# Evidenze nazionali e internazionali di impatto degli screening

Marco Zappa

ISTITUTO PER LO STUDIO
E LA PREVENZIONE ONCOLOGICA

# Cosa vogliamo valutare quando parliamo di “impatto”

Se i programmi di screening organizzato hanno determinato una modificazione dell’incidenza e/o della mortalità per cancro colorettale

# Evidenze nazionali e internazionali

Screening con ricerca del sangue occulto fecale
(Guaiaco e Immunologico)

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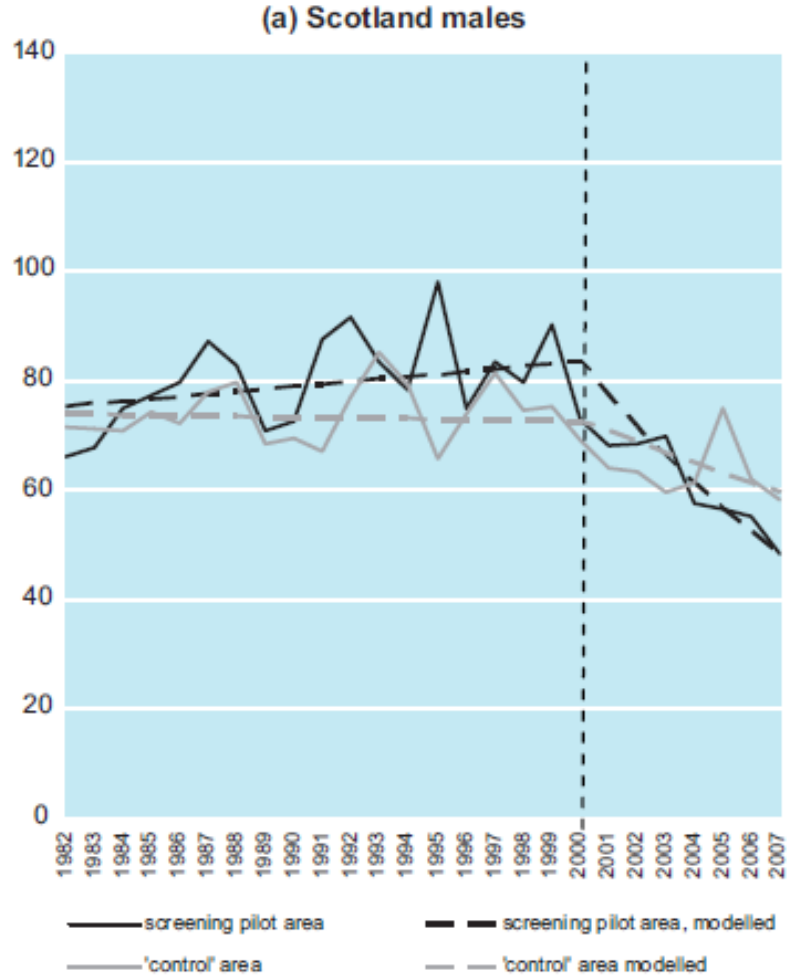
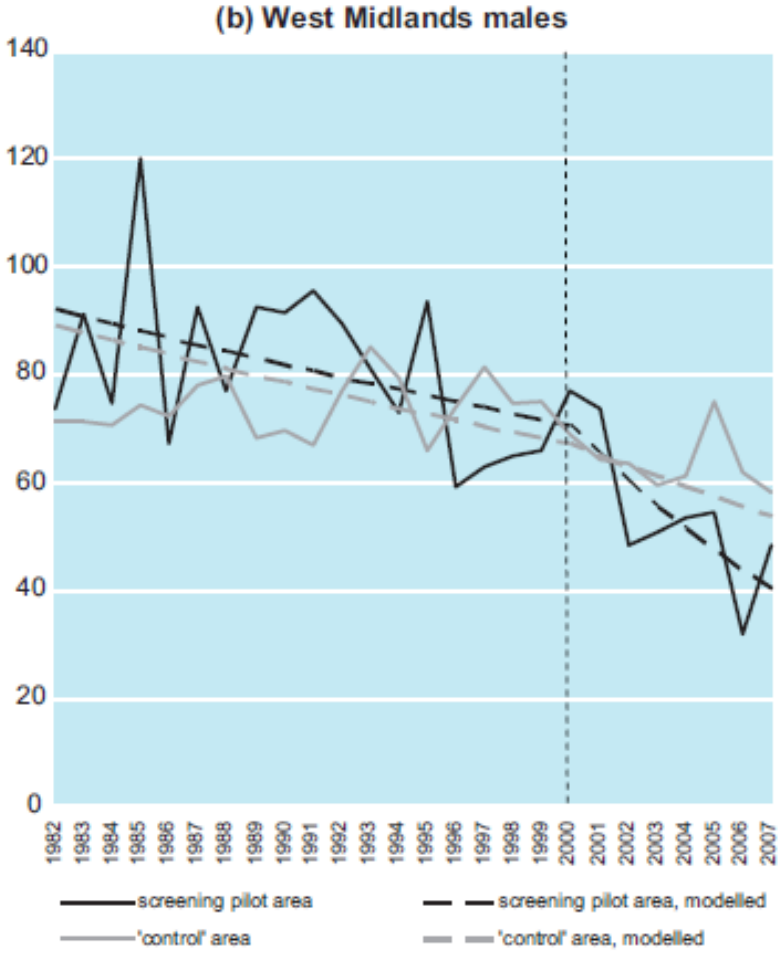
# Impact of the UK colorectal cancer screening pilot studies on incidence, stage distribution and mortality trends

Paula L. McClements [a,*], Vichithranie Madurasinghe [b,1], Catherine S. Thomson [b,1], Callum G. Fraser [c], Francis A. Carey [d], Robert J.C. Steele [e], Gill Lawrence [f], David H. Brewster [a,g]

*Objective*: To assess the impact of the UK colorectal cancer guaiac faecal occult blood test screening pilot studies on incidence trends, stage distribution and mortality trends. *Design*: Ecological study. *Setting*: Scotland and the West Midlands. *Data*: We extracted anonymised colorectal cancer (ICD-10 C18–C20) registration (1982–2006) and death records (1982–2007), along with corresponding mid-year population estimates. *Intervention*: Residents of the screening pilot areas, in the age group 50–69 years, were offered biennial guaiac faecal occult blood test screening from 2000 onwards. Screening was not offered routinely in non-pilot areas until the start of the roll-out of the national screening programmes in England and in Scotland in 2006 and 2007, respectively. *Main outcome measures*: We analysed trends in age-specific incidence and mortality rates, and Dukes' stage distribution. Within each country/region, we compared the screening pilot areas to non-screening pilot ('control') areas using Chi square tests and Poisson regression modelling. *Results*: Following the start of the screening pilots, as




In Scotland, for males in 2007, the difference in the modelled mortality rates between the two groups was 18.9% (modelled rate 48.4 per 100,000 in pilot study area compared with 59.7 in non-pilot study area); in the West Midlands, the corresponding difference was 24% (modelled rate 40.4 per 100,000 in pilot study area compared with 53.9 in non-pilot study area).

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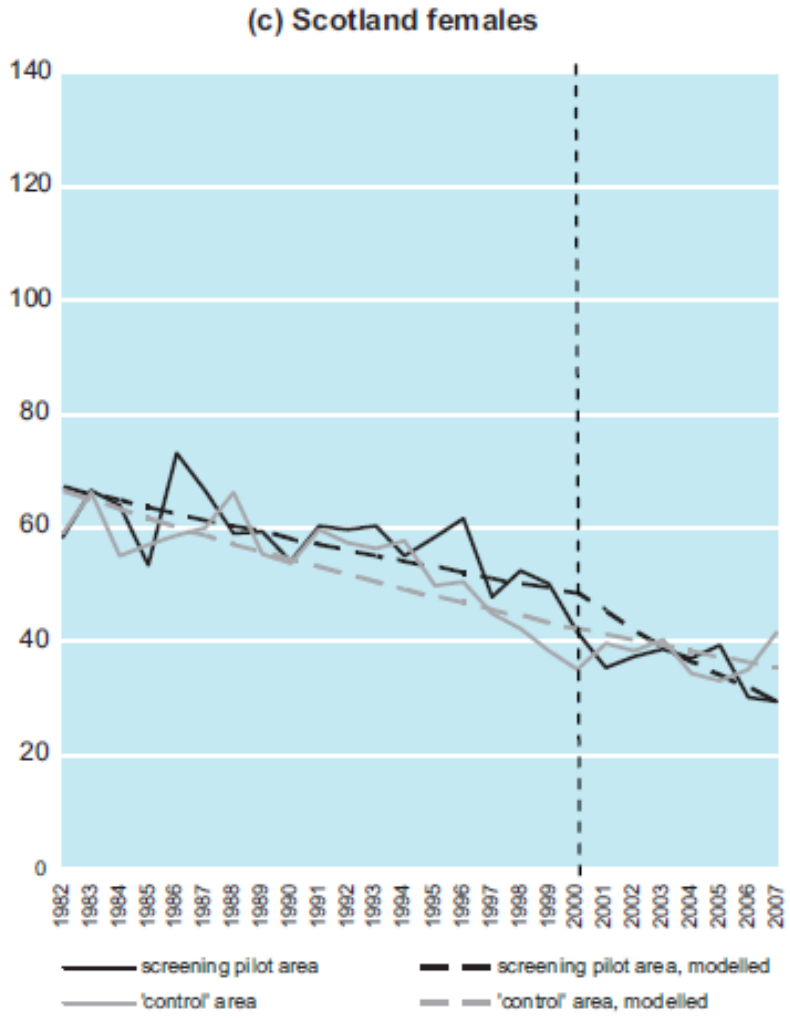
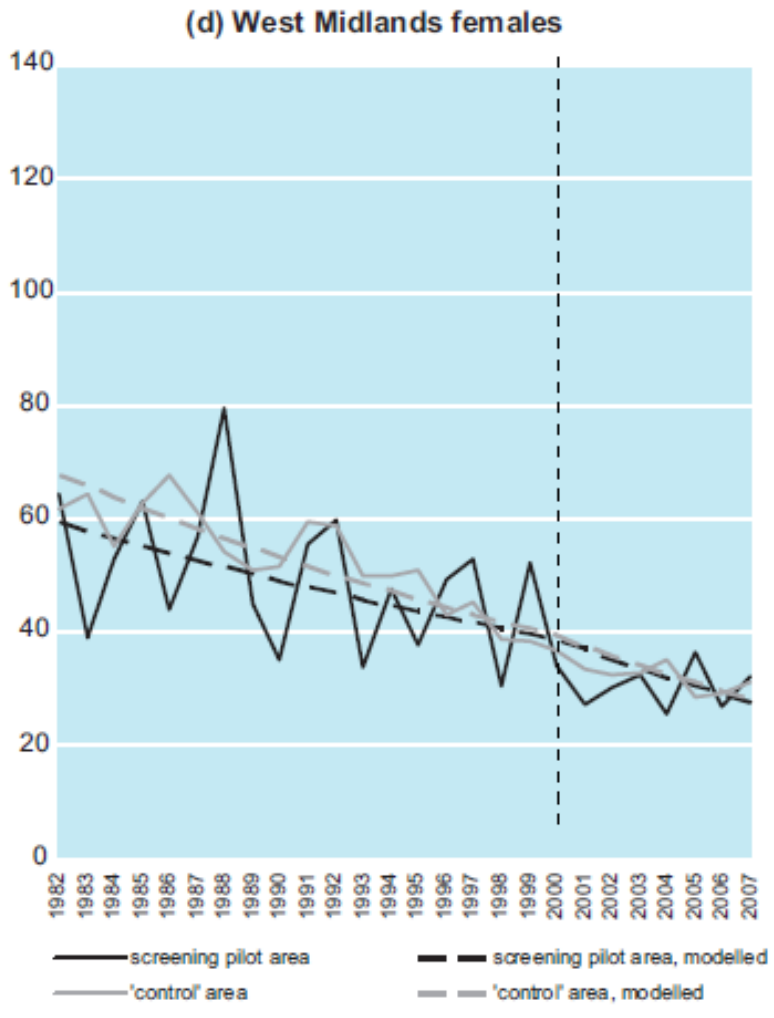


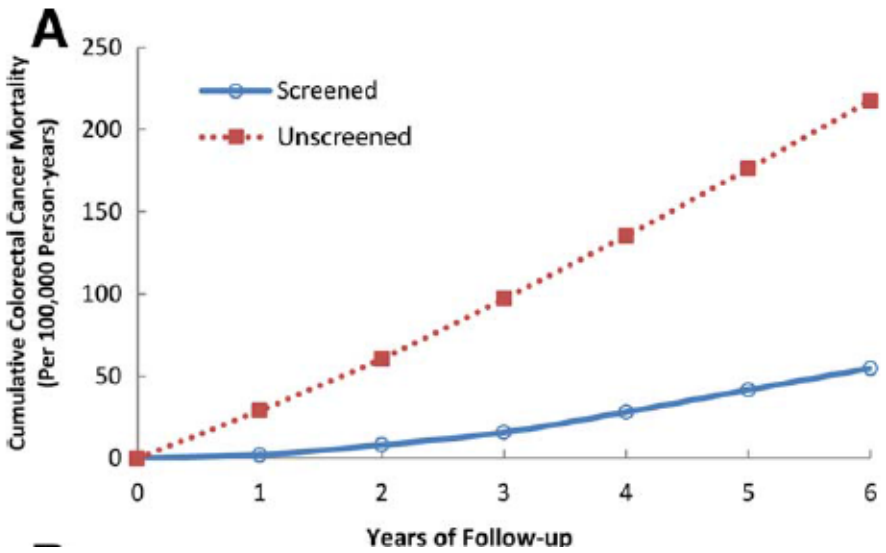

For Scottish females, the equivalent difference in modelled mortality rates in 2007 was 16.7% (modelled rate 29.4 per 100,000 in pilot study area compared with 35.4 in non pilot study area). There was, however, no significant effect in females in the West Midlands, a difference of only 2.1% (modelled rate 27.8 per 100,000 in pilot study area compared with 28.4 in non pilot study area).

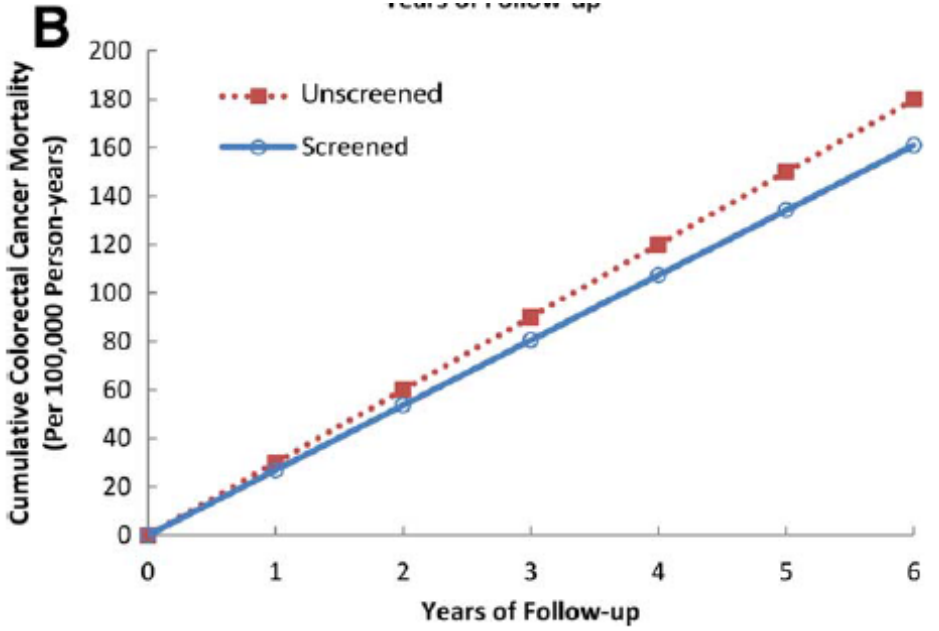
Cancer Month 00, 2015

# Effectiveness of Fecal Immunochemical Testing in Reducing Colorectal Cancer Mortality From the One Million Taiwanese Screening Program

Han-Mo Chiu, PhD[1]; Sam Li-Sheng Chen, PhD[2]; Amy Ming-Fang Yen, PhD[2]; Sherry Yueh-Hsia Chiu, PhD[3]; Jean Ching-Yuan Fann, PhD[4]; Yi-Chia Lee, MD, PhD[1]; Shin-Liang Pan, MD, PhD[5]; Ming-Shiang Wu, MD, PhD[1]; Chao-Sheng Liao, MD, PhD[6]; Hsiu-Hsi Chen, PhD[7]; Shin-Lan Koong, PhD[8]; and Shu-Ti Chiou, PhD[8,9]

**BACKGROUND:** The effectiveness of fecal immunochemical testing (FIT) in reducing colorectal cancer (CRC) mortality has not yet been fully assessed in a large, population-based service screening program. **METHODS:** A prospective cohort study of the follow-up of approximately 5 million Taiwanese from 2004 to 2009 was conducted to compare CRC mortality for an exposed (screened) group and an unexposed (unscreened) group in a population-based CRC screening service targeting community residents of Taiwan who were 50 to 69 years old. Given clinical capacity, this nationwide screening program was first rolled out in 2004. In all, 1,160,895 eligible subjects who were 50 to 69 years old (ie, 21.4% of the 5,417,699 subjects of the underlying population) participated in the biennial nationwide screening program by 2009. **RESULTS:** The actual effectiveness in reducing CRC mortality attributed to the FIT screening




The RR of cumulative CRC mortality between 2004 and 2009 for the screened subjects versus the unscreened ones was 0.38 (95% confidence interval, 0.35-0.42), and this yielded a significant 62% effectiveness of reducing deaths from CRC. The mortality rates were 13.77 per 100,000 persons in the screened group and 36.31 per 100,000 persons in the unscreened group. Figure 2A shows the difference in the corresponding cumulative CRC mortality curves for the screened and unscreened groups without adjustments for the self-selection bias.

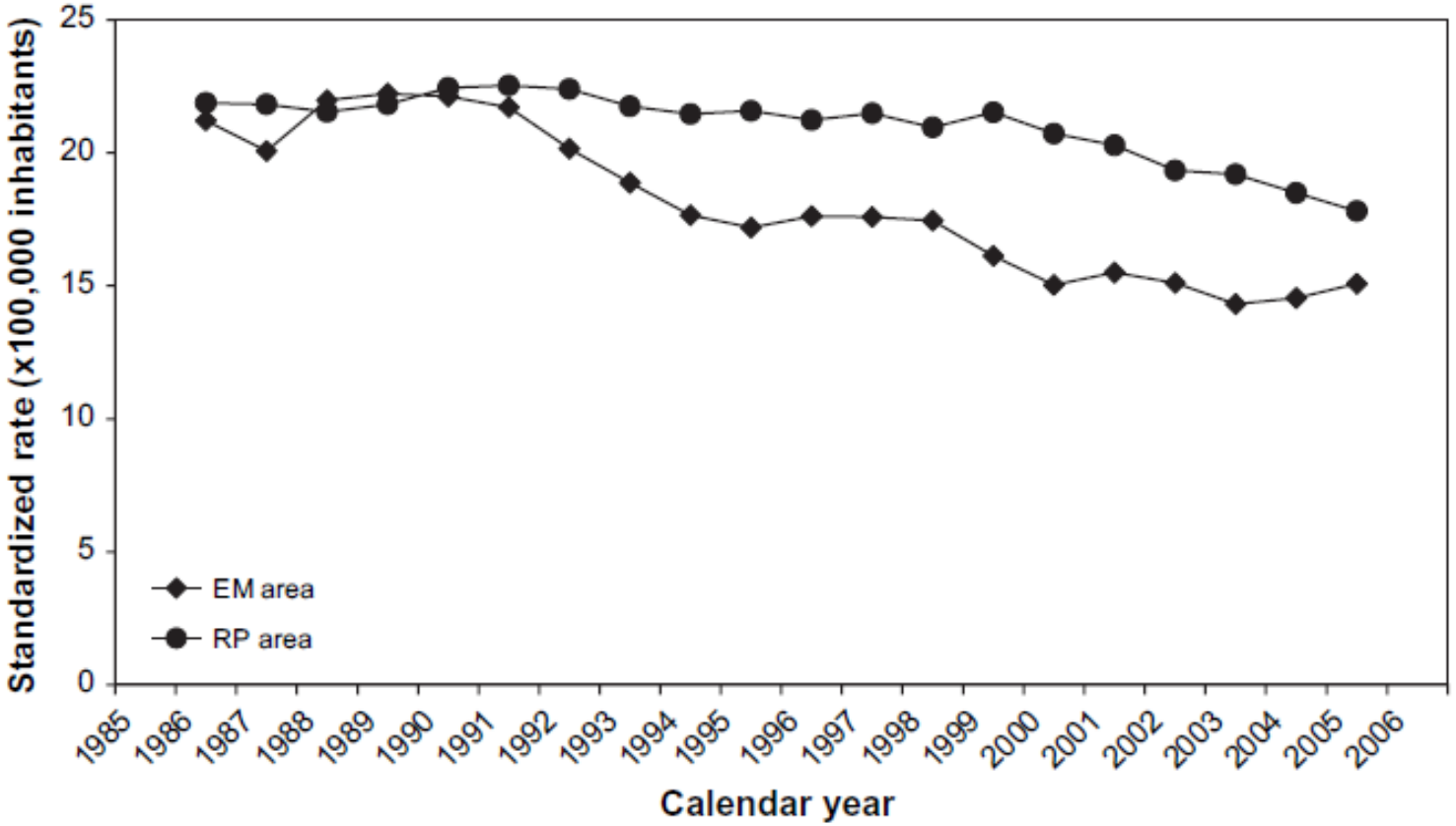
It is interesting to note that the RR of cumulative mortality between the invited and uninvited groups was 0.90 (95% confidence interval, 0.84-0.95) with adjustments for the self-selection bias and CRC incidence change. This suggests a significant 10% mortality reduction from CRC attributable to the 21.4% coverage of the FIT screening. Figure 2B shows a comparison of the 2 curves with adjustments for the self-selection bias.

# Colorectal Cancer Mortality in Two Areas of Tuscany With Different Screening Exposures

Adele Seniori Costantini, Andrea Martini, Donella Puliti, Stefano Ciatto, Guido Castiglione, Grazia Grazzini, Marco Zappa

**J Natl Cancer Inst 2008;100:1818–1821**

**an evaluation of population-based screening programs is still lacking. We compared the colorectal cancer mortality rates (both adjusted rates and 3-year moving average rates) during 1985–2006 for two geographic areas in the provinces of Florence and Prato in the Tuscany region of Italy that began active population-based screening for colorectal cancer at different times: the Empolese–Mugello district, in the early 1980s, and the rest of the Florence and Prato provinces, in early 2000. A log-linear Poisson**




whether geographic area modified the effect of calendar year on it. The Empolese–Mugello district had a greater decrease in colorectal cancer mortality than the rest of the Florence and Prato provinces (estimated annual percent change in age-adjusted colorectal cancer mortality rate, 2.7% decrease per year [95% confidence interval {CI} = 1.7% to 3.7%] vs 1.3% decrease per year [95% CI = 0.8% to 1.7%], respectively). The interaction between calendar period and area was statistically

*Gut* 2015;**64**:784–790.

# Impact on colorectal cancer mortality of screening programmes based on the faecal immunochemical test

Manuel Zorzi,[1] Ugo Fedeli,[2] Elena Schievano,[2] Emanuela Bovo,[1] Stefano Guzzinati,[1] Susanna Baracco,[1] Chiara Fedato,[1] Mario Saugo,[2] Angelo Paolo Dei Tos[1,3]

**Design** In the Veneto Region (Italy), biennial FIT-based screening programmes that invited 50–69-year-old residents were introduced in different areas between 2002 and 2009. We compared CRC mortality rates from 1995 to 2011 between the areas where screening started in 2002–2004 (early screening areas (ESA)) and areas that introduced the screening in 2008–2009 (late screening areas (LSA)) using Poisson regression models. We also compared available data on CRC incidence rates (1995–2007) and surgical resection rates (2001–2012).

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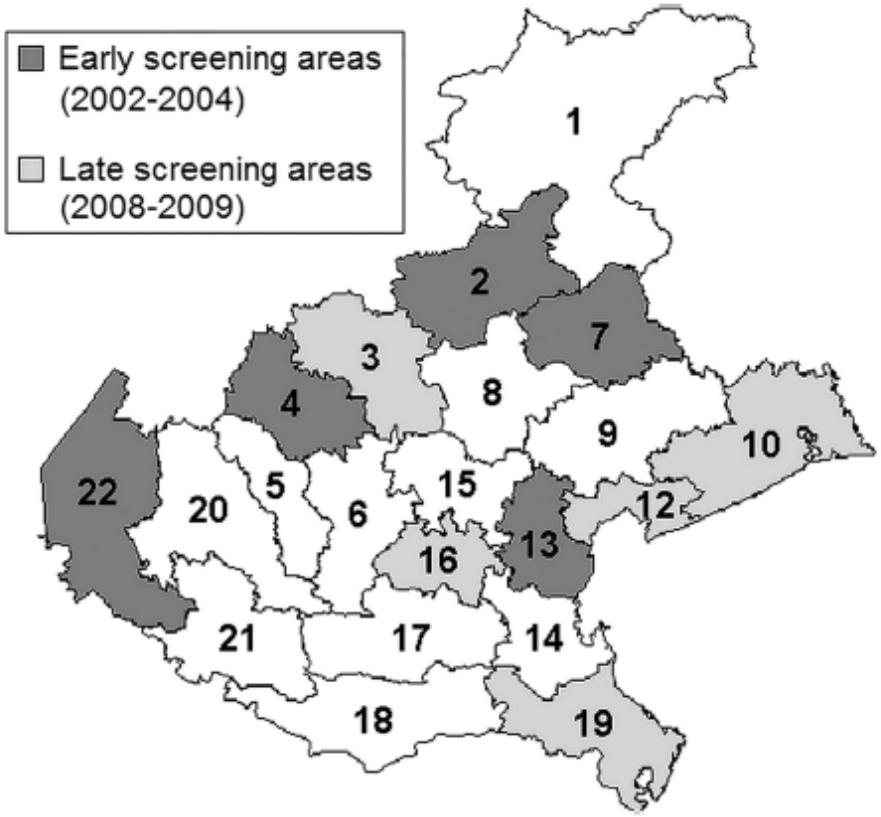
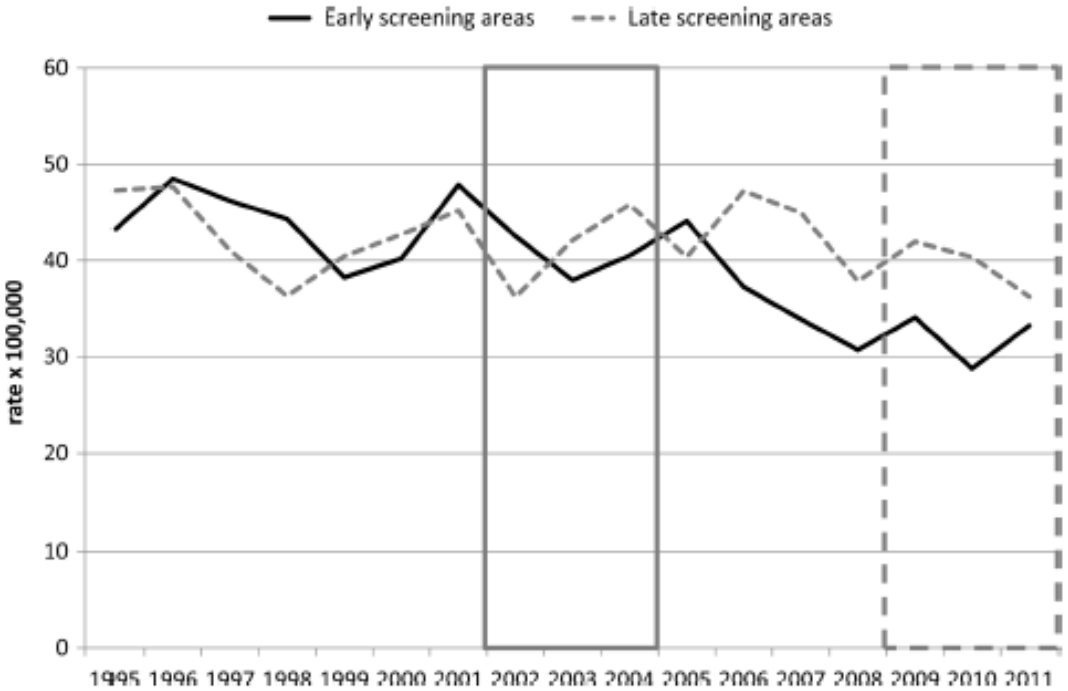
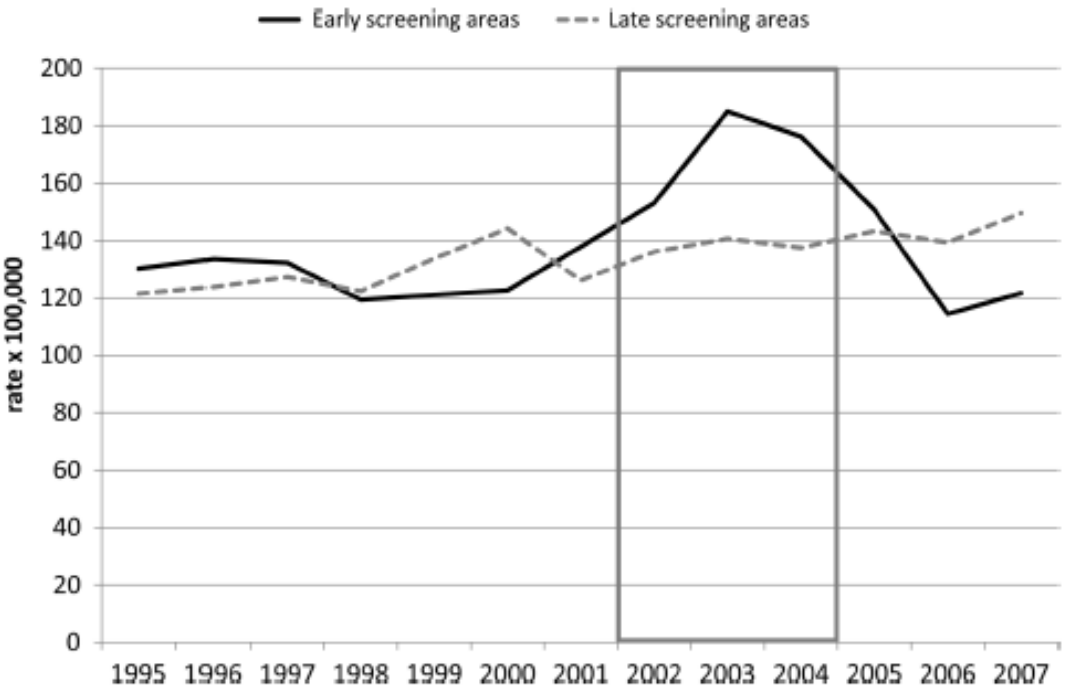



**Figure 1** Map of local health units of the Veneto Region by period of activation of a colorectal screening programme.

FIT screening programmes were established in different LHUs between 2002 and 2009. The LHUs where screening was set up in 2002–2004 were classified as 'early screening areas' (ESA) and those where screening started in 2008–2009 as 'late screening areas' (LSA). All the following analyses have been restricted to the ESA and the LSA, thus excluding LHUs that instituted screening programmes between 2005 and 2007.




In the ESA, mortality rates in 2006–2011 were compared with those observed in 1995–2000 and showed an overall decline of 24% (22% in men and 32% in women). In the LSA, a smaller decrease was observed among men, whereas mortality among women remained almost unchanged. Figure 3 shows that mortality (both genders combined) was similar at the beginning of the study period, whereas after the introduction of the screening programmes, the rates observed in the ESA fell below the values registered in the LSA.




Incidence rates were available for only part of the LHUs included in the ESA and the LSA. They showed a major peak during the introduction of screening programmes in the ESA, and then returned to the baseline in 2006–2007, which are the last years with incidence figures. The incidence rates in the LSA increased progressively between 1995 and 2007 (figure 4).

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Oncology

# The impact of immunochemical faecal occult blood testing on colorectal cancer incidence

Leonardo Ventura, Paola Mantellini, Grazia Grazzini, Guido Castiglione, Carlotta Buzzoni, Tiziana Rubeca, Claudio Sacchettini, Eugenio Paci, Marco Zappa*

*Cancer Prevention and Research Institute, Florence, Italy*

*Methods:* Two cohorts were analyzed: subjects who underwent an initial faecal immunochemical test between 1993 and 1999 ("attenders"), and unscreened residents in the same municipalities invited to perform the faecal immunochemical test in the same period ("non-attenders"). Kaplan–Meier and Cox regression analysis were performed to evaluate the risk of developing colorectal cancer.

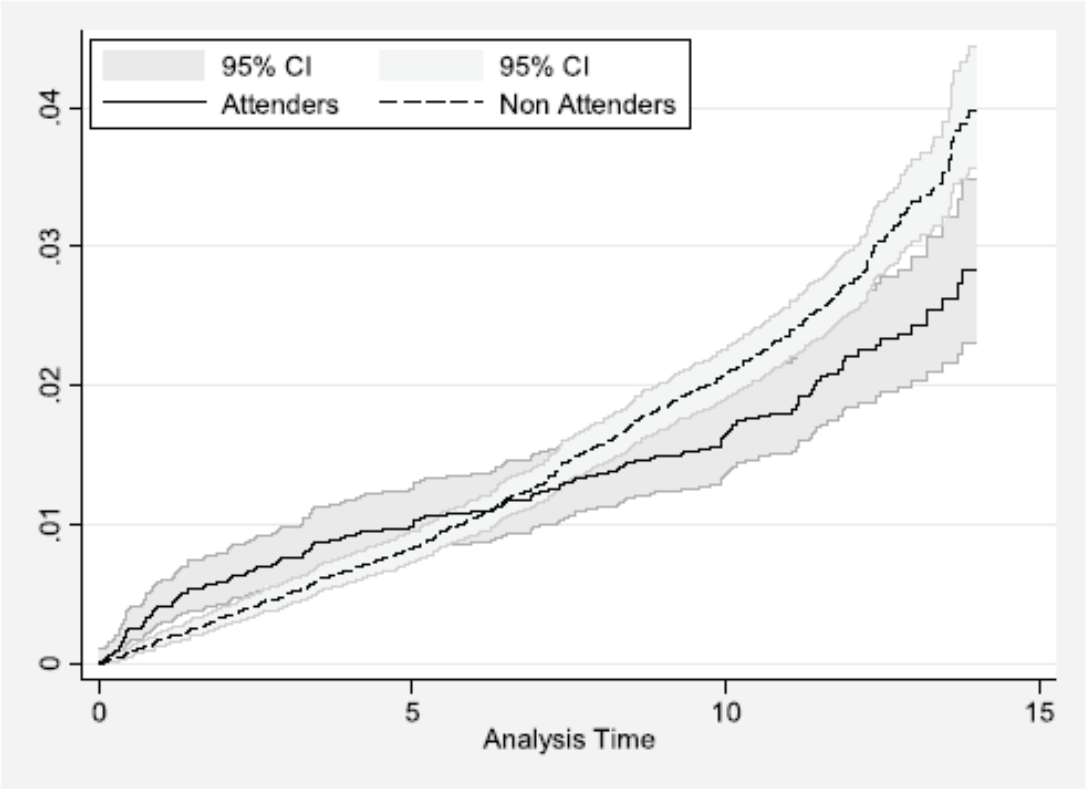


**Fig. 2.** Colorectal cancer Cumulative Incidence (%) for the attenders' (6961 subject and 78,027 person years) and non-attenders' (26,285 subject and 277,878 person years) cohorts.

**Table 1**
Hazard ratios of developing a Colorectal Cancers for attenders versus non-attenders subjects. Cox model during the entire time period.

| | HR | 95% CI |
|---|---|---|
| Non-attenders | Ref. | |
| Attenders | 0.78 | 0.65–0.93 |
| Males | Ref. | |
| Females | 0.55 | 0.48–0.63 |
| ≤54 years | Ref. | |
| 55–59 years | 1.39 | 1.12–1.73 |
| 60–64 years | 1.67 | 1.35–2.06 |
| ≥65 years | 2.60 | 2.14–3.17 |

Prima del catch-up

HR = 1.12

95% CI: 0.87-1.44

Dopo il catch-up

HR = 0.57

95% CI: 0.43-0.75

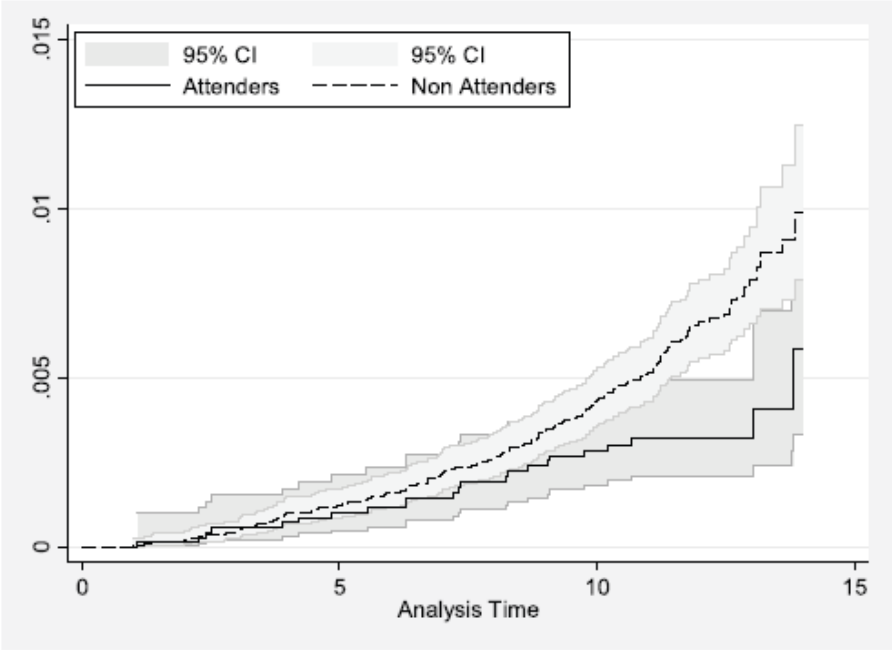


**Fig. 3.** Colorectal cancer Cumulative Mortality (%) for the attenders' (6961 subject and 80,808 person years) and non-attenders' (26,285 subject and 286,675 person years) cohorts.

Comparison of the mortality for CRCs in the 2 cohorts showed a significant reduction of CRC mortality in the attenders' cohort as compared to the non-attenders' cohort (SMR = 0.59, 95% CI: 0.37–0.93).

The Kaplan–Meier estimates (Fig. 3) showed the cumulative risk of death from CRC of the attenders' and non-attenders' cohorts. The mortality risk seemed to be similar in the 2 cohorts for the first 5 years of follow-up; thereafter the risk of the non-attenders increased more rapidly than that of the attenders.

# Impact of Screening Program on Incidence of Colorectal Cancer: A Cohort Study in Italy

Paolo Giorgi Rossi, PhD[1,2], Massimo Vicentini, MSc[1,2], Claudio Sacchettini, MSc[1,2], Enza Di Felice, MSc[1,2], Stefania Caroli, MSc[1,2], Francesca Ferrari, MSc[1,2], Lucia Mangone, MD[1,2], Annamaria Pezzarossi, MSc[1,2], Francesca Roncaglia, PhD[1,2], Cinzia Campari, MSc[2,3], Romano Sassatelli, MD[4], Roberto Sacchero, MD[5], Giuliana Sereni, MD[4], Luisa Paterlini, MD[3] and Marco Zappa, MD[6]

*Am J Gastroenterol* advance online publication, 25 August 2015;

**An organized screening program was implemented in 2005 in the province of Reggio Emilia (Northern Italy). The program invites the resident population aged 50–69 for FIT every 2 years. Subjects who test positive are referred for colonoscopy. Incidence was studied through cancer registry. Person-times of people aged 50–74 from 1997 to 2012 were classified for exposure to screening according to age and period. Furthermore, two open cohorts—one never screened (aged 50–69 in 1997) and one invited for screening (aged 50–69 in 2005)—were followed up for 8 years.**

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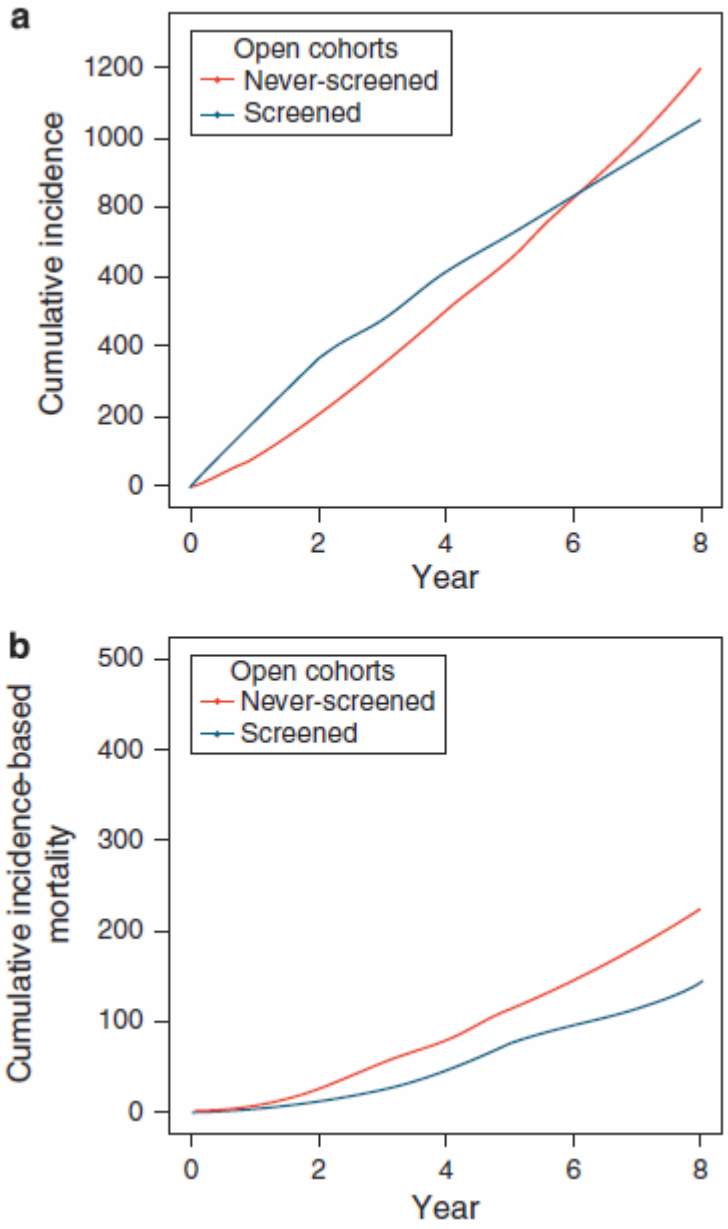
# Incidence rate according to screening period

**Table 2. Colorectal cancers, person years, and IRRs with 95% CI by sex, age, and screening exposure**

| Exposure definition | Cases | Person - years | IRR | 95% CI |
|---|---|---|---|---|
| *Sex* | | | | |
| Men | 1,760 | 1,032,392 | 1 | |
| Women | 1,136 | 1,100,102 | 0.58 | (0.55–0.63) |
| Age (as continuous variable) | | | 1.08 | (1.07–1.08) |
| *Screening exposure* | | | | |
| Pre-screening | 1,659 | 1,120,038 | 1 | |
| Prevalence round | 437 | 262,499 | 1.60 | (1.43–1.79) |
| Incidence rounds | 625 | 633,002 | 0.86 | (0.78–0.94) |
| II round | 252 | 215,318 | 1.01 | (0.88–1.15) |
| III round | 203 | 220,312 | 0.80 | (0.69–0.92) |
| IV round | 170 | 197,372 | 0.75 | (0.64–0.88) |
| Post-screening | 175 | 116,955 | 0.59 | (0.50–0.69) |

CI, confidence intervals; IRR, incidence rate ratio.
IRR for II, III, and IV rounds are estimated by a separate Poisson model.
Age 50–74, years 1997–2012.

# Comparison between pre-screening and invited cohort




After 8 years, the cohort screening shows significantly reduced risk of incidence (IRR=0.90 (95% CI, 0.83–0.97)) compared with the control cohort. Initially, incidence was higher in the screening cohort, but after 3 years, the slope of the curve became less than that of the control, and after 6 years, the two curves are reversed (**Figure 3a**).

***Incidence-based mortality.*** Using this approach, we could also compare the incidence-based mortality, i.e., the mortality among those who had a CRC diagnosed during the follow-up in the two cohorts. We observed 315 deaths in the cohort invited for screening and 429 deaths in the control cohort. The screened cohort had a 27% decrease in incidence-based all-cause mortality (IRR=0.73, (95% CI 0.63–0.85)) (**Figure 3b**).

# Conclusioni

- Vi è evidenza che lo screening colorettale attraverso la ricerca del sangue occulto riduca sia l'incidenza che la mortalità per tumore colorettale

- Nonostante lo screening colorettale sia un LEA, esso non è ancora garantito ad una quota rilevante dell apopolazione

- La crescente mole di dati sullo screening colorettale permetterà di mettere in luce risultati sempre più solidi