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Comparative analysis of the protective effect of different screening strategies for colorectal cancer

Submission date
01/08/2023

Recruitment status
No longer recruiting

Registration date
19/10/2023

Overall study status
Completed

Last Edited
04/10/2023

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Colorectal cancer (CRC) is the third most common cancer in men and the second in women. However, CRC is a highly preventable disease and effective screening methods are available. Several effective methods are available for colorectal cancer screening: stool-based tests, which can detect minimal quantities of blood lost in faecal material by bleeding lesions (cancer and cancer precursor lesions), and endoscopic methods, which use optical instruments to directly examine the rectum and colon. Comparative data about the impact of different strategies on cancer incidence and mortality rates are needed to estimate their effectiveness and the balance between benefits and harms. Among stool tests, the faecal immunochemical test (FIT) can specifically detect human blood in the stool, while among endoscopy tests sigmoidoscopy (FS) requires a limited preparation and a short examination time, showing a satisfactory sensitivity for relevant lesions. Colonoscopy is used as a follow-up test for patients who have tested positive with other screening methods. This is the first large study comparing the impact on CRC incidence and death rates, as well as the yield of colorectal lesions, of strategies using FIT and sigmoidoscopy, alone or in combination, in an average-risk population.

Who can participate?
All people resident in one of the participating centres from 55 to 64 years of age, without a history of terminal illness or inflammatory bowel disease, polyps or colorectal cancer, or two first-degree relatives with colorectal cancer. A sample of subjects in the stipulated age range was drawn in each centre and the subjects included in those samples were offered the option to participate, if eligible

What does the study involve?
Participants were mailed a personal invitation letter signed by their general practitioner. The mailing included a leaflet that briefly described the screening procedure and its possible side effects. Participants were randomly assigned to:
1. Biennial faecal immunochemical test (FIT): the kit is delivered by the GP or included in the invitation letter
2. Patient’s choice of FIT or “once-only” FS

3. “Once-only” FS
4. FS followed by biennial FIT
5. FS and FIT followed by biennial FIT for participants with a negative screening result

Participants allocated to the FS screening groups were offered an appointment at a specified time and were asked to call the screening centre to confirm, modify, or cancel their appointment. Those who agreed to schedule a test date were advised to visit their general practitioner or the screening centre to obtain the required enema kit. Participants allocated to the FIT screening arms received a letter that included instructions for performing the test and for storing and returning the sample

What are the possible benefits and risks of participating?
The tested strategies can reduce individuals’ risk of dying of CRC as well as the likelihood of getting the disease. Sigmoidoscopy is likely associated with a larger reduction in the risk of getting the disease than FIT.

FS is more invasive, but the test does not need to be repeated for the rest of the life, while the protective effect of non-invasive FIT can be achieved if the test is regularly repeated every second year. Subjects with a positive result at screening need to perform a colonoscopy, which is an invasive test associated with a small probability of side effects like perforation or bleeding (less than 10 in 1000 exams).

Where is the study run from?
Piedmont Region Health Authority (Italy)

When is the study starting and how long is it expected to run for?
July 1997 to December 2016

Who is funding the study?
Italian Association for Cancer Research (Italy)

Who is the main contact?
Dr Carlo Senore, carlo.senore@cpo.it

Contact information

Type(s)
Scientific

Contact name
Dr Carlo Senore

ORCID ID
http://orcid.org/0000-0003-1023-7477

Contact details
Via Cavour 31
Turin
Italy

10123
+39 (0)116333890
carlo.senore@cpo.it

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Randomized trial of different screening strategies for colorectal cancer

Acronym
SCORE2

Study objectives
There is a general consensus that screening for colorectal cancer is effective in reducing the burden of the disease. There are several methods available for colorectal cancer screening: stool-based tests to detect blood include the guaiac faecal occult blood test and the more sensitive faecal immunochemical test (FIT); endoscopic methods, which use optical approaches to directly examine the rectum and colon, include flexible sigmoidoscopy (FS) and colonoscopy. FIT and FS are currently used in Italy, while colonoscopy is used as a follow-up test for persons who have tested positive with other screening methods. Comparative data about cancer incidence and mortality rates of the different screening strategies are needed, to estimate the effectiveness and the balance between benefits and harms of screening interventions.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 24/11/1998, Piedmont Region Department of Health, Health Planning Management, Health Planning Sector (Corso Regina Margherita 153, Turin, 10100, Italy; None available; no_longer@available.com), ref: 436DO28.1

Study design
Multicentre randomized parallel trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Community

Study type(s)
Screening

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Colorectal cancer

Interventions
Eligible subjects were randomized in the trial through a computer-generated random sequence (Randomized blocks sequence) within general practitioner (GP).

During the initial phase involving all centers, eligible patients were randomly assigned (ratio 2:5: 3:3:9), within the rosters of their GP, to:
1. Biennial faecal immunochemical test (FIT); kit sent by mail with the invitation
2. Biennial faecal immunochemical test (FIT); kit delivered at the pharmacies of by GPs
3. Patient’s choice of FIT or “once-only ” sigmoidoscopy
4. “Once-only” sigmoidoscopy
5. Sigmoidoscopy followed by biennial FIT for subjects with negative screening result

During the second phase, conducted only in Turin, eligible subjects were randomly allocated to:
1. Biennial faecal immunochemical test (FIT); kit sent by mail with the invitation
2. Biennial faecal immunochemical test (FIT); kit delivered at the pharmacies of by GPs
3. Patient’s choice of FIT or “once-only ” sigmoidoscopy
4. "Once-only” sigmoidoscopy
5. Sigmoidoscopy followed by biennial FIT for subjects with negative screening result
6. Sigmoidoscopy and FIT followed by biennial FIT for subjects with negative screening result

Please note:
The study enrolment was extended in Turin, which resulted in a substantial increase in the number of people enrolled (following the same protocol and randomization schemes). The Piedmont Regional Health Authority's decision to approve and fund the study referred to the extended enrolment.

The overall study end date is the end of follow-up for incidence and mortality analyses. Some centers could provide data about screening outcomes in the local programs for the following years (up to 2017-2018), but those data will not be used for the incidence and mortality follow-up analysis.

Intervention Type
Other

Primary outcome measure

1. Colorectal cancer (CRC) incidence and mortality measured using a record linkage of the trial database with local population cancer and mortality registers at 15-year follow-up

Secondary outcome measures
All-cause mortality measured using an automated record linkage of the trial database and the local population mortality registries at 15-year follow-up

The study aims also to study the screening outcomes with different strategies. The outcome indicators include participation, positivity rate, positive predictive value, DR of CRC and advanced adenomas. Cumulative estimates are used to compare strategies based on the offer of a single test over the lifetime (FS and TC) and those requiring regular repetition of the test (FIT).

Overall study start date
01/07/1997

Completion date
31/12/2016

Eligibility

Key inclusion criteria
In Turin and Milan, the target population included all patients aged 55 – 64 years who were listed in the rosters of a random sample of general practitioners who had not been involved in a previous trial (SCORE ISRCTN27814061 of 08/12/2010).

In the other centers, the target population was recruited from those districts not yet involved in the SCORE trial (Biella and Rimini) or in the ongoing regional colorectal cancer screening program (Florence). All residents aged 55 – 64 years in those districts were targeted for recruitment: the researchers identified and contacted their general practitioners, who were invited to collaborate in the study.

In all centers, GPs were asked to review the list of their patients targeted for recruitment to exclude subjects not eligible for the trial.

Participant type(s)
Population

Age group
Senior

Lower age limit
55 Years

Upper age limit
64 Years

Sex
Both

Target number of participants

Initial phase target: 22,000: 3000 each in Biella, Florence, and Rimini, 5000 in Milan, and 8000 in Turin

Total final enrolment
30180

Key exclusion criteria
1. Unable to give informed consent
2. Diagnosed with a terminal illness or inflammatory bowel disease
3. History of polyps or colorectal cancer or two first-degree relatives with colorectal cancer
4. Undergone a colorectal endoscopy or a FOBT within the previous 2 years
5. Already included in a previous trial (SCORE ISRCTN27814061 - 08/12/2010) and had changed their general practitioner to one that was included in this study or who had moved to a district included in the current study area

Date of first enrolment
01/11/1999

Date of final enrolment
30/09/2002

Locations

Countries of recruitment
Italy

Study participating centre
Epidemiology and Screening Unit - A.O.U. Città Della Salute e della Scienza di Torino
Via Cavour 31 (Via San Francesco da Paola 31 at the time of starting the trial)
Turin
Italy
10123

Study participating centre
Gastroenterology Unit - Infermi Hospital
Via dei Ponderanesi 2 (Via Rodolfo Caraccio 5 at the time of recruitment)
Biella
Italy
13875

Study participating centre
Edo and Elvo Tempia Foundation
Via Malta 3

Biella
Italy
13900

Study participating centre
Clinical Epidemiology Unit - ISPRO (formerly ISPO)
Via Villa delle Rose 2 (Viale Volta 171 at the time of recruitment)
Florence
Italy
50139

Study participating centre
Epidemiology Unit - ASL Città di Milano
Corso Italia 19
Milan
Italy
20122

Study participating centre
Gastroenterology Unit - Infermi Hospital
Viale Luigi Settembrini, 2
Rimini
Italy
47923

Sponsor information

Organisation
AIRC Scientific Directorate

Sponsor details
Formerly Piedmont Region Health Authority
Corso Regina Margherita 153
Turin
Italy
10100
None available
administrative.office@airc.it

Sponsor type
Government

Website
https://www.direzionescientifica.airc.it/contact-us/

Funder(s)

Funder type
Research organisation

Funder Name
Associazione Italiana per la Ricerca sul Cancro

Alternative Name(s)
Italian Association for Cancer Research, The Italian Association for Cancer Research, AIRC

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
Italy

Results and Publications

Publication and dissemination plan
The baseline results of the trial, together with a description of the study protocol, have been published in 2005.

The report of the 15-year incidence and mortality follow-up will be submitted for publication in early autumn 2023

Intention to publish date
01/09/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyses during the current study are not expected to be made available due to the change in privacy legislation. The original consent form filled by the recruited subjects did not include specific indications about data sharing. Moreover, data about subjects undergoing screening in the local programs (six regional programs) are not publicly available. Data can be shared only among researchers from the participating centres.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Results of the recruitment phase of the trial referring to the first phase of the study, which involved all centers. The data from the extended enrolment in Turin were not available yet for this analysis.	02/03/2005	14/08/2023	Yes	No