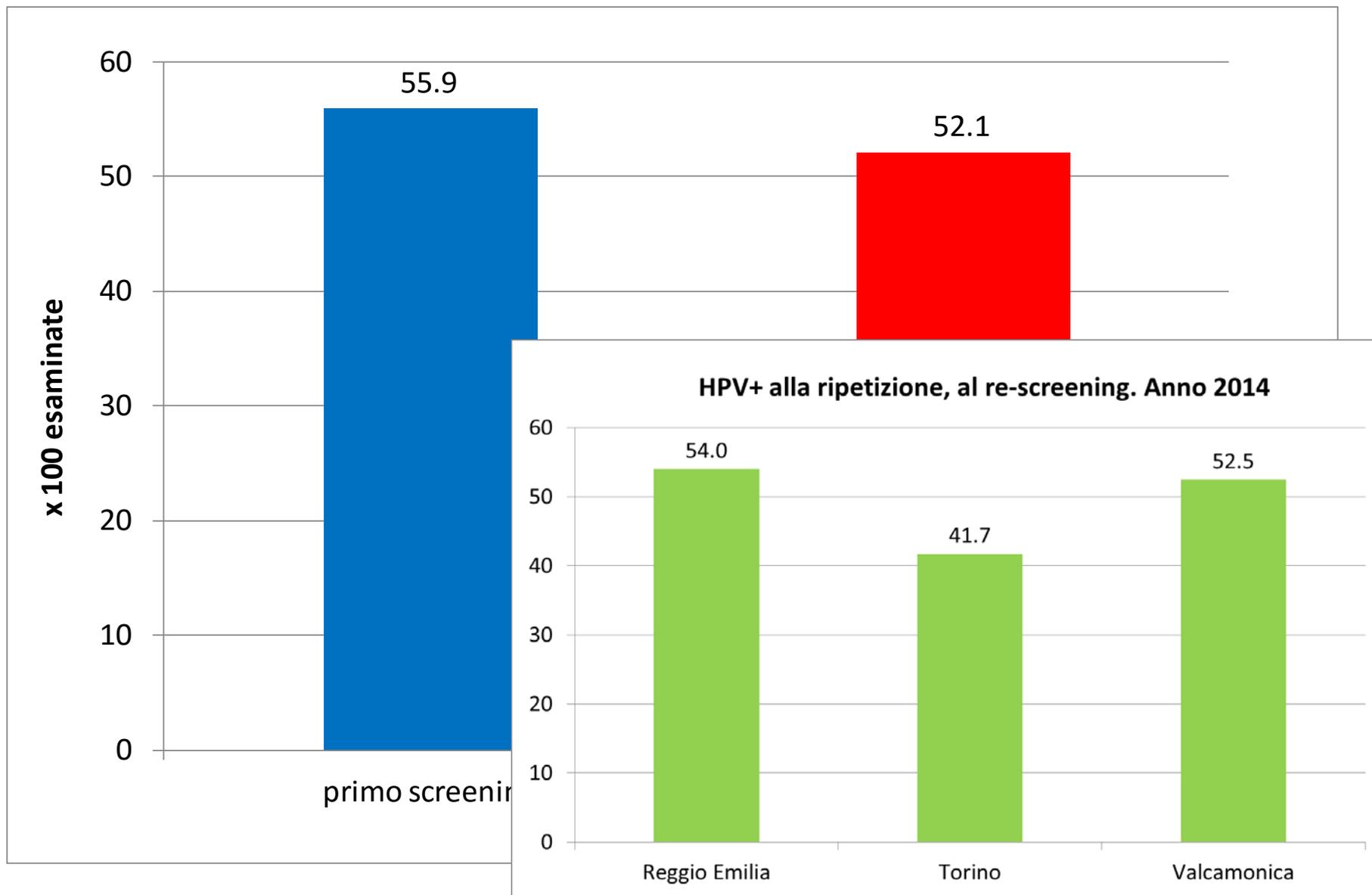
Positività al test HPV al baseline



Positività al pap test di triage

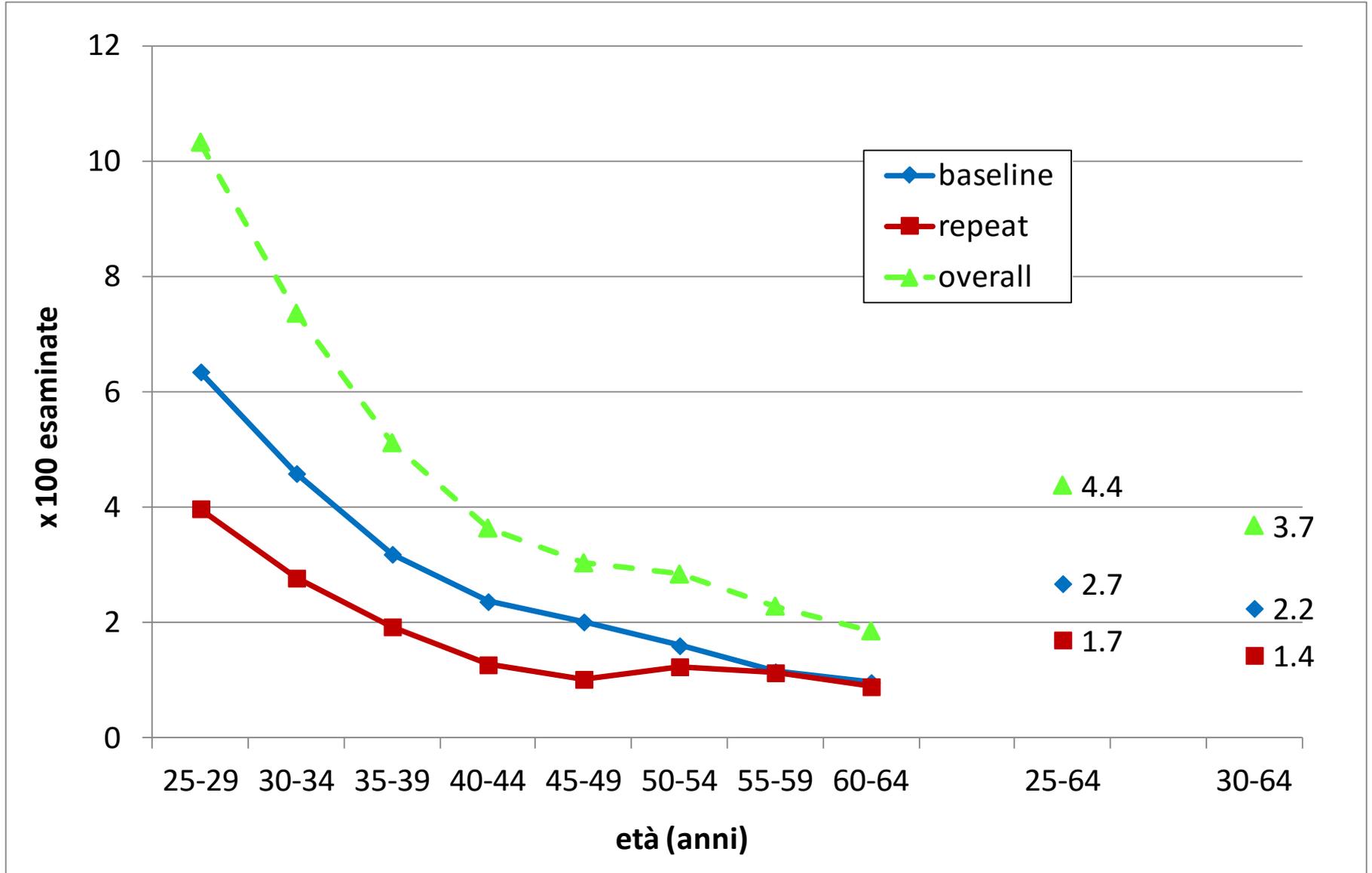


Positività al test HPV alla ripetizione a 1 anno



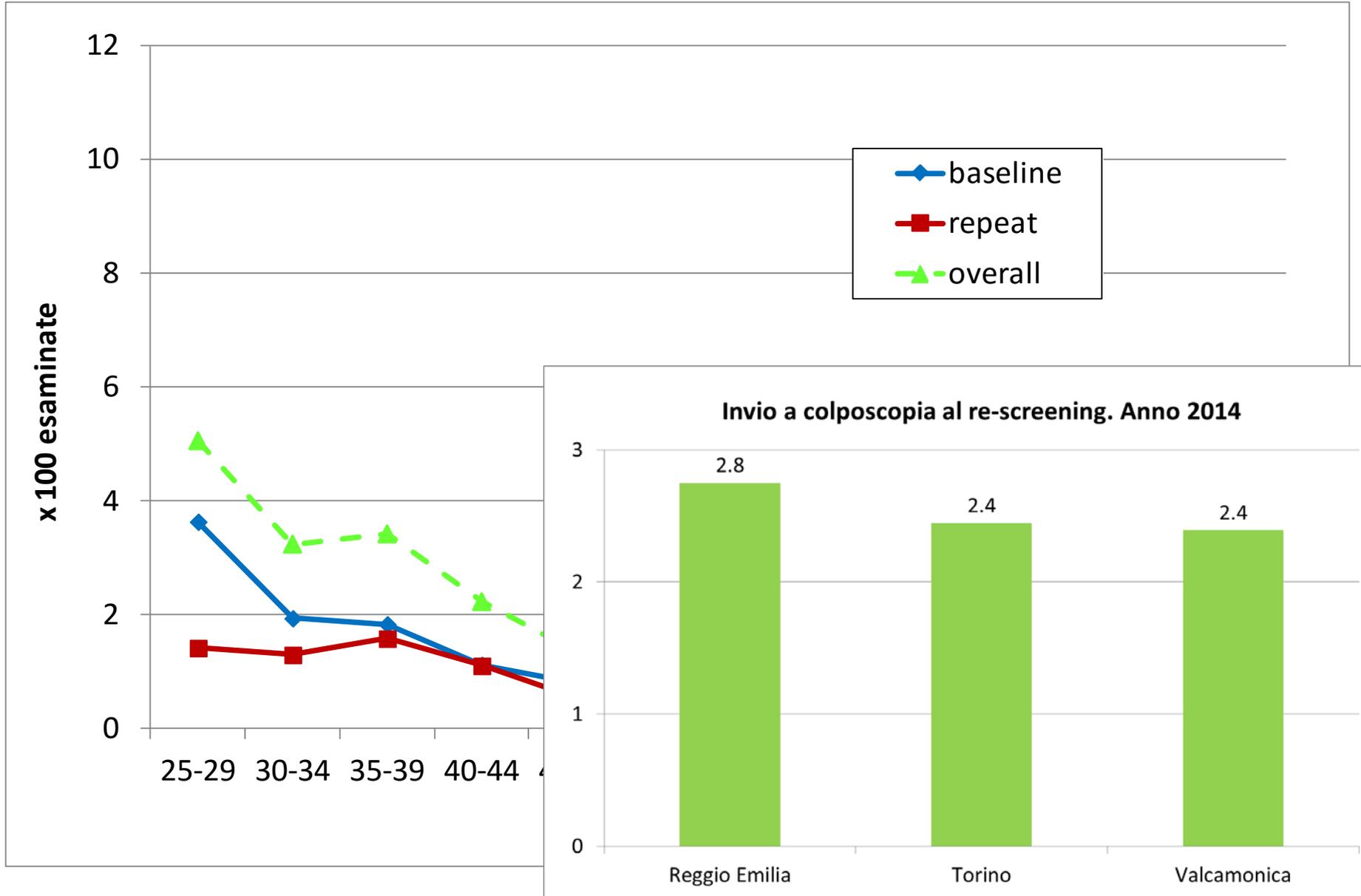
Invio a colposcopia al baseline e alla ripetizione a un anno

Donne al primo screening con test HPV

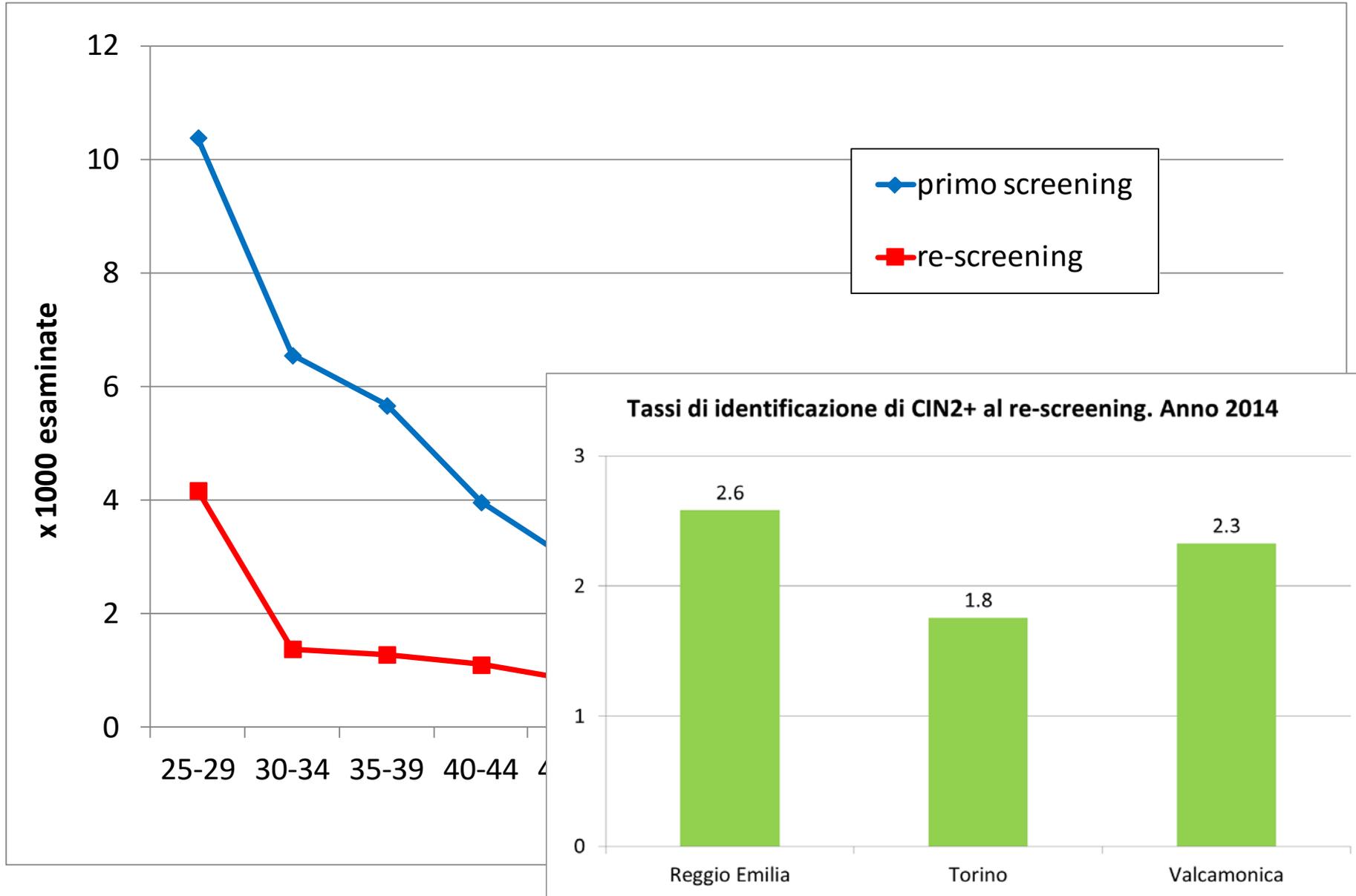


Invio a colposcopia al baseline e alla ripetizione a un anno

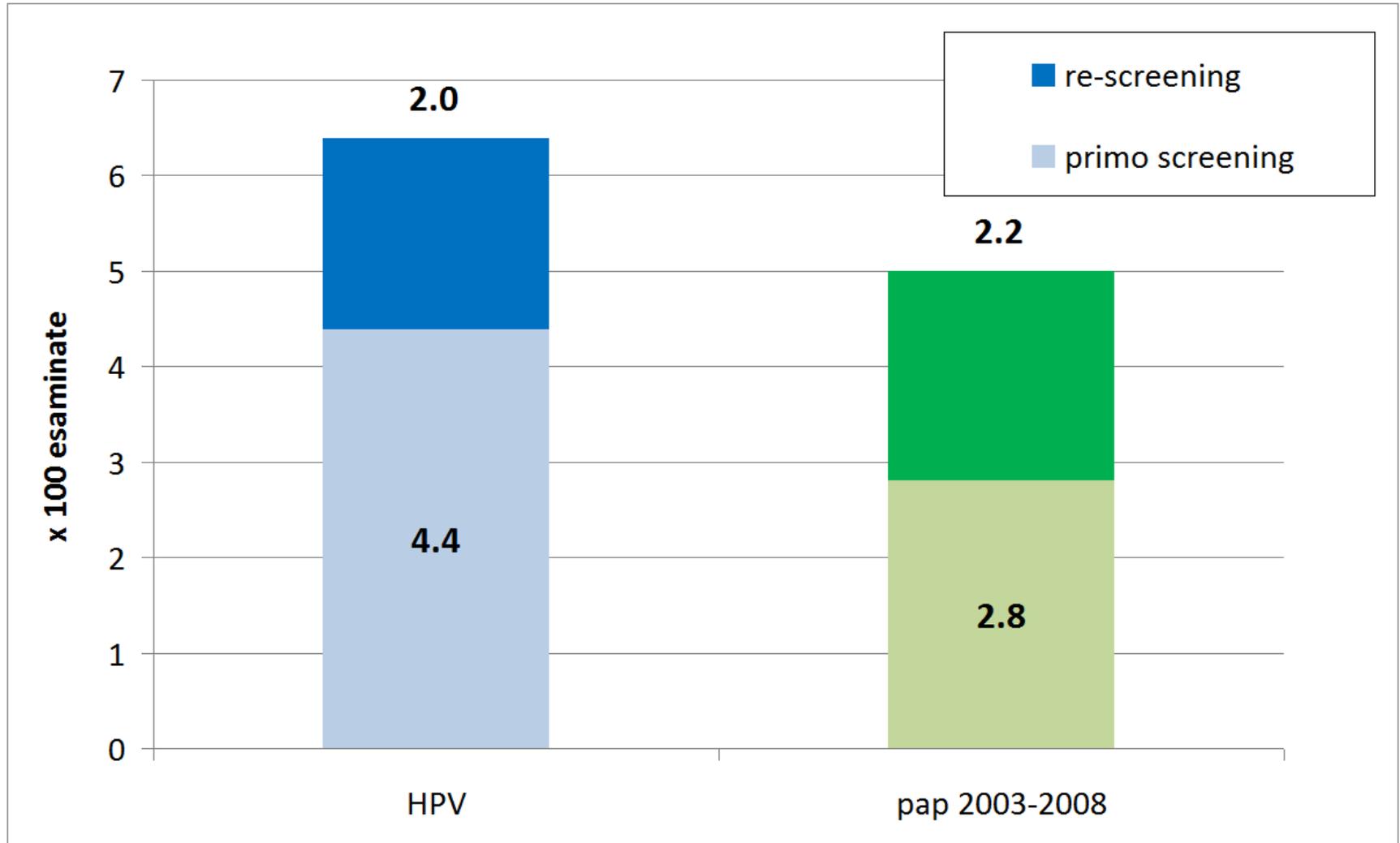
Donne al re-screening con test HPV



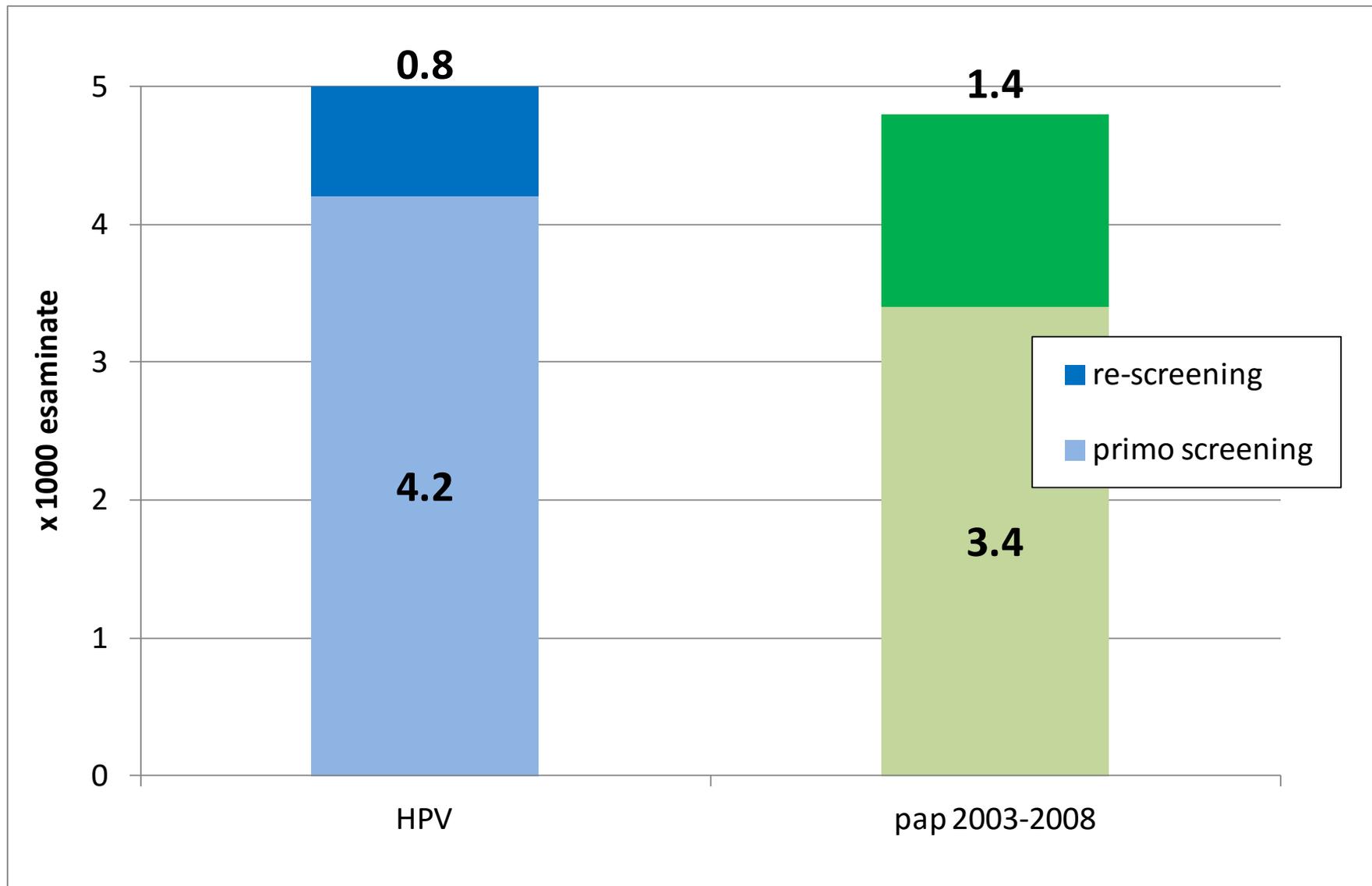
Tassi di identificazione di CIN2+



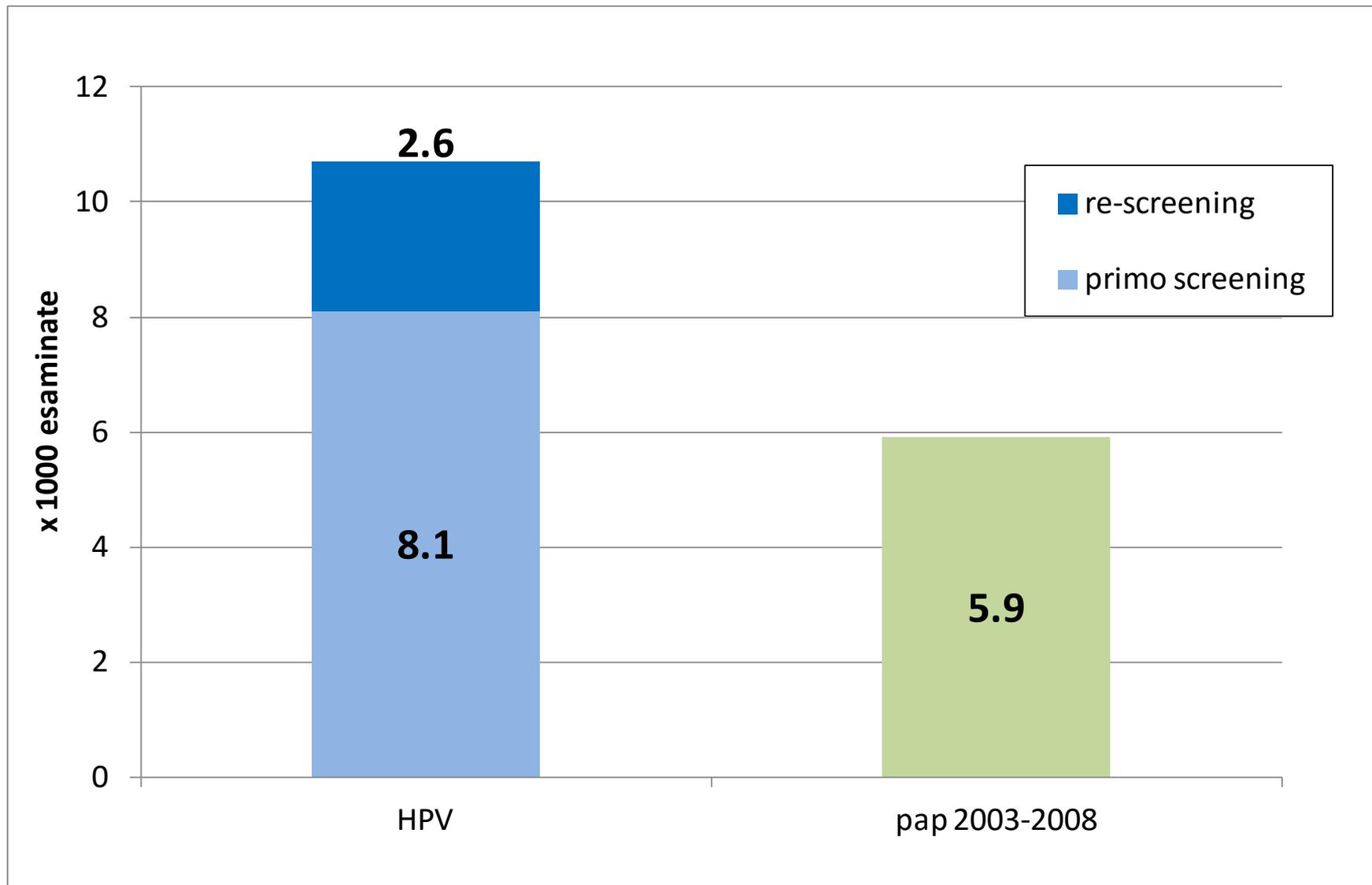
Invio a colposcopia cumulativo dopo due round di screening HPV vs. pap test. Donne 25-64enni



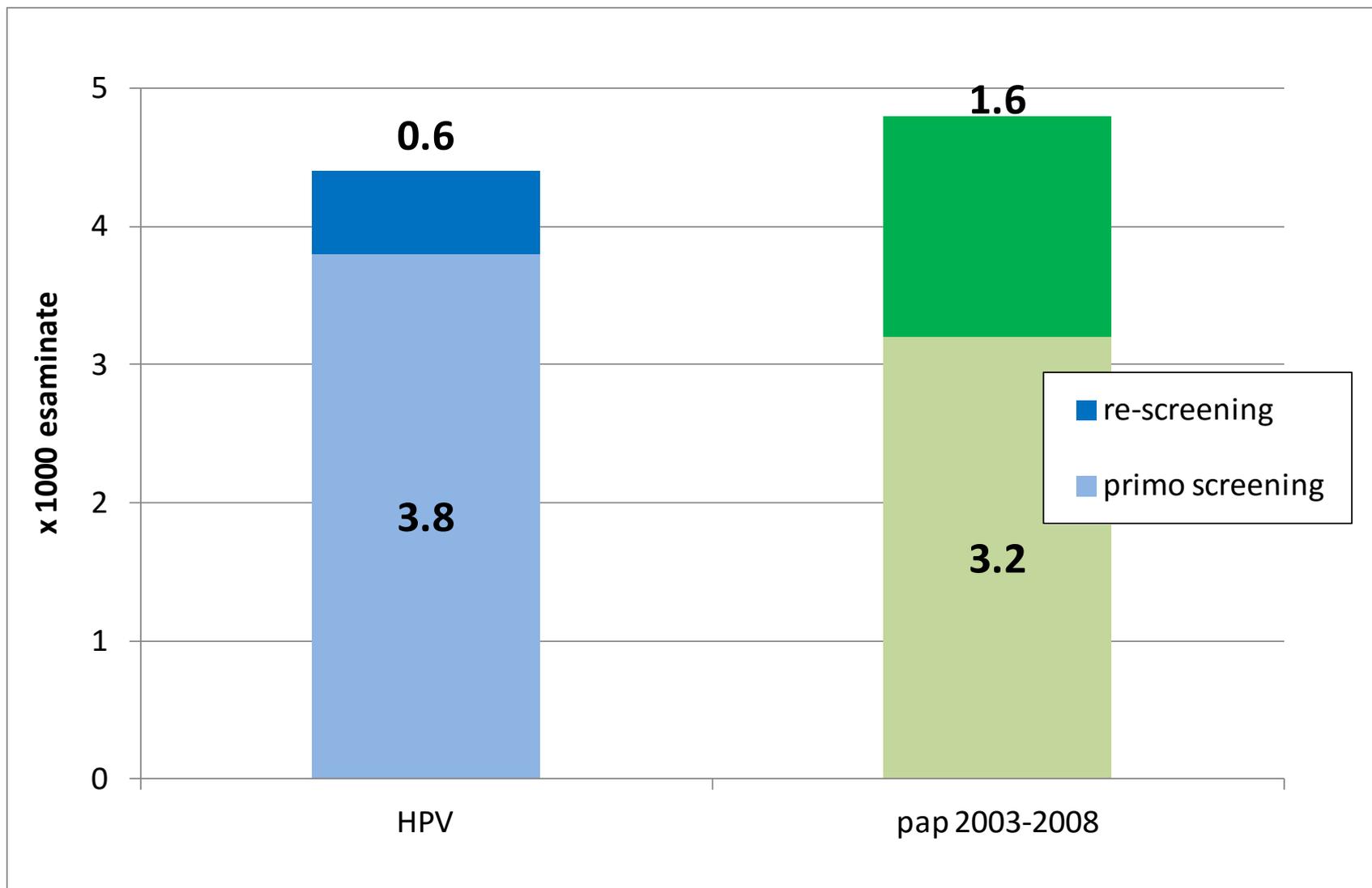
Tassi di identificazione cumulativi dopo due round di screening HPV vs. pap test. Donne 25-64enni



Tassi di identificazione cumulativi dopo due round di screening HPV vs. pap test. Donne 25-29enni



Tassi di identificazione cumulativi dopo due round di screening HPV vs. pap test. Donne 30-64enni



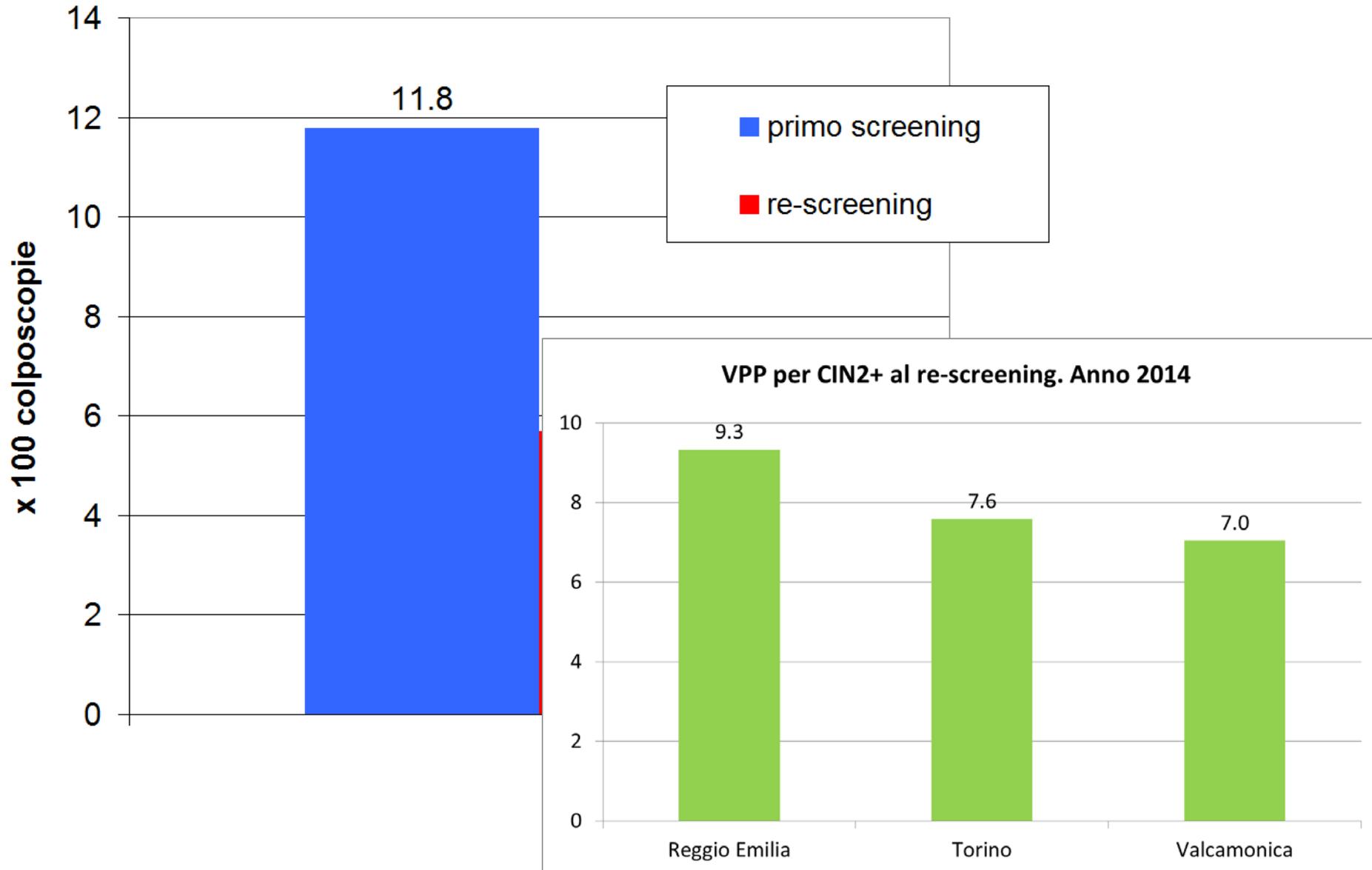
Comparison of CIN2+ detection rates (DR) at two consecutive screening rounds in women screened with HPV-DNA test* and cytology**, by age class.

| | Screened women | CIN2+ | | | | | | % diagnosed at re-screening |
|------------------------|----------------|-----------------|---------------------|--------------|---------------------|-------|---------------------|-----------------------------|
| | | first screening | | re-screening | | total | | |
| | | N° | DR (‰) | N° | DR (‰) | N° | DR (‰) | |
| 25-29 years | | | | | | | | |
| HPV test | 2,712 | 22 | 8.1 | 7 | 2.6 | 29 | 10.7 | 24.1 |
| Cytology | 1,536 | 9 | 5.9 | 0 | 0.0 | 9 | 5.9 | 0 |
| Relative Rate (95% CI) | | | 1.38 (0.61-3.42) | | - | | 1.82 (0.84-4.39) | - |
| p-values | | | 0.41 | | - | | 0.11 | - |
| 30-64 years | | | | | | | | |
| HPV test | 26,135 | 100 | 3.8 | 16 | 0.6 | 116 | 4.4 | 13.8 |
| Cytology | 15,940 | 51 | 3.2 | 25 | 1.6 | 76 | 4.8 | 32.9 |
| Relative Rate (95%CI) | | | 1.20 (0.84-1.71) | | 0.39 (0.19-0.76) | | 0.93 (0.69-1.26) | 0.42 (0.19-0.88) |
| p-values | | | 0.30 | | 0.002 | | 0.63 | 0.01 |
| 25-64 years | | | | | | | | |
| HPV test | 28,847 | 122 | 4.2 | 23 | 0.8 | 145 | 5.0 | 15.9 |
| Cytology | 17,476 | 60 | 3.4 | 25 | 1.4 | 85 | 4.9 | 29.4 |
| Relative Rate (95% CI) | | | 1.23 (0.90-1.71) | | 0.56 (0.30-1.02) | | 1.03 (0.78-1.37) | 0.54 (0.27-1.06) |
| p-values | | | 0.19 | | 0.040 | | 0.81 | 0.051 |

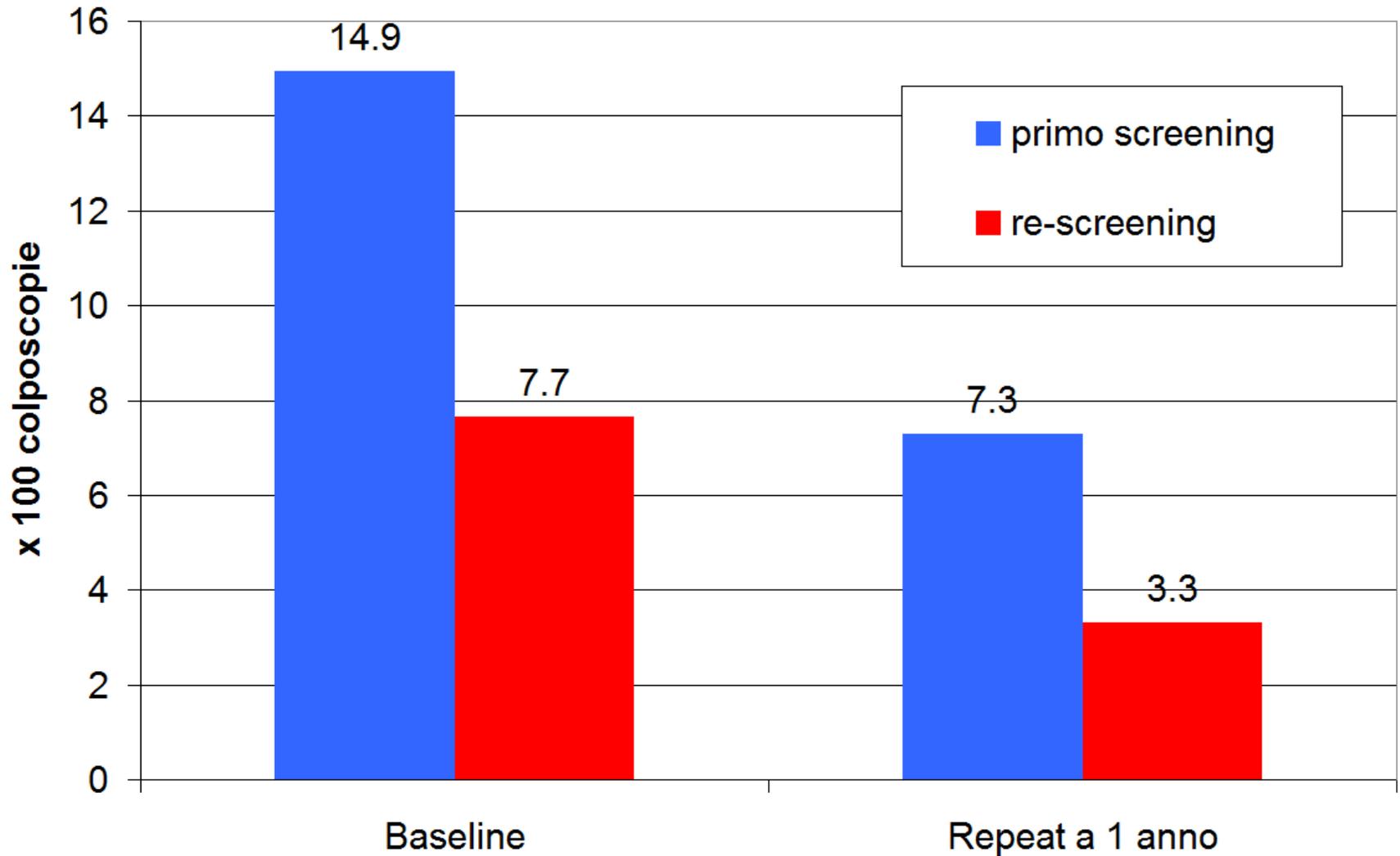
* Women with first HPV screening test performed before 01/01/2012, who were invited for re-screening during the study period (including 1-year repeat in HPV+ pap-)

** 2002-2008

Valore predittivo positivo per CIN2+ (25-64 anni)



Valore predittivo positivo per CIN2+ (età 25-64 anni)



Conclusioni

- Adesione molto elevata
- Positività al test HPV dimezzata
- Crollo dell'invio a colposcopia
- Forte riduzione dei tassi di identificazione
- Drastica riduzione del VPP
- Anticipo diagnostico rispetto al pap test

Impatto rilevante del primo round di screening con HPV

Intervallo di 3 anni inefficiente

Necessità di confronti intra-programma

Per approfondire...

DOI: 10.1111/1471-0528.14575

www.bjog.org

A 3-year interval is too short for re-screening women testing negative for human papillomavirus: a population-based cohort study

M Zorzi,^a H Frayle,^b M Rizzi,^b C Fedato,^c M Ruggie,^{a,d} MG Penon,^e A Bertazzo,^e S Callegaro,^f M Campagnolo,^f F Ortu,^f A Del Mistro,^b and the Veneto HPV-screening Working Group*

13.30 – 16.00

Sessione 7: Highlights dalla ricerca e quality assurance dello screening organizzato

Moderano Gian Piero Fantin e Antonella Pellegrini

Presentazione 4 abstract dai poster

That's all Folks!

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