
51° CONGRESSO NAZIONALE SItI
SOCIETÀ ITALIANA DI IGIENE
Medicina Preventiva e Sanità Pubblica
I PRIMI 40 ANNI DEL SERVIZIO SANITARIO NAZIONALE: IL CONTRIBUTO DELL'IGIENE ALLA SALUTE E ALL'EQUITÀ
RIVA DEL GARDA
17-20 OTTOBRE 2018

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RIVA DEL GARDA 17-20 OTTOBRE 2018

Registri tumori e screening organizzati

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GdL SItI Prevenzione tumori
Università di Perugia

Riva del Garda - venerdì 19 ottobre 2018

Screening oncologici

- Opportunistici o spontanei o non organizzati
- Organizzati o programmati
- Effetto collaterale

- Misto, laddove le due modalità coesistano

Lo screening di popolazione organizzato o programmato

Table 6.1 . Defining criteria for organized screenings according to Hakama and colleagues

a. The target population has been identified;

b. individual people are identifiable;

c. mechanisms are implemented to guarantee high coverage and attendance (e.g., a personal letter of invitation);

d. there are adequate field facilities for performing the screening tests;

e. there is a defined quality control program concerning how the tests are performed and interpreted;

f. adequate facilities exist for diagnosis and for the appropriate treatment of confirmed abnormalities;

g. there is a carefully designed and agreed upon referral system, an agreed link between the participant, the screening center, and the clinical facility for diagnosis of an abnormal screening test, for management of any abnormalities found, and for providing information about normal screening tests; and

h. evaluation and monitoring of the total program is organized in terms of incidence and mortality rates among those attending, among those not attending, at the level of the total target population. Quality control of the epidemiologic data should be established.

Hakama M, Chamberlain J, Day NE, Miller AB, Prorok PC (1985). Evaluation of screening programmes for gynaecological cancer. Br J Cancer 52,669 – 673.

Strategia esplicita e definita

- Lo screening opportunistico e quello organizzato potenzialmente si avvalgono dello sesso test ma l'utilizzo è esplicitamente definito e valutato solo nel secondo caso (*analogia con vaccinazioni e percorsi diagnostico terapeutici*)
- Inoltre nel modello organizzato il test è attivamente proposta ad una popolazione bersaglio definita

12. Take part in organised cancer screening programmes for:

bowel cancer (men and women);

breast cancer (women);

cervical cancer (women).

European Code against Cancer 4th Edition: 12 ways to reduce your cancer risk. Schutz et al. Cancer Epidemiology 2015

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LO SCREENING PER LA PREVENZIONE DEL CERVICO-CARCINOMA – I DATI DEI REGISTRI TUMORI

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I NUMERI DEL CANCRO IN ITALIA 2018

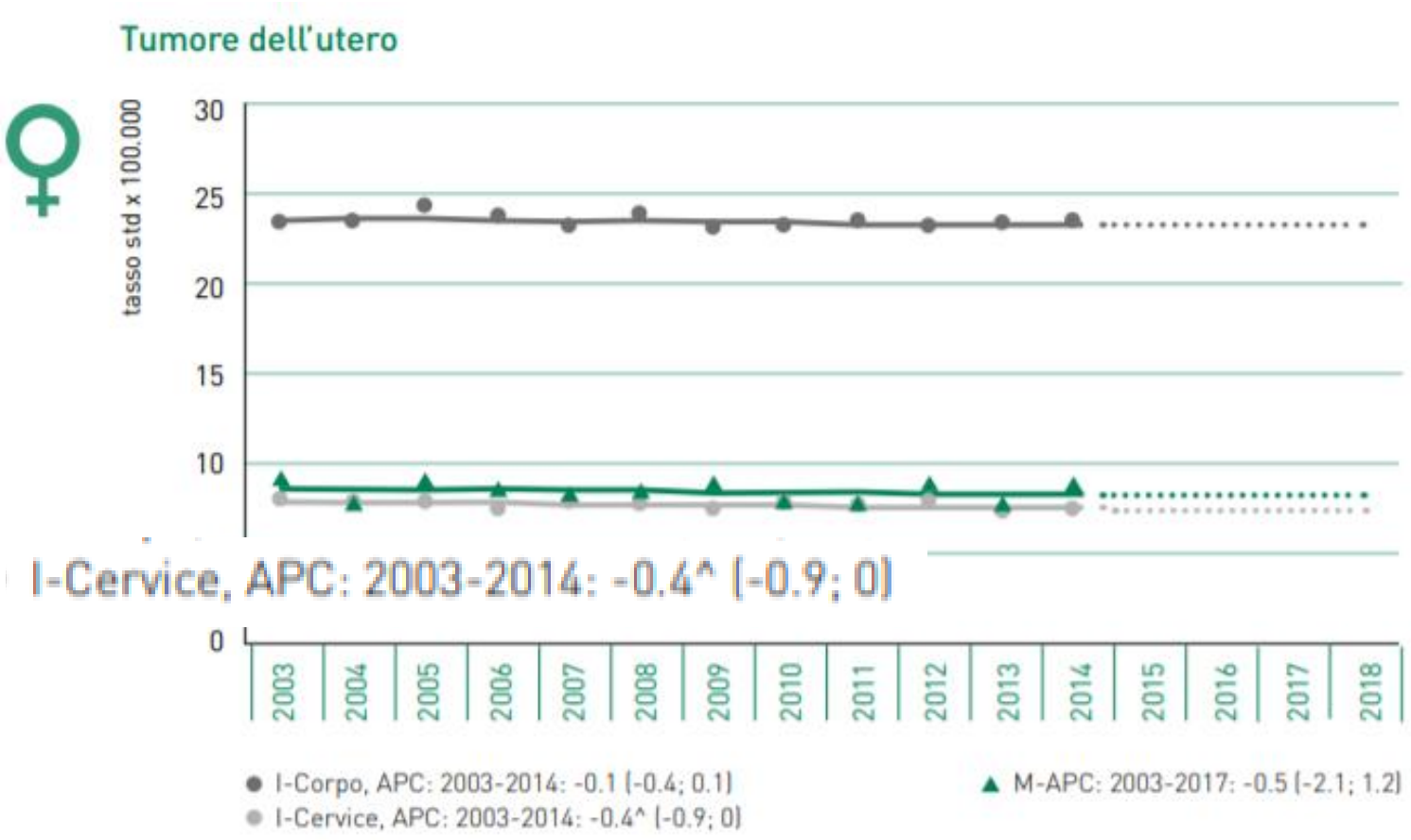

FIGURA 25. Tumore del corpo dell'utero e della cervice uterina. AIRTUM: stima dei trend tumorali di incidenza e mortalità (utero totale) 2003-2018. Tassi standardizzati nuova popolazione europea 2013

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RIVA DEL GARDA 17-20 OTTOBRE 2018

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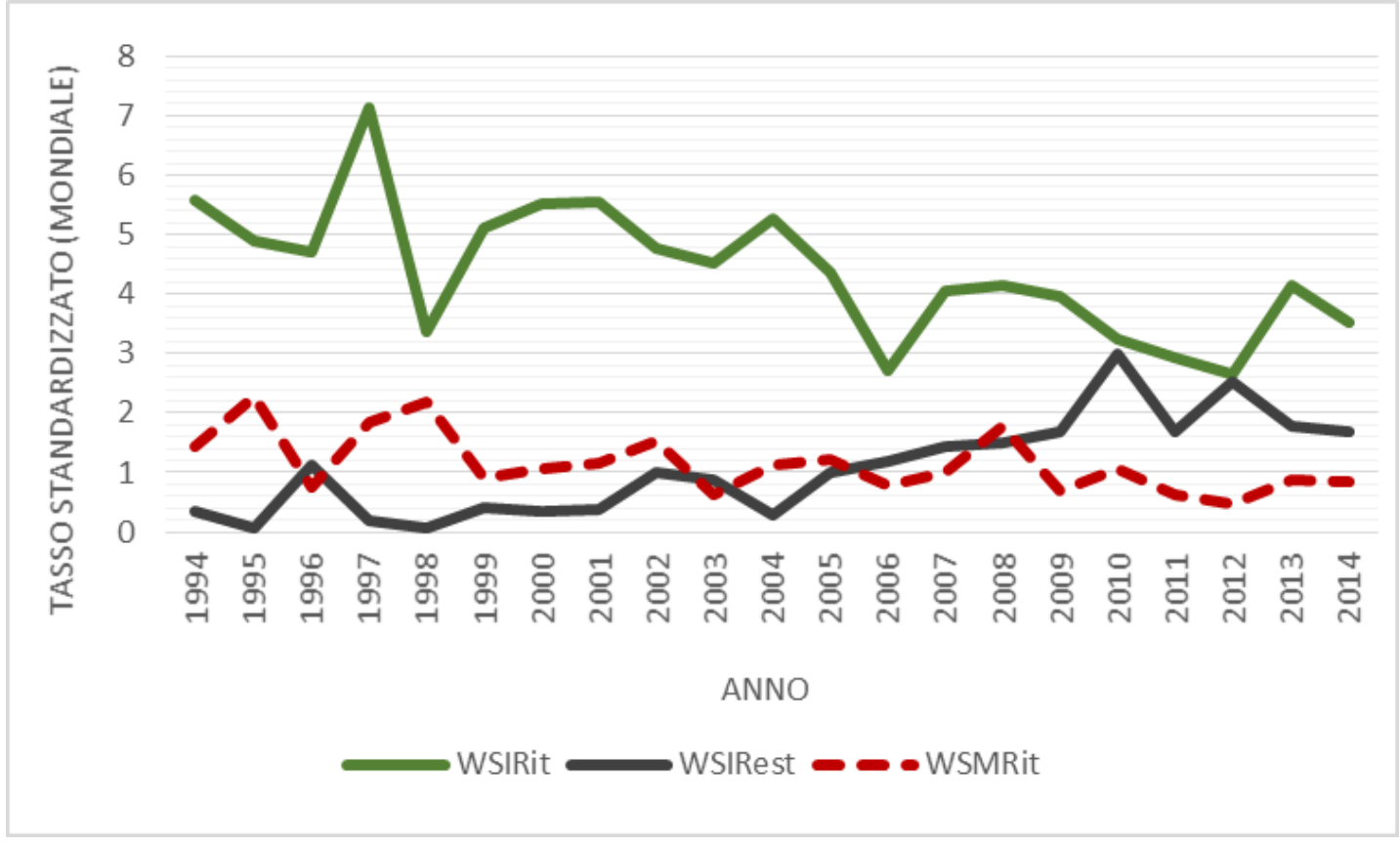
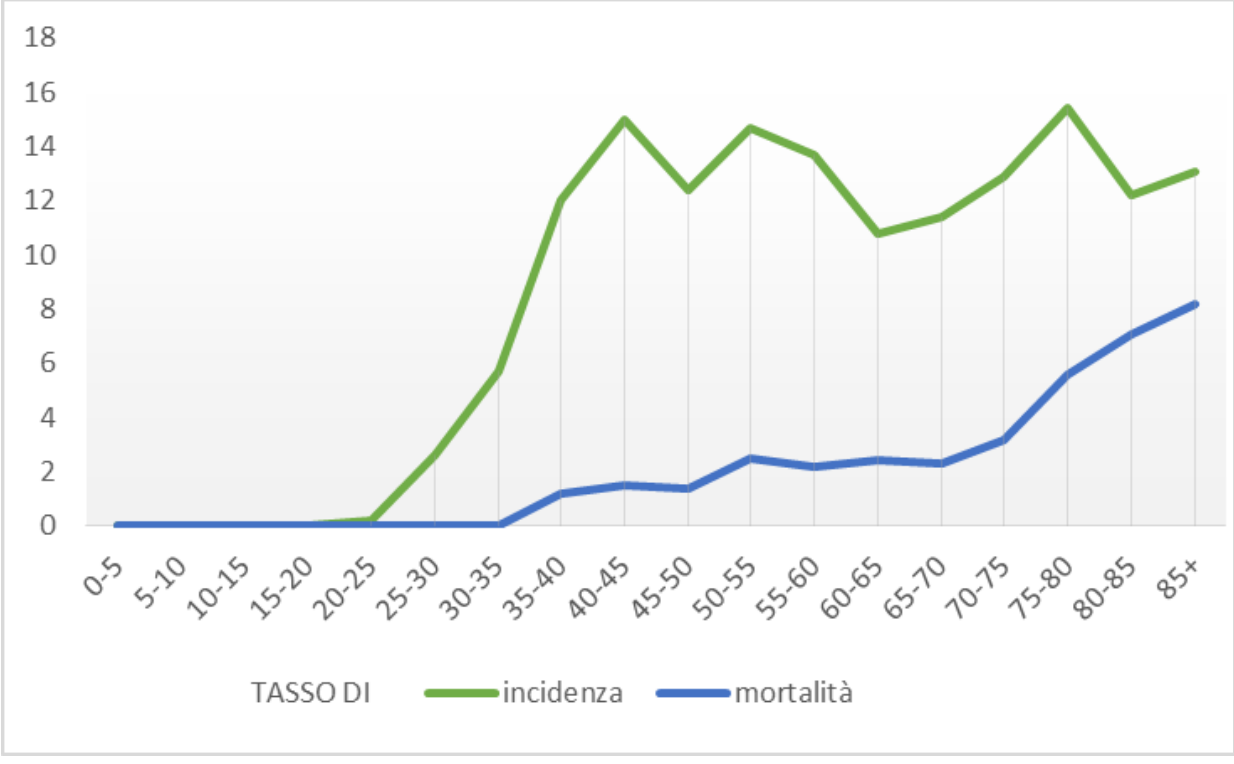
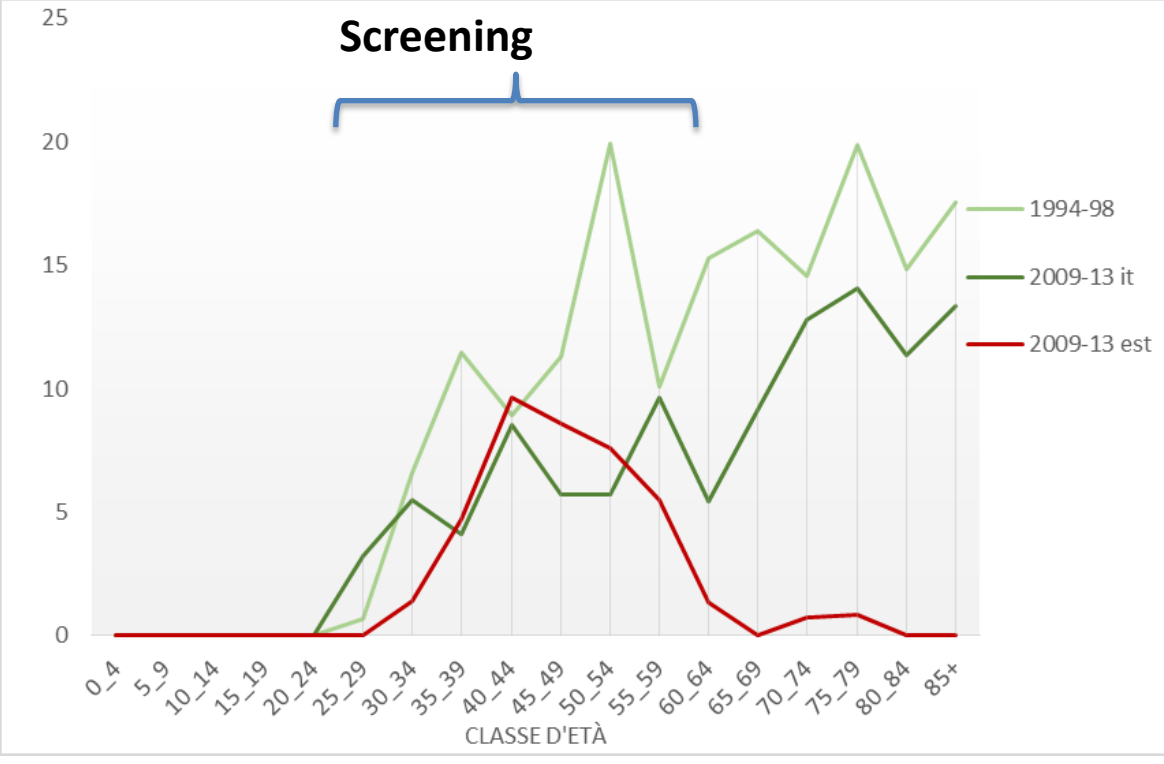
SEZIONE TRIVENETO

Tassi standardizzati di incidenza di carcinoma della cervice uterina per nate in Italia (verde) verso nate all'estero (grigio) e di mortalità per nate in Italia (rosso); periodo 1994 – 2014

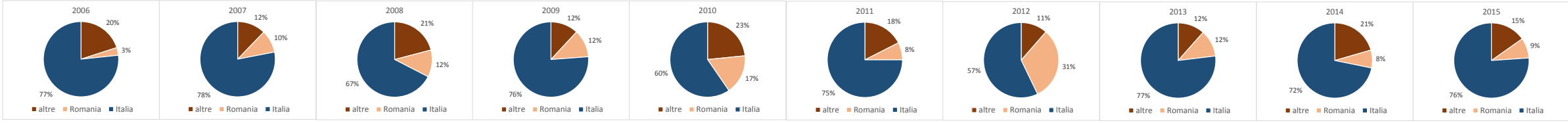


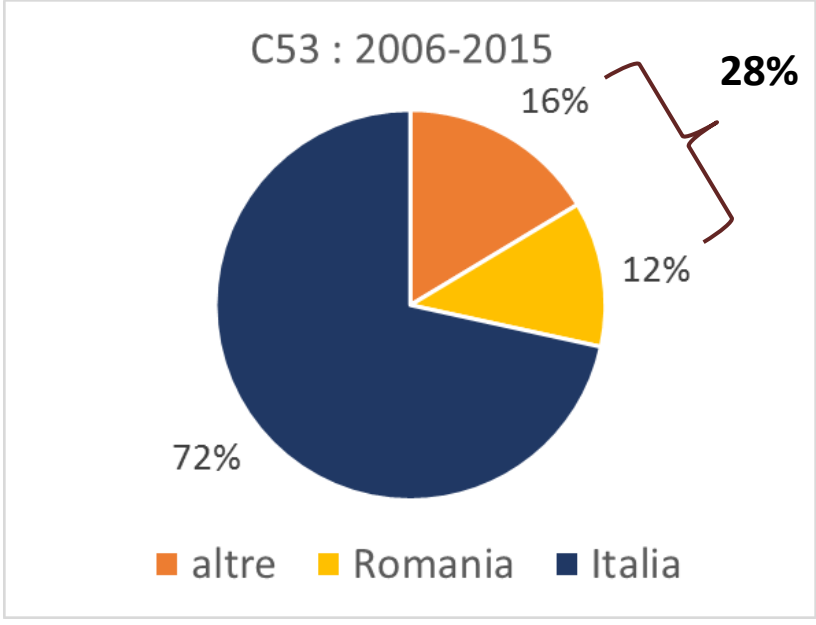
Tassi età specifici 1994-2014

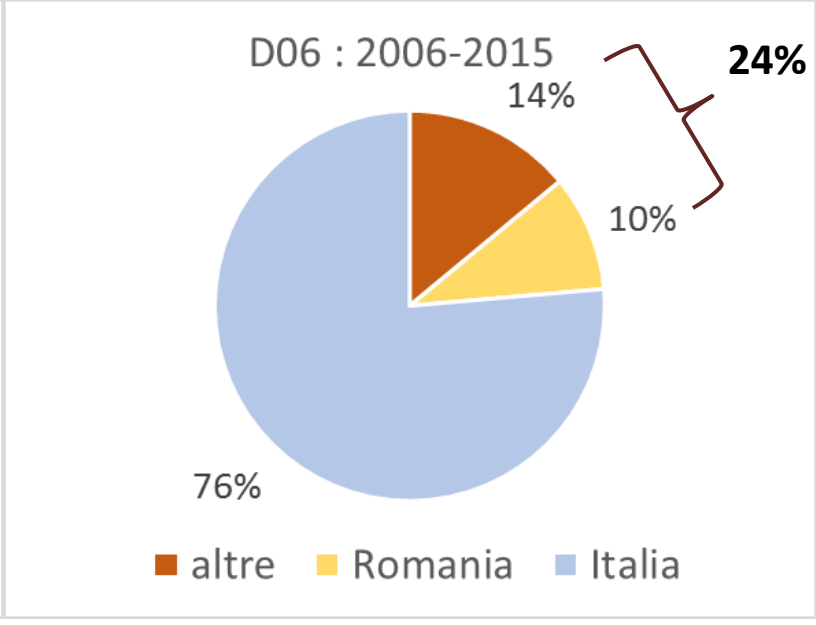


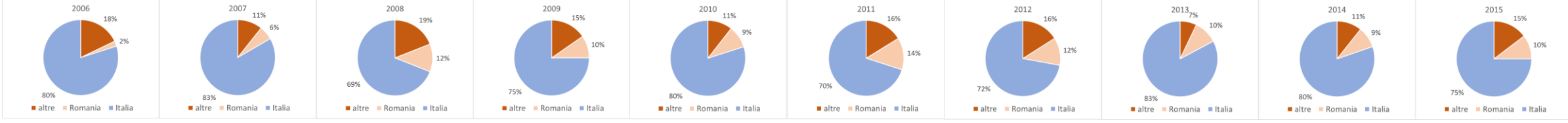


Distribuzione % dei casi di carcinoma infiltrante e CIN III per comune di nascita 2006-15









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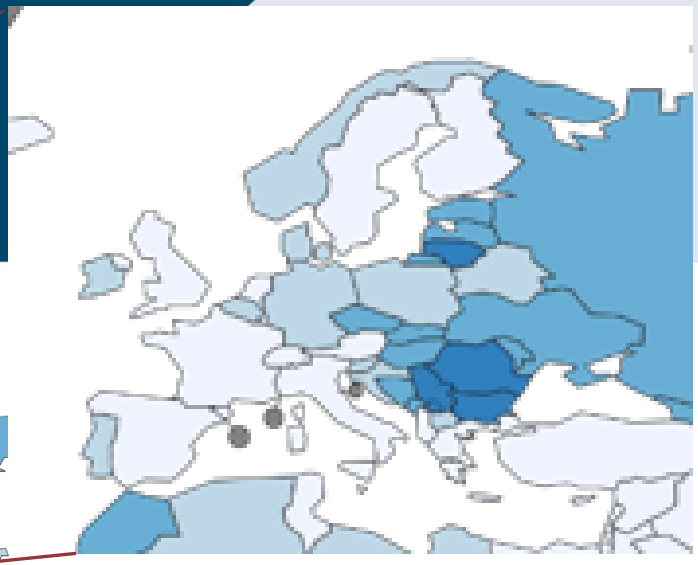
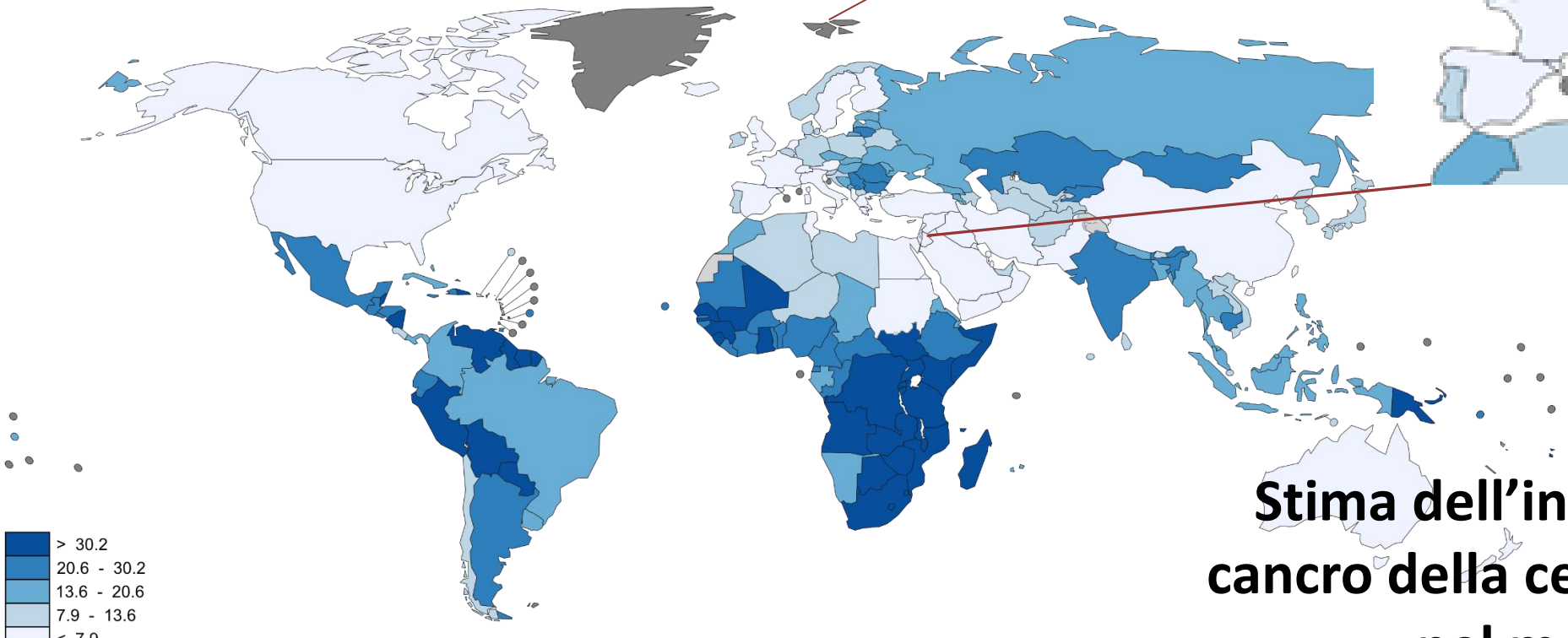
RIVA DEL GARDA 17-20 OTTOBRE 2018





Stima dell'incidenza del cancro della cervice uterina nel mondo

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: GLOBOCAN 2012
Map production: IARC
World Health Organization

World Health Organization

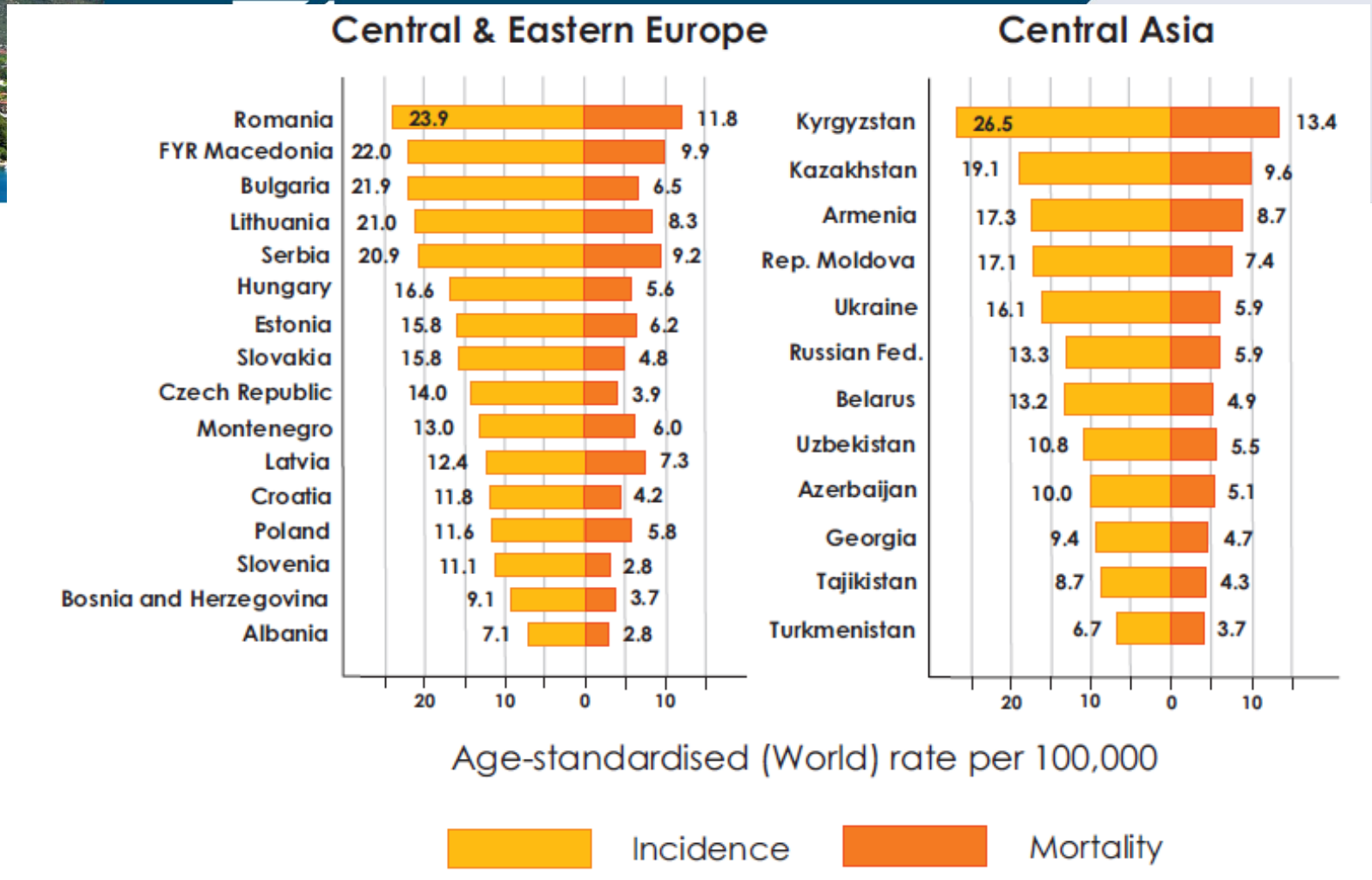


Fig. 1. Estimated cervical cancer age standardised(world) incidence (left), mortality (right), all ages, in the regions of Central and Eastern Europe and in Central Asia, 2008. Data source: Globocan2008 [4].

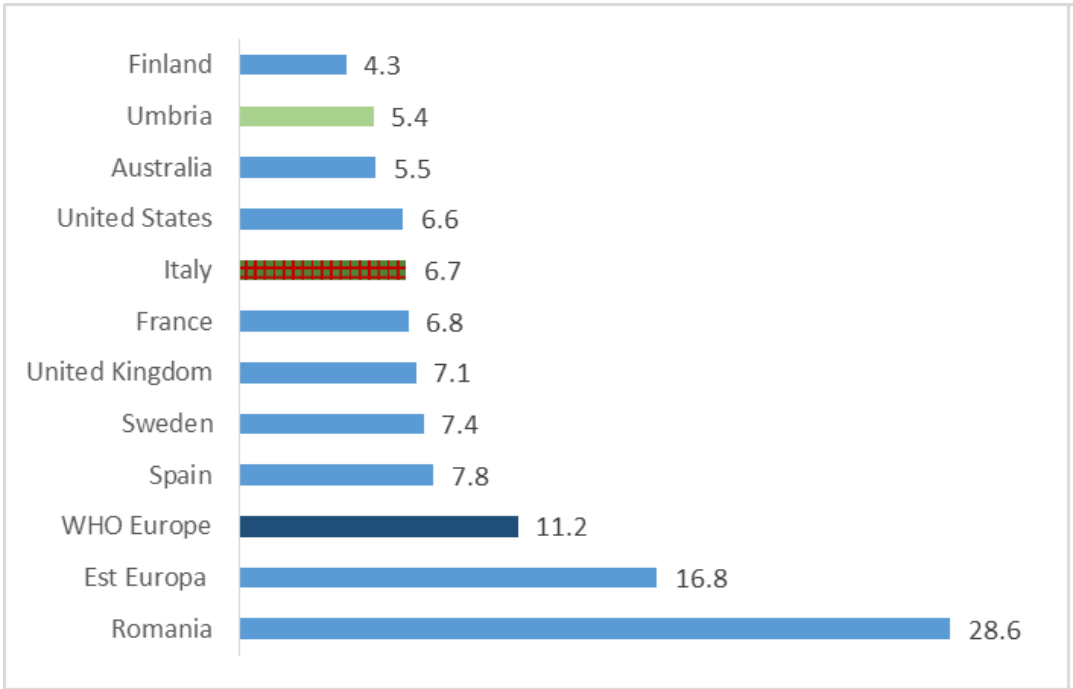
Trends in cervical cancer incidence and mortality in the Baltic countries, Bulgaria and Romania. Arbyn M et al. International Journal of Cancer 2011

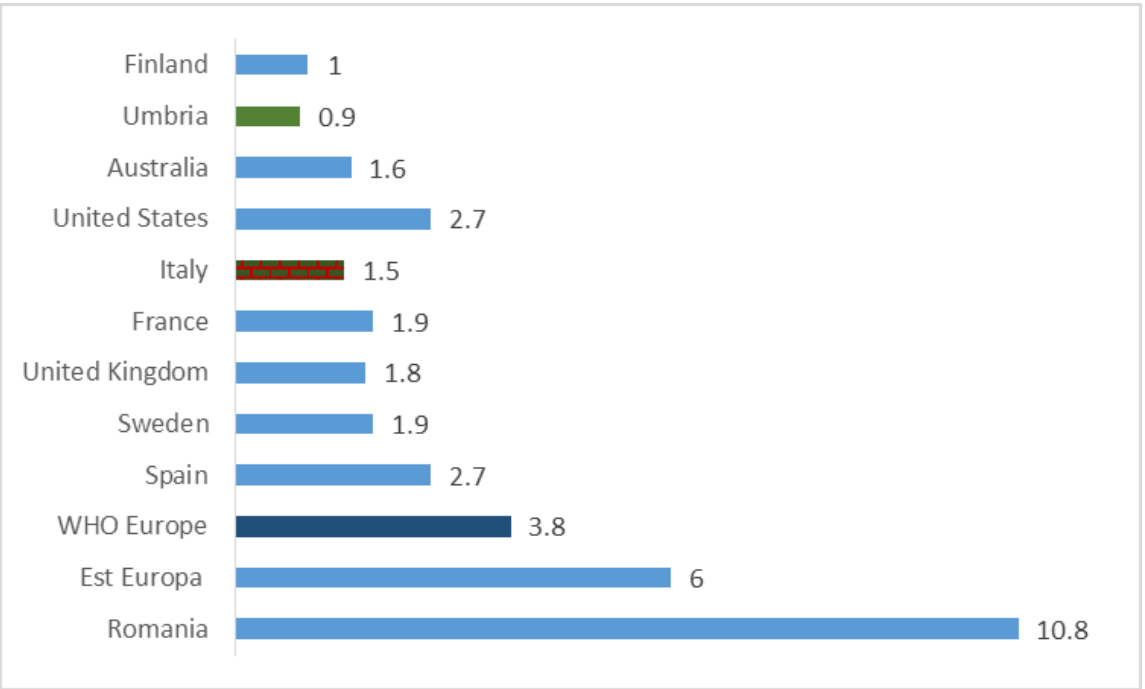
Lotta ad HPV e patologie HPV correlate: la situazione in Romania

- Romania performs opportunistic screening based on regional organization…The reported coverage in this opportunistic setting is extremely low—between 0.6 and 3.2%...the screening infrastructure in the country is insufficient and financial resources are less than 10% of the necessary amount…
- In Romania, a national school-based programme to vaccinate females aged 11 was first launched in 2008, but was temporarily suspended during the first year due to low acceptance—only about 2% of the target population received the vaccine.
- The government analysed the reasons for the low uptake and subsequently implemented a novel information campaign prior to a re-launch in February 2010. To the best of the authors' knowledge, the relaunched HPV vaccination programme in Romania was stopped at the end of 2011 due to a negative public reaction and lack of proper communication.
- This resulted in low coverage in the target population, which did not reach 5%.

Poljak M et al. Cervical Cancer Screening Practices and Current Status of Vaccination Implementation in Central and Eastern Europe. Vaccine 2013

Tasso standardizzato di incidenza (mondo) e mortalità, 2012. Confronto internazionale (Globocan)





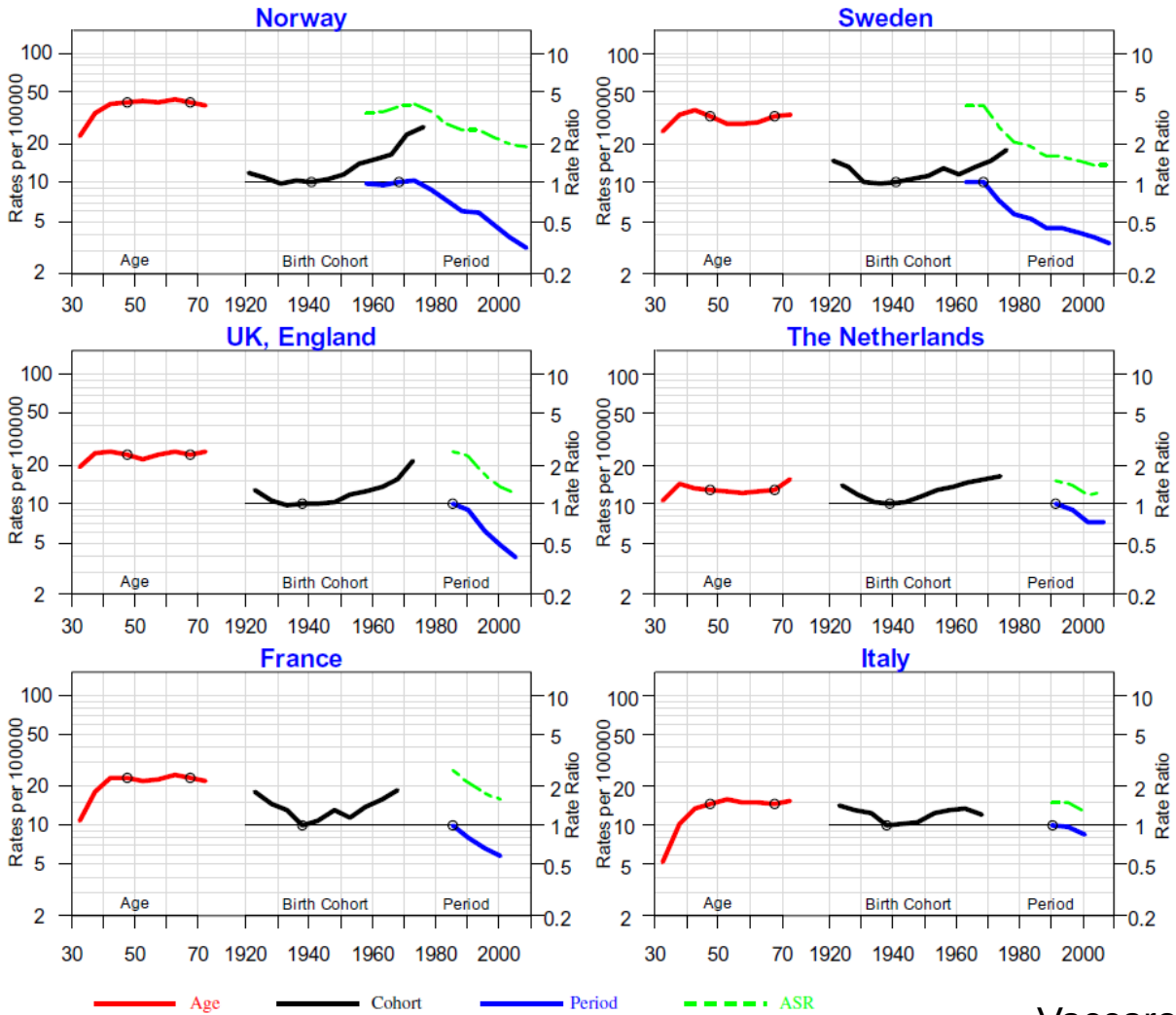
Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on day/month/year.

Finland

- The mass screening programme in Finland introduced in the mid-1960s and the 80% declines seen there from the mid-1960s to the early-1990s is a cornerstone of the evidence for the effective- ness of organised cytological screening [36]; it is worth noting that the age-adjusted (world) incidence rates of cervical cancer at their peak in Finland (circa 1962–65 [6], of 17.3) are of a similar or lesser order of magnitude than the corresponding rates observed today in almost half of the countries studied in the combined regions (*i.e. Central and Eastern Europe and Central Asia*)

Patterns and Trends in Human Papillomavirus-Related Diseases in Central and Eastern Europe and Central Asia Bray F et al. Vaccine 2013

Worldwide trends in cervical cancer incidence: Impact of screening against changes in disease risk factors



Effetto coorte di nascita,

- (*meno marcato in Italia rispetto agli scandinavi*) «Many aspects of sexual behaviour,…have changed substantially starting from generations of women born during or after the Second World War”

Effetto periodo

- “the beneficial impact of screening in counteracting the underlying cohort-specific increases in ICC risk”

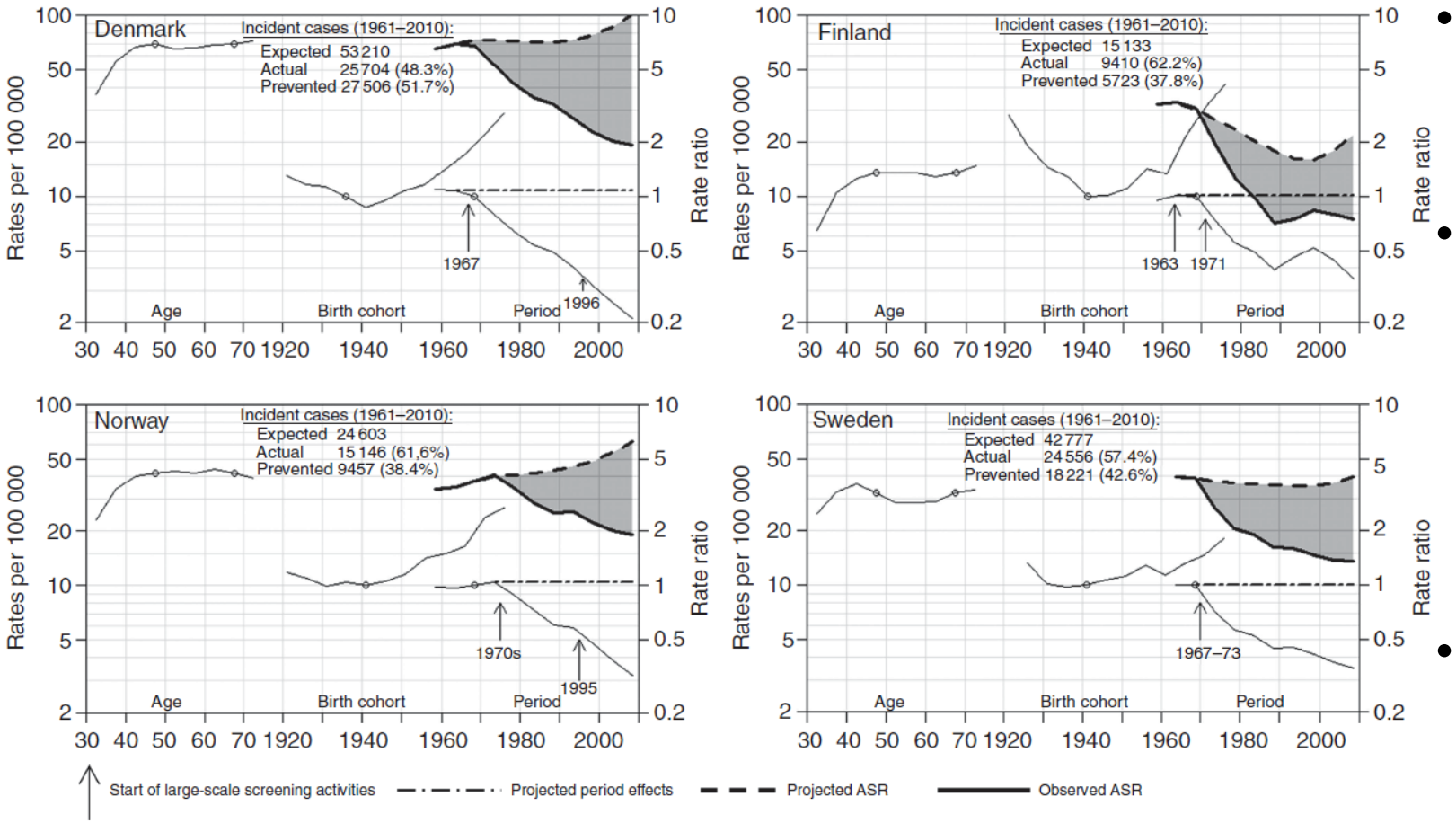
Vaccarella S et al. European Journal of Cancer 2013; 49, 3262– 3273

- The varying period and cohort patterns in ICC trends across countries can be largely attributed to two independent factors:

(1) the existence, duration, and quality of screening programmes over calendar time; and

(2) changes in ICC risk factors, notably sexual behavior and, hence, the probability of HPV exposure, affecting consecutive generations of women

Vaccarella S et al. European Journal of Cancer (2013) 49, 3262– 3273



50 years of screening in the Nordic countries: quantifying the effects on cervical cancer incidence Vaccarella S et al. BJC 2014

- **Screening programmes might have prevented a HPV-driven epidemic of cervical cancer in Nordic countries**.
- According to extrapolations from cohort effects, cervical cancer incidence **rates** in the Nordic countries **would have been otherwise comparable to the highest incidence rates currently detected in low-income countries**
- might not exclude, however, that the initial impact of screening may be partly obscured by the early detection of microinvasive cancers

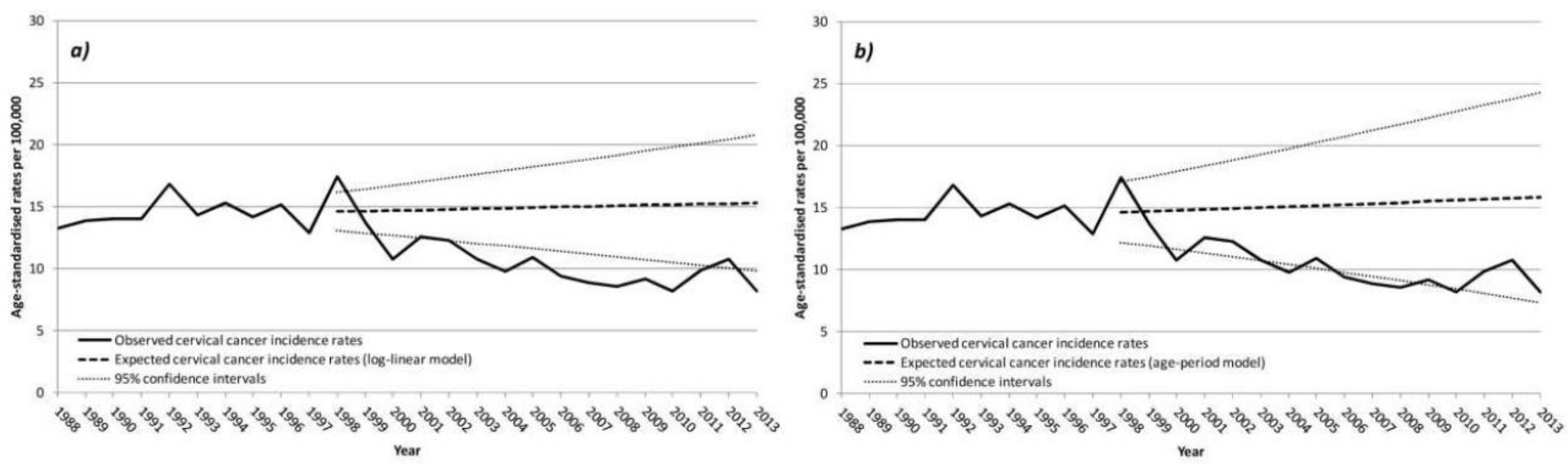
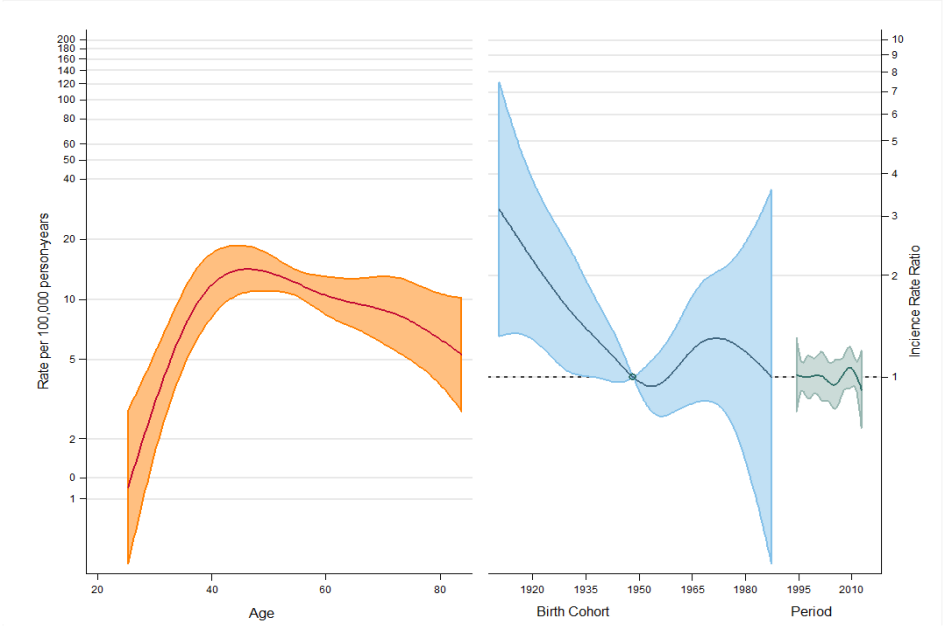


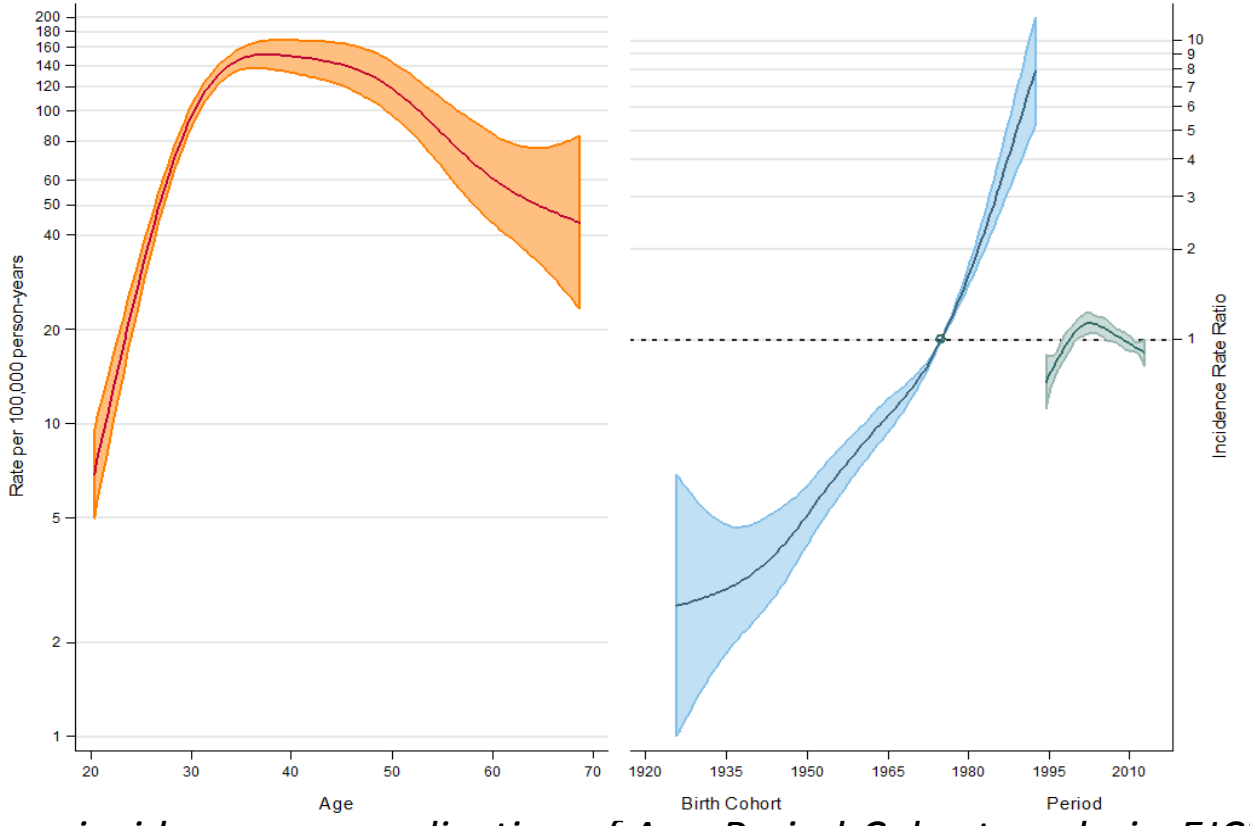
Figure 1. Curve of **observed total annual cervical cancer incidence rates** per 100,000 women aged 25-64 years in 1988-2013 and curve of **total annual rates that would be expected in 1998-2013 in the absence of screening**.

*"*We found many consistent circumstantial evidences for a causal relationship between the introduction of the screening programme in the Emilia-Romagna Region and a significant decrease in CC incidence in the target population. The decrease reached 40% after approximately 10 years and stabilised thereafter.»

Bucchi L et al. Estimating the impact of an organised screening programme on cervical cancer incidence: a 26-year study from northern Italy. Int J Cancer 2018

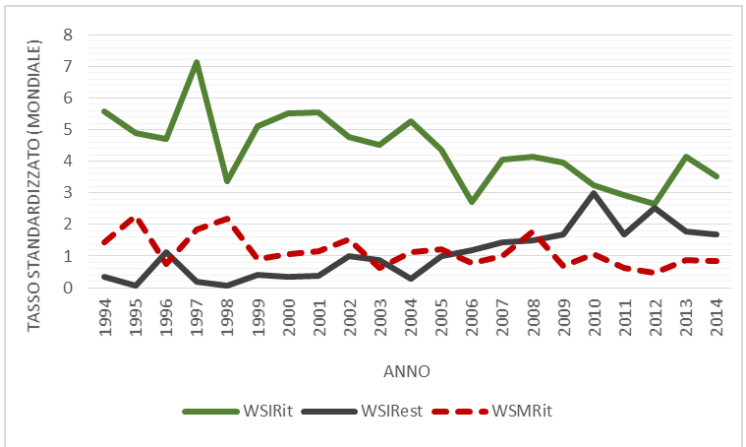
Modello età-coorte-periodo - Umbria



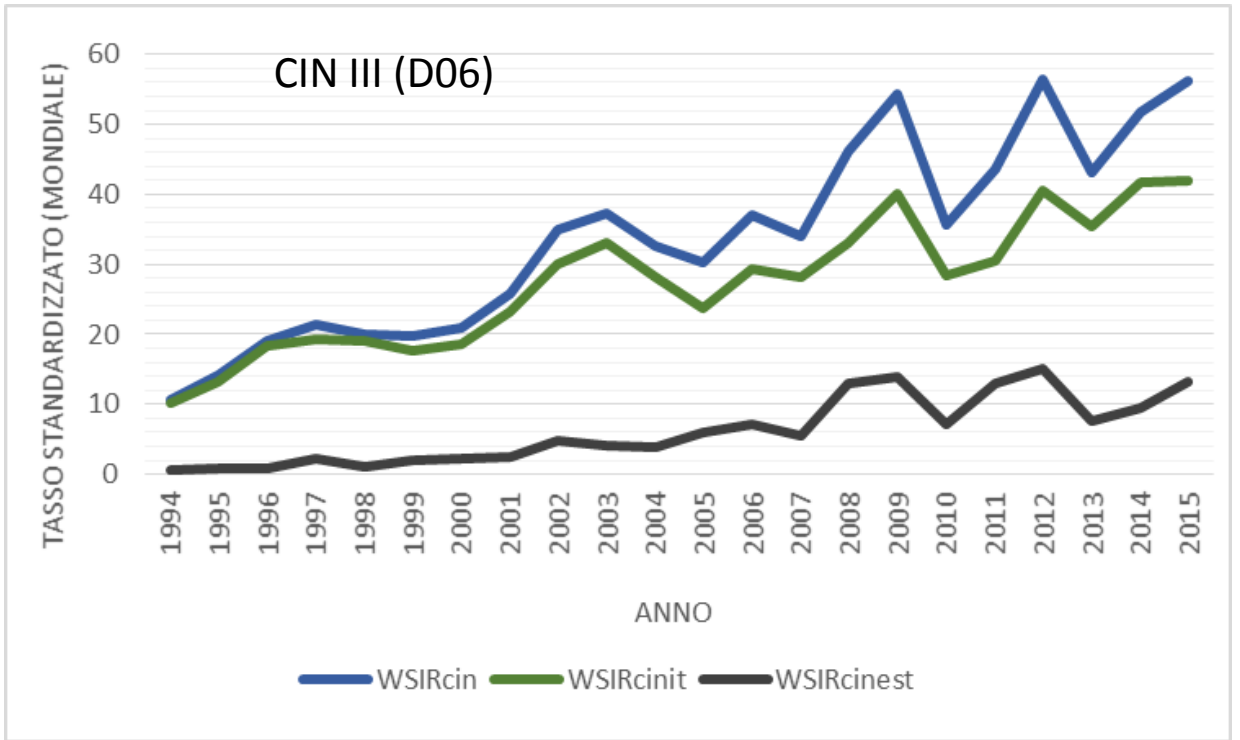


Bucchi D. et al. Immigration, screening and cervical cancer incidence: an application of Age-Period-Cohort analysis. EJCP 2018; accepted

Tassi standardizzati di incidenza di CIN III (D06) - periodo 1994 – 2015 ; complessivo (blu), nate in Italia (verde), nate all'estero (grigio)



Carcinoma infiltrante (C53)



APC +5.9%

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LO SCREENING PER LA PREVENZIONE DEL CANCRO DEL GROSSO INTESTINO

Tumore del colon-retto

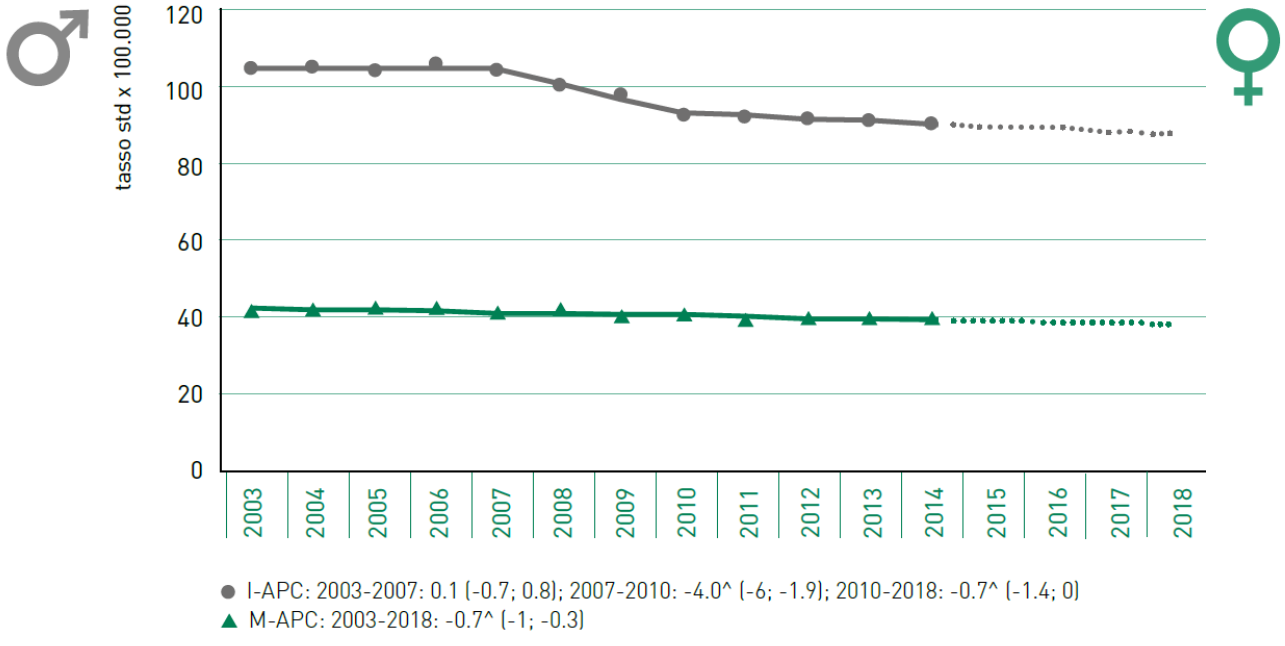


FIGURA 15A. Tumore del colon-retto, maschi. AIRTUM: stima dei trend tumorali di incidenza e mortalità 2003-2018. Tassi standardizzati nuova popolazione europea 2013

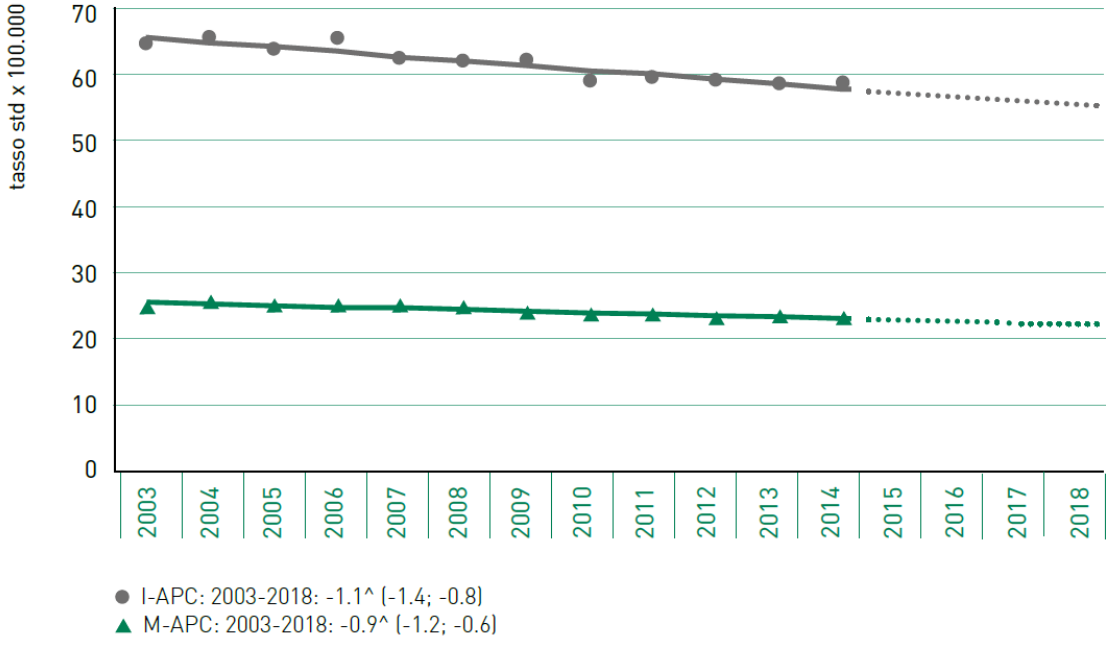
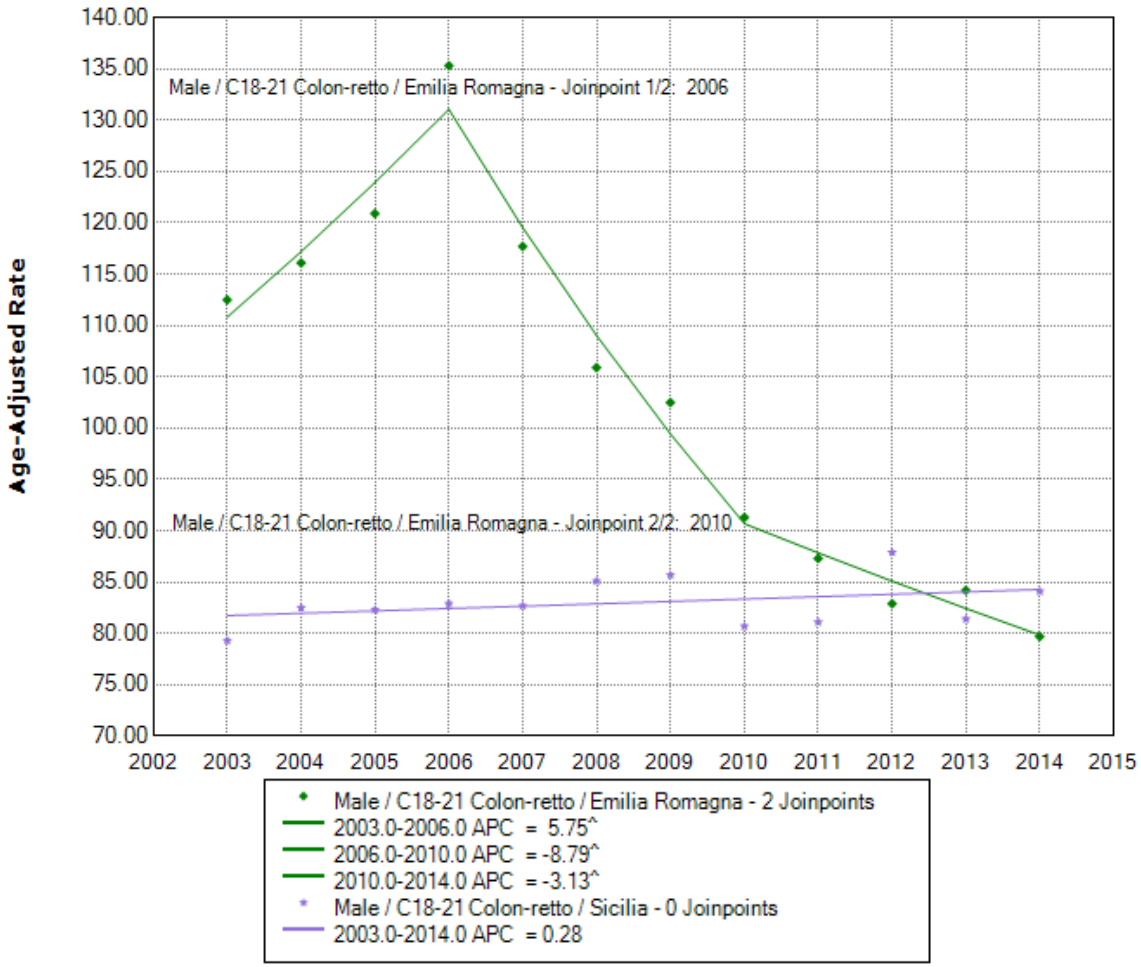
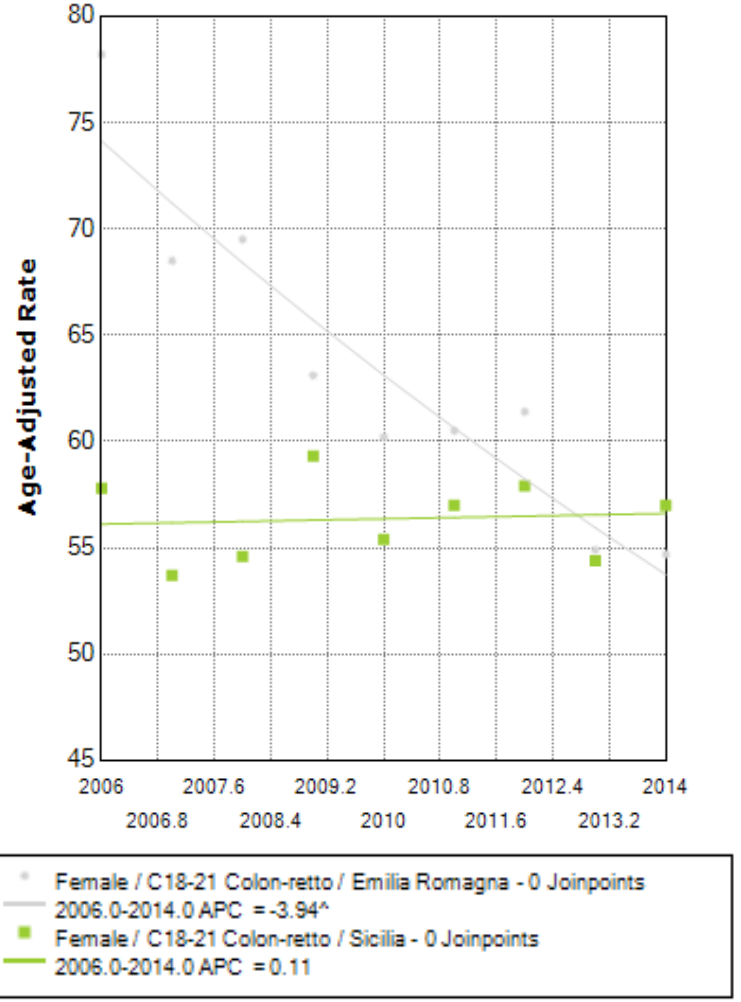


FIGURA 15B. Tumore del colon-retto, femmine. AIRTUM: stima dei trend tumorali di incidenza e mortalità 2003-2018. Tassi standardizzati nuova popolazione europea 2013

I trend per **regione -** COLON RETTO. *Grazie allo screening l'Emilia Romagna (area ad elevata frequenza) ha meno carcinomi infiltranti della Sicilia (area a bassa frequenza)*





Cortesia Dr Stefano Guzzinati – convegno nazionale AIRTum Venezia 11-13 aprile 2018

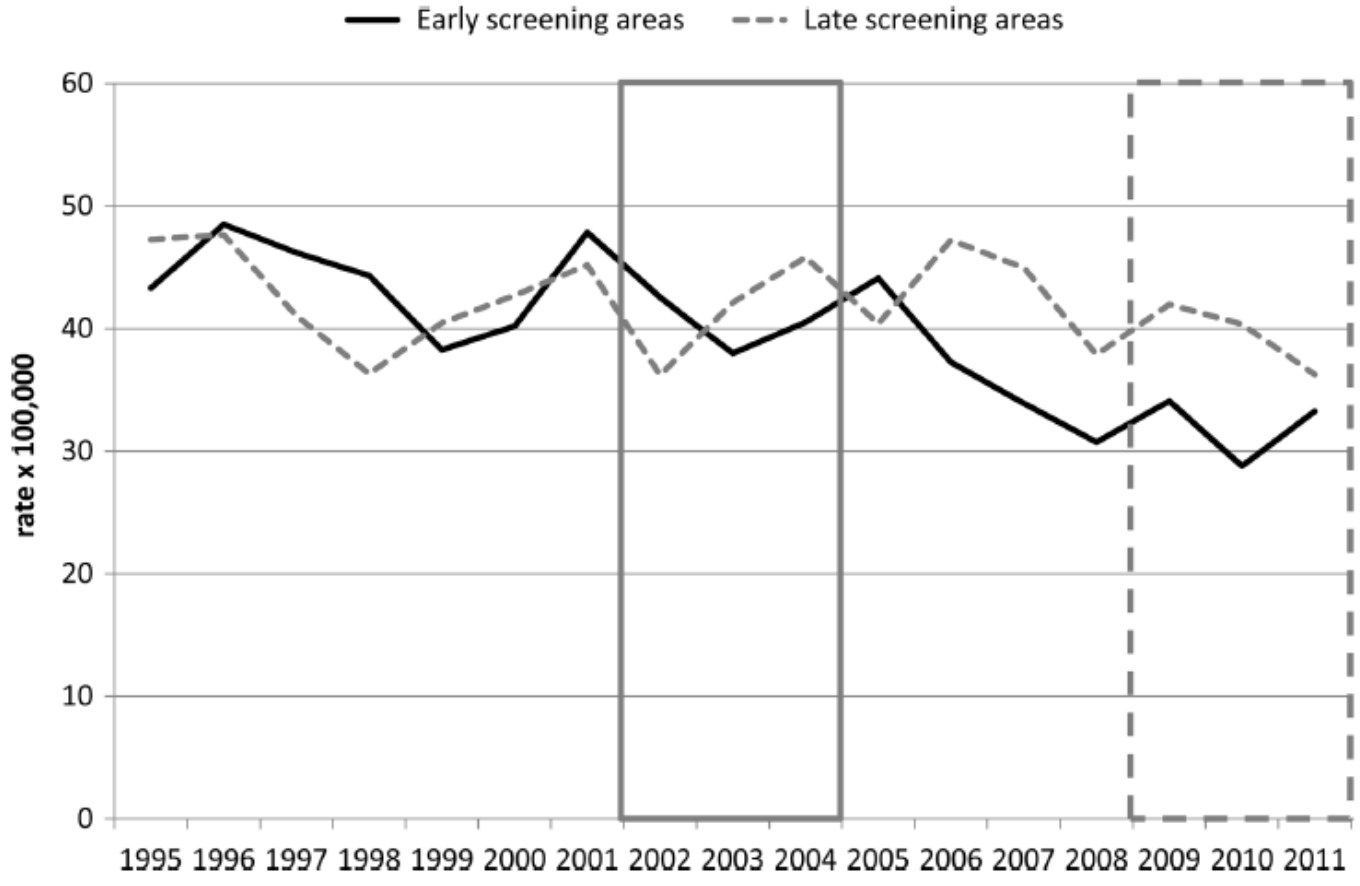


Figure 3 Age-standardised (European standard population) colorectal cancer mortality rates, by year and period of activation of the screening programme; 50–74-year-old subjects, 1995–2011. Grey and dotted boxes: period of activation of colorectal screening programme in early and late screening areas, respectively.

Mortalità in riduzione in seguito alla introduzione dello screening (FIT) Zorzi M, et al. Gut 2014;0:1–7

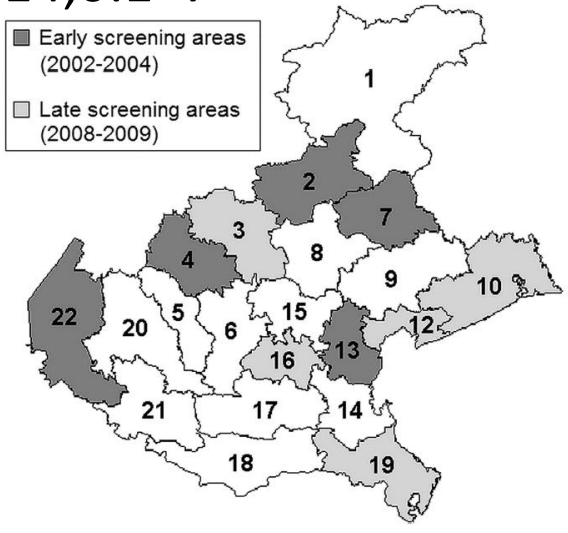
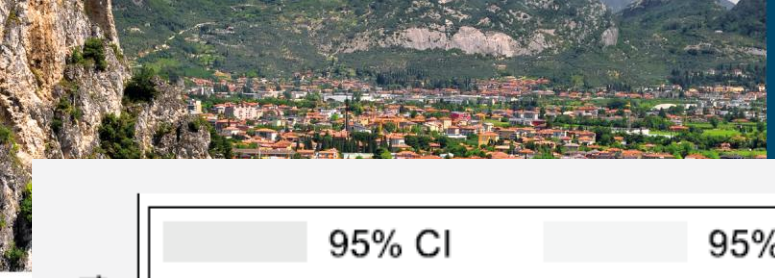
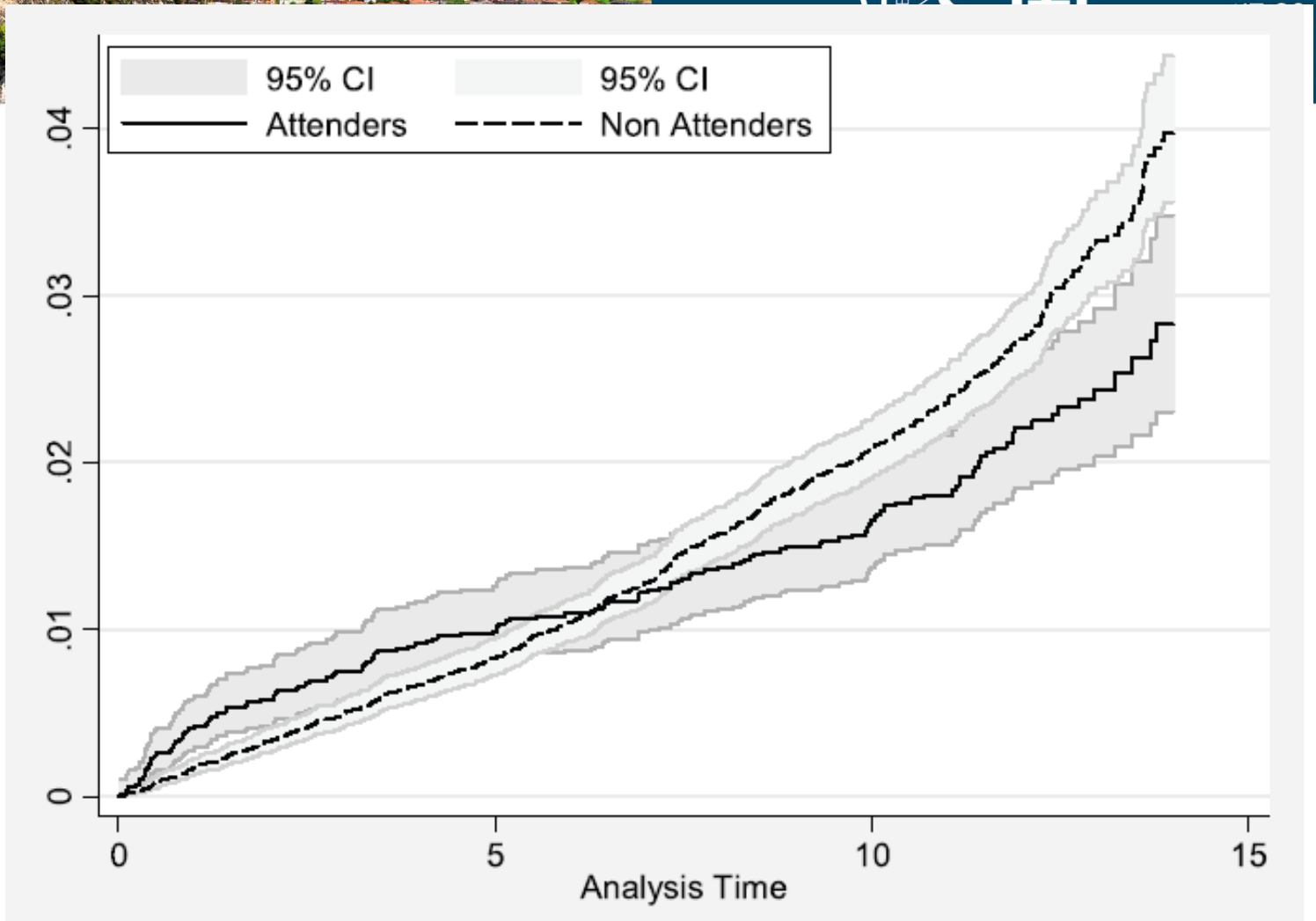


Figure 1 Map of local health units of the Veneto Region by period of activation of a colorectal screening programme.





Le evidenze disponibili indicano che il FIT determina una riduzione dell'incidenza di CRC grazie alla diagnosi delle lesioni pre-maligne

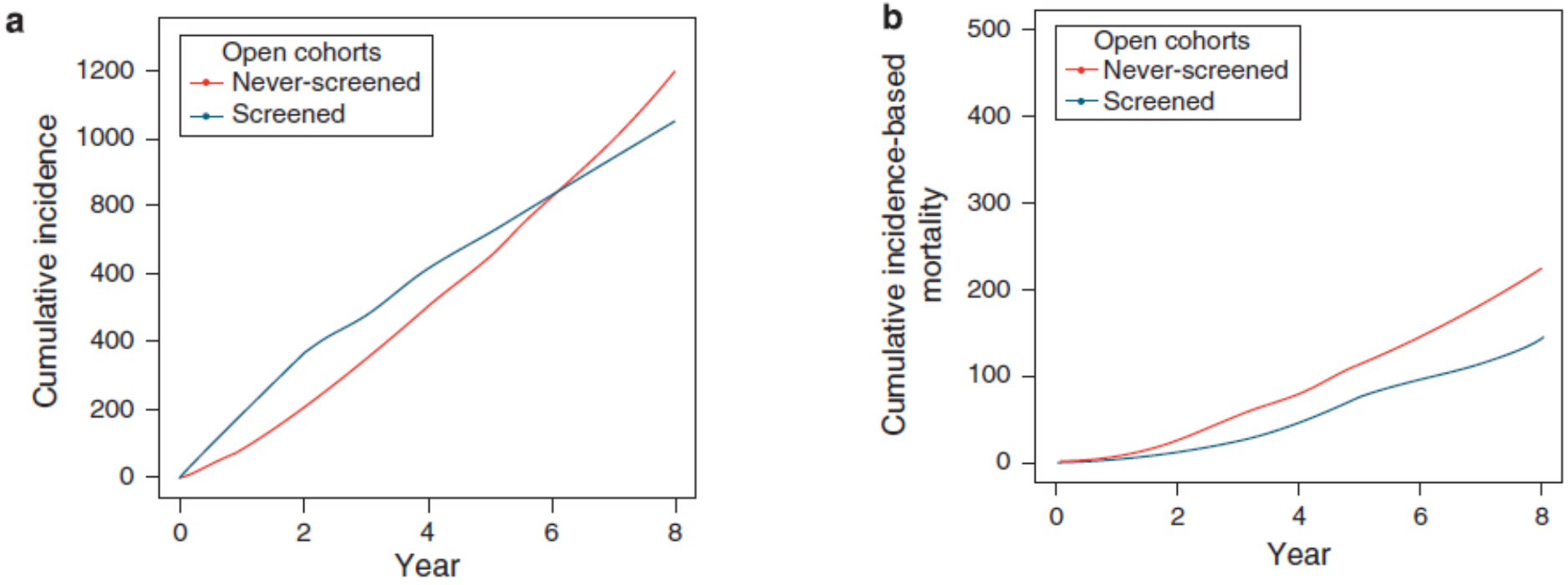
"The Cox model…, adjusted for sex and age, showed an overall statistically significant reduction in CRC incidence of 22% (HR = 0.78, 95%CI: 0.65–0.93) in the attenders' versus the nonattenders' cohort."

Ventura L, et al. The impact of immunochemical faecal occult blood testing on colorectal cancer incidence. Dig Liver Dis. 2014; 46:82-6

Influenza dello screening colorettale su incidenza e mortalità nella provincia di Reggio Emilia

L'effetto di remozione delle lesioni premaligne prevale dopo 6-8 anni

Precoce differenza di mortalità a favore dello screening



Conclusion. FIT screening leads to a decrease in the incidence of CRC and in its mortality.

Giorgi Rossi P et al. Am J Gastroenterol 2015

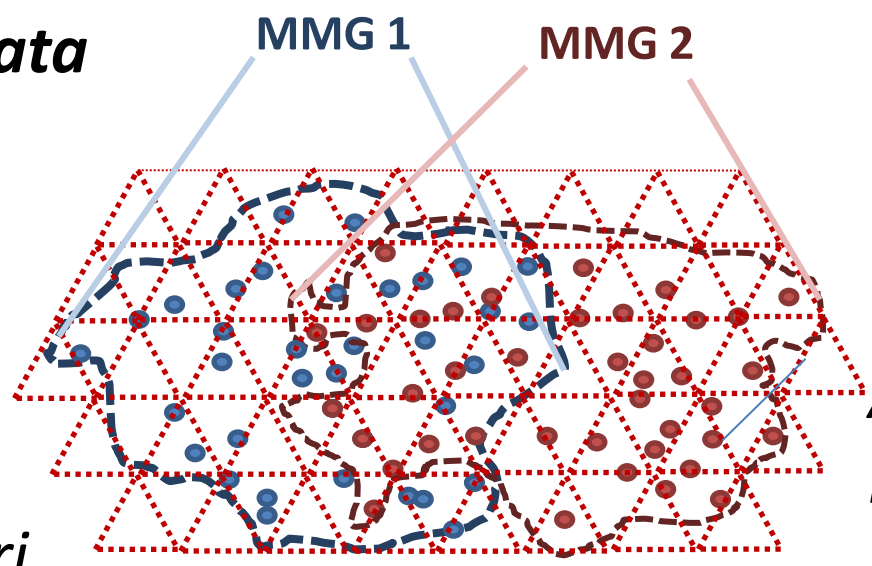
51° CONGRESSO NAZIONALE SItI
RIVA DEL GARDA 17-20 OTTOBRE 2018

NUOVE TECNOLOGIE SVILUPPATE DAI REGISTRI TUMORI E COLLABORAZIONE CON I SERVIZI DI SCREENING

Valutazione dell'adesione per MMG basata sulla geocodifica di popolazione

SAR-MMG Adesione standardizzata e ponderata

Adesione assistibili



Adesione popolazione residente nelle aree degli assistibili

Popolazione residente suddivisa in aree triangolari (area 0.68 km², numero medio invitati 111, Maschi 48%)

Odds di non adesione allo screening (***effetti fissi nel modello a 2 livelli***)

Fattore	Categorie	N.	OR	IC 95%
Sesso (ref. femmine)	Maschi	*118.649*	1.16	1.14 - 1.17
Età (ref. 50-54)	55-59	*56.379*	0.83	0.82 -0.85
	60-64	*48.194*	0.81	0.79 - 0.83
	65-69	*50.524*	0.84	0.82 - 0.86
Comune di nascita (ref. italiano)	Estero		1.62	1.54 - 1.70
Deprivazione (ref. I quintile)	II quintile		0.98	0.96 - 1.01
	III quintile		1	0.98 - 1.03
	IV quintile		1.03	1.01 - 1.06
	V quintile		1.12	1.09 – 1.14

Variabilità spiegata dalla variabile di clustering MMG

VPC variance partition coefficient (=ICC: intraclass correlation coefficient)
the proportion of the total observed individual variation in the outcome that is attributable to between-cluster variation (Austin 2017)

Modello	VPC %	IC 95%
Intercetta random + effetti fissi		
MMG	6	5.1-7.6
Intercetta random + coeff. + effetti fissi		
Nazionalità	3.8	2.7-5.5
MMG	4.1	3-5.7

LR test p<0.0001

51 CONGRESSO NAZIONALE SItI

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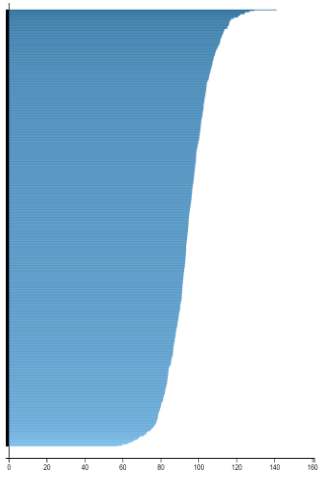
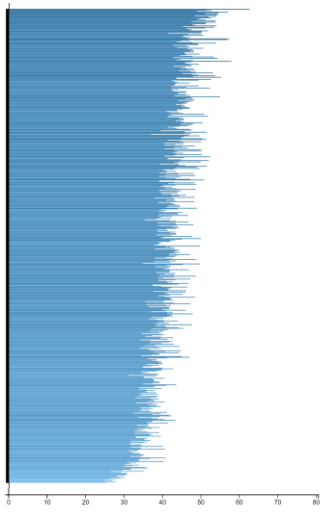
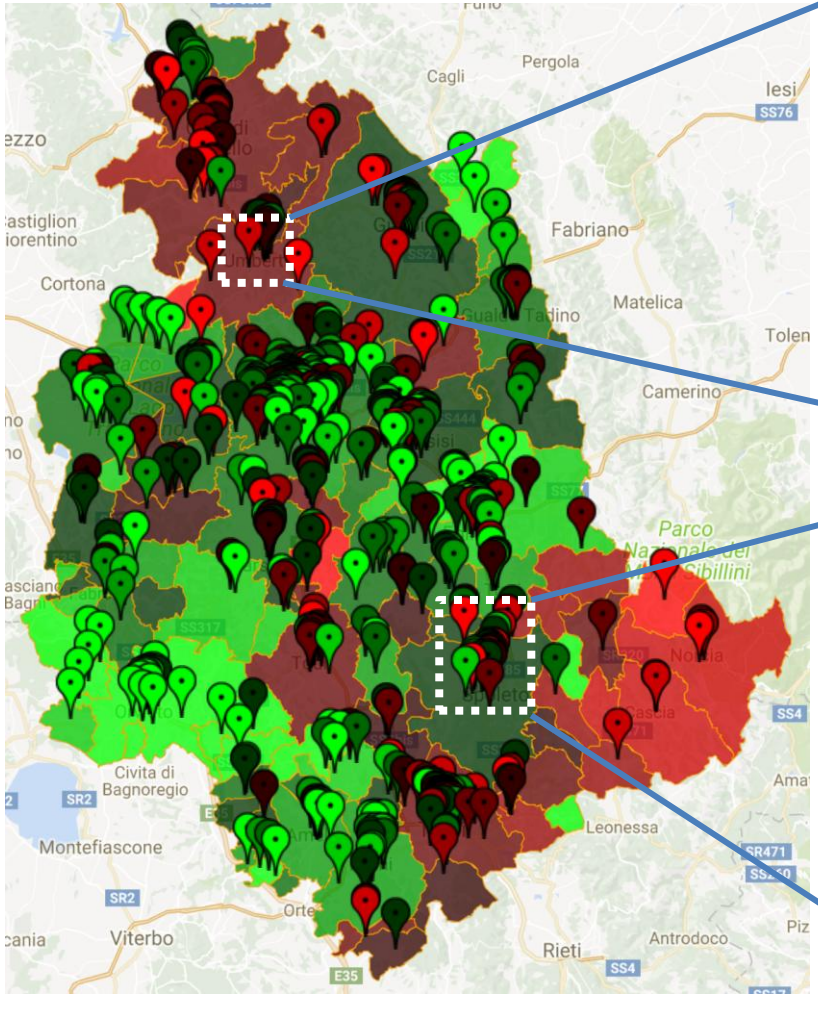
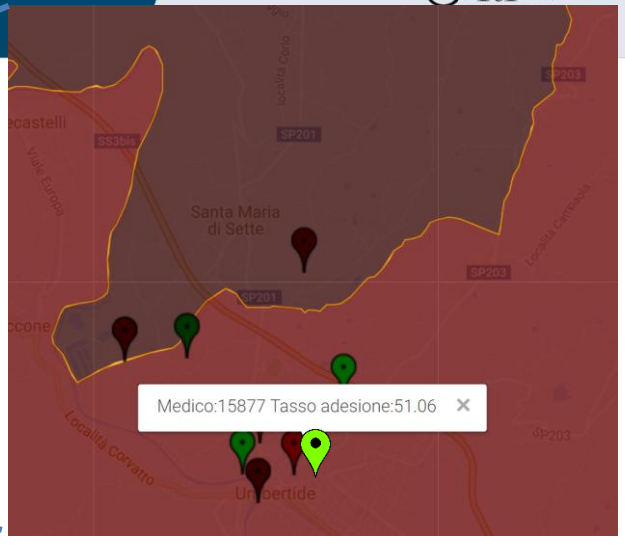
SAR

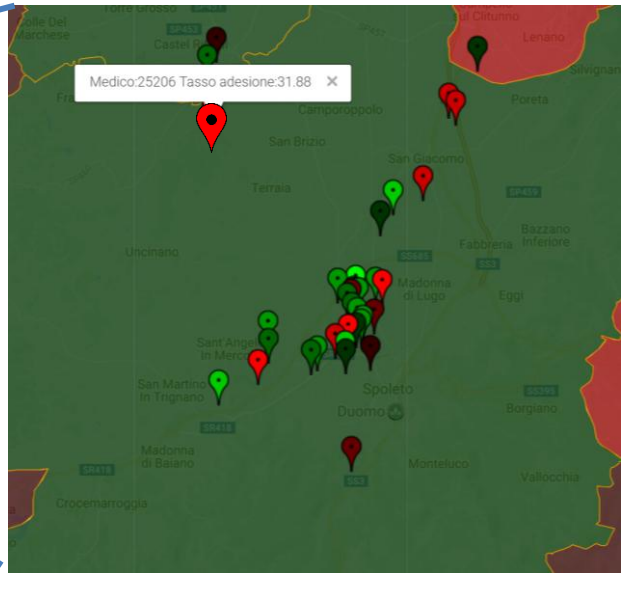


Rapporto grezzo ordinato SAR

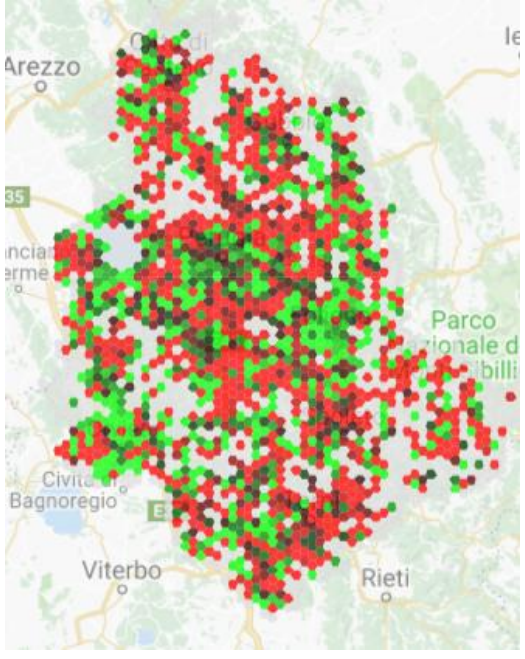


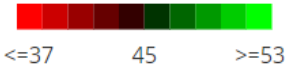




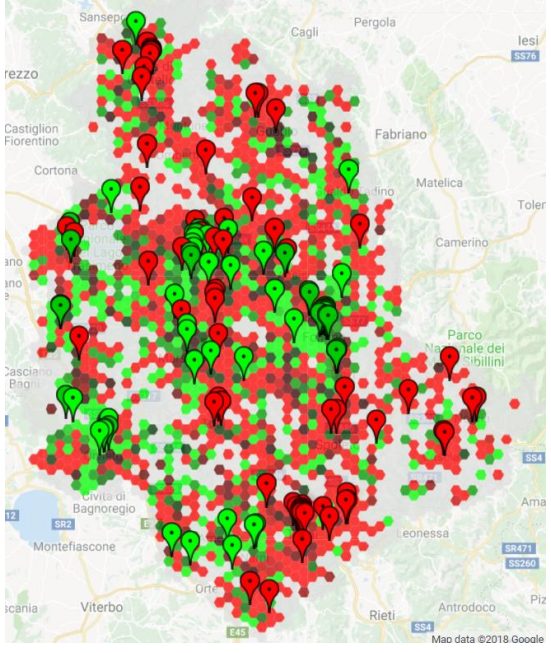


Tasso di adesione standardizzata per MMG, SAR-MMG aggiustato per sesso, età, deprivazione





MMG 65
MMG 78



51° CONGRESSO NAZIONALE SItI
RIVA DEL GARDA 17-20 OTTOBRE 2018

Il progetto IMPATTO

LA RICOSTRUZIONE DELLA STORIA INDIVIDUALE DI SCREENING MEDIANTE INCROCIO DELLE BASI DATI DEI SERVIZI E DEL REGISTRO TUMORI

IMPATTO

- Attraverso l'incrocio con gli archivi della popolazione invitata allo screening, per ogni donna e stata ricostruita l'intera storia di screening precedente alla diagnosi del tumore, con la prima data di invito e tutte le date dei test di screening eseguiti
- Mammella, colon retto, cervice, dati ad elevata risoluzione

51 CONGRESSO NAZIONALE SItI
RIVA DEL GARDA 17-20 OTTOBRE 2018

Decreasing Incidence of Late-Stage Breast Cancer After the Introduction of Organized Mammography Screening in Italy

Flavia Foca, BStat[1]; Silvia Mancini, BStat[1]; Lauro Bucchi, MD[1]; Donella Puliti, PhD[2]; Marco Zappa, MD[2]; Carlo Naldoni, MD[3]; Fabio Falcini, MD[1]; Maria L. Gambino, PhD[4]; Silvano Piffer, MD[5]; Maria E. Sanoja Gonzalez, PhD[6]; Fabrizio Stracci, MD, PhD[7]; Manuel Zorzi, MD[8]; Eugenio Paci, MD[2]; and the IMPACT Working Group

BACKGROUND: After the introduction of a mammography screening program, the incidence of late-stage breast cancer is expected to decrease. The objective of the current study was to evaluate variations in the total incidence of breast cancer and in the incidence of breast cancers with a pathologic tumor (pT) classification of pT2 through pT4 after the introduction of mammography screening in 6 Italian administrative regions. **METHODS:** The study area included 700 municipalities, with a total population of 692,824 women ages 55 to 74 years, that were targeted by organized mammography screening between 1991 and 2005. The year screening started at the municipal level (year 1) was identified. The years of screening were numbered from 1 to 8. The ratio of the observed 2-year, age-standardized (Europe) incidence rate to the expected rate (the incidence rate ratio [IRR]) was calculated. Expected rates were estimated assuming that the incidence of breast cancer was stable and was equivalent to that in the last 3 years before year 1. **RESULTS:** The study was based on a total of 14,447 incident breast cancers, including 4036 pT2 through pT4 breast cancers. The total IRR was 1.35 (95% confidence interval, 1.03-1.41) in years 1 and 2, 1.16 (95% confidence interval, 1.10-1.21) in years 3 and 4, 1.14 (95% confidence interval, 1.08-1.20) in years 5 and 6, and 1.14 (95% confidence interval, 1.08-1.21) in years 7 and 8. The IRR for pT2 through pT4 breast cancers was 0.97 (95% confidence interval, 0.90-1.04) in years 1 and 2, 0.81 (95% confidence interval, 0.75-0.88) in years 3 and 4, 0.79 (95% confidence interval, 0.73-0.87) in years 5 and 6, and 0.71 (95% confidence interval, 0.64-0.79) in years 7 and 8. **CONCLUSIONS:** A significant and stable decrease in the incidence of late-stage breast cancer was observed from the third year of screening onward, when the IRR varied between 0.81 and 0.71. ***Cancer*** **2013;119:2022-8.** © *2013 American Cancer Society.*

KEYWORDS: breast cancer, incidence, mammography, screening, tumor stage.

51 CONGRESSO NAZIONALE SItI
RIVA DEL GARDA 17-20 OTTOBRE 2018

Effectiveness of service screening: a case–control study to assess breast cancer mortality reduction

D Puliti[1], G Miccinesi[1], N Collina[2], V De Lisi[3], M Federico[4], S Ferretti[5], AC Finarelli[6], F Foca[7], L Mangone[8], C Naldoni[6], M Petrella[9], A Ponti[10], N Segnan[10], A Sigona[11], M Zarcone[12], M Zorzi[13], M Zappa[1] and E Paci[*,1], the IMPACT Working Group

The aim of this study was the evaluation of the impact of service screening programmes on breast cancer mortality in five regions of Italy. We conducted a matched case–control study with four controls for each case. Cases were defined as breast cancer deaths occurred not later than 31 December 2002. Controls were sampled from the local municipality list and matched by date of birth. Screening histories were assessed by the local, computerised, screening database and subjects were classified as either invited or not-yet-invited and as either screened or unscreened. There were a total of 1750 breast cancer deaths within the 50 to 74-year-old breast cancer cases and a total of 7000 controls. The logistic conditional estimate of the cumulative odds ratios comparing invited with not-yet-invited women was 0.75 (95% CI: 0.62–0.92). Restricting the analyses to invited women, the odds ratio of screened to never-respondent women corrected for self-selection bias was 0.55 (95% CI: 0.36–0.85). The introduction of breast cancer screening programmes in Italy is associated with a reduction in breast cancer mortality attributable to the additional impact of service screening over and above the background access to mammography.

British Journal of Cancer (2008) **99,** 423–427. doi:10.1038/sj.bjc.6604532 www.bjcancer.com

La ricostruzione della storia individuale di screening

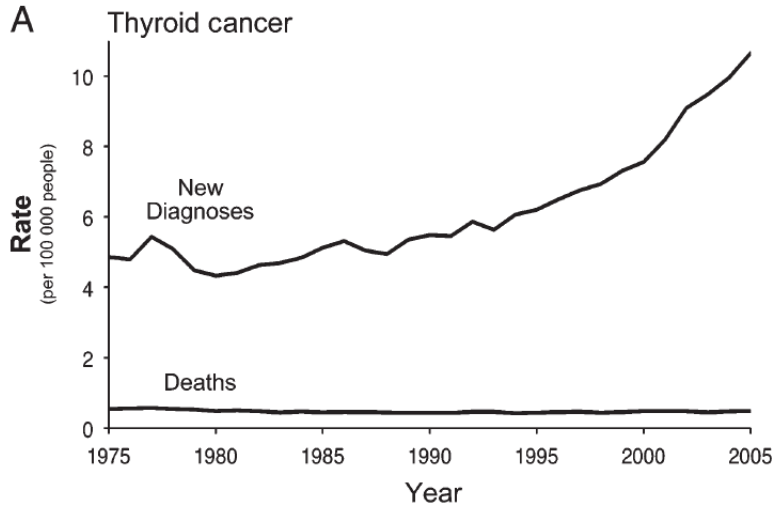
- È stata utile per la ricerca, dato che si è basata su dati storici
- Potrebbe avvenire con una relazione di scambio dati in tempo reale (*richiede la pre-registrazione o registrazione rapida*)
- *La costruzione di un sistema informativo intelligente (incluso RT) per il dipartimento oncologico dovrebbe consentire*
  - *La produzione tempestiva di indicatori di valutazione*
  - *La definizione condivisa nel dipartimento oncologico degli obiettivi*

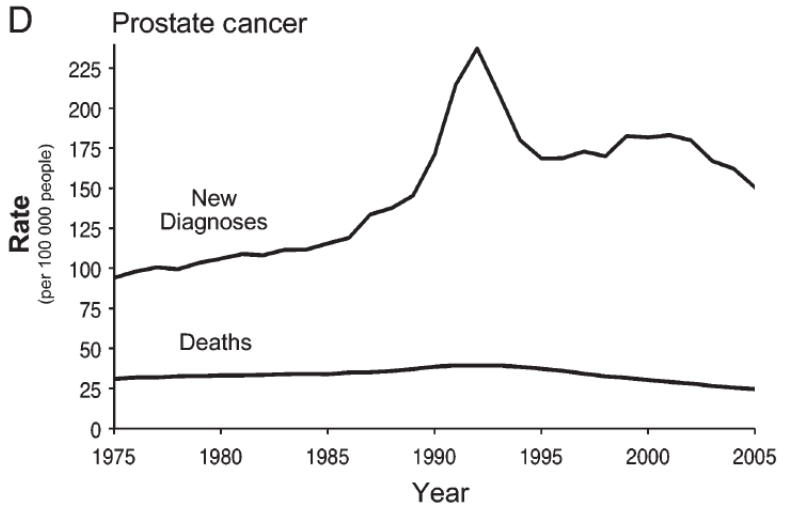
51° CONGRESSO NAZIONALE SItI
RIVA DEL GARDA 17-20 OTTOBRE 2018

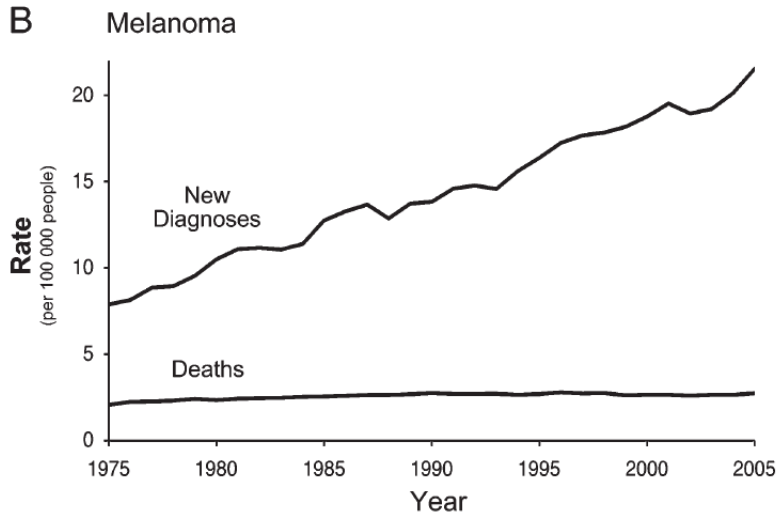
LA SANITA' PUBBLICA E GLI SCREENING IN-ORGANIZZATI O INCONTROLLATI

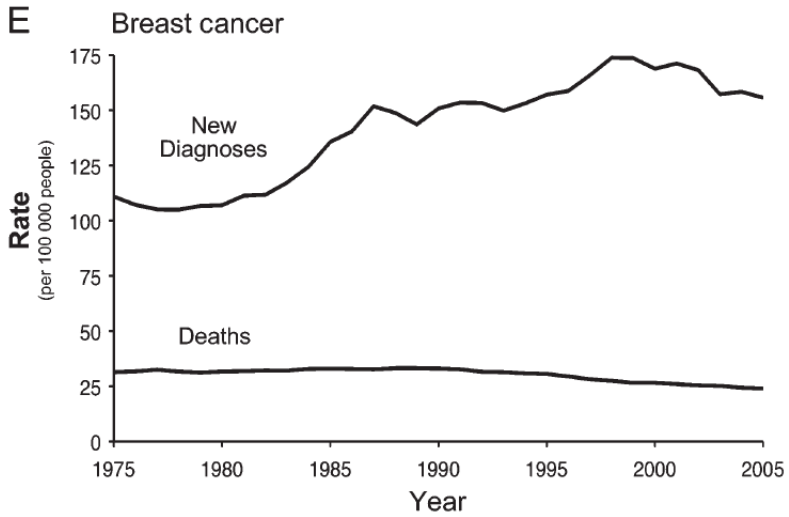
Overdiagnosis in Cancer

H. Gilbert Welch, William C. Black J Natl Cancer Inst 2010;102:605–613









Worldwide Thyroid-Cancer Epidemic? The Increasing Impact of Overdiagnosis

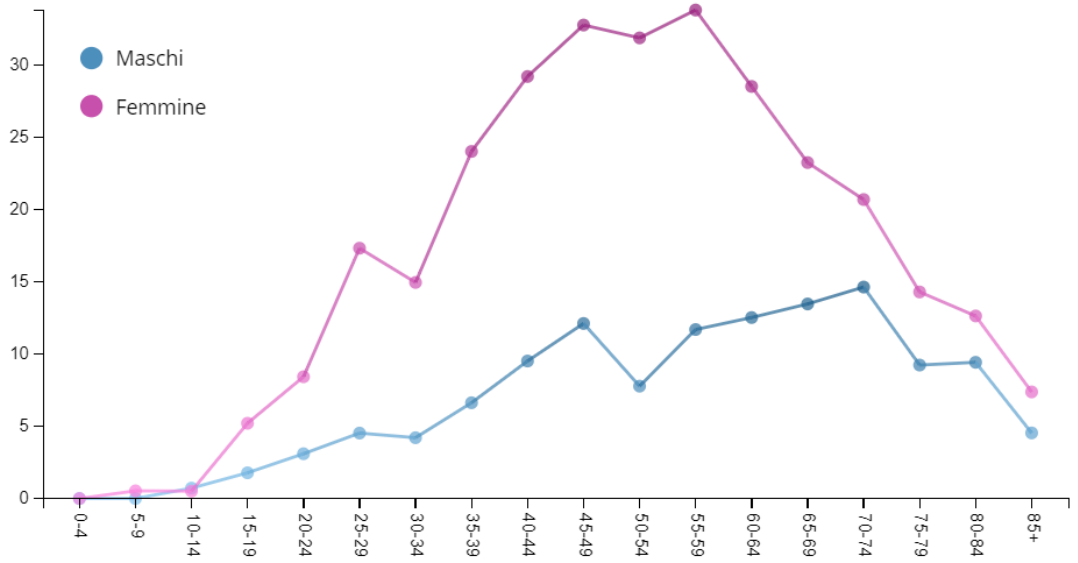
Salvatore Vaccarella, Ph.D., Silvia Franceschi, M.D., Freddie Bray, Ph.D., Christopher P. Wild, Ph.D., Martyn Plummer, Ph.D., and Luigino Dal Maso, Ph.D.

Observed versus Expected Changes in Age-Specific Incidence of Thyroid Cancer per 100,000 Women, 1988–2007. The expected rates were based on the observation that before the introduction of ultrasonography and other novel diagnostic techniques, thyroid cancer incidence increased exponentially with age in all countries with available long-term data, in keeping with the multistage model of carcinogenesis (rate proportional to age k, where the exponent k is to be estimated from incidence data).

Tassi età specifici in Umbria

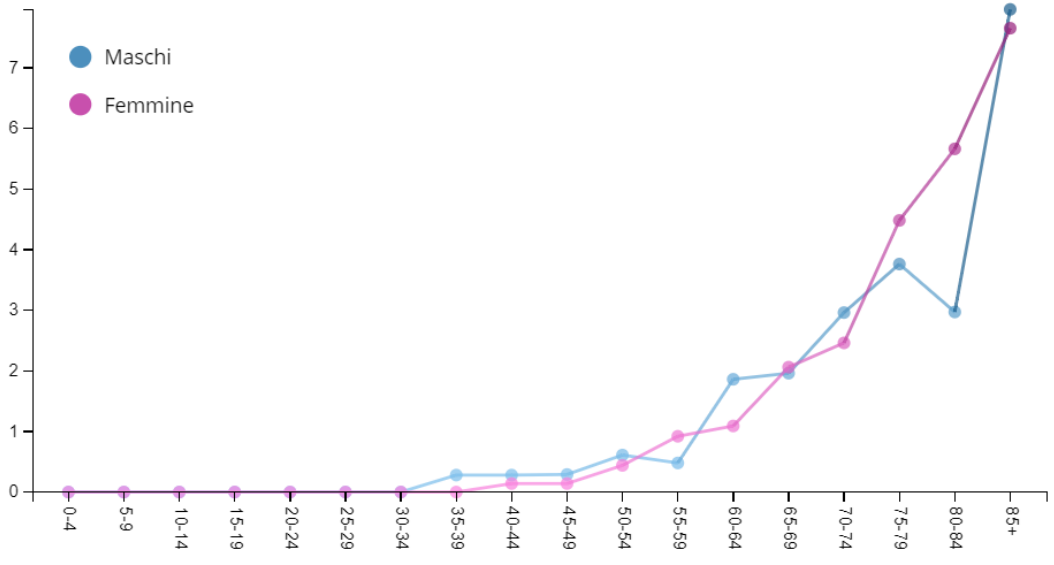
Tasso di incidenza per sesso e classi di età - tiroide 1994-2015

Tasso per 100.000 abitanti - Popolazione standard Italia 2011



Tasso di mortalità per sesso e classi di età - tiroide 1994-2016

Tasso per 100.000 abitanti - Popolazione standard Italia 2011



Variabilità dell'incidenza del cancro della tiroide

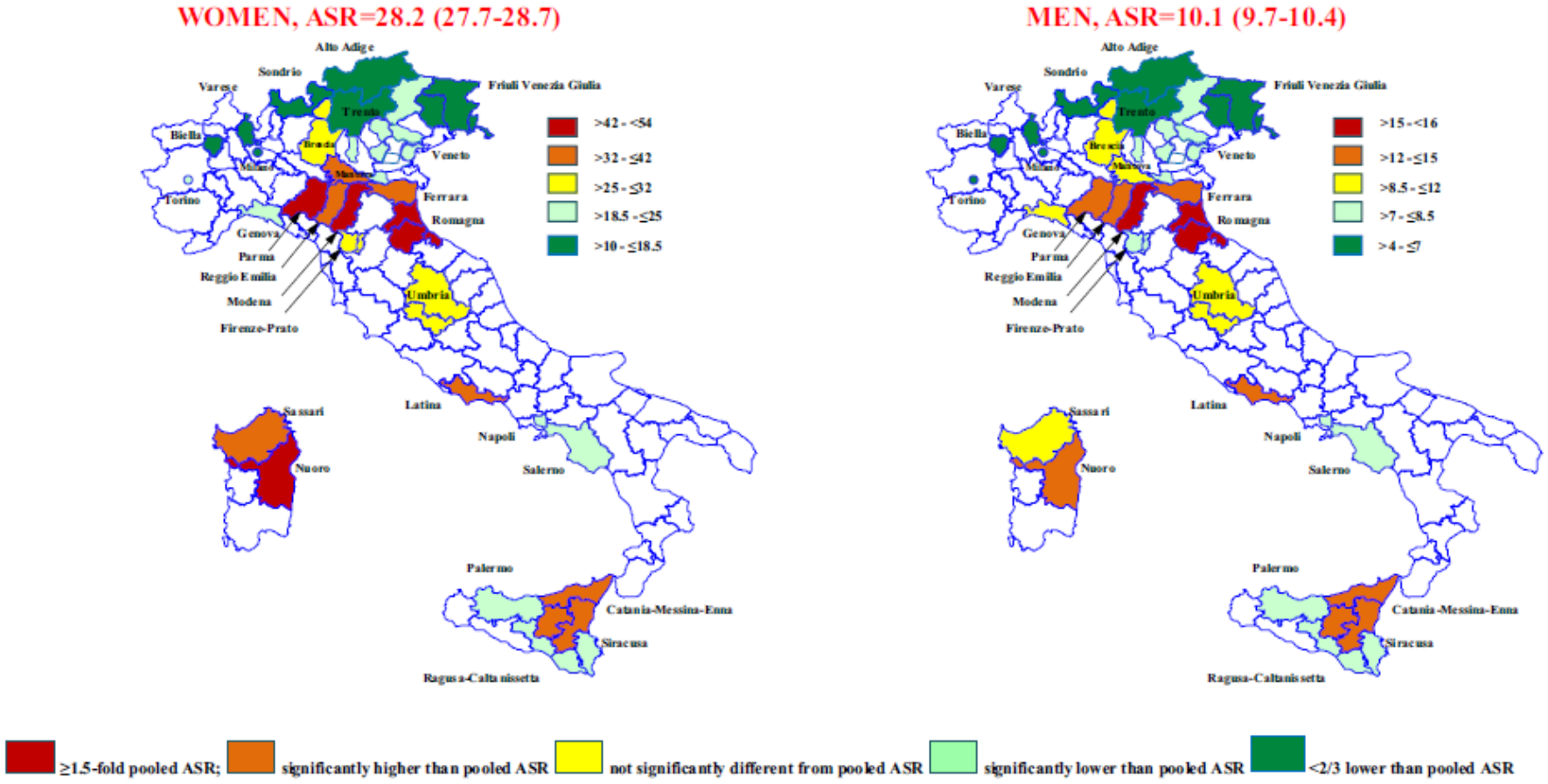


Fig. 1. Age-standardised incidence rates (ASR) (Per 100,000 age standardised to the Italian Population [2008]) and 95% confidence intervals for thyroid cancer by sex, Italy, 2008–2012, age 0–84 years.

The impact of overdiagnosis on thyroid cancer epidemic in Italy 1998-2012. Dal Maso L et al. *European Journal of Cancer (2018)*

Carcinoma tiroideo occulto

"…They (Harach et al.) went on to calculate that, if sectioned finely enough, virtually every person would be found to harbor a thyroid cancer."

Davies L, Welch HG. **Increasing incidence of thyroid cancer in the United States, 1973-2002**. *JAMA*. 2006;295:2164-7.

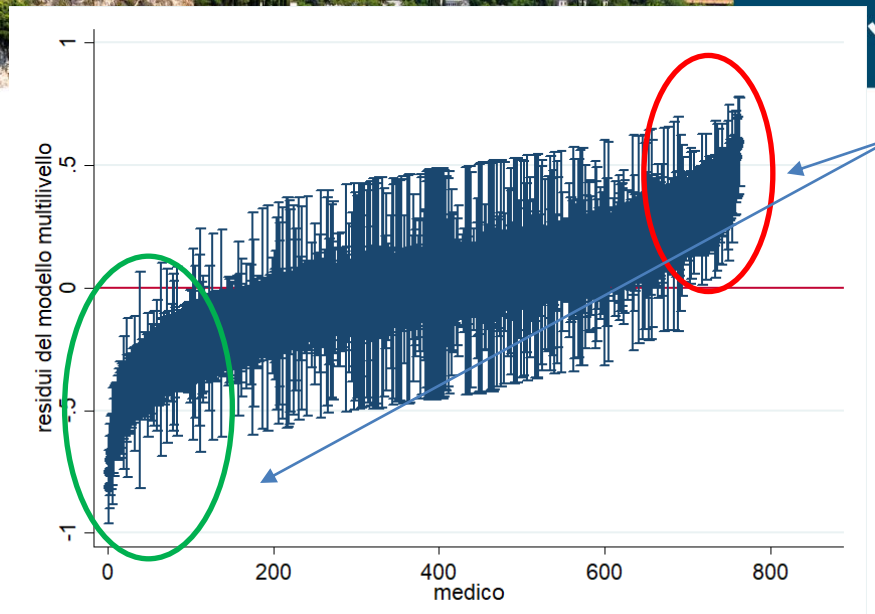
Harach HR,FranssilaKO,WaseniusVM. **Occult papillary carcinoma of the thyroid: a "normal" finding in Finland**. Cancer. 1985;56:531-538.

Table 1. Estimated size of the disease reservoir for three cancers, the lifetime risk of death or metastatic disease, and the probability of overdiagnosis where the entire disease reservoir detected

Cancer	Population	% With cancer (disease reservoir) (*a*)	Lifetime risk of death or metastatic disease* (*b*), %	Probability of overdiagnosis where entire disease reservoir detected† ($c = [a - b]/a$), %
Prostate	Men older than 60 y	30–70	4	87–94
Thyroid	Adults aged 50–70 y	36–100	0.1	99.7–99.9
Breast	Women aged 40–70 y	7–39	4	43–90

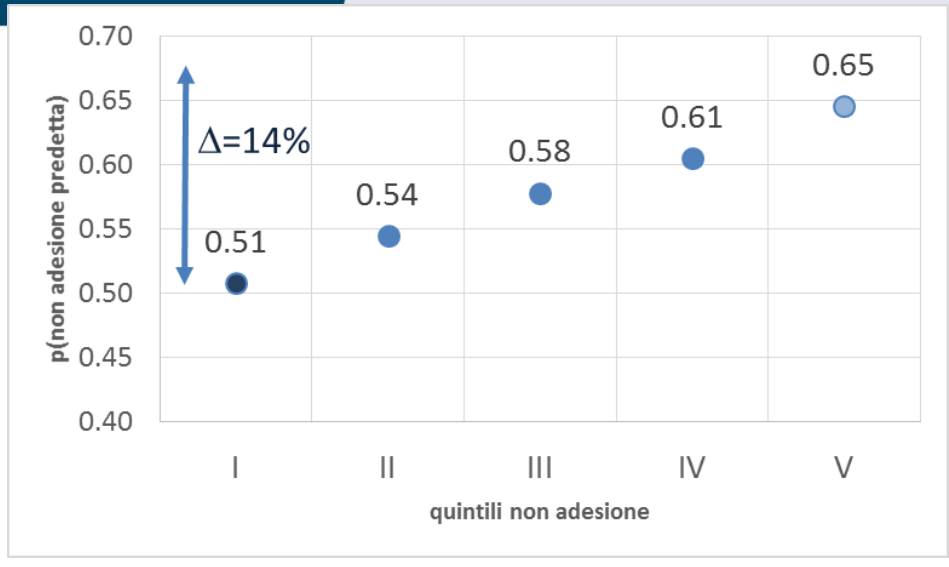
Se individuassimo tutti i cancri occulti avremmo una sovradiagnosi del **99.7-99.9%**

FINE



Alcuni medici sono significativamente sotto o sopra la media di adesione

Tra il quintile con la migliore adesione e quello con la peggiore vi è una differenza del **14%**



	Stima (%)	95% Int. Conf.
VPC Varianza spiegata dalla nazionalità	3.8	2.7-5.5
VPC Varianza residua medico di famiglia	4.1	3-5.7
LR test vs effetti fissi	p<0.0001	-

$$VPC = \frac{\sigma_u^2}{\sigma_u^2 + \sigma_{e^*}^2}$$ where $\sigma_{e^*}^2$ = 1 for a probit model and 3.29 for a logit model.

Il 3,8% della variabilità è spiegata dalla nazionalità degli assistibili all'interno dei singoli cluster (assistibili del MMG)

Rimane un 4,1% di variabilità legata a caratteristiche non osservate del medico di famiglia