

# Observational study to evaluate the impact of internet reminders for GPs on colorectal cancer screening uptake in Northern Italy in 2013

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## Keywords

Colorectal cancer • Screening uptake • Reminder interventions

## Summary

**Introduction.** Colorectal cancer (CRC) is the third most common cancer worldwide and CRC-related mortality can be effectively reduced by population-based screening. Screening uptake is a key indicator of performance, susceptible of several implementation methods. Participation in ASL Milano 1 area (northern Italy) is increasing thanks to reminder invitation sent to non-responders. Here we evaluate the implementation of another strategy among those proved to be effective.

**Methods.** In the years 2013-2014 we conducted an observational study in patients non-responder to first invitation and subsequent mailed reminder. A list of them was sent to their own GP, who had the task to evaluate possible exclusion criteria and make a reminder, either by personal interview, telephone call or via e-mail. Intervention could be conducted either by the GP himself

or by an assistant. Primary outcomes were to assess the overall efficacy of the intervention and the efficacy of its single features (type of intervention and provider), measuring the consequent uptake of CRC screening.

**Results.** Participation in CRC screening was significantly higher (33,5%) in patients who received a reminder from GP, regardless of the type, vs those who did not (19,0%,  $p < 0.01$ ). No statistically significant difference was detected either by method or by provider of the intervention.

**Discussion.** The results of our study demonstrate that even a modest intervention can have a significant effect in improving compliance to screening for CRC, one of the cancers with highest incidence in developed countries, for which an effective treatment is available in case of early diagnosis.

## Background

Colorectal cancer (CRC) is the third most common cancer worldwide, causing approximately 1,360,000 new cases every year, and the fourth leading cause of cancer-related death. Almost 55% of the cases occur in more developed regions [1].

In Italy, CRC is by far the most common cancer in our population, ranking third in men and second in women, with nearly 59,000 estimated diagnoses in 2013. Moreover, it represents the second cause of cancer-related death [2]. In Lombardy, a northern region of Italy with nearly 11 millions inhabitants, CRC has a great impact in public health, accounting for 9,126 new cases and 3,215 deaths estimated in 2013 and 1,500 hospitalizations every year and representing the second leading cause of cancer-related death, as reported by the Local Health Unit of one large metropolitan area in Lombardy (ASL Milano 1) [3, 4].

Therefore, reducing mortality from CRC represents an important and challenging problem for public health and this target may be achieved by the introduction of population-based screening programs that allows to effectively reduce cancer deaths by detecting cancers at an early stage and by detecting and removing precancerous polyps before cancer develops [5-7].

In 2005 Lombardy started a screening program using fecal immunochemical blood test (FIT), implemented by ASL Milano 1 in 2006. The CRC screening campaign of ASL Milano 1 is addressed to a target population of nearly 240,000 subjects resident in this area, that covers 73 municipalities with a total population of 940,000 subjects [8].

In organised screening programs, broad participation in screening is critical to reduce CRC mortality at the population level. Screening uptake is a key indicator of performance because is susceptible of several implementation methods [9, 10]. Postal reminders, telephone calls, General Practitioners (GPs) signing the invitation have all proved to be effective in increasing participation [9-11].

Screening uptake in ASL Milano 1 area is steadily growing from 30% in 2006 to 47% in 2012, in line with reference data at the national level. One of the approaches locally used to increase participation is mailing a reminder invitation to non-responders three months after the first one. In 2014 a second reminder invitation was introduced for non-responder patients.

Our aim was to describe and evaluate the implementation of another strategy among those proved to be effective to increase CRC screening uptake by involving GPs in recruitment of their eligible non-responder patients.

## Methods

### STUDY DESIGN AND SETTING

In the years 2013-2014 we conducted an observational study in patients non-responder to first invitation and subsequent mailed reminder after 3 months in a large metropolitan area north-west of Milan, covered by a Local Health Unit called ASL Milano 1. This area has population of nearly 1,000,000 inhabitants distributed in 73 municipalities and 604 GPs.

Target population is invited every two years by a personal letter to collect the FIT kit at the local pharmacies and to return the sample to the same pharmacies, that provide to send it to the central laboratory (Parabiago Public Health Laboratory). If FIT results positive, subjects are informed by a phone call from the Screening Center inviting them to an interview with a gastroenterologist, who will explain them the second level test, a colonoscopy.

The study was divided in two phases each year:

- In the first phase we analysed health administrative data to retrieve a list of non-responder patients, resident in ASL Milano 1 area and aged 50-69, who already received a reminder invitation from our Screening Center in the period January-May; each GP then received an email with a personal link with the list of their patients to be evaluated for a possible reminder.
- In the second phase (August - November), the GP had the task to check and report any reason for exclusion from reminder intervention, such as a colonoscopy performed in the past 5 years. Then the GP contacted eligible patients checking if they had received the invitation and asking them to participate and to contact the Screening Center for any further explanation.

### STUDY PARTICIPANTS

Participants were GPs in charge in the ASL Milano 1 area that agreed to join the ASL project about CRC screening.

### INTERVENTION

GPs received from ASL an e-mail reminder concerning a list of non-responder patients, as described above. After evaluating among possible exclusion criteria (performing a colonoscopy in the past 5 years, a concomitant severe disease, moving elsewhere, not being assisted by that GP), each GP could in turn choose among three different types of patient reminder: personal interview, telephone call or via e-mail. Intervention could be conducted either by the GP himself or by an assistant (i.e. a nurse or a secretary), if available.

The flow-chart of the project is shown in Figure 1.

### OUTCOME MEASURES

The primary outcomes were to assess the overall efficacy of the intervention and the efficacy of its single features (type of intervention and provider), measuring the consequent uptake of CRC screening. Rates were adjusted for age and sex using as standard population the non-responder population of ASL Milano 1 area that received a reminder invitation in 2012.

An additional analysis performed on 2013 data evaluated the screening participation related to GP activity level by dividing GPs into four groups accordingly to the rate of patients contacted:

- Group 1 =  $\leq 25\%$  of patients contacted;
- Group 2 = 26%-50% of patients contacted;
- Group 3 = 51%-75% of patients contacted;
- Group 4 = 76%-100% of patients contacted.

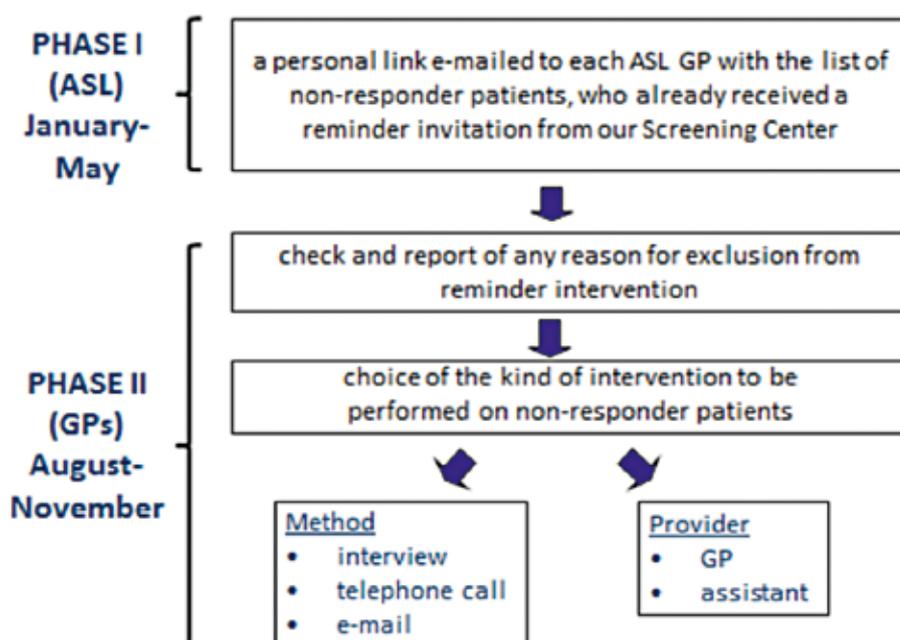


Fig. 1. Study flow-chart.

**Tab. I.** Patients non responder to the first invitation letter: participation rate by intervention type (year 2013; Rates were adjusted for age and sex using as standard population the non-responder population of ASL Milano 1 area that received a reminder invitation in 2012).

2013 participation rate by intervention type		Interventions by		Overall
		GP	Assistant	
Patients of GPs joining ASL project	Interview	33.4%	32.7%	33.3%
	Telephone call	35.8%	27.1%	32.6%
	E-mail			28.0%
	Intervention (all)	33.8%	28.8%	33.1%
	No intervention			16.7%
Patients of GPs not joining ASL project	No intervention			13.7%
All	Overall uptake 2013			26.7%

**Tab. II.** Patients non responder to the first invitation letter: participation rate by intervention type (year 2014; Rates were adjusted for age and sex using as standard population the non-responder population of ASL Milano 1 area that received a reminder invitation in 2012).

2014 participation rate by intervention type		Interventions by		Overall
		GP	Assistant	
Patients of GPs joining ASL project	Interview	33.9%	32.4%	33.8%
	Telephone call	31.8%	33.7%	32.3%
	E-mail			28.5%
	Intervention (all)	33.5%	32.9%	33.1%
	No intervention			20.4%
Patients of GPs not joining ASL project	No intervention			16.8%
ALL	Overall uptake 2014			27.6%

**Tab. III.** Patients non responder to the first invitation letter: participation rate by intervention type (pooled data years 2013+2014; Rates were adjusted for age and sex using as standard population the non-responder population of ASL Milano 1 area that received a reminder invitation in 2012).

2013+2014 participation rate by intervention type		Interventions by		Overall
		GP	Assistant	
Patients of GPs joining ASL project	Interview	33.6%	32.1%	33.5%
	Telephone call	33.4%	30.2%	32.4%
	E-mail			28.7%
	Intervention (all)	33.5%	30.9%	32.8%
	No intervention			19.0%
Patients of GPs not joining ASL project	No intervention			15.4%
All GP	Overall uptake 2013+2014			27.3%

**Tab. IV.** Non-responder patients participation rate according to the level of GP's activity volume (Year 2013).

	Activity volume (rate of their patients contacted)	GPs distribution according to activity volume N°(%)	Non-responder patients participation rate
Group 1	≤ 25%	103 (19%)	16.3%
Group 2	26-50%	25 (5%)	24.0%
Group 3	51-75%	135 (26%)	26.2%
Group 4	76-100%	267 (50%)	31.6%

## STATISTICAL ANALYSIS

Results, after being collected and recorded in the personal link provided at the beginning of the study, were analysed using the statistical software package IBM SPSS (version 21.0).

We assessed the impact of the intervention and its features comparing screening uptake between patients who received the intervention and those who did not, using a Chi-square test. Finally, we compared the rate of screening uptake according to the level of participation of the GP in the study. For all analyses, a p-value of less than 0.05 was considered significant.

All data were been used according to the privacy laws and according to ethical standards.

## Results

A total of 59,579 (23,373 in 2013 and 36,206 in 2014) non-responder patients were identified using health administrative database. The mean age was 58 years old (SD 6.3) and 50% were female.

8,594 patients (14.4%) met exclusion criteria. The remaining 50,985 patients (85.5%) were included in the analysis. 23,281 (45.6%) did not receive any kind of intervention. 27,704 (54.3%) received one: 72% an interview, 27% a telephone call, 2% an e-mail. The interventions were been conducted in person by GP (87%), or their assistants (11%), or with (e-mail 2%).

Results separately for year are shown in Tables I and II. Overall results are shown in Table III. 33.5% of the 27,704 patients who received a reminder from GP, regardless of the type, subsequently participated to CRC screening. Conversely, only 19.0% of the 23,281 who did not receive any type of intervention participated. The difference resulted statistically significant ( $p < 0.01$  Chi squared, Yates correction, equals 1269.130 with 1 degrees of freedom).

Analysing each year separately, response rate without intervention increased from 15.0% in 2012, to 16.7% in 2013 and to 20.4% in 2014. Screening participation after intervention was 33.1% in 2013 and 32.6% in 2014 (Tab. IV). Concerning the type of reminder from GP, no statistically significant difference was detected either by method (interview vs. telephone call) or by provider of the intervention (physician vs assistant).

Interview response rates were 33.3% in 2013, either performed by GP or assistant, and 33.8% in 2014 (33.9% if performed by GP and 32.4% if performed by an assistant), while telephone and e-mail reminders passed from response rates of respectively 32.6% and 28.0% in 2013 to 32.3% and 28.5% in 2014.

Screening uptake in non-responder patients raised from 15.0% in 2012 with only invitation reminder from ASL to 26.7% in 2013 and 27.6% in 2014 after GP or assistant intervention.

Evaluating screening uptake according to the level of participation of the GP in the study in 2013, the 530 GPs enrolled were stratified as follows according to the rate of patient contacted (Tab. IV).

Noteworthy, GPs most active in contacting non-responder patients had a significantly higher uptake rate compared to less active groups of physicians. Results were statistically significant ( $p < 0.01$  Chi squared, Yates correction, equals 377.489 with 3 degrees of freedom.).

The overall screening participation, including patients in the study and patients that had responded to the first call were: 45% in 2012, 49% in 2013, 53% in 2014.

## Discussion

The results of our study showed that receiving any kind of intervention in addition to invitation and mailed reminder from Screening Center can significantly affect uptake of CRC screening.

Public screening programs must achieve high compliance to be effective and efficient, yet participation is low in many countries despite standard invitations and recall systems. As high participation in screening is the primary goal of all organised programs, more and more attention has been paid recently to how to engage citizens in public health programs [11]. A systematic review showed that individuals who previously participated in screening were more likely to be screened subsequently, so efforts could be focused on identifying and encouraging attendance among those who have never previously participated in screening [12]. Several interventions have been proposed to increase participation. Scientific evidence confirmed that organised screening programs, based on invitation letter or on GP involvement, were consistently effective in increasing participation compared to spontaneous screening [9]. Although among the measures to increase participation in organised screening there is solid evidence of a modest positive effect of interventions such as postal reminders, telephone calls, GP signing the invitation, it is still controversial the efficacy of active GP involvement [9, 13-15].

In our case, the results show clearly that even a modest intervention, conducted either by the GP or by an assistant, can have a significant effect in improving compliance to screening for CRC, one of the cancers with highest incidence in developed countries, for which it is available an effective treatment if diagnosed early. Moreover, in 2013 screening uptake seemed to increase accordingly to GP's activity level and the result was significant also for groups with intermediate level of activity in comparison with the one with low or no activity.

It is important to underline how screening uptake increase without GP intervention from 16.7% in 2013 to 20.4% in 2014 may be due to the introduction of a second reminder invitation from ASL for non-responder patients. A possible explanation for the uptake improvement following the introduction of the second reminder can be that this kind of intervention is likely to involve people already disposed to participate in screening program. Conversely, GP intervention can be more effective in involving patients less prone to participation through a targeted counselling. The effect of second reminder alone can be showed in patients without intervention: uptake improves from 16.7% to 20.4% (+3.4%) in pa-

tients of GPs joining ASL project, and from 13.7% to 16.8% (+3.1%) in patients of GPs not joining ASL project. So we can suggest that the second reminder can help to improve the uptake of 3% in patients non responder. The effect of second reminder looks to be hide by the interventions of the GPs or their assistants. To confirm this hypothesis and compare these possible effects, a further study with a four-arm design is required.

Among limitations concerning our study, the observational design instead of a randomized controlled trial can limit the strength of the results. In fact the method of reminder (call, interview, mail) were simply due to a choice of the GPs. Furthermore the GPs were not randomized but they decided to join or not to ASL project. In this way probably GPs more interested in “CRC screening” attended ASL project. An other limit of this study is that we can't describe socio-economical status of responders/non responders.

But we have to consider that others studies [9, 10] already said us that the provider intervention is effective to improve uptake to screening. This study wants to show how literature suggestions can be applied to real setting. In fact our aim was to describe and evaluate the implementation of evidence-based strategies to increase CRC screening uptake. With this study we want to share our result to starts a factual benchmark with other “screening centers”.

## Conclusions

In conclusion, our findings stress the pivotal role of health providers in counseling and could be relevant also in the light of the recent Italian reform concerning territorial health care, according to which similar interventions could be systematically operated by health care professionals other than GPs [16]. Moreover, Lombardy is going to review its Health System to improve the organisation of GPs and this could further facilitate the implementation of counseling concerning cancer screening.

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## Authors contributions

Study conception and design: DC, GB, PC, MEP. Acquisition of data: DC, GBi, PC. Analysis and interpreta-

tion of data: EG, AJBi, DC. Drafting of manuscript: EG, AJB. Critical revision: EG, PC, AJBi, MP

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